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MEDICAL DEPARTMENT

UNITED STATES ARMY

IN WORLD WAR II

NOTE

This volume was written under the direction of Col. John Boyd Coates, Jr., MC, USA, former Director and Editor in Chief, The Historical Unit, U.S. Army Medical Service, and processed for publication under the supervision of his successor, Col. Arnold L. Ahnfeldt, MC, USA, now retired.

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MEDICAL DEPARTMENT, UNITED STATES ARMY

INTERNAL MEDICINE IN WORLD WAR II

Volume III

INFECTIOUS DISEASES AND GENERAL
MEDICINE

OFFICE OF THE SURGEON GENERAL

DEPARTMENT OF THE ARMY

WASHINGTON, D.C. 1968

INTERNAL MEDICINE IN WORLD WAR II

Volume III

INFECTIOUS DISEASES AND GENERAL MEDICINE

MEDICAL DEPARTMENT, UNITED STATES ARMY

The volumes comprising the official history of the Medical Department of the United States Army in World War II are prepared by The Historical Unit, U.S. Army Medical Service, and published under the direction of The Surgeon General, U.S. Army. These volumes are divided into two series: (1) The administrative or operational series; and (2) the professional, or clinical and technical, series. This is one of the volumes of the latter series.

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Foreword

History of medical experience looks in two directions: in surveying and reporting on the past it suggests, by inference and implication, the impact that past experience will have on future practice.

This observation is dramatically illustrated by the many volumes now published in which are recorded the activities of the Medical Department, U.S. Army, in World War II. The stresses of global war impose extraordinary responsibilities on the physicians and surgeons charged with maintaining the combat capabilities of the Nation's fighting men. Meeting and discharging these responsibilities often means compressing into months or even weeks the formulation and testing of new medical concepts involving unfamiliar or obscure medical conditions—tasks that under normal circumstances might take years. It means, too, the opportunity to evaluate results under unified direction and under controlled circumstances to the ultimate benefit of all mankind; and on a scale that finds no counterpart in civilian medical practice.

This volume is the third and last in that medical series reporting on the experience of the U.S. Army Medical Department with internal medicine in World War II. The first of the internal medicine volumes, published in 1962, dealt with the activities of consultants in medicine in all parts of the world. The second volume (1963) contained an account of the infectious diseases encountered in a global war. This final volume continues the account of infectious diseases and considers various aspects of other internal medicine problems. It continues, also, the impressive account of the expansion of our knowledge of the etiology, clinical picture, control, and management of a wide variety of infectious diseases, including some about which little or nothing was known before the war. Such a disease is "Bullis Fever," a tickborne illness which is described in chapter VI. The account of the discovery of this new disease entity, and of the clarification of its epidemiology within a very short period of time, is a tribute to the Army medical officers who participated in its clinical and laboratory investigation.

In the broad field of internal medicine, military medical practitioners were provided an unparalleled opportunity to study disease and to acquire new knowledge in a variety of climes and circumstances. In hot climates, we had to rediscover that man has remarkable heat adaptation mechanisms and that adherence to sound physiological principles permits him to work hard, efficiently, and effectively in any naturally occurring hot environment. The problem of living and working under these adverse climatic conditions was solved at the expense of a considerable number of casualties and with some loss of life, but the basic principles, once learned, should not be for-

gotten and should form the basis for the proper handling of troops in hot climates in future years.

During the Second World War, to the fevers and fluxes of previous wars were added the hazards of exposure to high altitudes and the devastating effects of blast and bombs. It was, therefore, inevitable that the diseases and disorders, which affect the stability of the circulatory system, should have attracted particular attention and detailed study. Thus, the special attention given to the heart and vascular system in the process of selection of persons for military service provided an insight into the strength as well as the weakness of our eligible population. Although this effort proved disturbing in certain respects, it stimulated the thoughtful planning of special studies in the fields of hypertension and of latent coronary disease.

An outstanding example of medical effort in World War II which had significance both in the spheres of infectious disease and cardiovascular physiology was the new and detailed information gained about tsutsugamushi fever (scrub typhus). This acute and serious disease was widely encountered by the Army in the Southwest Pacific Area and in Burma, where more than 5,000 cases were reported. Three major epidemics occurred in northern Burma and in Netherlands New Guinea in 1944, and as a direct result of the Army experience, several concepts of the nature of this rickettsial disease were changed. It was discovered that there were no typical scrub typhus areas, a wider geographic distribution of the disease was established, the etiology was confirmed, vector species were proved, strains were isolated, a new complement fixation test was developed, and the clinical pattern and pathological features were described.

War, with its characteristic situation changes, dramatically brings to the forefront the environmental aspects of man's struggle for existence. The chapter on nutritional diseases presents a vivid description of the progressive states of starvation following improper or inadequate food intake, as seen in the unfortunate inmates of prisoner-of-war and concentration camps during World War II. The findings, initial, intermediate, and terminal, provided clinicians with a clear portrayal of the pathognomonic symptoms of the various vitamin nutritional deficiencies, which they could utilize in predicting the effects of various restricted diets.

Dermatological diseases, although seldom severe enough to cause death, nevertheless are among the most common and chronic medical conditions with which an army in the field must cope. Particularly is this true in semitropical and tropical climates where heat and humidity favor such diseases. Under these circumstances, crippling results requiring prolonged hospitalization are not unusual. We are fortunate, indeed, in having a splendid description of our experience in this regard based on the report and recommendations of Dr. J. Gardner Hopkins, following his tremendously helpful consultant visit to the Southwest Pacific Area for The Surgeon General during World War II.

In addition to a better understanding of symptoms and complaints referable to bodily dysfunction or defect, military physicians in World War II learned to appreciate psychological and sociological influences upon disease and adjustment. This experience in military medicine fostered the growth of the psychosomatic viewpoint, so well recognized today. Although psychosomatic concepts had some vogue before World War II, they received a major impetus during the war years, for here was a vast laboratory of stress where physicians could observe firsthand the effects of mind-body interrelationships upon symptoms, treatment, and disposition in a wide variety of diseases and injuries.

The evolution of military medical practice, as related in this third volume of the internal medicine series, is interesting and professionally highly informative reading. Much of the experience was gained in remote and unfamiliar areas of the world. It is, also, a record of achievement and progress which is a testament to the devotion to duty and the diligence of medical personnel, and especially to the many experienced physicians and investigators, both military and civilian, who pursued their studies under circumstances which were always difficult and frequently dangerous.

As with the other volumes in the history of the Medical Department, I take great pleasure in expressing my gratitude to the many authors whose contributions made possible this additional volume; to its editor, Dr. W. Paul Havens, Jr.; to the Advisory Editorial Board on the History of Internal Medicine of which Dr. Garfield G. Duncan is chairman; and to the Director and his staff of The Historical Unit who are doing the prodigious work of producing these volumes.

LEONARD D. HEATON,
Lieutenant General,
The Surgeon General.

Preface

This is the third volume of the history of internal medicine in World War II. In the preface of the first volume, which contains the reports of the medical consultants, is recounted the story of the development of the organization that ultimately produced the history. The early enthusiastic efforts of Brig. Gen. Hugh J. Morgan and Cols. Walter Bauer, John S. Hunt, and Francis R. Dieuaide to implement its writing were described. At the suggestion of Col. Calvin H. Goddard, MC, former Director, The Historical Unit, U.S. Army Medical Service, an Advisory Editorial Board on the History of Internal Medicine, with Dr. Garfield G. Duncan as Chairman, was formed in 1952. Early in 1953, an editorial office was established at the Jefferson Medical College of Philadelphia, with Dr. W. Paul Havens, Jr., as Editorial Director. Col. John Boyd Coates, Jr., MC, succeeded Colonel Goddard as Director of The Historical Unit.

In the preface of the second volume, which contains the clinical descriptions of certain infectious diseases, attention is called to the fact that World War II was the first great conflict in which fewer of our troops died of infectious diseases than of injuries. Mention was made of the numerous productive clinical and laboratory investigations initiated by the Armed Forces and by the various civilian commissions working under their aegis.

This volume—the third and last of the series—is a potpourri, with chapters on subjects concerned with infectious diseases, general medicine, and dermatology. It is making its appearance 15 years after the formation of the Advisory Editorial Board and 22 years after the end of World War II. Several of those who contributed greatly to the production of this history have died. The long lapse of time between the experiences recounted here and their publication in this volume does not detract from their value or interest. Although most of the information has long since appeared in our medical journals, volume III serves to bring it together in its proper relationship with place and time in history. Of necessity, there is overlapping of the material contained in this book and in volume I. However, in contrast to the more general aspects of various medical problems described by the medical consultants in the first volume, the chapters in this book, like those in volume II, were based on the observations of many medical officers and were written by physicians directly concerned with the responsibilities for the care of patients and the clinical investigations of their diseases.

The editor wishes to express his sincere thanks to the medical officers who made the material for these chapters available and to the contributors who have written them. In addition, thanks are due to Dr. Duncan

and the entire Advisory Editorial Board for their constant support and to Colonel Coates and his successors, Col. Arnold L. Ahnfeldt, MC, and Col. Robert S. Anderson, MC, for their many courtesies and vigorous assistance. In particular, appreciation is expressed again to Miss Eleanor S. Cooper, whose tireless and painstaking attention to the preparation and editing of most of these manuscripts was an invaluable aid in the compilation of this history.

The editor and the authors are also greatly indebted to Mr. E. L. Hamilton, Director, Medical Statistics Agency, Office of The Surgeon General, and Mr. A. J. McDowell, Chief, and Mr. M. C. Rossoff, Assistant Chief, Statistical Analysis Branch, Medical Statistics Agency, who not only provided essential data but also checked and reviewed all statistical information contained herein.

Finally, grateful acknowledgment is made to Mrs. Rebecca L. Levine, Chief, Editorial Section, Editorial Branch, The Historical Unit, who performed the final publications editing and prepared the index for this volume.

W. PAUL HAVENS, Jr., M.D.

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CHAPTER I

Leishmaniasis

Harry Most, M.D.

Part I. Cutaneous Leishmaniasis

Cutaneous leishmaniasis did not constitute an important or a disabling medical problem in World War II, and the effective troop strength in the areas involved was not appreciably altered. An estimated 1,000 to 1,500 cases occurred, and all but the few reported from Latin America,[1] North Africa,[2] and Panama[3] originated in stations of the Persian Gulf Command, mainly in the vicinity of Ahvāz, Iran. In this command, the first case was discovered in October 1943, and as a result of special attention to the problem of cutaneous leishmaniasis, that is, by altering dispensary officers to the appearance of the lesion and by establishing a central area for the administration of treatment, 630 cases were reported within the next 3 months. The peak incidence was over by 1 February 1944, and during the next 12 months, the average number of new cases was only 23 per month[4] (chart 1).

CLINICAL ASPECTS

In a report from the 113th General Hospital, Quarry Camp, Ahvāz, based on an analysis of 499 cases, detailed information was furnished concerning the clinical aspects of cutaneous leishmaniasis in American military personnel.[5] White and Negro enlisted personnel as well as male and female officers were involved.

Incubation Period

The incubation period for the development of cutaneous leishmaniasis, based on human inoculation experiments with cultures or material from

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[1] Report, Medical Statistics Division, Office of The Surgeon General, U.S. Army, 15 Dec. 1945.

[2] Kranes, A.: Leishmaniasis Among American Troops in the Mediterranean Theater of Operations. (One case of cutaneous leishmaniasis proved by biopsy at the 17th General Hospital.) [Unpublished; official paper.]

[3] Kean, B. H.: Cutaneous Leishmaniasis on the Isthmus of Panama. Arch. Dermat. & Syph. 50: 237–238, October 1944.

[4] (1) Essential Technical Medical Data, Persian Gulf Command, U.S. Army, for March 1944, dated 15 Apr. 1944. (2) Essential Technical Medical Data, Persian Gulf Command, U.S. Army, for December 1944, dated 19 Jan. 1945.

[5] Ball, D., and Ryan, R. C.: Cutaneous Leishmaniasis. Bull. U.S. Army M. Dept. No. 79, 65–73, August 1944.

1

CHART 1.—*Incidence rates for cutaneous leishmaniasis in Persian Gulf Command, U.S. Army, 1943–45*

[Rate expressed as number of cases per annum per 1,000 average strength]

RATE
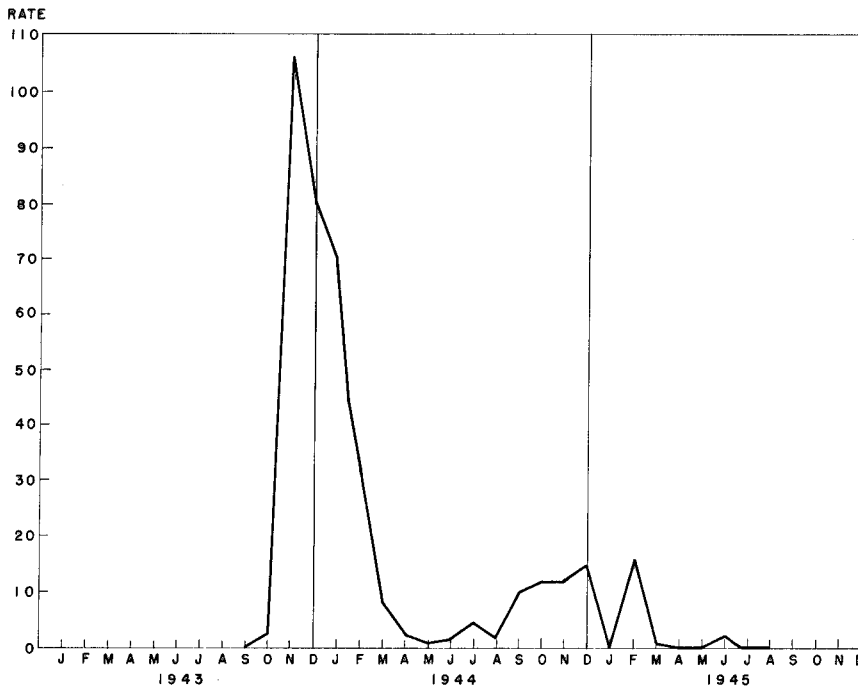
proved ulcers, is known to vary from a few weeks to 56 months.[6] In the group of 499 cases just mentioned, the disease developed in one patient within 10 days of exposure; in others, presumably infected while in India, it developed within 3 weeks after arrival in Iran. The maximum incubation period for the latter group, which had spent about a month in India and about 10 days en route to Iran, would be approximately 6 weeks. Of interest in regard to the prolonged incubation period in some instances was the development of cutaneous leishmaniasis in military personnel following their return to the United States after having served in endemic areas.

Lesion

The characteristic lesion at onset was an indolent papule, resembling an insect bite. At first, it was painless and did not itch. Subsequently, the small red papule enlarged and the center developed a thin crust, becoming slightly dimpled. Ulceration occurred in the center and formed a thick, rough crust or scab which was difficult to remove. The ulcer, from 1 to 1½

    [a] Berberian, D. A.: Cutaneous Leishmaniasis (Oriental Sore); Incubation Period. Arch. Dermat. & Syph. 50: 231–232, October 1944.

inches in diameter, was surrounded by a raised red, firm, liplike edge. The number of lesions ranged from 1 to 3 in 204 patients and from 4 to 29 in 193 patients. The majority of the lesions occurred on the extremities, but the face, ears, and neck were also involved. In two patients, lesions were present on the penis.

DIAGNOSIS

The diagnosis was established without difficulty in the majority of patients. A stained smear of material removed from beneath the crust provided the most valuable diagnostic information. In 387 cases, the first smear was found to contain *Leishmania tropica;* in 9 cases, 2 smears were necessary; and in 1 case, 3 smears were made before *L. tropica* could be demonstrated. Fifty-three patients with a clinical diagnosis of cutaneous leishmaniasis had two or three negative smears and were not treated. In 49 of these patients, spontaneous healing occurred in an average time of 7.3 weeks. It was assumed that these patients were in the healing stage when first seen. Treatment was almost entirely carried out in dispensaries, and those affected could perform their usual military functions. No patients were returned to the United States because of this infection, and no patient was given a medical discharge because of it.

TREATMENT

The average age of the lesions when treatment was begun was 9.7 weeks. Sixty-five patients with one to four noninfected lesions were treated with ethyl chloride spray every 5 days. Fifty-seven of these showed no evidence of healing in an average of 3 weeks, and only eight patients were cured in an average of 5.5 weeks. Only small young lesions were amenable to freezing with ethyl chloride, and this form of treatment failed in 87.7 percent of the patients for whom it was used. Injections of acid berberine sulfate, 1–2 cc. of a 1-percent solution, were given once a week to 138 patients. After an average of 5.5 weeks, 31.8 percent of these patients failed to respond to the treatment. The interval to cure, after treatment with acid berberine sulfate alone, was 6.8 weeks and was 4.5 weeks after prior failure with ethyl chloride spray.

Neostam (stibamine glucoside) was given intravenously to 221 patients of whom 155 had had no prior therapy. The others had previously been treated without success with ethyl chloride, acid berberine sulfate, Neostam locally, or X-ray. Cure was accomplished in all cases in 2 to 20 weeks (average 14.5). Toxic manifestations of nausea, vomiting, diarrhea, and collapse were encountered in 5 percent of the patients who initially received Neostam in maximum single doses of 0.2 gram. Reduction in maximum doses to 0.15 gm. given at least 5 hours after a meal diminished

the incidence of toxic symptoms to 0.83 percent in the last 950 injections. The initial dose was 0.5 gm. and subsequent doses, 0.1 and 0.15 gram. Injections of 0.15 gm. were given twice weekly and continued until cure was accomplished. Healing began with as little as 0.7 gm. total dosage of Neostam and was manifested by disappearance of the redness of the lesion, by the development of a copper-colored area around the lesion, and by the formation of new epithelium when the crust fell off. The average amount of Neostam to accomplish cure was 1.14 grams.

Neostam (1–2 cc. of a 2-percent solution) was administered locally at weekly intervals in 35 cases, and in 32, cures resulted in an average of 3.3 weeks, the shortest interval for cure of any group.

Of 10 patients treated locally with roentgen radiation and adequately followed, 9 were cured in an average of 8.3 weeks after the last exposure to X-ray therapy. The initial X-ray dose was 60 R. (roentgen), and three subsequent doses of 75 R. were given at 4-day intervals. One patient failed to respond to this course of treatment.

Penicillin was ineffective in one patient treated, in Panama, for cutaneous leishmaniasis of the face. No clinical response was noted during 5 days of therapy, and apparently viable parasites were still found in the tissues 8 days after completion of treatment.[7]

In summarizing the results of treatment, it appeared that ethyl chloride spray and acid berberine sulfate locally were not highly effective in the treatment of cutaneous leishmaniasis. Neostam locally injected into noninfected lesions cured 90 percent of them in a month. X-ray treatment was effective in selected cases. Neostam, intravenously, was effective in all cases but produced considerable toxicity unless the maximum dose was not greater than 0.15 gram. Neostibosan (ethylstibamine), a less toxic drug than Neostam, which can be given at short intervals (daily) in relatively large amounts is more effective in the treatment of leishmaniasis. Unfortunately, its use was not recommended in 1941,[8] and although recommended for use in 1943,[9] its designation as a standard item was not approved until 1944.

Complications occurred in 0.7 percent of the patients with proved cutaneous leishmaniasis and consisted of such infections as cellulitis, lymphangitis, and thrombophlebitis. It was observed that 35 percent of these secondary infections occurred in patients who were receiving local injections of acid berberine sulfate. The patients with these complicating infections were hospitalized for periods from 5 to 93 days (average 25). Only one recurrence or reinfection was observed in the group of patients discussed in this chapter. No deforming scars remained after treatment.

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[7] Snow, J. S.: The Unsuccessful Treatment of American Leishmaniasis With Penicillin; Report of Case. Arch. Dermat. & Syph. 50: 324–325, November 1944.

[8] Circular Letter No. 56, Office of The Surgeon General, War Department, 9 June 1941, subject: Notes on the Treatment and Control of Certain Tropical Diseases.

[9] Circular Letter No. 33, Office of The Surgeon General, War Department, 2 Feb. 1943, subject: Treatment and Control of Certain Tropical Diseases.

An interesting observation by local health authorities with regard to control measures of reservoir hosts and the effect of such measures on the rate of infection in the natives in known endemic areas was cited in the report from the 113th General Hospital. In one such area, 60 percent of the gerbils (burrowing rodents related to the mouse, native to Africa and Asia) were found infected. Intensive rodent destruction with chloropicrin resulted in a reduction of the incidence of leishmaniasis in the natives in the area from 70 to 0.4 percent.

Part II. Visceral Leishmaniasis

Visceral leishmaniasis, or kala-azar, was not a serious problem in troops of the United States. In all, an estimated 50 to 75 cases occurred in military personnel from North Africa, Sicily, southern Italy, the Riviera, and India. The individual case, however, often posed a problem in diagnosis to medical officers, owing chiefly to lack of prior experience. In the United States before World War II, cases of kala-azar were rare, with the disease occurring in persons who had resided in India, China, or countries bordering the Mediterranean Sea.[10] Many medical officers were unaware of the possibility of encountering kala-azar in American troops stationed in areas where the disease was endemic. This frequently resulted in a long delay in diagnosis and in inadequate or inappropriate treatment.

As many of these patients were hospitalized early, and for long continued periods, for unexplained chills and fever and other symptoms, and as many patients were sent for specialized study to the Zone of Interior, the opportunity was presented to observe the entire course of the disease and its response to treatment. Some studies on individual cases were reported.[11] A group of 30 patients were admitted to the Moore General Hospital, Swannanoa, N.C., for diagnosis, institution of treatment, re-treatment, or observation. Clinical, biochemical, and hematological studies were made. The observations, reported by Most and Lavietes,[12] will be summarized and discussed here, with a few case histories (pp. 42–48). The case numbers used in the Most and Lavietes report have been retained in this chapter.

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[10] (1) Price, F. L., and Myer, R. A.: Kala-azar (A Case). J.A.M.A. 125: 490, 1944. (2) Munter, E. J., and Packchanian, A.: Two Exogenous Cases of Visceral Leishmaniasis (Kala-azar) in the United States With Notes on Cultivation of Leishmania-Donovani in Vitro. Am. J. Trop. Med. 25: 507, November 1945. (3) Rose, H. M.: Cold Hemagglutinins in Visceral Leishmaniasis (Kala-azar). Proc. Soc. Exper. Biol. & Med. 58: 93, January 1945. (4) Mathieson, D. R., and Watson, B. A.: Kala-azar. J.A.M.A. 112: 309, January 1939.

[11] (1) Kaminsky, F., and Wever, G. K.: Visceral Leishmaniasis. New York State J. Med. 46: 522–525, 1 Mar. 1946. (2) Marple, C. D.: Visceral Leishmaniasis (Kala-azar): Report of a Case. Ann. Int. Med. 26: 787–795, May 1947. (3) Burchenal, J. H., and Woods, R. P.: Visceral Leishmaniasis; Report of 3 Cases of Its Occurrence in Members of Armed Forces of United States. War Med. 7: 173–177, March 1945. (4) Kranes, A.: Leishmaniasis Among American Troops in the Mediterranean Theater of Operations. (Report of 5 Cases Submitted to The Surgeon General's Office.) [Unpublished; official paper.]

[12] Most, H., and Lavietes, P. H.: Kala-azar in American Military Personnel; Report of 30 Cases. Medicine 26: 221–284, September 1947.

By the end of World War II, not a single death had been reported as a result of kala-azar. Subsequently, one death occurred 66 months after the diagnosis of kala-azar, complicated by nephritis, had been established (Case 23). As the incubation period, though indeterminate, is frequently long, a small number of cases occurred in the United States; the disease developed in men who had previously served in endemic areas, in some, after separation from military service.[13] In a few patients, there was slight residual splenomegaly. Posttreatment cutaneous leishmaniasis did not develop in any of the patients, and only the one (Case 23) who died had suffered relapse after return to civilian life.

In the present series of 30 cases, the average interval from the onset of acute symptoms to definitive diagnosis and specific treatment was 10 weeks, varying from 2 to 23 weeks. In 50 percent of the cases, the disease was active and under observation in a military hospital for 3 months or more before diagnosis was made, and in only five patients was the diagnosis established within a month after onset. In six patients, the disease was continuously active during 4 to 6 months of uninterrupted hopitalization before the correct diagnosis of kala-azar was proved. Most of these men lost a year or more of active duty.

From this experience, it may be hoped that, if troops are again exposed to infection by *Leishmania donovani*, they will have suitable protection [14] against the vector, the sandfly of the genus *Phlebotomus*, and, if cases do occur, that early diagnosis will be made and appropriate, intensive therapy given promptly.

PRECLINICAL HISTORY

Age and occupation.—Of the 30 patients, 13 were from 21 to 25 years of age; 12, from 26 to 30; 2, from 31 to 35; and 3, from 36 to 40. There were 28 enlisted men and 2 officers. One of the officers was attached to an air forces headquarters in India, and the other was an infantry platoon commander, also in India.

Geographic origin of infection.—Of the 30 cases, 15 originated in India and 15 in the Mediterranean theater, with the infected soldiers having spent enough time in North Africa, Sicily, and southern Italy to make more exact localization impossible, with one exception. This patient, stationed near Paris, France, had a 1-week furlough in Nice, 3 weeks before

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[13] A review, in 1951, of records of veterans drawing compensation from the Veterans' Administration and carrying leishmaniasis as a major discharge diagnosis, disclosed no significant disability attributable to kala-azar.—H. M.

[14] The extensive research program which the Office of The Surgeon General, U.S. Army, instituted in 1941 for improved insecticides and insect repellants led to the discovery of the insecticide DDT and such insect repellants as Indalone (butopyronoxyl), dimethyl phthalate, and Formula No. 612 of Rutgers University. All of these were tested, not only against mosquitoes but also against the Phlebotomus sandfly of kala-azar and the tsetse fly of African sleeping sickness and found quite effective. However, their full-scale production did not become available until the latter part of 1943 and early 1944.—A. L. A.

the onset of symptoms. It is reasonably certain that his infection was acquired in the vicinity of Nice.

Mode of infection.—Several species of *Phlebotomus* are known to act as vectors in the transmission of leishmaniasis. The 30 patients all said that they had been bitten by mosquitoes and other "insects and bugs," but they were not specifically aware of the sandfly. This is not surprising, since *Phlebotomus* is only from 1.5 to 2.5 mm. in length, and the local irritation caused by its bite may easily be attributed to the more readily visible arthropods.

Kala-azar occurs mostly in native villages and frequently is a household infection. One patient was one of three officers sharing an apartment in Calcutta, India, in two of whom leishmaniasis developed. Three patients were from the same company quartered at an airbase on the outskirts of Calcutta. Six patients said they had occupied native huts in a village recently vacated. One patient, a truckdriver, slept repeatedly in a stable on the outskirts of a village. Five other truckdrivers traveled at night along the coast of North Africa and often had to sleep in their trucks in towns or villages. In the majority of the 30 patients, there was thus ample opportunity for acquiring infection in or near native villages, but for some of the patients, there was no history obtained of time spent in native huts or villages.

Incubation period.—The incubation period is not definitely known and apparently varies widely, instances being reported in which it was as short as 2 weeks and as long as 18 months. In the patient who became ill 3 weeks after spending a week at Nice, it is fairly certain that the incubation period was 3 weeks, since previously this man had been on duty only in England and Paris. In two of the cases, the incubation period, based on the interval between the last possible exposure in an endemic area and the development of the clinical disease in the United States, was at least 2 months. The longest possible incubation period, as indicated by the interval between arrival in an endemic area and the onset of symptoms, was 33 months. Our attention has been called [15] to a soldier who had served in North Africa, Sicily, and Italy. In Italy, in February 1944, he was taken prisoner and sent to Germany where he remained until his liberation and subsequent return to the United States. He was discharged from the Army in August 1945. Symptoms developed insidiously during the next 2 months, and the patient was finally hospitalized in December 1945. The last possible exposure was in Italy, in early February 1944, and the shortest possible incubation period extended from his arrival in Germany until he became ill in the United States, an interval of 19 months. Accordingly, when there are suggestive clinical and laboratory findings, a diagnosis of kala-azar should be considered, even if the patient has long since left the endemic area.

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[15] Hayman, J. H., Jr.: Personal communication.
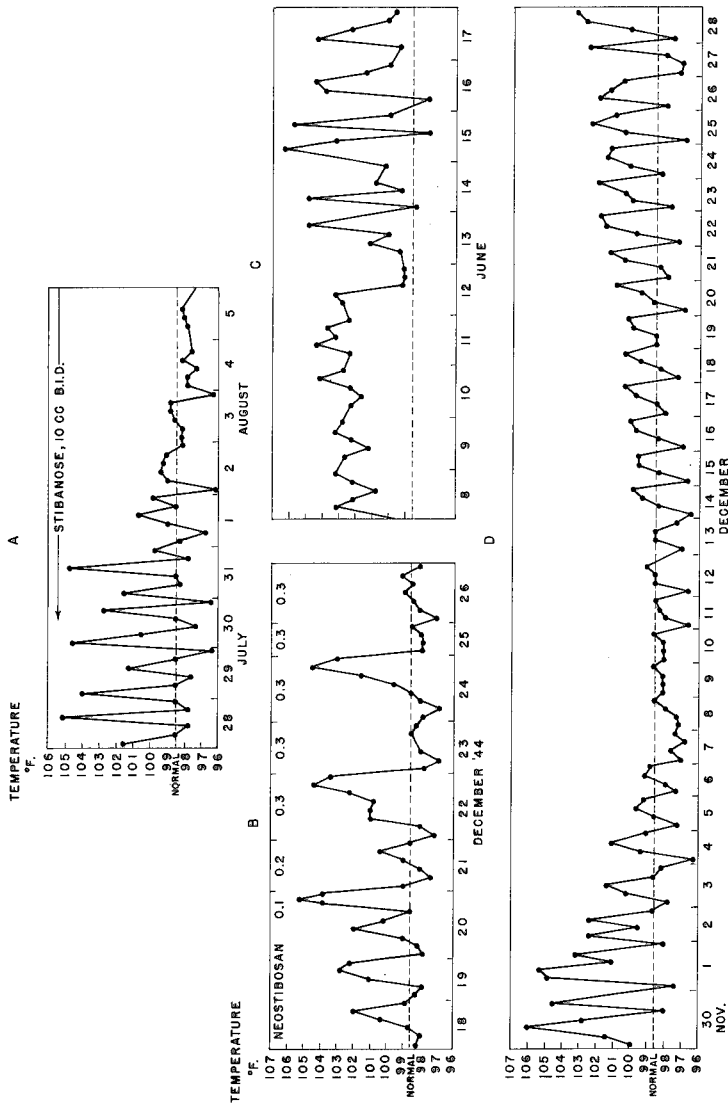
FIGURE 1.—Types of fever in untreated kala-azar and response to specific therapy. A. Daily intermittent fever before treatment. Note double daily peaks. This type of fever was present in this patient for almost 3 months before treatment. Note prompt control of fever after institution of specific therapy (200 cc. stibanose). No relapse occurred during 6 months' observation. B. Note control of fever in this patient within 6 days after institution of specific treatment (Neostibosan, 5.0 gm.). Before treatment, two rises in temperature (101°–105° F.) occurred daily for 4 months. The tertian periodicity that occurred during treatment may also occur in untreated patients and may simulate the form of malaria caused by *Plasmodium vivax*. C. Period of sustained fever simulating typhoid. Note characteristic double peaks later. D. Spontaneous remission and exacerbation of fever without treatment simulating undulant fever.

CLINICAL ASPECTS AT ONSET

Fever.—In this group of 30 patients, the onset of fever was abrupt. In 29 (96 percent) of them, the first symptom was fever, with a chill of sufficient severity to warrant their seeking medical attention.

In the acute phase of the disease, the fever was intermittent, with one or two daily temperature rises to 101° to 106° F. The phenomenon of double peaks in daily temperature was observed in 50 percent of the patients (fig. 1A). Although this may be seen in other infections, it occurs so frequently in kala-azar as to suggest this possible diagnosis in cases of prolonged fever. The second rise may occur late at night and may be overlooked unless temperature readings are taken every 2 or 3 hours, day and night, and are charted graphically.

In some patients, the maximum rise occurs at approximately the same time every day. In a few patients, there may be an exact tertian periodicity of chills and fever, recurring on alternate days for several days and weeks, and suggesting the form of malaria caused by *Plasmodium vivax* (fig. 1B). Occasionally, the temperature, although intermittent, may show very irregular variations in the height as well as in the hour of each maximum rise. Intercurrent infection may alter the temperature curve with periods of sustained high fever, which may be confusing in evaluating response to treatment. A typhoidlike fever early in the disease occurs commonly in China, but this was observed in only one patient whose high fever was sustained for 10 days before it became intermittent (fig. 1C). Recurring febrile waves resembling the temperature pattern in brucellosis have been described in kala-azar, particularly when its course is prolonged (fig. 1D), but this was not a characteristic curve even in patients who were febrile as long as 6 months before diagnosis or treatment. It occurred in four patients; after from 10 to 30 days, it subsided gradually, and a period of from 10 days to 6 weeks elapsed before it recurred. In only one patient was fever entirely absent throughout the observed course of the disease.

Many patients had one or more chills daily, for weeks at a time, and all but three had chills at some time during the disease. The aching in the back and the extremities and the vomiting that frequently occur following a paroxysm of malaria were not noted with the chill or fever of kala-azar. Profuse sweating followed the chill.

Splenomegaly.—Splenomegaly was the most prominent physical finding in most patients. In 27 (90 percent), the spleen was found enlarged on first examination, and in the 3 others, it became enlarged later. The liver was enlarged in 73 percent on first examination or subsequently. No patient had hepatomegaly without splenomegaly, and in all patients, the spleen was enlarged much more than the liver, varying in size from an edge readily palpable just below the costal margin to a gross mass below

the level of the umbilicus. The edge of the spleen was usually firm and smooth and, often, tender. The spleen often enlarged with remarkable speed.

Cervical adenopathy.—Cervical adenopathy was prominent in seven patients. There was also slight to moderate generalized lymphadenopathy in these patients, which, together with coexisting splenomegaly and hematological changes, helped to establish the differential diagnosis. In lymph node biopsies, *L. donovani* were demonstrated in six of these patients, either on first examination or on review of the sections. In still another patient, the only complaint at onset and throughout the whole course of the disease was painless progressive enlargement of lymph nodes of the neck.

Other complaints.—Other complaints at onset, aside from chills and fever, were remarkably few. In practically every patient, there was loss of weight, usually evident when first seen, but only two complained of weakness. Many observers noted that these patients usually did not seem acutely ill—"toxic" or "septic"—even after prolonged periods of chills and high temperature. The skin was warm and dry except following a paroxysm or during the profuse sweating of defervescence.

No striking changes were found in the heart and the lungs. One patient, admitted with chills and fever, had a history of an unproductive cough for 3 weeks, but physical and roentgenographic examinations of the chest were negative in all patients except two with intercurrent pneumonia. Blood pressures were normal, or below normal, in all patients but one. This patient had hypertension associated with acute nephritis (Case 23). This may or may not have been related to the onset of kala-azar. The pulse averaged about 80 per minute except during fever, when it ranged from 100 to 120 per minute. There were no disturbances in cardiac rhythm or in electrocardiograms made before treatment.

In one patient (Case 27), hospitalized because of jaundice, presumably infectious hepatitis, kala-azar was suspected and was later confirmed by the clinical and laboratory findings. This patient had slight icterus of the skin and sclerae. Otherwise, the eyes and fundi were normal in all patients; there were no pigmentary changes in the skin; and no purpura was observed. In one patient (Case 11), the chief complaint was bleeding from the gums, which were spongy, infected, and receded from the teeth.

One patient (Case 23), hospitalized because of edema of the lower extremities, had hypertension, azotemia, and hematuria. A bone marrow examination performed in an attempt to explain the persistent leukopenia in this case of diffuse glomerulonephritis led to the diagnosis of kala-azar.

DIFFERENTIAL DIAGNOSIS

Various acute or chronic infections and neoplastic diseases were sometimes suspected in this group of patients. Intermittent fever, spleno-

megaly, and hematological changes were suggestive, early in the clinical course, of acute infection and, later, of some primary disease of the hematopoietic organs. Frequently, there were intensive studies directed along these lines and numerous therapeutic trials with antimalarial drugs, sulfonamides, and penicillin. These remedies are of no benefit in kala-azar except to control intercurrent infections. The diagnoses most frequently made are discussed here briefly and in more detail in the article by Most and Lavietes (p. 5).

Differentiation from other infections.—In almost every case, malaria had been suspected at onset, suggested by the chills and fever and other findings and by the fact of military service in areas endemic for malaria. Invariably, however, repeated blood smears were negative for *Plasmodia,* and antimalarial drugs were ineffective.

Brucellosis had been seriously considered in five patients from the Mediterranean theater and one from India, but blood cultures were sterile and agglutination tests negative for *Brucella.* In brucellosis, there are usually no double peaks in daily temperature; the white count is rarely so depressed and the spleen rarely becomes so huge as in leishmaniasis.

Subacute bacterial endocarditis was suspected in one patient but was not confirmed. Military tuberculosis was suspected in one patient, a Negro, but was not found in roentgenograms. Dengue was suspected in two patients. Amebiasis was seriously considered in three cases, but there was no leukocytosis, and specific therapy was ineffective. Fortunately, these patients were not subjected either to laparotomy or to aspiration.

Typhoid fever or typhus was considered for several weeks in five patients. In one of these, the temperature was very suggestive of typhoid fever during the first 10 days. However, the blood, urine, or stool cultures, and the Widal reaction, characteristic for typhoid fever, are negative in kala-azar.

Pneumonia may complicate leishmaniasis, particularly in poorly nourished natives. The diagnosis of pneumonia was made early in the course of kala-azar in two patients, one of whom in fact had pneumonia, with leukocytosis. It is of interest that intercurrent bacterial infection in the course of kala-azar is frequently associated with leukocytosis. Proper treatment of the intercurrent infection may result in clinical improvement but as a rule the temperature curve follows the pattern and the white blood count falls to the leukopenic levels of kala-azar.

Infectious hepatitis was suspected in two patients. One may have had hepatitis with kala-azar, an unusual combination. One case was suspected of being histoplasmosis, which may be difficult to differentiate clinically from leishmaniasis since leukopenia, anemia, lymphadenopathy, splenomegaly, and remittent fever occur in both, and the diagnosis ultimately depends upon demonstration of *Histoplasma capsulatum* in smears, cultures, or sections of tissue.

Nephritis was suspected in two patients, and in one (Case 23), there undoubtedly was an acute glomerulonephritis. Although its coexistence with kala-azar may have been a coincidence, the two may be related, for the association has been commented on in the literature.[16] In Case 23, as noted, bone marrow examination was done to explain the persistent leukopenia and anemia. Proteinuria is a common occurrence in leishmaniasis.

Of the 30 patients, 9 were transferred to general hospitals under the classification F.U.O. (fever of undetermined origin).

Differentiation from diseases of the hematopoietic organs.—In approximately 50 percent of the cases of kala-azar, Hodgkin's disease, acute aleukemic leukemia, aplastic anemia, and infectious mononucleosis were seriously considered, and in some, one of these diagnoses was regarded as tenable for at least 3 months. In kala-azar, the peripheral blood picture does in fact resemble aplastic anemia, but the presence of reticulocytes and young white cells indicates continuous regeneration of the blood. Further comparison with these several conditions is discussed elsewhere.[17]

It should be emphasized that progressive, painless enlargement of lymph nodes without fever, splenomegaly, or blood changes may occur in visceral leishmaniasis. This condition has been reported from China and Brazil and more recently in two American soldiers.[18] One case was observed in the present series. The diagnosis is made by finding *L. donovani* in smears and sections of lymph nodes. Accordingly, this diagnosis should be considered in patients presenting progressive cervical adenopathy together with a history of residence or sojourn in a region where visceral leishmaniasis is endemic.

Certainly, it should not be inferred that kala-azar is the correct diagnosis in all febrile cases associated with such findings as leukopenia, splenomegaly, or lymphadenopathy, but only that the possibility should not be overlooked. In a general hospital in the United States, splenectomy was performed on an Italian prisoner of war more than a year after his arrival in the United States.[19] This man had fever, leukopenia, anemia, hyperglobulinemia, and splenomegaly. The spleen, after operation, weighed 1,660 gm. and contained large numbers of *L. donovani*. Before operation, various hematological, neoplastic, and infectious diseases (including kala-azar) were considered. Bone marrow smears examined at the hospital were negative, but *Leishmania* were reported in specimens submitted to the Army Institute of Pathology (now Armed Forces Institute of Pathology), Washington, D.C.

[16] (1) Lee, C. U., and Chung, H. L.: A Clinical Study of the Early Manifestations of Chinese Kala-azar. Chinese M.J. 49: 1281, December 1935. (2) Knowles, R., cited by Strong, Richard P., in Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases. 7th edition. Philadelphia: The Blakiston Co., 1944, vol. I.

[17] See footnote 12, p. 5.

[18] Angevine, D. M., Hamilton, T. R., Wallace, F. G., and Hazard, J. B.: Lymph Nodes in Leishmaniasis. Am. J.M. Sc. 210: 33, July 1945.

[19] Sweeney, J. S., Friedlander, R. D., and Queen, F. B.: Kala-azar (Visceral Leishmaniasis) Simulating Splenic Anemia. J.A.M.A. 128: 1020, 4 Aug. 1945.

Awareness of this disease should not interfere with studies designed to establish other possible diagnoses but may materially shorten the interval from clinical onset to correct diagnosis. Early diagnosis is important in kala-azar because adequate therapy is dramatically effective and in most patients results in complete cure.

DIAGNOSIS

The diagnosis of leishmaniasis is suggested by a history of possible exposure in endemic areas and by such clinical manifestations as (1) prolonged intermittent fever, frequently with double daily peaks; (2) enlargement of the spleen or lymph nodes or both with, in some cases, enlargement of the liver; (3) leukopenia; (4) anemia; and (5) elevation of serum globulin. The diagnosis is established by demonstration of *L. donovani* in smears, sections, cultures (on N.N.N. medium), or by hamster inoculation of material from spleen, liver, bone marrow, lymph nodes, or blood. These sources are listed in the order of relative abundance with which the parasites are said to occur in them.

The results of various diagnostic procedures in the 30 cases are summarized in table 1. The micro-organisms were found in the blood in only one case in which the diagnosis was previously unsuspected. In another series of 300 proved cases, there were positive smears in only 3, and in a series of 23 cases, there were 9 positive smears.[20]

Sternal marrow aspiration was done in 29 patients of the present series. Of 49 punctures, only 21 were positive. The diagnosis was established with one puncture in 14 cases, with a second puncture in 3, and with a third puncture in 4 cases, leaving 8 undiagnosed by this method. The average age of the disease was the same (10 weeks) in those with negative, and in those with positive, bone marrow smears.

In the four sternal punctures in this series that were done at the Moore General Hospital, *Leishmania* were demonstrated by smear and culture but in small numbers compared with the numbers seen in splenic preparations. Bone marrow material may be negative on smear, but positive after culture on N.N.N. medium. Cultures should not be discarded before 1 month, as growth may be slow.

Splenic puncture was performed in 18 cases and gave positive results in all. Three positive specimens of splenic material produced the infection in inoculated hamsters. The age of the disease when diagnosis was made by this means varied from 2 to 23 weeks (averaging 10 weeks).

Lymph node biopsy was done on seven patients with prominent lymphadenopathy. In three, the initial biopsy report was negative, but in two of these, *Leishmania* were found when the sections were reviewed because of

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[20] Henderson (1936) and Wang (1938), cited by Strong, Richard P., *in* Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, 7th edition. Philadelphia: The Blakiston Co., 1944, vol. I, p. 277.

TABLE 1.—*Results of diagnostic procedures* [1] *in 30 cases of proved kala-azar*

Case No.	Bone marrow		Spleen		Lymph node		Blood	
	Smear	Culture	Smear	Culture	Section	Smear	Smear	Culture
1	+		+	+				
2	+							
3	+		+	+			0	0
4	0		+	+			0	0
5			+					
6 [2]	0 / 0	+ / 0	+	+			0	0
7	0 / +	+ / +	+	+				
8	+				+			
9			+	+				
10	0		+	+			0	0
11	0 / +		+	+	0 / +		0	0
12			0		+	+		
13	+		+	+	+		0	0
14	+		+	+			0	0
15	+							
16	0		+	+				
17	0 / +		+	+				
18	+							
19	+		+	+			0	
20	+		+	+				
21	+		+	+			+	
22	0 / 0		+	+	0			
23	+							
24	0 / +							
25	+				+			
26	+							
27	+							
28	0		+	+	0			
29	+							
30	0		+					

[1] Multiple reports for same procedure represent results of trials on different occasions before treatment.
[2] Other diagnostic procedures (skin, tonsil) gave negative results.

KEY.— +, positive result; 0, negative result.

additional clinical and laboratory evidence. In four, the diagnosis was estab-
lished from smears or sections of lymph nodes, making a total of six out of
seven. However, *Leishmania* may easily be overlooked, unless search for
them is directed by a record of stay in endemic areas.

Notes on Technique

Puncture of the spleen.—As this proved to be the most reliable procedure in this series and as it is not widely used in the United States, a general description of the technique of spleen puncture is presented in the paragraph which is to follow and is described in detail elsewhere.[21] The procedure is simple and safe, if done carefully. It should be performed only when kala-azar is suspected from a history of possible exposure, supported by clinical evidence, and only when the edge of the spleen is well below the costal margin. The blood-clotting time and bleeding time should be determined beforehand, and transfusions of whole blood should be given if required.

One hour before puncture, 0.1 gm. pentobarbital sodium is given by mouth. The patient is placed on an abdominal binder and the site of puncture selected. This should be midway between the edge of the spleen and the costal margin, never immediately below the costal margin or between the ribs. A 1-percent procaine hydrochloride solution is injected so as to produce a wheal in the skin about 2 cm. in diameter. The patient is told to breathe deeply in and out 10 times, and a dry sterile needle (17 to 19 gage and 1¾ inch long) is then thrust deeply into the spleen. It should be held firmly but not rigidly. If a stylet has been used, it is withdrawn, and a sterile, airtight 5 cc. syringe attached. Suction is produced, and a little blood enters the syringe. The plunger is then gently released and the needle withdrawn quickly. A sterile pad is applied for a few minutes with gentle pressure to the site of injection, then the abdominal binder is closed. The patient should stay in bed and his pulse and blood pressure should be watched closely for 24 hours.

Smears.—Material from tissue puncture should be spread as thin as possible and allowed to dry. After staining with Giemsa's or Wright's stain, it should be painstakingly examined under an oil immersion lens, with care not to confuse blood platelets and Leishman-Donovan bodies that have been liberated from broken mononuclears.

From blood specimens, both thick and thin smears should be made. The latter require special attention to the edges and ends of the smear where aggregations of white cells may include parasitized mononuclears. Here again, platelets and free parasites may be confused.

If lymph nodes are enlarged, one may be aspirated or removed, and smears and thin sections made, also cultures on N.N.N. medium. Sections should be examined under an oil immersion lens, to avoid overlooking parasites which shrink in fixation.

Summary

Bone marrow smears and cultures may be diagnostic in 60 to 75 percent of cases if suitable specimens (marrow material rather than blood) are obtained and if sufficient care is taken in the search for parasites. These methods failing, splenic puncture remains the most reliable, with due care

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[21] See footnote 12, p. 5.

given to the technique of this procedure. Delays in diagnosis were caused not so much by the difficulty in finding the micro-organisms as by the failure to look for them. Of 14 cases reported to The Surgeon General from India [22] during 1944 and the first 5 months of 1945, 8 were studied at the 142d General Hospital in Calcutta. The interval to diagnosis ranged from 12 to 121 days (average 2½ months). Following presentation of one or two cases at staff conferences, the "index of suspicion" was raised, and delay in diagnosis was materially shortened. Other cases were also reported from the North African and India-Burma theaters.[23]

TREATMENT AND RESPONSE

Specific treatment with antimony compounds was instituted as soon as the diagnosis was made. The results of treatment and the relative efficiency of the drugs used are presented in tables 2 and 3.

The response was frequently dramatic. Fever, which may have been hectic for months, in some cases subsided within a few days after the first dose.

Comparative effectiveness.—Two patients had previously been treated, without benefit, with the trivalent compound Fuadin (stibophen). All were ultimately treated with Neostam (stibamine glucoside), Neostibosan (ethylstibamine), or stibanose (sodium antimony gluconate, 20 mg. antimony per centimeter) in one or more courses of one or more of these pentavalent compounds. Two failures were re-treated, successfully, with stilbamidine (4, 4'–diamidinostilbene isethionate).

Neostam was slower in bringing down fever (average 22 days) than Neostibosan (average 12 days) even when the total dosage was as high. The majority of patients reacted to Neostam with toxic symptoms, principally severe nausea and vomiting, and one patient had shock and convulsions after a single dose of 0.3 gram.

Stibanose eliminated fever rapidly, and no toxic symptoms were observed in four patients in whom it was used for kala-azar, in four others who were given 200 cc. experimentally for schistosomiasis japonica, and in one patient, with Bancroft's filariasis, who was given 400 cc. within 20 days. Two patients, one of whom had failed of cure with Neostibosan, were not, however, cured with stibanose. Stibanose was not found to be superior to Neostibosan.

Stilbamidine, a potentially dangerous drug, is effective in treating antimony-resistant strains (from the Sudan) as well as the more readily susceptible strains (from India, China, and Mediterranean countries).

[22] Blumgart, Herrman L., and Pike, George M.: *In* Medical Department, United States Army. Internal Medicine in World War II. Volume I. Activities of Medical Consultants. Washington: U.S. Government Printing Office, 1961, p. 796.

[23] (1) Essential Technical Medical Data, North African Theater of Operations, U.S. Army, for April 1944. (2) Essential Technical Medical Data, U.S. Forces, India-Burma Theater, 1 July 1945.

TABLE 2.—*Results of treatment in 30 cases of proved kala-azar*

Case No.	Treatment	Fuadin (cc.)	Tartar emetic (gm.)	Neostam (gm.)	Neostibosan (gm.)	Stibanose (cc.)	Stilbamidine (gm.)
1	I.V				[1] 3.5 [2] 5.0		
2	do				[2] 2.9		
3	do			[1] 3.6 [1] 4.25	[2] 5.0		
4	do					[2] 200	
5	do			[2] 4.05			
6	I.M			[1] 3.5	[2] 3.9		
7	do	[3] 30		[1] 2.9	[2] 3.9		
8	do			[2] 3.5			
9	do				[2] 3.6		
10	I.V				[2] 5.1		
11	I.M				[2] 3.6		
12	do			[2] 3.9			
13	do				[2] 4.7		
14	I.V			[4] 6.4	[4] 2.9		
15	I.M			[2] 3.9			
16	do				[2] 3.9		
17	I.V			[1] 4.7	[1] 2.4 [2] 5.0		
18	I.M			[1] 4.0	[2] 5.0		
19	I.V	[3] 43		[3] .8	[1] 2.7 [1] 5.0 [1] 10.0	[1] 240	[2] 4.0
20	do			[1] 4.6	[2] 5.0		
21	I.M			[1] 4.5		[2] 200	
22	do				[2] 5.0		
23	do					[1] 200	[2] 4.0
24	I.V			[2] 3.8			
25	I.M		[4] 1.9		[4] 2.6		
26	I.V			[2] 3.8			
27	do			[4] 2.6	[4] 2.6		
28	I.M			[1] 2.5	[2] 5.0		
29	I.V				[2] 3.4		
30	do				[1] 3.4 [2] 5.0		

[1] Clinical improvement followed by relapse.
[2] Amount which produced cure.
[3] No effect.
[4] Continuous course of two drugs which produced cure.

NOTE.—I.V. (intravenous injection); I.M. (intramuscular injection).

In general, Neostibosan proved to be the drug of choice in these cases, regardless of their origin (Indian or Mediterranean), duration before diagnosis, or previous medication. Fever was controlled promptly; hematological recovery was complete. The optimum total dosage appeared to be 4.0 gm. or more, although several patients were cured with less. In 18

TABLE 3.—*Summary of relative efficiency of drugs used in treatment of 30 proved cases of kala-azar*

Drug	Patients treated	Number of treatments	Percent treatment cures	Percent patients cured
Fuadin	2	2	0	0
Neostam	14	15	40	42
Stibanose	4	4	50	50
Neostibosan	18	23	74	95
Stilbamidine	2	2	100	100

patients, one given 0.5 gm. daily for 20 consecutive days, there were no toxic symptoms. In another case (Case 16), however, subsequent to a course of 3.9 gm. of Neostibosan, there developed a kidney lesion characterized by fixed urinary specific gravity, diminished output of P.S.P. (phenol-sulfonphthalein), and constantly elevated BUN.(blood urea nitrogen) without hypertension or proteinuria. These changes persisted for 9 months. This is a very uncommon manifestation of antimony toxicity. It may be encountered during or after treatment either with trivalent or pentavalent compounds.

Failures in treatment (p. 22) have been principally the result of the use of Neostam overseas or in a few hospitals in the United States or to inadequate dosage with Neostibosan.

Neostam was recommended for the treatment of leishmaniasis in 1941.[24] Previously, the chairman of the Subcommittee on Tropical Medicine of the National Research Council had pointed out that Neostibosan was a superior drug; however, not having been approved by the Food and Drug Administration, Neostibosan was not recommended until 2 February 1943,[25] and its standardization was not approved until 1 June 1944. As a result, this drug did not become available as a standard item of medical supply until most of the patients had already been treated with Neostam at least once.

Of these, in the present series, relapse occurred in more than 50 percent, irrespective of the total dosage of Neostam that had been given. In several patients, failure or relapse resulted from the use of inadequate amounts of Neostibosan. Antimony refractoriness was the probable explanation for repeated relapse in one patient (Case 19) after each of two intensive courses of Neostibosan (5.0 and 10.0 gm., respectively) and one course of 240 cc. of stibanose. Previous treatment with small amounts of Fuadin, Neostam, and Neostibosan had produced only temporary improvement after the latter two. Ultimately, cure followed administration of 4.0 gm. of stilbamidine. The treatment and response to various drugs in this patient is shown in figure 2.

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[24] See footnote 8, p. 4.

[25] See footnote 9, p. 4.

Treatment.—Neostibosan, a light brownish powder containing 42 per-
cent antimony, is available in ampules of 0.3 gram. It is dissolved as a
5-percent solution in sterile, saline, or distilled water and is administered
intravenously. A total of 5.0 gm. over a period of 17 days is usually given,
although in several patients 0.5 gm. daily for 10 days gave excellent results.
Liberal fluid intake and diet are encouraged during treatment. No adjuvant
therapy is prescribed. Complications are not an indication for the dis-
continuance of the specific therapy, unless there should be evidence of a
causal relation, which was not seen in the 30 patients of this series. Penicil-
lin or sulfonamides, or both, may be given to control bacterial infections
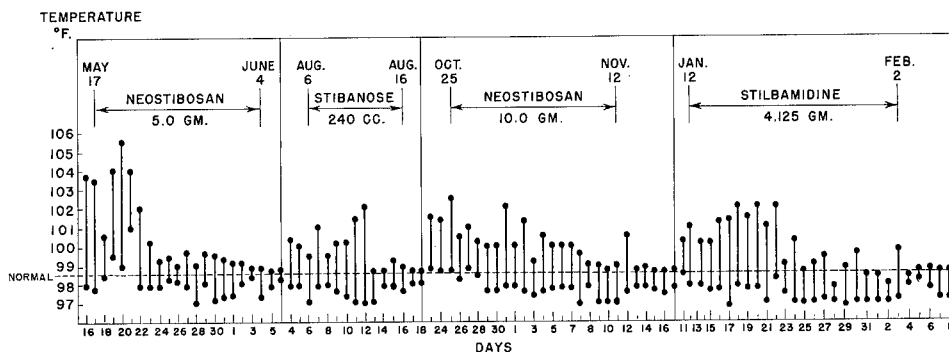
FIGURE 2.—Response of temperature to four courses of treatment in the same patient
(Case 19). Note that fever subsided promptly after each therapeutic course but recurred
after each course but the last. This patient had received, before the first course shown
in the figure, small noncurative amounts of Fuadin, Neostibosan, and Neostam and, as a
result, may have developed an antimony-resistant strain of *Leishmania*. Relapse occurred
even after 10.0 gm. of Neostibosan. Stilbamidine is recommended only after relapse, fol-
lowing adequate amounts of antimony. The necessity of prolonged observation after
treatment is apparent from this case.

during a course of Neostibosan. In the 30 patients, the anemia of kala-azar
responded to Neostibosan therapy, and no patient required any blood trans-
fusions.

Stilbamidine, a nonmetallic organic compound, may produce shock,
hemolysis, hepatic necrosis, and severe neuritis. It should be used with
caution only after failure with several intensive courses of Neostibosan. Of
the 30 patients, only 2 were treated with this drug. It is given intra-
venously in at least 200 cc. fluid, beginning with 25 mg. and increasing by
24 mg. daily until 300 mg. are given at one time. The total dose in the
patients was 4.0 gm., although the usual curative dosage is said to be
between 1 and 2 grams. There is some indication that the more severe toxic
reactions do not occur if the solutions are prepared daily before use.
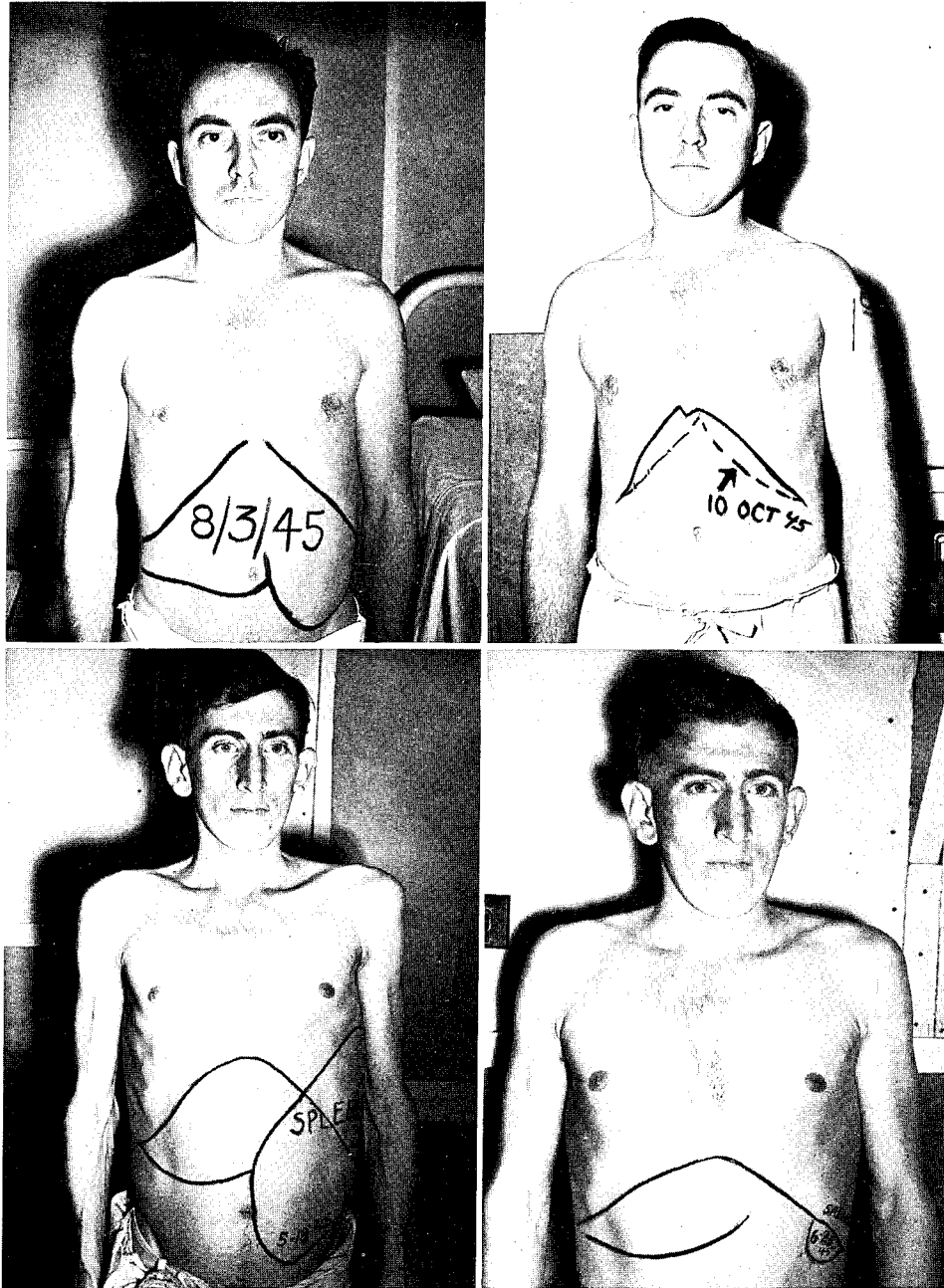
FIGURE 3.—Enlargement of liver and spleen in patients with kala-azar, and response to treatment. Note marked diminution in size of liver and spleen within a month after completion of treatment. Note also improved nutritional state.
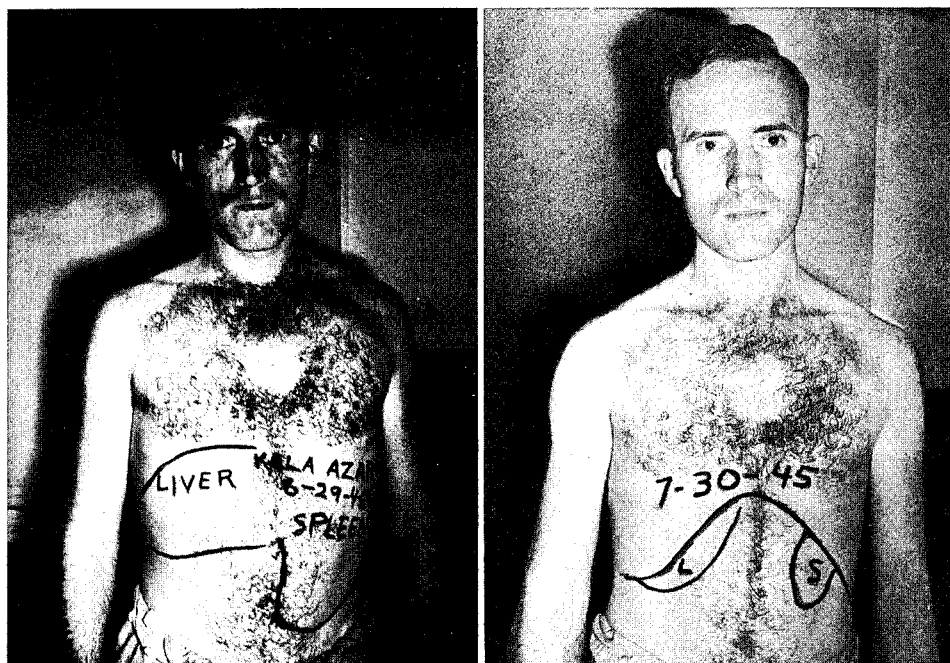
FIGURE 3.—Continued.

Clinical response to Neostibosan treatment.—Symptomatic improvement is frequently noted within a few days after beginning treatment. Most patients have a normal temperature when about half of the total amount of Neostibosan has been given, although a few may still have a low-grade fever 7 to 10 days after completion of treatment. In some, the maximum daily temperature becomes progressively lower each day during treatment until it is normal. In others, chills and high fever continue daily for the first 5 to 8 days of treatment, and then the temperature suddenly becomes, and remains, normal. A striking response to treatment is shown in figures 1A and B and 2.

With subsidence of fever and chills, appetite improves. One patient gained 30 pounds during the first 5 weeks of treatment, and most patients have regained normal weight in from 3 to 8 weeks after completion of treatment.

The spleen frequently shrinks very rapidly and, in practically all the patients, was no longer palpable within 2 months after completion of treatment. In one patient, who had been ill for 6 months before institution of therapy, the spleen, whose edge was in the pelvis at the start of treatment, was barely palpable 1 month thereafter. Typical changes in the size of the spleen and liver after treatment are shown in figure 3.

Correction of the accompanying anemia is seen in the frequently striking reticulocyte response and in the gradual increase in the number of leukocytes to normal within, usually, a month. The typical alterations in serum proteins may take 6 months to return to a normal balance. Hematological and biochemical changes observed in these cases of kala-azar before, during, and after treatment are discussed fully in the report by Most and Lavietes and briefly in this chapter.

Complications.—Whether related to treatment or to other infections, complications were infrequent in the patients in this series. Pneumonia developed in one before the diagnosis of kala-azar was established, and in two others, it occurred during or shortly after the course of antimony therapy. Another patient, while being treated with Neostibosan, developed an acute exacerbation of a previous otitis media. Penicillin brought these intercurrent infections promptly under control without interruption of the Neostibosan schedule. In another patient, a gluteal abscess, which had developed overseas following injection of liver extract, was controlled by incision, drainage, and penicillin. Intercurrent infections were associated with a leukocyte count of 13,000 to 20,000 which returned to the previously low level characteristic of kala-azar when the infection was controlled.

No ulcerative stomatitis occurred in this series, possibly because of the relatively healthy condition of the mouth of the American patient as compared to the native in whom this complication does occur. Acute agranulocytosis was not observed. This rare complication has been described [26] and may be recognized clinically and by leukocyte and differential counts. If it occurs during antimony treatment, such treatment is suspended until the complication has been overcome by blood transfusions, penicillin, and crude liver extract. Treatment with antimony is then reinstituted.

Relapse.—Treatment failures, observed in the United States and occurring overseas, fall into two categories. In one group, there is seen little or no effect on fever, anemia, enlargement of liver and spleen, and leukopenia during treatment or for a month after its completion. Such failures occurred with Fuadin and in many cases with Neostam. In the second group of failures, there is a satisfactory response to treatment, but after an interval of several weeks or months, fever recurs and there is clinical and laboratory evidence of relapse.

The average interval to relapse was 5.8 weeks (range 4 to 13 weeks) after Neostibosan treatment and 5.2 weeks (range 1 to 16 weeks) after Neostam. In this series, all patients were observed for more than 16 weeks after completion of therapy, the average being 6 months. In most cases, relapse is apparent within 2 months of treatment, but in some it may occur later. Relapses were suspected in 2 of the 30 cases only after 4 months of continued observation. One patient (Case 30) was clinically well at this

[26] (1) Huang, C. H.: Acute Agranulocytosis in Kala-azar. Chinese M.J. 57: 119, February 1940. (2) Zia, L. S., and Forkner, C. E.: The Syndrome of Acute Agranulocytosis and Its Occurrence as a Complication of Kala-azar. Am. J.M. Sc. 188: 5, November 1934.

time, but discharge was not advised because leukopenia persisted. In the next 2 weeks, he lost 10 pounds. The other patient (Case 23) was improved in all respects at 4 months, but weight and strength were still subnormal. Sternal puncture done 3 weeks later revealed viable *Leishmania*. These patients were re-treated, and one of them (Case 23) relapsed again with kala-azar and nephritis, eventually becoming the only fatality reported in American troops.

In this series of cases, splenic punctures were performed in all relapses and were invariably found positive. However, a positive splenic puncture 1 or 2 months after treatment is, by itself, not proof of failure or relapse since, in several instances, viable *Leishmania* were obtained from the spleen from 4 to 8 weeks after treatment; these patients were cured without any further treatment. Nevertheless, splenic puncture is important in excluding suspected relapse especially if no *Leishmania* are found on smear or culture of material from other tissues. Negative results indicate a search for a cause other than active kala-azar to explain the symptoms or signs in question, before additional antimony or other therapy is contemplated.

Treatment of relapse.—If relapse has followed treatment with Neostam, or with less than 5.0 gm. of Neostibosan, at least 5.0 gm. of Neostibosan should be administered as has been outlined (p. 19). Relapse after 5.0 gm. of Neostibosan can be treated with 10.0 gm. of the same drug (0.5 gm. daily for 20 days). Relapse after 10.0 gm. should be treated with stilbamidine. In the event of repeated relapse following intensive therapy with Neostibosan and other pentavalent compounds, or when other drugs are not available, a trial of tartar emetic (potassium or sodium antimony tartrate) may be attempted. A satisfactory dose schedule is as follows: First day, 10 cc. of freshly prepared 0.5 percent solution; third day, 20 cc.; fifth day, 30 cc., and this repeated every other day until a total of 360 cc. (1.8 gm.) has been given. Toxic manifestations consist of a hacking cough immediately after an injection; severe aching in joints and muscles, beginning 6 to 12 hours after the injection and lasting for about 12 hours; nausea; and electrocardiographic changes (principally inversion of T waves). Severe cough can be minimized or avoided by giving the 30-cc. doses in two injections of 15 cc. each, with an interval of 1 hour between the two. The rate of injection should not be more rapid than 1 cc. per 15 seconds.

Failure following intensive pentavalent and trivalent antimony and stilbamidine treatment of kala-azar is rare. Careful clinical and laboratory studies are necessary to determine whether some other condition is responsible for continued illness. A patient with kala-azar unsuccessfully treated with several intensive courses of pentavalent antimony compounds and stilbamidine was submitted to splenectomy (p. 44). A dramatic clinical and hematological response followed. Splenectomy must, therefore, be considered as a last resort if all other attempts at treatment have failed.

BLOOD STUDIES

Serum Proteins

Before treatment.—Data on serum proteins available in 19 cases before specific therapy, and within from 1 to 5 months after onset of symptoms, are presented in table 4.

Briefly, it is seen that a fall in albumin and rise in globulin are regularly manifested within 2 months of the clinical onset. Hyperglobulinemia became marked, but hypoalbuminemia never became severe in this series, although more extreme values have been reported.[27]

TABLE 4.—*Serum proteins before any specific therapy in 19 cases of proved kala-azar*

Case No.	Albumin (gm. percent)	Globulin (gm. percent)	Time from onset of symptoms (days)
10	4.1	2.1	9
	4.2	2.2	27
	3.8	2.0	37
16	2.8	5.2	152
	3.1	6.2	168
24	3.1	4.6	61
28	3.9	5.1	40
30	3.4	4.5	54
22	3.5	3.5	70
18	5.7	4.0	59
27	3.2	4.1	18
11	3.2	3.6	53
23	3.0	5.8	123
19	3.7	4.1	134
4	4.1	3.1	97
9	3.5	3.9	83
	2.7	3.9	115
	2.9	4.2	117
20	3.8	3.7	77
12	4.8	8.9	81
1	3.2	3.8	56
13	4.9	3.1	39
	4.5	3.5	186
	4.0	5.9	223
14	3.1	2.9	61
6	4.8	2.7	62
	3.4	6.8	120

[27] (1) Ling, S. M.: Distribution of Protein Fractions in the Serum of Kala-azar Patients. Proc. Soc. Exper. Biol. & Med. 27: 247, January 1930. (2) Chung, H. L.: The Sedimentation Rate of the Blood of Patients With Kala-azar, Chinese M.J. 48: 1101, November 1934.
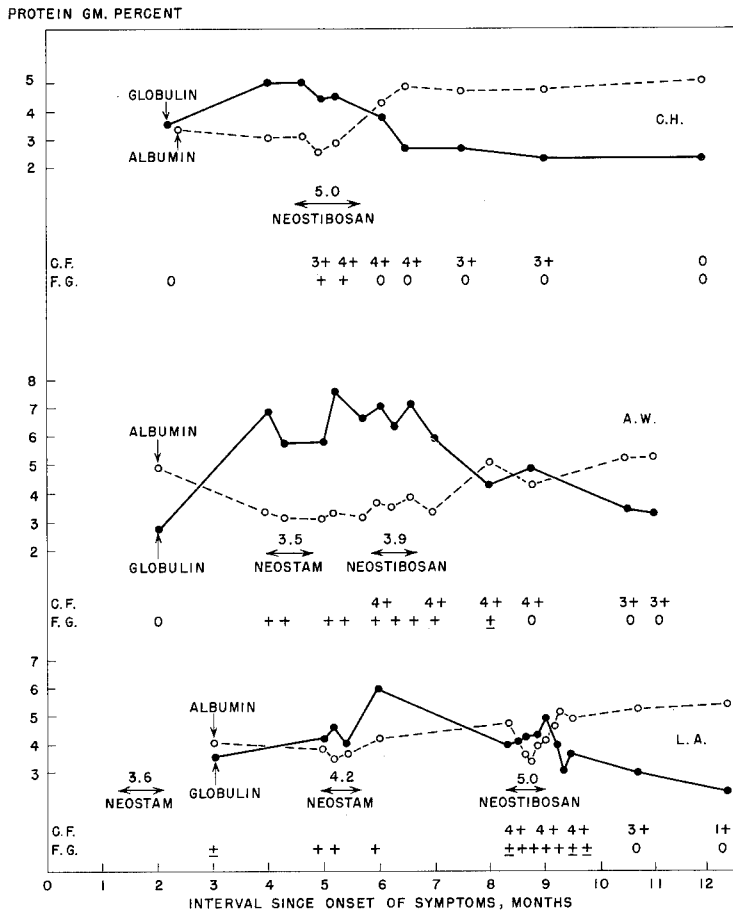
FIGURE 4.—Course of serum proteins, with results of formol-gel test and cephalin flocculation before, during, and after specific antimony treatment in individual cases. Note slow fall of globulin, persistence of positive results in cephalin flocculation test, and more prompt reversion of serum albumin and formol-gel to normal.

Response to treatment.—Data before beginning treatment and at monthly intervals thereafter are presented in table 5. With few exceptions, serum albumin rises to exceed 4 percent in 1 to 2 months, usually reaching maximum values 3 months after the start of therapy. Serum globulin returns to normal more slowly, remaining above normal, in the majority of cases, even after 5 months. The course of serum proteins, in three cases, in relation to the onset of symptoms and to therapy is shown in figure 4. Note the slow descent of globulin into the normal range, the reversion of the formol-gel reaction to normal shortly after treatment, and the prolonged persistence of positive cephalin flocculations.

TABLE 5.—*Serum proteins in relation to start of successful therapy, in leishmaniasis*
[Rate for albumin and globulin expressed as gram percent]

Case No.	Before therapy Albu-min	Before therapy Glob-ulin	1 month Albu-min	1 month Glob-ulin	2 months Albu-min	2 months Glob-ulin	3 months Albu-min	3 months Glob-ulin	4 months Albu-min	4 months Glob-ulin	5 months Albu-min	5 months Glob-ulin	6 months Albu-min	6 months Glob-ulin	7 months Albu-min	7 months Glob-ulin	8 months Albu-min	8 months Glob-ulin	9 months Albu-min	9 months Glob-ulin
3	4.7	3.9	4.8	3.5	5.2	2.9	---	---	5.3	2.3	---	---	---	---	---	---	---	---	---	---
10	3.8	2.0	5.4	2.2	4.4	1.9	---	---	---	---	---	---	---	---	---	---	---	---	5.5	2.5
15	---	---	---	---	---	---	4.1	5.1	---	---	---	---	---	---	---	---	---	---	---	---
16	3.1	6.2	---	---	---	---	3.4	5.3	4.6	4.1	4.2	3.6	---	---	5.2	2.6	---	---	---	---
17	4.3	3.1	4.8	2.9	---	---	5.4	1.4	---	---	5.2	2.0	---	---	---	---	---	---	---	---
24	3.1	4.6	---	---	4.1	4.5	---	---	4.5	3.8	---	---	4.8	3.3	---	---	4.9	2.4	---	---
28	3.0	5.8	3.7	6.0	---	---	---	---	4.8	2.7	---	---	---	---	---	---	---	---	---	---
26	---	---	---	---	---	---	---	---	---	---	5.4	1.5	---	---	---	---	---	---	---	---
30	3.4	4.5	4.4	3.7	4.6	4.0	---	---	4.8	3.6	---	---	---	---	5.2	2.1	---	---	---	---
22	3.0	5.5	3.5	4.7	4.8	2.6	4.7	2.6	4.8	2.4	---	---	---	---	---	---	---	---	---	---
21	3.2	5.8	---	---	3.7	5.1	---	---	3.9	5.3	4.2	5.0	4.1	4.4	---	---	---	---	---	---
18	3.9	5.4	---	---	---	---	5.1	2.8	---	---	4.9	3.0	---	---	---	---	---	---	---	---
27	3.2	4.1	---	---	---	---	5.2	2.0	---	---	4.8	1.9	---	---	---	---	---	---	---	---
11	3.0	4.6	3.1	5.7	4.0	5.5	4.1	3.4	---	---	4.2	3.7	---	---	---	---	---	---	---	---
23	3.0	6.2	3.6	6.4	3.3	4.7	---	---	2.7	6.2	5.1	2.2	---	---	---	---	---	---	---	---
19	3.7	5.9	4.3	4.2	4.4	3.8	4.8	3.3	4.4	8.1	---	---	---	---	---	---	---	---	---	---
5	---	---	4.7	3.4	4.8	3.3	3.6	3.1	3.5	2.9	5.1	2.2	3.9	3.2	4.8	2.8	---	---	5.1	2.0
4	4.1	3.1	4.4	3.2	4.8	3.3	---	---	5.2	3.2	---	---	---	---	---	---	---	---	---	---
9	2.9	4.2	4.0	4.9	---	---	4.2	3.2	---	---	4.2	2.0	---	---	---	---	---	---	---	---
25	---	---	4.9	3.9	---	---	4.9	2.6	4.9	2.9	4.7	2.5	---	---	5.0	2.1	---	---	---	---
20	3.9	4.5	2.3	10.1	3.4	7.4	5.5	2.3	4.4	5.2	5.0	2.8	5.1	3.8	---	---	---	---	---	---
12	4.8	8.9	3.7	4.9	4.6	2.8	4.5	2.7	5.3	1.8	4.2	4.4	4.5	2.5	---	---	---	---	---	---
1	4.0	4.4	---	---	5.4	1.3	5.4	1.3	4.9	3.3	5.2	2.3	5.0	1.5	---	---	---	---	---	---
2	---	---	3.6	5.1	3.5	5.1	4.8	3.9	5.5	1.7	---	---	5.0	2.6	---	---	---	---	---	---
13	4.0	5.9	5.2	3.3	4.3	2.8	---	---	---	---	4.7	3.1	---	---	---	---	---	---	---	---
7	3.8	4.6	3.4	5.8	5.0	4.3	4.3	4.6	---	---	5.2	3.3	---	---	---	---	---	---	---	---
6	3.1	6.5	---	---	---	---	5.0	3.3	---	---	4.5	3.1	4.6	3.5	5.2	2.1	---	---	---	---
14	---	---	4.2	7.1	3.7	6.7	---	---	---	---	4.7	3.7	---	---	---	---	---	---	---	---
8	---	---	---	---	4.5	4.5	---	---	4.4	4.5	---	---	---	---	---	---	---	---	---	---
29	---	---	---	---	---	---	---	---	5.0	3.3	---	---	---	---	---	---	---	---	---	---

¹ During this period, patient was convalescing from acute lymphogranuloma inguinale.

In Case 3, the fall in serum albumin during the first few days is not exceptional. In six of eight cases, a fall in albumin of 0.4 percent or more was noted between the second and seventh day of treatment. This is probably not due to blood dilution, although at this time the hemoglobin and erythrocyte count also usually fall, for the globulin usually increases, and the leukocytes and platelets may decrease disproportionately. It seems probable that these changes are all related to an initial stimulation of *Leishmania*.

Phenomena due to hyperglobulinemia.—Phenomena dependent largely upon hyperglobulinemia were studied as used diagnostically, as follows: *A* flocculation of protein from blood or serum by dilution with water; *B* flocculation from serum by solutions of pentavalent antimony compounds, and *C* opalescent gel formation when two drops of 40 percent formalin are mixed with 1 percent of serum (Napier's formol-gel test). Two or more of these tests were run on the same serum in 14 cases, with agreement between them in 12. In one case, *A* was negative while *C* was positive; in another, *B* was negative while *A* and *C* were positive. The formol-gel test, done 31 times in untreated cases, was positive 8 times, doubtful twice, and negative 7 times in the first 3 months after onset of symptoms; positive 12 times, and negative only twice, after 3 months.

As the formol-gel test depends primarily upon hyperglobulinemia,[28] it is not specific for leishmaniasis. In the 30 patients, the result was usually positive when serum globulin was 4.2 percent or more (fig. 5) but sometimes was negative, usually within a month or two after completion of successful treatment, when serum albumin had increased considerably before serum globulin had fallen markedly. Occasionally, a doubtful positive becomes definitely positive during treatment,[29] as it did in Cases 3 and 19 on the third and fourth days of treatment.

These observations suggested, and in vitro experiments (fig. 6) described by Most and Lavietes confirmed the suggestion, that the opalescence of the formol-gel reaction in the serum of patients with kala-azar is obtained only in hyperglobulinemia in the presence of hypoalbuminemia. Opalescent gels may be obtained with normal euglobulin in physiologic saline solution. Gel formation is common in serum with elevated globulin content in conditions other than kala-azar, but is rarely as opalescent, despite equal reduction in albumin concentration. This suggests that the globulin in kala-azar yields stronger opalescence than that in other conditions with hyperglobulinemia.

The cephalin flocculation and thymol turbidity tests are dependent upon hyperglobulinemia primarily and, the former at least, upon hypoalbuminemia secondarily. Both are strongly positive in active cases. They remain positive for months after successful treatment, even after the globulin con-

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[28] Wise, C. R., and Gutman, A. B.: Formol-Gel Reaction: Convenient Preliminary Test for Hyperglobulinemia. Am. J.M. Sc. 194: 263, August 1937.

[29] See footnote 16 (1), p. 12.

SERUM GLOBULIN (GM.PERCENT)
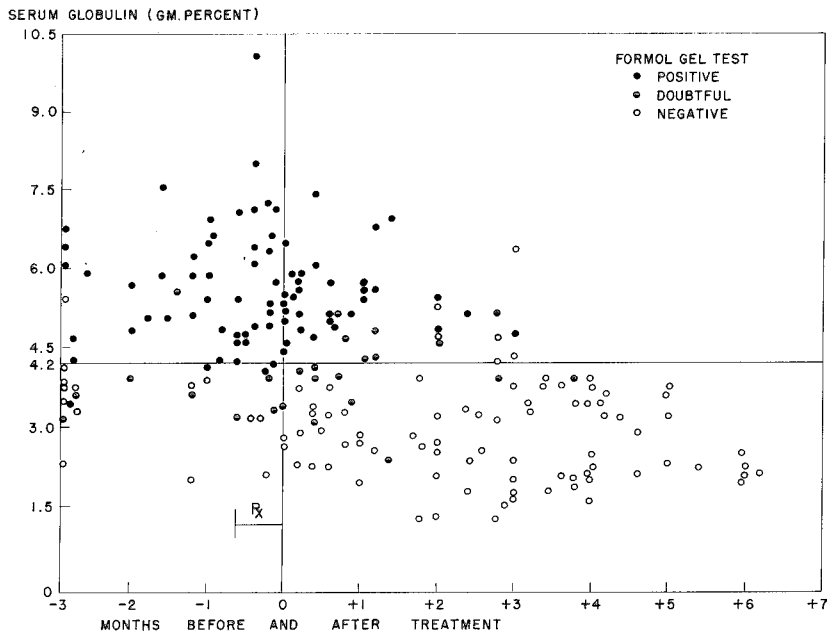
FIGURE 5.—Correlation of serum globulin and result of formol-gel test. Note that, when the serum globulin is 4.2 gm. percent or above, the formol-gel test is positive in most instances. Note also that the serum globulin may be elevated for as long as 6 months after completion of successful treatment although the formol-gel test becomes negative within a month after treatment.

centration has fallen to normal range, suggesting that some of the serum globulin peculiar to leishmaniasis is still present at this time. Tests of liver function (p. 39) showed no evidence of damage.

Nature of the hyperglobulinemia.—The increase in globulin, as in previously reported cases,[30] was chiefly in the euglobulin fraction. Curves of electrophoretic studies (fig. 7) made in 2 of the 30 cases indicate an increase in gamma globulin without abnormal concentration of alpha or beta globulin.

A cold precipitable serum protein which redissolves readily on return to room temperature has been described [31] and was found in approximately one-third of the active cases. In one, 1.9 gm. of protein per 100 cc. came out of solution at 5° centigrade.

The globulin in leishmaniasis serum binds subnormal amounts of calcium. Total serum calcium was in the lower normal range in the presence of marked hyperproteinemia, but ultrafilterable calcium was within normal

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[30] See footnote 27, p. 24.

[31] Wertheimer, E., and Stein, L.: Cold-Susceptible Globulin Fraction of Pathologic Sera. J. Lab. & Clin. Med. 29: 1082–1089, October 1944.

limits (table 6). Hyperglobulinemia of certain other diseases has likewise been shown to possess subnormal base-binding power.[32]

The globulin peculiar to leishmaniasis is, in summary, a sparingly soluble gamma globulin which binds subnormal amounts of calcium (and presumably of total base as well). It probably arises in an immune reaction or, conceivably, from continuous destruction of parasitized reticuloendothelial cells.
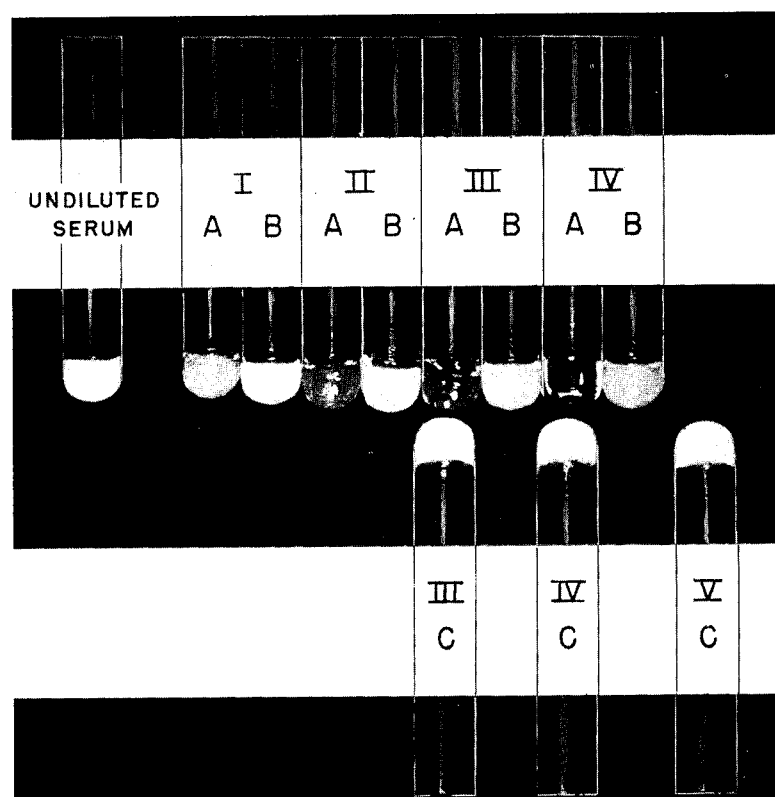
FIGURE 6.—Effect of albumin on the formol-gel reaction. Serum from Case 23 was diluted I (20 percent), II (30 percent), III (40 percent), IV (50 percent), and V (60 percent) with A (17 percent solution of normal human albumin in physiologic saline solution), B (normal serum), and C (physiologic saline solution). One-half cc. portions of the diluted serum were mixed with 1 drop of commercial formalin in 8-mm. tubes. Photographs were made with the samples lying on a black background after 24 hours. Note marked diminution of opalescence in I-A, its almost complete disappearance in II-A, and loss of gelation as well in IV-A. This is in striking contrast to the gelation and intense opalescence after even greater dilution with physiologic saline in V-C. The dilution with normal serum gives intermediate results.

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[32] Gutman, A. B., and Gutman, E. B.: Calcium-Protein Relation in Hyperproteinemia: Total and Diffusible Serum Calcium in Lymphogranuloma Inguinale and Myeloma. Proc. Soc. Exper. Biol. & Med. 35: 511–515, December 1936.

TABLE 6.—*Calcium in serum and in ultrafiltrate of serum, in leishmaniasis*

Case No.	Serum albumin (gm. percent)	Serum globulin (gm. percent)	Serum calcium (mg. percent)	Ultrafiltrate calcium (mg. percent)
15	3.3	7.0	9.5	
11			9.2	
9	2.5	6.1	9.0	
12	4.8	8.9	10.0	
19	3.6	6.4	9.7	5.4
21	3.9	5.3	10.4	6.2
23	3.1	6.1	9.0	5.7
28	2.5	6.4	10.3	6.3
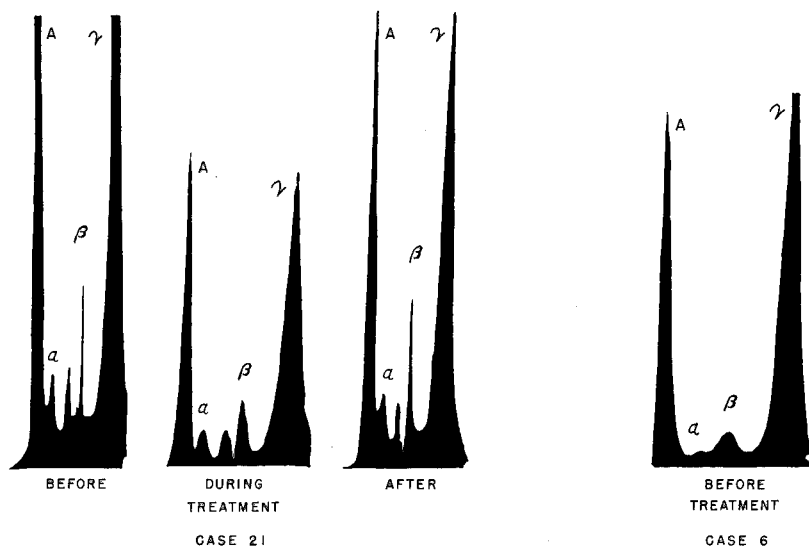
FIGURE 7.—Electrophoretic pattern of sera from two cases of active kala-azar. In both instances, gamma globulin makes up more than half of the total protein and albumin, little over one-fourth of the total. (A, albumin; γ, gamma globulin; β, beta globulin; α, alpha globulin (1 and 2)). There is no significant change during or immediately after completion of treatment in Case 21 (200 cc. stibanose during 10 days). (These studies were made by Mrs. M. Costello and Dr. Dan Moore, Department of Anatomy, College of Physicians and Surgeons, Columbia University, New York, N.Y.)

Leukopenia

Leukopenia is an early and striking manifestation of leishmaniasis. Counts done early in the course of most of these cases are available and are summarized in table 7.
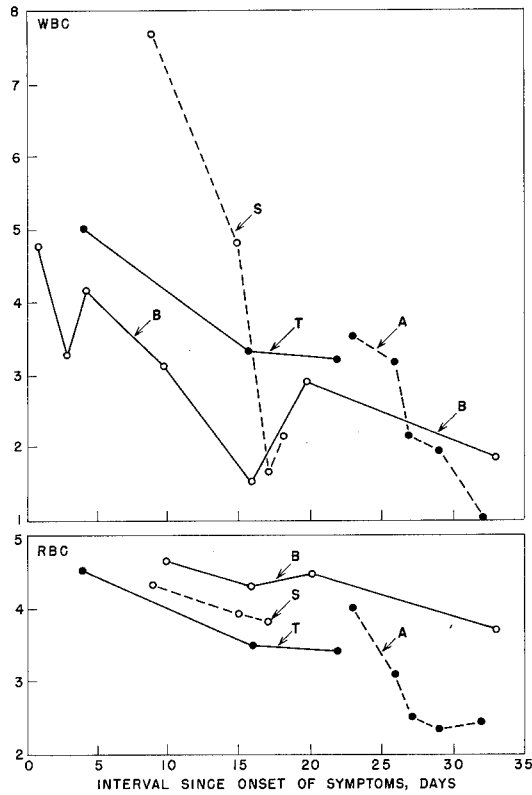
FIGURE 8.—Early changes in the red and white blood counts in active kala-azar. Note rapid development of anemia and leukopenia in patients under observation shortly after onset of symptoms.

TABLE 7.—*Leukocyte counts in 28 cases of proved kala-azar*

Number of cases	Days after onset of symptoms	Number of patients with leukocyte counts of—			Poly-morphonuclear cells, <3,000
		<4,000	<6,000	>7,000	
11	<10	3	7	1	4
	<30	9	2		
9	11–30	5	4		2
	30+	9			
8	>30	7	1		
	>44	8			

TABLE 8.—*Blood counts before and after successful treatment of leishmaniasis in Moore General Hospital*

Case No.	Time from onset of symptoms (weeks)	Previous treatment	Before treatment						After treatment [1]					
			Red blood count (millions)	Hemoglobin (percent)	Color index	White blood count (thousands)	Neutrophils (percent)	Platelets (thousands)	Red blood count			White blood count		
									3 days	1 week	1 month	3 days	1 week	1 month
3	31	A (T)	3.03	56	0.93	1.8	--	160	2.73	2.69	4.30	1.65	2.50	5.50
10	5	--	3.75	68	.90	1.85	33	119	3.56	3.63	4.28	1.35	2.05	5.10
16	24	--	3.22	54	.84	3.7	--	--	2.80	3.42	4.50	4.60	4.75	5.85
17	27	A	3.22	62	.97	2.9	45	184	--	3.86	--	--	3.15	4.65
28 [2]	7	A	2.91	48	.83	2.05	44	--	--	--	--	--	--	--
28	13	T	3.39	61	.90	2.8	49	169	3.01	2.87	4.09	3.00	2.55	4.45
22 [2]	16	--	2.88	55	.96	1.75	50	82	--	--	--	--	--	--
22	20	T	3.67	71	.97	1.8	38	106	--	--	3.51	--	--	6.00
21	24	A	3.30	62	.94	2.1	36	180	--	2.80	3.60	2.55	2.88	3.40
18	15	A	3.78	68	.90	4.65	46	--	4.05	4.10	--	3.00	7.20	--
11	19	--	3.60	77	1.07	2.9	--	69	--	3.69	3.90	3.40	2.75	5.75
23	39	A	3.62	70	.97	3.25	--	--	3.74	3.64	4.36	6.85	6.0	--
19	72	A	3.28	56	.86	2.60	--	--	2.90	3.02	4.14	2.20	1.95	4.60
4	13	--	3.50	71	1.01	2.1	51	101	--	4.08	4.15	3.45	4.60	5.15
9	16	--	3.63	68	.94	4.8	35	--	3.56	3.70	4.20	1.85	2.40	6.80
20	33	A	3.86	65	.84	2.85	40	165	--	--	4.07	--	1.80	7.10
1	26	A	3.00	62	1.03	2.9	34	136	--	3.60	4.00	--	4.40	5.60
13	31	--	3.50	71	1.01	4.0	46	148	2.70	--	3.90	2.50	--	3.50
7	21	A	3.65	74	1.01	4.85	63	102	4.58	--	--	7.00	--	--
6	24	A (T)	3.36	65	.97	5.7	56	148	3.35	3.3	--	3.90	3.40	--

[1] Data presented, where available, at 3 ±1 days, 7 ±2 days, and 30 ±5 days.

[2] Data from hospitalization immediately before admission to Moore General Hospital given because in these two cases transfusions were given shortly before transfer.

NOTE.—A: indicates antimony therapy; T: indicates that transfusions were given in the preceding month.

Thus, only 2 of 20 cases observed in the first month after onset of symptoms failed to develop a leukocyte count of less than 4,000, and 1 of these had a mild persistent granulopenia. Another patient was noted as having both leukopenia and anemia in the first month of clinical illness but is not included in the analysis because the early data are not available. The speed with which leukopenia may develop is illustrated in figure 8.

The data obtained in active cases before (and after) successful treatment at the Moore General Hospital are shown in table 8. During spontaneous remissions of the disease, the blood count reverts to or toward normal.[33] There are no observations during remissions in this series. In two cases, leukocytosis developed with the occurrence of pyogenic complications (otitis media and pneumococcic pneumonia).

Anemia

A common early symptom of kala-azar is a lowered erythrocyte count. Observations made soon after the onset of symptoms are presented in table 9.

At or near the time of first observation, 16 of 26 cases had erythrocyte counts of 4.0 million or less. In 13 of 17 patients with counts done during the first month after the clinical onset, the red cells fell to 4.0 or less.

In this series, anemia never progressed to extreme levels. The median count in 16 patients during the first month of symptoms was 3.7 million, range from 2.4 to 4.6. For the 28 cases as a whole, the minimal pretreatment count had a median of 3.2, range from 2.2 to 4.5. Pretreatment counts at the Moore General Hospital, recorded in table 8, range from 2.9 to 3.9, median 3.4, in close agreement with pretreatment data from other hospitalizations.

Color indices (Sahli's technique) in the active cases were rarely less than 0.90, and in several exceeded 1.00 (table 10), again in close agreement

TABLE 9.—*Erythrocyte counts in 26 cases of proved kala-azar*

Number of cases	Days after onset of symptoms	Number of patients with erythrocytes		
		>4.8 (millions)	>4.0 (millions)	>2.8 (millions)
6	<10	--------------	5	1
	<30	--------------	2	4
11	11–30	--------------	3	8
	30	--------------	2	9
9	>30	--------------	2	7

[33] See footnote 16 (1), p. 12.

with hemoglobin determinations made before admission, technique not specified. In these, color indices were usually between 0.90 and 1.00, rarely below 0.85 and never below 0.82, with a few between 1.00 and 1.10. As a rule, there was but slight hypochromia in relation to the number of erythrocytes (color index) but more marked hypochromia in relation to cell volume (mean corpuscular hemoglobin concentration) ; that is, the red cells were often abnormally large and pale, as was readily apparent in some of the smears.

Other findings included reticulocyte counts, before treatment, of 0.5 percent or less in six active cases and of 1.0 and 1.4 percent in two active cases. Normal values had been noted elsewhere in three of these patients and in one other. The test for erythrocyte fragility to hypotonic saline made in four active cases gave normal results. The icterus index was normal in all active cases upon admission. In early determinations in 15 patients, it was within normal range in all except 1 patient who probably had concurrent hepatitis, 2 who had single observations of 9 and 11 shortly after transfusions, and 2 with unexplained single observations of 9 and 18. In blood smears, normoblasts were not observed; metamyelocytes were present in normal numbers, and no younger forms of leukocytes were found in the peripheral blood.

TABLE 10.—*Hematological observations in seven cases of active kala-azar*

Case No.	Previous treatment (antimony)	Time from onset of symptoms (weeks)	Red blood count (millions)	Hemo-globin (percent)	Hema-tocrit volumes (percent)	Color index	Mean corpuscular volume (cubic microns)	Mean corpuscular hemoglobin concentration (percent)
10	0	5	3.46	68	28	0.98	81	35.2
28	+	19	3.03	57	27	.94	89	30.6
22	0	17	2.88	55	27	.96	94	29.5
11	+	22	3.67	77	36	1.05	98	32.1
23	0	32	3.62	70	36	.97	100	28.2
9	0	16	3.63	68	33	.95	91	29.9
16	0	12	2.65	54	26	1.02	98	30.0

NOTE.—0, negative result; +, positive result.

These findings indicate that the changes in the blood observed in kala-azar are not characterized by excessive blood destruction or by increased blood formation.

Clotting Mechanism

The clotting mechanism was studied during active disease in all but two cases. Bleeding time was 4 minutes or less, with rare exceptions, and never exceeded 5 minutes. Clotting time was usually in the upper normal

range, with none definitely abnormal. The quality of the clot was often poor, and clot retraction was occasionally retarded; none being apparent at 2 hours in four patients and none at 24 hours in one, in which bleeding from the gums had occurred in its course (Case 11).

Thrombocytopenia developed early and regularly in the 30 patients but never became extreme. Platelet counts made before treatment (table 8) were uniformly subnormal, the lowest being in the case with the poorest clot retraction. In Case 23, with nosebleed at the onset of illness, platelets were 105,000 only 12 days thereafter; in Cases 11 and 7, they numbered 132,000 and 159,000, respectively, 5 and 7 weeks from clinical onset; and in Cases 3 and 22, they were 70,000 and 63,000, respectively, at approximately 20 weeks from onset of symptoms. The occasional defect in clot retraction was presumably due to thrombocytopenia. That the hyperglobulinemia was not responsible is suggested by the fact that globulin from patients with kala-azar added to normal serum did not prevent normal clot retraction.

Although total serum calcium was in the lower normal range (table 6), normal values for ultrafilterable calcium showed that an abnormally high portion of total calcium was not bound to protein, as might have been expected in view of the hyperglobulinemia.

Fibrinogen, measured in three patients, was normal, as in previously reported cases.[34] Prothrombin time, determined in four active cases, was within normal limits. In one patient (Case 14), who was successfully treated before admission, the prothrombin time was 56 percent before treatment, with slow reversion to normal subsequently.

Deficiency in calcium, fibrinogen, or prothrombin cannot have been responsible for the bleeding observed in this disease. The thrombocytopenia, although occurring regularly, was not of the degree seen in purpura. In previous observations, also, a lack of correlation between bleeding and platelet counts has been noted.[35] Only the two patients in this series had any abnormal bleeding, the one (Case 11), from his gums early in his disease; the other (Case 23), from the nose at the onset of illness and again during an exacerbation 4 months after treatment with stibanose. During this relapse, examination of the anterior nares revealed some areas of hyperemia, superficial ulceration, and crusting. The bleeding of kala-azar may be due, in part at least, to actual leishmanial lesions of the mucous membranes.

Response of Blood Count to Treatment

Circulating erythrocytes and leukocytes usually decreased during the first week of treatment. A progressive rise ensued, which was usually well marked within 1 month of beginning treatment. The counts after approximately 3 days, 1 week, and 1 month of therapy are presented in table 8.

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[34] See footnote 27 (2), p. 24.

[35] Scovel, F. G.: Kala-azar: A Review of Its Incidence and Epidemiology in China and Clinical Observations on 585 Cases. Ann. Int. Med. 21: 607, October 1944.
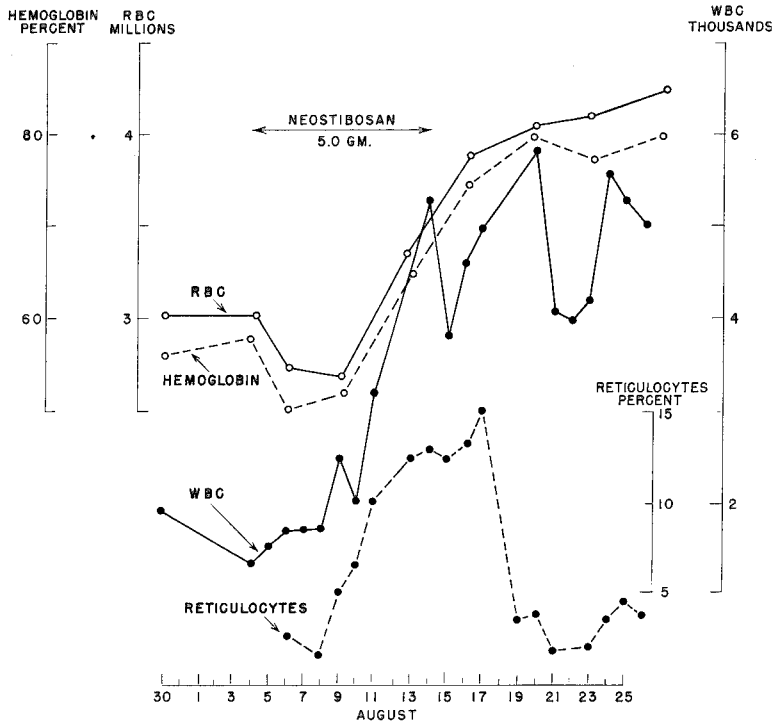
FIGURE 9.—Hematological response to treatment. Note reticulocyte rise and reversion of red blood cells, white blood cells, and hemoglobin toward normal.

Available data on patients treated before admission showed a similar trend. Red cell count and hemoglobin usually became entirely normal in the 30 cases only 3 to 4 months after start of treatment. No medication was given for the anemia per se. Platelets were followed through treatment in only one patient (Case 28). The pretreatment level was 169,000, with fall to 115,000 on the 7th day of treatment and return to 171,000 on the 14th day. This is in accord with previous observations.[36] Frequent reticulocyte counts during treatment in six cases invariably showed a significant rise, in three of them occurring within 2 days after the first injection. The peak (up to 15 percent) was reached in approximately 2 weeks in most instances (table 11). A typical hematological response is shown in figure 9, and a composite chart of the leukocyte counts before, during, and after treatment is shown in figure 10. The speed of restoration of the leukocyte count to normal is not related to the ultimate outcome, although one should suspect therapeutic failure or relapse if leukopenia is prolonged for several months after treatment.

[36] Yang, C. S., and Ch'en, K. T.: Blood Platelets in Kala-azar. Nat. Med. J. China 16: 34–42, February 1930.

WBC (THOUSANDS PER CMM)
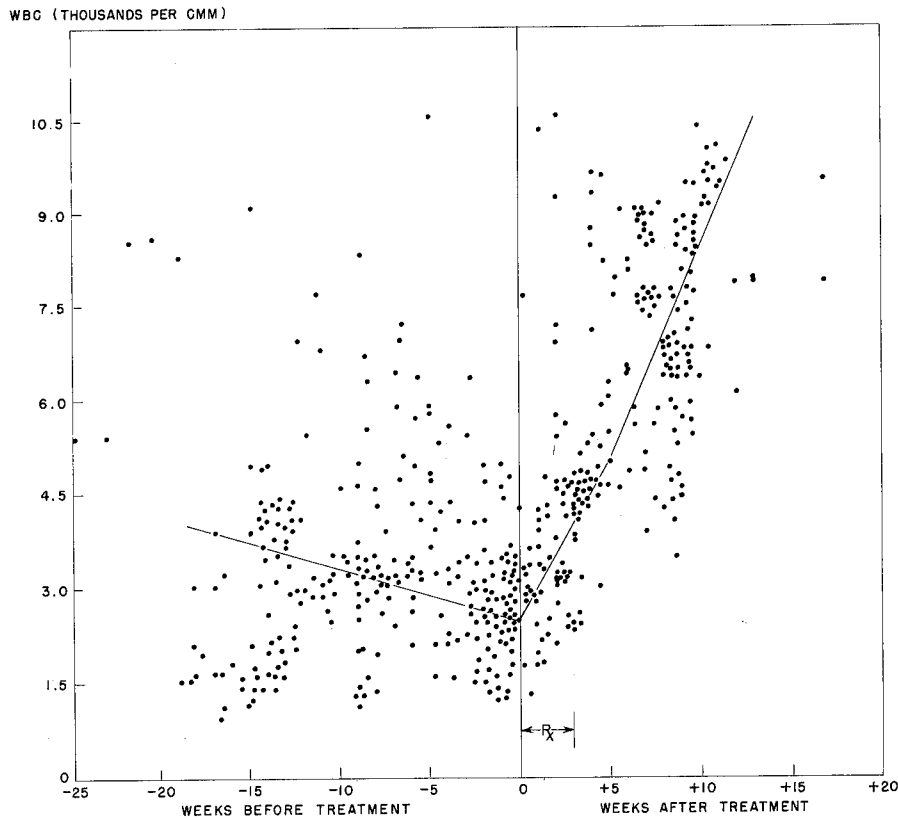
FIGURE 10.—White blood counts before and after treatment. Composite chart of all white blood counts in 25 cases. Note the marked and maintained leukopenia before treatment and the response after therapy.

TABLE 11.—*Reticulocyte response to specific treatment in proved cases of kala-azar*

Case No.	Before treatment		Maximal reticulocyte count	
	Red blood count (millions)	Reticulocytes (percent)	Days from first injection	Level (percent)
3	3.03		13	15.0
19 [1] (a)			13	9.4
(b)			18	3.9
(c)		1.0	27	5.3
4	3.50		7	4.6
21	3.3		18	14.8
28	3.39	.5	15	7.0
18	3.78	.5	15	3.4

[1] Response to 3 different courses of treatment, as follows: Relapse after (a) 10.0 gm. Neostibosan and (b) 240 cc. stibanose and cure after (c) 4.0 gm. stilbamidine.

Erythrocyte Sedimentation Rate

Regular increase in sedimentation rate in kala-azar has been described [37] and is usually so great that, in blood from untreated cases, the cells settle out to a large degree before clotting occurs. Sedimentation rates, determined by the method of Wintrobe in 19 of 30 cases before specific therapy, are summarized in table 12. It is apparent that the sedimentation rate is usually, but not necessarily, elevated during active disease. The following cases are illustrative:

Case 11.—This patient had had a sedimentation of 35 mm. before treatment with a small dose of antimony, which produced a brief remission. On admission to Moore General Hospital, 7 weeks later, he was febrile and splenic puncture was positive, yet the sedimentation rate was 2 mm. per hour.

Case 23.—This patient, with marked elevation of sedimentation rate before treatment, had a rate of 9 mm. per hour 19 weeks after treatment with stibanose. Because this patient failed to gain weight and strengh, splenic puncture was done and viable Leishmania were recovered. Activity of the disease in this patient could not be predicted by the sedimentation rate.

TABLE 12.—*Pretreatment sedimentation rate (millimeter per hour) in 19 cases of proved kala-azar*

Number of cases	Pretreatment sedimentation rate (mm. per hour) after onset of symptoms			
	2 weeks	3 weeks	7 weeks	>8 weeks
4	25	30		
		20		
		26		
		32		
13				> normal
1 [1]			8	
1 [2]				[3] 4

[1] Case 7.
[2] Case 13.
[3] 32 weeks after onset of symptoms but only 1 week after spontaneous remission of 3 weeks.

Other Tests

Agglutination of group 0 erythrocytes in the cold by serum from patients with kala-azar has been reported.[38] Of 5 of the 30 cases tested, 3 were negative and 2 were positive in low titer (1:5, 1:4). Complement fixation tests were more often negative than positive in the active cases.

Bone marrow smears were examined in only four active cases. Prior reports in most instances had noted only the presence or absence of Leishmania. In 7 cases, however, in which complete examinations were recorded

[37] See footnote 27 (2), p. 24.
[38] See footnote 10 (3), p. 5.

and in 4 of the 30 of this series, marrow of average cellularity and differential count was observed. In this cellular marrow, Leishman-Donovan bodies usually were sparsely scattered.

Nature of the Hematological Disturbance

There is no apparent hemolytic component, since red cell fragility and icterus index are normal. There is no deficiency of antianemic principle, since the bone marrow is not megaloblastic nor the anemia hyperchromic. Liver extract was used before admission in several of the 30 patients, without therapeutic effect. The hematological disturbance is not nutritional in the ordinary sense, since it may develop with extreme rapidity, is associated with marked leukopenia, and is characterized by only minimal hyperchromia.

The peripheral blood picture is that of aplastic anemia, but the bone marrow is not morphologically aplastic. The anemia and leukopenia have been described as myelophthistic, a hypothesis which seems hardly tenable in view of the cellular marrow and relative paucity of Leishman-Donovan bodies. The picture in the periphery and in the marrow resembled that described in benzol and other poisoning.[39] It seems quite possible that the anemia of kala-azar is likewise toxic either in the sense that a metabolic product of *Leishmania* interferes with cell production or that the metabolic needs of rapidly dividing *Leishmania* or rapid formation and destruction of reticuloendothelial cells deprive the marrow of essential nutrients. The early appearance of reticulocytes when the temperature falls during antimony treatment, while viable *Leishmania* are still present in abundance in spleen and marrow, is compatible with this hypothesis.

LIVER FUNCTION

There is no indication that liver function has suffered significantly in the 30 patients of this series. The icterus index was normal in all of the cases that were active on arrival in Moore General Hospital and in almost all observations made before hospitalization here. Bromsulphalein (sulfobromophthalein) excretion was studied in six active febrile cases, using the 5 mg. per kilogram dose and the 45-minute interval. Dye retention was only between 2 and 10 percent. The strongly positive cephalin flocculation and thymol turbidity probably were not indicative of liver damage but were rather a manifestation of the marked hyperglobulinemia.

Icterus index, serum bilirubin, and BSP (Bromsulphalein) excretion were determined during and after treatment with Neostibosan or stilbamidine in several instances, but no evidence of liver damage was found. The

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[39] Rhoads, C. P., and Miller, D. K.: Histology of the Bone Marrow in Aplastic Anemia. Arch. Path. 26: 648–663, September 1938.

icterus index in the patient (Case 27) convalescent from apparent infectious hepatitis fell from 31 to 20 in 4 days of febrile kala-azar immediately before treatment with antimony and to 10 during the first 2 weeks of treatment. On admission to Moore General Hospital, 3 months later, the icterus index was 4.

RENAL COMPLICATIONS

There were only two patients with clinically important renal complications in this series. One, Case 16, an instance of chronic renal insufficiency following successful treatment of kala-azar with Neostibosan, will be discussed later (p. 41). The other, Case 23 (p. 46), developed classical acute glomerulonephritis at approximately the same time as the onset of kala-azar. At the time of first observation, 2 weeks after the onset of symptoms, marked leukopenia was already present in addition to the edema, hypertension, azotemia, albuminuria, and hematuria of acute nephritis. Since leukopenia rarely develops in less than 2 weeks from the clinical onset in kala-azar, this disease was probably of at least 2 weeks' duration. That it was not much longer than this is indicated by the fact that splenomegaly and lymphadenopathy developed 1 week after the initial observation and that serum protein rose from 6.2 to 6.9 gm. percent in the first 10 days and to 10.4, 2 months later. Coincident onset does not, of course, indicate a causal relationship between the two diseases. In fact, progressive improvement in the nephritis was marked before treatment of the kala-azar, and the subsequent course to apparent cure was not inconsistent with the natural history of the ordinary severe acute nephritis. The very few cases of acute nephritis that have been reported in connection with kala-azar may be of an accidental association.

Incidence and course of albuminuria and hematuria in the patients of this series during the course of kala-azar are summarized as follows:

Of 25 patients, 16 were observed to have albuminuria during active kala-azar, and 12 were known to have microscopic hematuria. The albuminuria was usually slight and the hematuria usually mild. In only one case were many red blood cells reported with urinary findings so prominent that renal function tests and intravenous pyelograms were made; both were normal. In most cases, hematuria was observed on several occasions. Many specimens contained from 3 to 10 leukocytes per high-power field without relation to other urinary findings and usually without change following treatment. With the exception of Case 23, none of the patients had hypertension, edema, azotemia, and all were able to concentrate urine and to excrete phenolsulfonphthalein.

Hematuria, albuminuria, and cylindruria disappeared during treatment or within a few days thereafter. Neither albuminuria nor hematuria was constantly present during fever. The frequency of hematuria in the

patients of this series suggests that the albuminuria of leishmaniasis is due to focal leishmanial lesions, analogous to focal nephritis in bacteremias, and not to fever. In fatal cases, parasitized macrophages may be seen in the interstitial tissues of the kidneys.[40]

The other patient (Case 16) developed chronic renal insufficiency during convalescence from kala-azar, presumably from toxic effect of Neo-stibosan. Previous data in this case are scant. Urinalysis 12 weeks from onset of symptoms of kala-azar was normal. Four weeks later, from six to eight red blood cells per high-power field were reported. Five weeks after this, just before treatment, urinalysis showed specific gravity of 1.023, no albumin, and no formed elements. Clinical response to treatment with 3.9 gm. of Neostibosan in 23 days was prompt and satisfactory with no un-toward reactions noted. Unfortunately, the urine was not examined during treatment or for 10 weeks thereafter. Casual urine specimens then showed low specific gravity, and concentration tests revealed marked hyposthenuria. Excretion of P.S.P. was only 22.5 percent in 15 minutes (normal 25 to 50 percent) and the BUN. was elevated to 22 mg. percent. The urine contained no albumin or formed elements. There was no hypertension or edema, and serum albumin was normal. For $9\frac{1}{2}$ months after completion of treatment, urine concentration was never greater than specific gravity 1.015, P.S.P. excretion ranged between 17.5 and 20 percent in 15 minutes, BUN. varied between 21 and 27 mg. percent, and maximal urea clearance was only 38 cc. per minute. The patient remained asymptomatic, except for slight nocturia, with normal blood pressure and without albumin or formed elements in the urine. In summary, this man had a diffuse, nonprogressive lesion with marked reduction of renal function but without signs of inflammation. This was presumably due to toxicity from antimony, although documentation is admittedly poor.

In all other cases in this series, urine examinations and renal function were normal at the end of the observation period. Therapy with the various pentavalent antimony preparations did not affect normal urines, and those with initially abnormal findings cleared during treatment. Excretion of P.S.P. was determined shortly after completion of treatment in many instances and urea clearance in four instances; all were within normal limits. In one patient (Case 19), during treatment with stilbamidine, slight albuminuria developed without other abnormality. Three consecutive speci-mens before treatment and repeated specimens after the last day of treat-ment were all negative. Routine urinalysis before, during, and after treat-ment had specific gravity in excess of 1.024. No appreciable change in slight albuminuria present before treatment was observed in the course of treating Case 23 with stilbamidine.

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[40] Strong, Richard P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases. 7th edition. Philadelphia: The Blakiston Co., 1944, vol. I, p. 256.

CASE HISTORIES

Five case histories, of unusual interest, are presented in this section. Three (Case 22, Case 19, and Case 23) are from the series of cases discussed in the preceding sections of this chapter. One (Case 5c) is from another series, and one (unnumbered) is of a patient who was seen at the Walter Reed General Hospital, Washington, D.C.

Case 22.—Prolonged interval to diagnosis; leukemia considered for 2 months; prompt response to 5.0 gm. Neostibosan; no relapse.

This patient, white, 23 years old, a carpenter, had served in the Mediterranean theater (north Africa and Italy) from 13 May 1943 to 24 March 1945. Onset of illness in December 1944 was gradual, with progressive enlargement of the abdomen, with pallor, and, in January, with chills, fever, sweats, and anorexia. Admitted to the 81st Station Hospital, Leghorn, Italy, on 16 February 1945, he had lost 38 pounds; the liver and spleen were enlarged four fingers' breadth below the costal margin; there was generalized adenopathy; leukopenia (3.3) but no anemia; cephalin flocculation, 4 plus. Presumptive diagnoses were Hodgkin's disease, aleukemic leukemia, or kala-azar. Sternal puncture, blood culture, stool examinations, and malaria smears were all negative. An excised axillary lymph node showed nothing specific. Fever, with one or two chills daily, showed a temperature rise as high as 105° F. The liver and spleen continued to enlarge.

He was transferred to the 64th General Hospital, Ardenza, Italy, on 10 March 1945. Symptoms became progressively worse. A second sternal puncture was reported negative for kala-azar. An inguinal hernia developed. Evacuated to the United States with a transfer diagnosis of aleukemic leukemia, he was a patient at the Foster General Hospital, Jackson, Miss., from 19 April 1945 to 10 May 1945. Pallor and emaciation became more severe; the splenomegaly, hepatomegaly, and adenopathy persisted; and anemia was discovered. Total serum proteins were elevated. Sternal puncture and biopsy of an axillary node did not reveal parasites. A splenic puncture was performed, but the slides were lost. Temperature rose daily to 104° F. The patient was transferred to the Moore General Hospital on 10 May 1945.

Physical examination.—Pallor; weight, 132 pounds; * * * generalized adenopathy involving the anterior cervical, the occipital, the epitrochlear, the axillary, and the inguinal glands. In the left axilla, there was a hard gland of moderate size, freely movable, not tender. The spleen was nine fingers' breadth below the costal margin and descended further with respiration; it was tender to touch. The liver was six fingers' breadth below the costal margin. The clinical impression was kala-azar.

Admission laboratory findings.—RBC, 3.6 million; Hb. 71 percent; WBC, 1.8; serum albumin, 2.5, serum globulin, 4.6 gm. percent; cephalin flocculation test, 4 plus; formol-gel test, 4 plus; clotting time (Lee and White method), 16 minutes; bleeding time, 2.5 minutes; platelets, 106,430.

Hospital course.—A transfusion of 500 cc. blood was given on 13 May 1945. Splenic puncture on the following day showed Leishman-Donovan bodies. A course of 5.0 gm. Neostibosan was begun on 15 May and completed on 2 June 1945. In 10 days, the temperature became normal for the first time in 5 months. By 18 June 1945, the patient had gained 24 pounds, his spleen was only three fingers' breadth and his liver four fingers' breadth below the costal margin. The erythrocyte count had risen to 4.2 million, Hb. 84 percent, leukocyte count to 5,500. The formol-gel test was negative. Total serum proteins were normal at 7.4, albumin 4.8 and globulin 2.6. Cephalin flocculation was 4 plus.

Returning from a 30-day furlough, the patient reported feeling fairly well except for some pain in the left upper quadrant of the abdomen. His spleen was no longer palpable, and all laboratory findings were normal except for a positive cephalin floccula-

tion. Seen again in September, he complained only of tiring easily. He weighed 165 pounds, and neither liver or spleen was palpable. Bilateral hernias were repaired on 3 October 1945, and the patient was discharged as completely well in December 1945. The serum proteins were normal, the red and white blood counts were normal, and the cephalin flocculation test was negative. Microscopic hematuria and albuminuria, which had been repeatedly observed, cleared completely after treatment.

Comment.—The interval to diagnosis from the onset of symptoms was at least 4 months. The consensus at several hospitals was that the patient had leukemia. The correct diagnosis was established by splenic puncture, and complete recovery followed treatment with 5.0 gm. Neostibosan. No relapse occurred during 6 months' observation following treatment.

Case 19.—Protracted illness; long interval to diagnosis; repeated failure with antimony; cure with stilbamidine (see fig. 2).

The patient, white, 27 years old, a file clerk, served in various parts of India from 17 May 1942 to 25 August 1944, in contact with natives and quartered sometimes in barracks and sometimes in tents. Acute clinical onset, on 16 August 1944, with chills, fever, generalized aching, and headache. Admitted to the 263d General Hospital, Calcutta, India, on 25 August. One or two temperature elevations with chills daily. Treatment with quinine, Atabrine (quinacrine hydrochloride), sulfonamides, and penicillin had no effect on symptoms.

Physical examination.—Negative except for enlargement of the spleen shown by X-ray.

Laboratory findings.—WBC, on admission 5,200, fell gradually and subsequently remained between 2 and 3 thousand; RBC 2.8, Hb. 60 percent. Formol-gel tests negative during the first 4 months of illness. On 29 December 1944, serum albumin 2.7, globulin 4.1 gm. percent. Presumptive diagnoses during this time were dengue, malaria, amebiasis, and finally unexplained fever. On 30 December 1944, smears from sternal marrow were positive for *Leishmania*.

Treatment (30 December 1944–20 January 1945), 42.5 cc. Fuadin, with no effect on fever, anemia, and leukopenia; Neostibosan, 2.7 gm. (5 February–24 February 1945), with temporary clinical response. Fever absent for 1 month; recurred on 29 March 1945. Anemia, leukopenia, and splenomegaly persisted. Neostam, 0.75 gm. (31 March–14 April 1945), with temporary slight lowering of fever; no change in blood picture.

The patient was evacuated to the United States. On admission to Moore General Hospital on 6 May 1945, he was moderately undernourished; the spleen was palpable eight fingers' breadth below the left costal margin. In the axillae and the right epitrochlear region, there were palpable nodes, small (0.5–1.0 cm.), firm, discrete, freely movable, not tender. One or two rises in temperature daily, 104° to 105.6° F. RBC 2.9; Hb. 65 percent; WBC 1.8; serum albumin 3.0 and globulin 6.6 gm. percent; formol-gel and cephalin flocculation tests positive; platelets 134,000. Spleen puncture on 17 May 1945 positive for *Leishmania* by smear and culture.

Hospital course.—Treatment (17 May–4 June 1945) with Neostibosan 5.0 grams. Temperature normal on 15th day of treatment. Spleen receded somewhat. RBC 3.2; WBC 3.9. After a 30-day furlough, the patient returned with a history of chills, fever, loss of weight, and intermittent pain in left upper quadrant of the abdomen. The spleen had enlarged. Splenic puncture was again positive. Treatment (6 August–16 August 1945) with 240 cc. stibanose, with temperature becoming normal 1 day after completion of treatment; reticulocytosis 9.4 percent; rise of RBC to 3.9 and of WBC to 4.9. The patient, asymptomatic, was again given a 30-day furlough, during which chills and fever recurred. On readmission, the spleen was found to be still larger; RBC 2.8; WBC

2.8; serum globulin 6.6. Spleen puncture on 21 August 1945 again positive by smear and culture. Treatment with 10.0 gm. Neostibosan (24 October–12 November 1945), with prompt control of fever. Reticulocytosis, 13.9 percent, on last day of treatment. Relapse within 1 month, with spleen well into the pelvis; WBC 2.6; recurrence of fever. Spleen puncture on 10 January 1946 again positive.

Treatment (12 January 1946–2 February 1946) with stilbamidine. The dosage, initially 0.025 gm., was increased gradually to daily injections of 0.300 gram. Toxic symptoms included mild flushing of the skin, with some formication and burning; local venous irritation with resultant thromboses; moderate exacerbation of daily temperature peaks up to 102° F.; and moderate malaise with nausea, lasting from 4 to 6 hours after each injection. During the first 16 days of this therapy, all elements of the blood were mildly depressed; thereafter, all rose progressively. Reticulocytosis 5.3 percent on 7 February. Red blood count, hemoglobin, and white blood count rose progressively to peaks of 4.74 million, 84 percent, and 7.40, respectively, 22 days after cessation of treatment. Temperature (3 February) became and remained normal. The spleen, which enlarged during the early part of treatment, by the 15th day after its completion was only three fingers' breadth below the left costal margin. There was no relapse during observation continued for 5 months.

Comment.—The interval to diagnosis from onset of symptoms was 4 months. This patient had several courses of small amounts of antimony overseas. Subsequently, curative amounts of 5 and 10 gm. of Neostibosan and 240 cc. of stibanose were ineffective. The strain of *Leishmania* in this patient may possibly have developed resistance to antimony. Cure was ultimately accomplished with stilbamidine.

Patient seen at Walter Reed General Hospital.—Protracted illness; repeated failures with antimony and stilbamidine; cure with splenectomy.

The clinical record reads substantially as follows:

The patient began his current hospitalization on 27 February 1944 with fever, weakness, malaise, headache, and with laboratory findings: RBC 1.9 million, Hb. 40 percent, WBC 1500. * * * diagnosis of kala-azar was made 15 April 1944 by splenic puncture. * * * specific treatment between April 1944 and December 1945 consisted of inadequate dosages in three courses of Neostibosan, in one course of Anthiomaline (lithium antimony thiomalate), in one of Solustibosan, in four of diamidinostilbene, and in one of antimony by iontophoresis, and adequate dosage in two courses of diamidinostilbene, and in one of solustibanose.

Discussion as of 1 December 1945:

The problem, whether or not to remove this patient's spleen, has three aspects: The leishmaniasis, the anemia, and the general discomfort from this tremendously enlarged spleen.

The recent fever, increase in size of spleen on cessation of treatment, leukopenia, reversal of albumin globulin ratio, strongly positive aldehyde test, and the apparent temporary response to diamidinostilbene therapy all point to continued leishmanial infection despite three negative splenic punctures and one sternal puncture which appears to be negative so far. Physical examination has not disclosed any extraneous cause of fever and 10 blood cultures, both routine and under carbon dioxide, have shown no growth. Chest X-ray is negative. I know of no other disease which could produce this picture except possibly Hodgkin's and the lymphomas, neither of which have been ruled out by gland biopsies as yet. If this patient has continuing leishmanial infection despite his more than adequate treatment, it may well be that the organisms lying deep in this enormous spleen are not reached by concentrations of drug adequate to destroy them completely.

The anemia is severe and 83 transfusions of 500 cc. each have been needed in the past 22 months to maintain him at a level of 1.5–3.0 million RBC. Of these 83 transfusions 69, representing 39,500 cc. of whole blood, have been given in the past 6 months. Even under such intensive transfusion therapy his RBC rose only to 3.0 million and the highest Hb. revealed is 8.1 grams. Other blood studies have shown reticulocytes of 10 to 25 percent * * *, which would tend to rule out aplastic anemia * * *, and an osmotic fragility which is increased with hemolysis beginning at 0.48 percent, whereas control blood began at 0.42 percent. No sickling trait has been found * * *. The icteric index has varied from 5 to 12 for the past 3 months with one level of 25 in July 1945. The serum proteins have been consistently elevated with reversal of A/G [albumin/globulin] ratio, * * *. Last week the patient was given 4,000 cc. of compatible group A blood all less than 72 hours old but 3 days later the hematocrit was only 24 percent, RBC 2.4 and Hb. 6.7 Gm.

All these data point to an anemia of the hemolytic type. The leishmaniasis * * * provided two factors which might contribute to the hemolysis: The first would be the opportunity for pooling of blood in the enlarged spleen; second, the tremendous increase in the globulin fraction of the serum proteins may well be due at least in part to the tremendous increase in reticuloendothelial tissue in the spleen. From this point of view I feel splenectomy is advisable * * *.

From the point of view of the patient's present comfort * * * there have been many episodes when he complained of moderately severe pain over this region and a definite rub could be heard. The present distention interferes with his eating and makes maintenance of body weight difficult.

Realizing that the risk of splenectomy in this patient may be considerable, I still feel that with adequate pre- and post-operative transfusions the procedure * * * offers the only chance of cure.

Basis of diagnosis:

1. 14 April 1944. Splenic puncture showed *Leishmania donovani* in smear.

2. 25 July 1944. Sternal puncture showed inclusion bodies in R.°E. cells suggestive of Leishman-Donovan bodies. Culture consistent with *Leishmania*.

3. 2 October and 24 October 1945. Splenic punctures failed to show *Leishmania* in smear, culture, or in hamsters.

4. 9 November 1945. Sternal puncture failed to show *Leishmania* in smear, culture, or in hamsters.

5. 11 December 1945. Splenectomy.

   a. *Leishmania donovani* found in smear from spleen.

   b. *Leishmania donovani* cultured and growth in hamsters was demonstrated by culture.

Formol-gel test before splenectomy was repeatedly positive in less than 5 minutes. Thereafter, for 3 weeks, it was positive in less than 1 minute, and then at increasing long intervals, until by 13 March 1946 it was positive only after 5 hours.

Course of red and white blood counts (selected samples):

	RBC	WBC
18 Aug. 1944	2,100,000	2,050
21 Dec. 1944	1,900,000	3,050
17 May 1945	1,890,000	3,500
19 Oct. 1945	1,700,000	2,400
24 Nov. 1945	3,150,000	2,800
11 Dec. 1945	Splenectomy	
21 Dec. 1945	3,150,000	9,000
23 Feb. 1946	3,950,000	10,900
13 Mar. 1946		9,350

Course of proteins (selected samples):

	Total proteins	A/G ratio
16 Aug. 1944	11.60	1/2.18
25 Oct. 1945	8.73	1/2.28
3 Nov. 1945	8.4	1/1.372
11 Dec. 1945	Splenectomy	
12 Jan. 1946	8.30	1/1.22
19 Jan. 1946	7.96	1/1.08
2 Feb. 1946	7.7	1.08/1
13 Mar. 1946	8.00	1.09/1

By 1 April 1946, the patient had steadily continued to improve. He had gained 40 lbs. since the splenectomy; his proteins had continued to improve; he was asymptomatic; his RBC and WBC had been improving slowly and his formol-gel test was less positive. We feel this procedure saved the patient's life but that it was not necessarily a specific cure for his residual leishmaniasis.

Comment.—This case is most unusual. Repeated courses of treatment with small amounts of antimony and stilbamidine may have produced resistance of the *Leishmania* to these drugs. An underlying hemolytic disease or abnormal lesion in the spleen may have contributed to the continued anemia and illness of this patient.

Case 23.—Onset associated with acute nephritis. Diagnosis made incidentally by splenic puncture in attempt to explain the leukopenia in a case of nephritis; death 66 months later, the only fatality in a serviceman with kala-azar (see fig. 6).

The patient, 36 years old, Negro, a Quartermaster ration-dump worker, with service in north Africa and Italy, had had scarlet fever in childhood, when he was bedridden for 6 months with a complication of unknown nature. His health was good in service, until he was admitted, on 10 June 1945, to the 8th Evacuation Hospital with a 5-day history of dyspnea, dragging sensation in the abdomen, swelling of the legs, dizziness, and lethargy. He had had a productive cough for 1 week and daily nosebleeds for 2 weeks. On examination, there was some bleeding from the left nostril; a soft systolic mitral murmur; blood pressure 155/95; moist rales heard at the bases of both lungs; and edema of both legs. The urine contained red cells, white cells, and casts.

Improved after 10 days in bed, the patient was evacuated to the 33d General Hospital, Leghorn, Italy, on 20 June 1945. There he was dyspneic on exertion; blood pressure was 142/92 and 180/108; RBC 3.0 million with proportionate reduction in hemoglobulin; WBC 5,400 to 5,000; red cells, white cells, and casts in urine; serum albumin 3.2, globulin 3.7 on 25 June; N.P.N. (nonprotein nitrogen) 54 mg. percent, and urea nitrogen 33.4 percent. Temperature elevations reaching a peak of 102.8° F., began on 1 July. Anemia and a moderate leukopenia developed.

Improved with rest and transfusions, the patient was evacuated to the United States and admitted to the Fletcher General Hospital, Cambridge, Ohio, on 13 August 1945, with a transfer diagnosis of chronic glomerulonephritis. He was in some distress from a recent tooth extraction. There was a large discoid lesion on the shaft of the penis with several satellite sores. The systolic apical murmur persisted; blood pressure was 132/86. There was mild generalized adenopathy. There were daily elevations of temperature, finally reaching 104.6° F., on 23 August 1945. A course of penicillin, totalling 2,400,000 units, was begun, and within 24 hours the temperature fell abruptly and remained normal for 10 days. However, on 12 September, a low grade fever reappeared and con-

tinued throughout the rest of his hospital course. RBC 3.0 million; WBC 3.6; N.P.N. 41 mg. percent; serum albumin 3.8; globulin 6.6.

On 25 September 1945, a sternal puncture was done in an attempt to explain the leukopenia (ranging from 3,600 to 5,600) occurring in a case of nephritis, and numerous Leishman-Donovan bodies were found. Repeated dark-field examinations of the penile lesion were negative, and smears disclosed no *Leishmania*. Sedimentation rate was 65 mm. per hour. Electrocardiogram showed low voltage of T waves. Roentgenogram of the chest showed pleural thickening in the right costophrenic angle.

The patient was admitted to the Moore General Hospital for treatment, on 4 October 1945, with a transfer diagnosis of (1) leishmaniasis, (2) chronic glomerular nephritis, (3) herpes progenitalis.

Physical examination.—Examination confirmed previous findings, including mild narrowing of retinal arteries, slight cardiac enlargement with an apical systolic murmur, generalized enlargement of lymph nodes, about 1.5 cm. in diameter, not tender.

Laboratory findings.—RBC 3.61 million; Hb. 71 percent, WBC 4,700. Urine contained a heavy trace of albumin, 5 to 6 WBC, and a specific gravity of 1.018. P.S.P. test: 20.5 percent excretion in 1 hour, formol-gel test 4 plus; total protein 8.8 gm., albumin 3.0, globulin 5.8; clotting and bleeding time within normal limits; platelets 165,000.

Treatment.—In view of this patient's chronic glomerular nephritis, it was decided to treat his kala-azar with stibanose. A total of 200 cc. stibanose was given from 22 October to 1 November 1945. On the eighth day of treatment, the patient became, and remained, essentially afebrile. There was no apparent aggravation of the nephritic abnormalities. On return from convalescent furlough on 26 January 1946, he had intermittent irregular low grade fever, and the spleen was still down two fingers' breadth below the left costal margin; BUN 12; RBC 2.7 million; Hb. 6.1; WBC 4,350; serum albumin 3.1, globulin 6.1; formol-gel and cephalin flocculation tests 4 plus. He lost 5 pounds during the next month, and sternal puncture on 1 March 1946 was positive for Leishman-Donovan bodies. Treated with 4.0 gm. stilbamidine from 18 March to 7 April, with no untoward effect except mild phlebitis and transitory flushing and tingling during injections. WBC rose from 3,350 to 6,000 during treatment. Excretion of BSP and P.S.P. both normal at the end of treatment. He was asymptomatic on return from furlough on 29 April; WBC 5,900; RBC 4.2; Hb. 82 percent; serum albumin 3.9, globulin 4.7. After another furlough, he returned on 23 May with fever, chills, genital lesion, marked inguinal adenopathy; WBC 8,200; Frei test strongly positive. Fever subsided during treatment with sulfathiazole, but red cell count and hemoglobin fell, and serum globulin rose again following this episode. Subsequent convalescence was uneventful, with apparent cure of the kala-azar and with marked improvement in the kidney lesion.

Subsequent history and comment.—This is the only known case in which further relapse occurred after the patient was separated from military service. He continued to have periodic parasitic and clinical relapses despite all forms of chemotherapy, including trivalent and pentavalent antimony compounds in large amounts, various stilbene derivatives, and splenectomy. Bilateral optic atrophy, nephritis, and severe intractable anemia developed, and the patient died 66 months after the diagnosis of kala-azar was established. He was hospitalized almost continuously during his entire illness and received all known specific and symptomatic treatment. Autopsy disclosed an overwhelming parasitization of the reticuloendothelial cells in all tissues examined. Apparently, this strain of micro-organism was resistant to the available drugs used against this infection. Fortunately,

this was the only death recorded as the result of kala-azar in American military personnel during or after World War II.

Case 5c.—Onset by lymphadenopathy; no other positive clinical or laboratory findings, *Leishmania* demonstrated in lymph nodes.

This patient had been in northern Africa for 4 months before his arrival in Sicily, in September 1943, where he spent the next 5 months before coming to England. He had been in excellent health until about 1 January 1944, at which time he noted a slight swelling, without tenderness, of the posterior cervical and postauricular lymph nodes. These increased gradually in size until the largest was plainly visible. There were no other complaints, and he was admitted to a station hospital only for study of the enlarged nodes. There the physical examination revealed essentially normal conditions except for the enlarged suboccipital, postauricular and posterior cervical lymph nodes. The largest of these, in the left posterior cervical chain, measured 1.5 by 2.0 centimeters. Roentgenograms of the chest and neck revealed nothing significant. The blood counts were normal, and Kahn, Widal heterophile, and undulant fever agglutination tests were done, with negative results. Typical *Leishmania* were found in sections from a biopsy of a large node stained with Giemsa's stain.

He was transferred to the Moore General Hospital, on 23 March 1944, with a diagnosis of leishmaniasis. No history could be obtained of chills, fever, night sweats, loss of weight, diarrhea, or slowly healing sores.

Physical examination.—Examination showed a well-nourished man of 23, apparently in excellent health. The skin was clear. Small pea-sized lymph nodes were found in the posterior cervical chain and in the postauricular and suboccipital regions; they were not tender. The epitrochlear nodes were just palpable, and a few small, discrete axillary nodes were palpable but not tender. The liver descended 2 cm. below the costal margin on deep inspiration and was slightly tender. The spleen could not be felt. Otherwise the physical examination was essentially negative.

Laboratory studies.—RBC 4,800,000, Hb. 96 percent, WBC 5,000, with 68 percent polymorphonuclear leukocytes and no abnormal cells. Total serum proteins were 6.5 gm., albumin 4.8, globulin 1.7. The aldehyde test of Napier was negative. Smears of sternal marrow and material aspirated from lymph nodes were negative, and cultures of these materials on N.N.N. medium showed no leptomonad forms after 21 days' incubation at room temperature. A second biopsy of an enlarged cervical node, however, showed typical *Leishmania* parasites in smears, microscopic sections, and culture. Despite the patient's apparently excellent health, antimony therapy was started on the basis of the incontestable diagnosis of lymph node leishmaniasis. Fifteen daily injections of 6 cc. of solution of sodium antimony gluconate, representing 1,800 mg. antimony, were given. At the completion of this series, he was discharged to duty, with instructions to return in one month for further evaluation of results.

Comments.—This case is of unusual interest because the only symptom or finding was lymphadenopathy. It emphasizes the importance of *Leishmania* in the differential diagnosis of adenopathy in patients from endemic areas.

CHAPTER II

Coccidioidomycosis

Roger O. Egeberg, M.D.

The full clinical picture of coccidioidomycosis had been put together only a short time before the entry of the United States into World War II, and the very name was unfamiliar to the majority of physicians in the United States as the country began to take action against the eventuality of war.

What, then, was known to students of the disease as the United States began to mobilize and to prepare for training? By 1940–41, the clinical picture was fairly clear. It was recognized that coccidioidomycosis was a disease with an acute, relatively benign initial phase, usually localized in the lungs, and frequently associated with erythema nodosum. This acute phase was followed in a few patients by a generalized spread throughout the body with death occurring in more than 50 percent of white patients and in almost all dark-skinned patients. The causative agent was a biphasic fungus, *Coccidioides immitis,* which had been recovered from the soil of certain arid regions and from rodents. There were obvious similarities to tuberculosis, but analogies here were in many respects misleading.

HISTORICAL NOTE

In 1892, Posada [1] and, later in the same year, Wernicke [2] described a round parasite found on section in the autopsies of patients dying of a disease not unlike tuberculosis. This work was done in Argentina, and the patients were seen at infrequent but fairly regular intervals. In California, in 1894, Rixford [3] and, in 1896, Rixford and Gilchrist [4] were impressed with the similarity of this round parasite, which they also had seen at the autopsy table, to coccidiosis, a parasitic disease of chickens, and accordingly called

[1] Posada, A.: Un Nuevo Caso de Micosis Fungoidea con Psorospermias. An. d. Circ. Med. Argent. 15: 585–597, 1892. Cited by Moore, M.: Blastomycosis, Coccidioidal Granuloma, and Paracoccidioidal Granuloma. Arch. Dermat. & Syph. 38: 163–190, August 1938.

[2] Wernicke, R.: Ueber einen Protozoenbefund bei Mycosis fungoides. Centralbl. f. Bakt. 12: 859–861, 28 Dec. 1892. Cited by Moore, M.: Blastomycosis, Coccidioidal Granuloma, and Paracoccidioidal Granuloma. Arch. Dermat. & Syph. 38: 163–190, August 1938.

[3] Rixford, E.: A Case of Protozoic Dermatitis. Occidental M. Times 8: 704–707, December 1894. Cited by Smith, C. E.: The Epidemiology of Acute Coccidioidomycosis With Erythema Nodosum ("San Joaquin" or "Valley Fever"). Am. J. Pub. Health 30: 600–611, June 1940.

[4] Rixford, E., and Gilchrist, T. C.: Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs. Johns Hopkins Hosp. Rep. 1: 209–268, 1896. Cited by Smith, C. E.: The Epidemiology of Acute Coccidioidomycosis With Erythema Nodosum ("San Joaquin" or "Valley Fever"). Am. J. Pub. Health 30: 600–611, June 1940.

it *Coccidioides*. The disease, coccidioidal granuloma, was usually fatal and for years was described sporadically in the literature, almost always from post mortem examination. In 1900, Ophüls and Moffitt [5] showed clearly in a simple experiment that the spherules recovered from diseased tissue could develop into a mycelial mat and that *Coccidioides* was therefore a "mould."

Early in the settling of the southern part of the San Joaquin Valley, Calif., people noted a nonrecurring, relatively mild disease, primarily respiratory in nature, with symptoms similar to a cold or la grippe and associated with red "bumps" on the legs or with a blotchy eruption. This illness was called "Valley Fever," was common, and was considered to be a mild local condition. These "two" diseases continued to make themselves felt, side by side, one common, more of a nuisance or discomfort, the other relatively rare, severe, wasting, and usually ending in death.

In 1935 and 1936, Gifford and Dickson began to relate the two clinical pictures and in 1937–38 published their very important papers showing that coccidioidal granuloma was a relatively rare spread of the early mild disease and never occurred without the other.[6] This immediately focused more attention on the primary form with the grave threat overhanging it, in what Dr. Karl F. Meyer of The George Williams Hooper Foundation, University of California Medical Center, San Francisco, Calif., in discussion called "the renaissance of the disease." With this much fuller clinical picture, with the total number of patients infected with the fungus very much greater than previously thought, and with the great gaps of information still to be filled in, interest was aroused, cases were better described, symptomatology became better known, and the time relationship between the two stages became evident.

By 1940–41, it was possible to define the disease as an infection caused by the fungus *C. immitis*, characterized by an acute respiratory syndrome simulating a cold, influenza, or pneumonia and infrequently progressing to a generalized chronic infection of a granulomatous type fatal in well over 50 percent of the cases.

CAUSATIVE AGENT

Coccidioides immitis is a biphasic fungus growing as a mycelial mat with aerial hyphae in its saprophytic phase—as on culture media—and as spherules which multiply by endosporulation in the animal body.

[5] Ophüls, W., and Moffitt, H. C.: A New Pathogenic Mould. Phila. M. J. 5: 1471–1472, 30 Jan. 1900. Cited by Smith, C. E.: The Epidemiology of Acute Coccidioidomycosis With Erythema Nodosum ("San Joaquin" or "Valley Fever"). Am. J. Pub. Health 30: 600–611, June 1940.

[6] (1) Gifford, M. A.: San Joaquin Fever. *In* Annual Report, Kern County Health Department for Fiscal Year July 1, 1935, to June 30, 1936, pp. 22–23, and for Fiscal Year July 1, 1936, to June 30, 1937, pp. 39–54. (2) Dickson, E. C.: "Valley Fever" of San Joaquin Valley and Fungus Coccidioides. California & West. Med. 47: 151–155, September 1937. (3) Dickson, E. C.: Coccidioidomycosis. J.A.M.A. 111: 1362–1364, 8 Oct. 1938. (4) Dickson, E. C., and Gifford, M. A.: Coccidioides Infection (Coccidioidomycosis); II. The Primary Type of Infection. Arch. Int. Med. 62: 853–871, November 1938.

In its mycelial phase, the micro-organism sustains itself under a wide variety of meager nutritional situations. It remains alive in dry soils, even washed beach sand, in moderate temperatures for at least 7 years. Its ability to withstand higher temperatures is related to humidity. It grows abundantly in a pH range of 2.02 to 12.13.

On modified Sabouraud's medium, the mycelial mat or phallus may vary in appearance, but most commonly it is white and fluffy from above, very slightly yellowed underneath, and frequently has a whiteness and
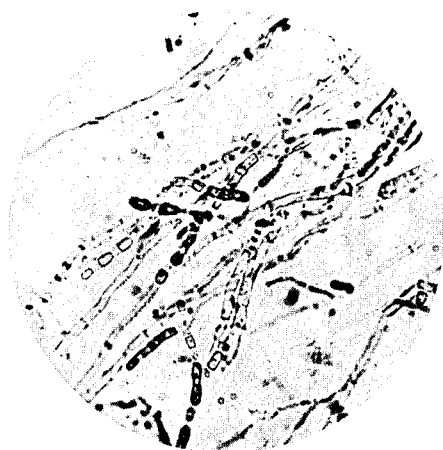
FIGURE 11.—Sputum culture of *C. immitis* on Sabouraud's medium, showing white, cottony fungus growth.
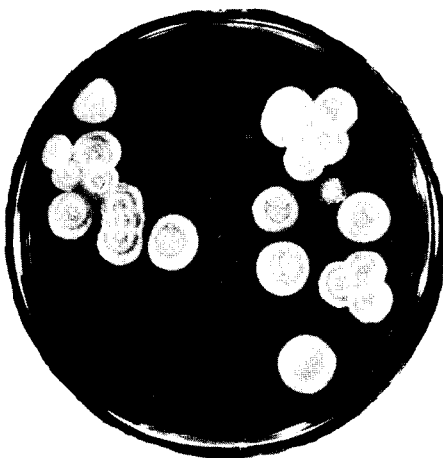
FIGURE 12.—Microscopic appearance of old culture *C. immitis*, showing fragmented chlamydospores. This is the infective form of the fungus occurring in nature.

translucence resembling a naphthalene mothball broken in two (fig. 11). A speck fished from a 10- to 20-day-old colony and teased in a drop of water on a slide has a very characteristic appearance when viewed under the dry high power of a microscope. In varying amounts scattered through the relatively dense mycelial mat are hyphae, with the following characteristics:

1. They branch at right angles.

2. They have swellings at irregular intervals best described as "racqueting."

3. They are segmented, and the more mature areas show an increasing difference between adjacent segments, so that every other one becomes barrel shaped while the ones in between atrophy. It is these barrel-shaped segments (arthrospores) that can infect animals or man or repeat the saprophytic cycle.

A culture of more than 10 days becomes increasingly dangerous as a source of laboratory infection, and a 4-week-old culture while showing the characteristics best is a menace (fig. 12).

A

B

E

C

D
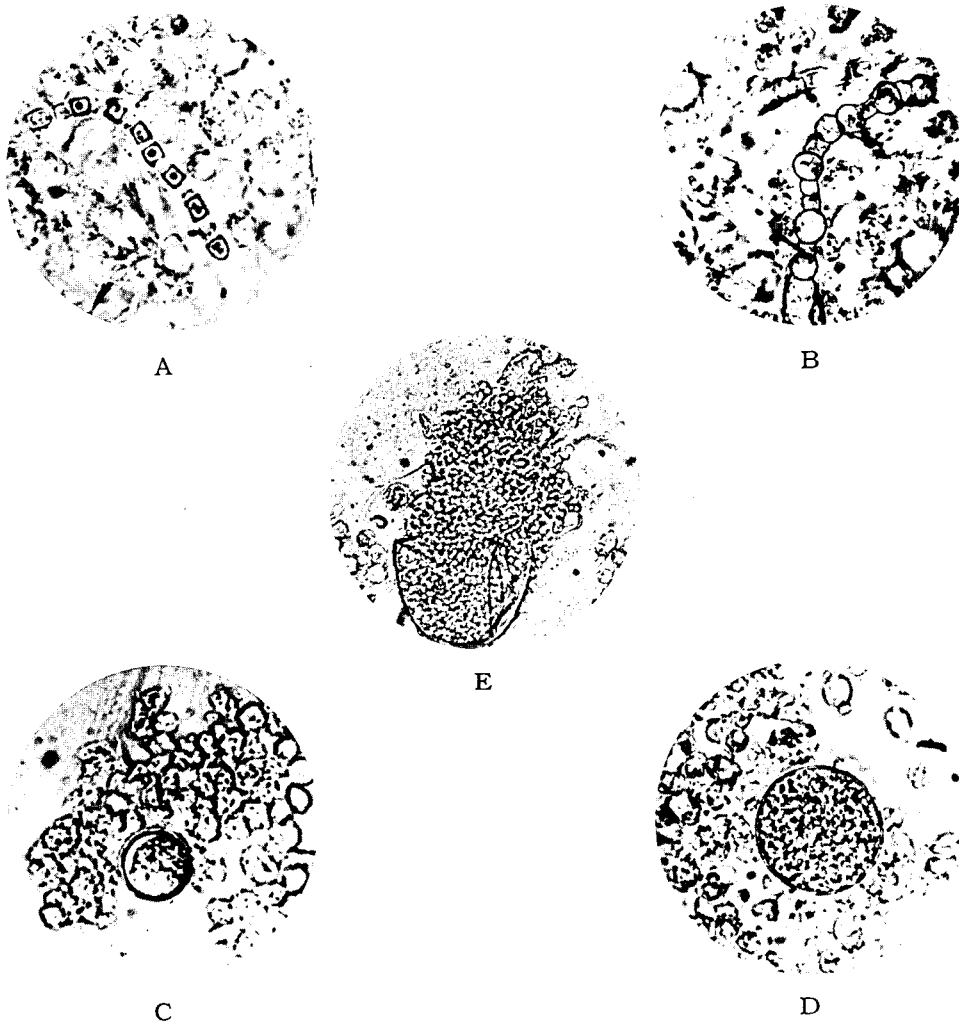
FIGURE 13.—Development of coccidioidal spherules. A. Chlamydospores in tissue.
B. Chlamydospores rounding up to form spherules. C. Protoplasm appearing within the
spherule. D. Protoplasm divides into endospores. E. Mature spherule ruptures, releasing
endospores which are carried by lymphatics or by the bloodstream. Each endospore
increases in size, becomes a mature spherule, and repeats stages C, D, and E.

The home of the mycelial or saprophytic phase of the fungus now
appears to be the soil of the endemic areas, where it can be recovered in as
high as 40 percent of soil samples collected from the surface in the early
summer. In the parasitic phase, in the tissues of man or lower animal, the
arthrospores quickly round out into spherules, usually from 20 to 40 microns
in diameter, which have a very characteristic doubly refractile wall. As
these mature septae form within them and gradually wall off, approximately

70 small pieces, which round out to become endospores, grow to the size of mature spherules and in turn endosporulate (fig. 13). Not infrequently, growth in a pulmonary cavity may resemble the saprophytic stage with mycelia and formation of hyphae, but it is doubtful that these ripen. It is thus apparent that spread of this disease is not by contagion from man to man but from the environment to man by inhalation of the arthrospores.

SYMPTOMATOLOGY

The symptoms and signs of coccidioidomycosis, in its primary phase, are best described as mimicing a cold, influenza, or primary atypical pneumonia; in its disseminated phase, as a generalized tuberculosis. About 60 percent of those infected, as evidenced by changing skin reactivity to coccidioidin, have no symptoms. In that 40 percent of infected people who become ill, the onset of coccidioidomycosis may be acute or gradual, and the patients exhibit one or more, or a combination of, symptoms, as follows:

1. Fever is relatively mild and most common. Usually, the temperature is not above 102° F., but it may reach 105° F. The fever lasts a short time—from 4 to 5 days in most instances—but may continue as a low grade fever for several months in uncomplicated primary coccidioidomycosis.

2. Chest pain varies from a mild sense of constriction to a pain severe enough to be mistaken for a myocardial infarction or an acute abdominal condition.

3. Cough, although most frequently present, is not very annoying to the patient. It is more often dry than productive. The slight amount of mucoid or mucopurulent sputum commonly raised frequently grows *C. immitis* on culture.

4. Arthralgia in the back or the peripheral joints is similar to the aching common in mild influenza and responds readily to salicylates.

5. Headache is usually mild and transitory; sometimes very severe, almost neuralgic in character. It is most often frontal, or when very severe postorbital, like the headache associated with malarial chills.

The symptoms just described occur in more than two-thirds of the patients. Malaise, of varying degree, chills, night sweats, anorexia, and pharyngitis occur in about one-third of the patients. Erythema nodosum (the early trademark of the disease), erythema multiforme, and urticaria—all of good prognostic significance—are seen in less than one-fifth of the patients, erythema nodosum occurring three times as often in women as in men.

The findings on physical examination vary somewhat with the symptoms and range from a reddened throat without exudate to the dullness, rales and rubs of a frank pneumonia, and include the allergic manifestations of erythema, nodosum or multiforme, and urticaria. Conjunctivitis is not infrequent, and pleural effusion can occur.
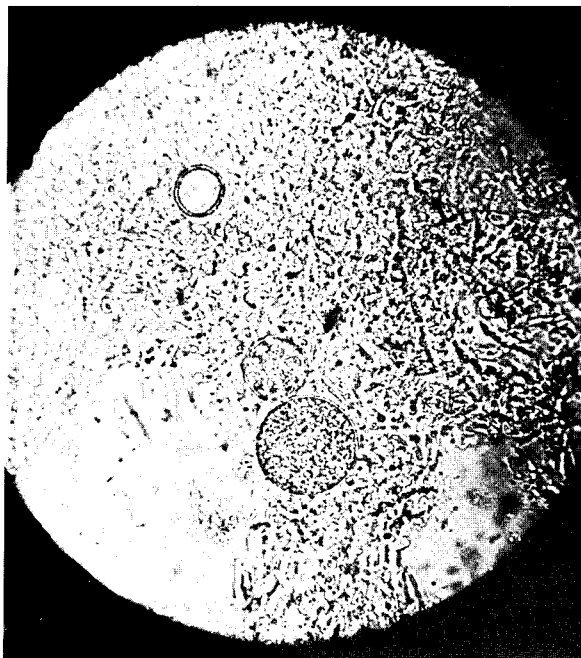
FIGURE 14.—Coverslip preparation showing a doubly contoured spherule without protoplasm, one with undifferentiated protoplasm, and a mature spherule with characteristic endospores.

LABORATORY EXAMINATIONS

Although the diagnostic proof of coccidioidomycosis could be said to depend on finding the spherule (fig. 14) in sputum, discharge or pleural fluid, or by growing out the saprophytic phase from such materials and identifying the spherule after animal passage, there are other tests that are most important. These are the coccidioidin skin test, the precipitin test, and the complement fixation test.

Coccidioidin test.—The intracutaneous test with coccidioidin, performed and read like the tuberculin test, is the means of determining whether a person has been infected with *C. immitis*. Of the greatest value in an epidemiologic survey, the coccidioidin test is also very useful as a diagnostic tool and in some cases indicates a degree of resistance. The reaction is almost always positive in a person who has been infected with the specific agent, although there is a slight cross-reactivity with histoplasmin or haplosporangin extract, and in an overwhelming disseminated case of coccidioidomycosis the reaction may be negative. Otherwise, this is a very dependable test; it can be repeated regularly without creating a positive reaction in a noninfected subject, while a reaction, once positive,

will remain positive for many years, if not for life. The material for the test can be obtained commercially, but in the early days of its use it was usually obtained from Dr. Charles E. Smith, Department of Public Health and Preventive Medicine, Stanford University School of Medicine, Calif. The material is prepared by growing 10 strains of *C. immitis* on the same asparagin culture medium used for making tuberculin. Grown for 1 to 2 months, it is tested at intervals, and when shown to be potent the suspension and extract are filtered through a Berkefeld filter and diluted with aqueous Merthiolate (thimerosal) to a concentrate of 1 : 10,000. This is standardized on infected and on normal individuals. This dilution is then referred to as undiluted coccidioidin and is very stable, keeping its potency at room temperature for at least 4 years. For testing purposes, it is diluted in normal saline to 1 : 100 and to 1 : 1,000. The 1 : 100 dilution is used for routine testing. The reaction is read at 36 to 48 hours.

Knowledge was at first inadequate concerning the immunologic meaning of the coccidioidin test and, particularly, of its implications for the soldier newly arrived in endemic regions. Subsequently, the important observation was made that the disease might occur, but did not progress to the severe disseminated form, in those who were positive to coccidioidin on their arrival at their posts. Dissemination occurred only in those who arrived uninfected, acquired infection, and then disseminated.[7] Furthermore, it was found that dissemination rarely occurred in patients with primary infection accompanied by erythema nodosum which was an early manifestation associated with high sensitivity to coccidioidin. The reaction was frequently weak or negative in cases of severe (anergic) disseminated disease. When negative personnel were retested, the incidence of change to a positive reaction indicated a higher incidence of the completely "inapparent" or asymptomatic than of the clinically recognizable disease.

Aronson and his associates,[8] in studies of large population groups in various parts of the United States including Alaska, had provided evidence that "clinched"[9] the question of the specificity of the coccidioidin test, in proper dosage. Within their wider field of inquiry, they found a significant incidence, notably in a highly endemic region of Arizona, of calcified pulmonary nodules in persons negative to tuberculin, positive to coccidioidin. Forbus and Bestebreurtje[10] found little evidence of calcifi-

[7] Smith, C. E., Beard, R. R., and Saito, M. T.: Pathogenesis of Coccidioidomycosis With Special Reference to Pulmonary Cavitation. Ann. Int. Med. 29: 623–655, October 1948.

[8] Aronson, J. D., Saylor, R. M., and Parr, E. I.: Relationship of Coccidioidomycosis to Calcified Pulmonary Nodules. Arch. Path. 34: 31–48, July 1942.

[9] Smith, C. E., Whiting, E. G., Baker, E. E., Rosenberger, H. G., Beard, R. R., and Saito, M. T.: The Use of Coccidioidin. Am. Rev. Tuberc. 57: 330–360, April 1948. (Studies supported from 1937 to 1941 by the Rosenberg Foundation, subsequently an activity of the Commission on Acute Respiratory Diseases, Army Epidemiological Board, Office of The Surgeon General, carried out by the Department of Public Health and Preventive Medicine, Stanford University School of Medicine.)

[10] Forbus, W. D., and Bestebreurtje, A. M.: Coccidioidomycosis: A Study of 95 Cases of the Disseminated Type With Special Reference to the Pathogenesis of the Disease. Mil. Surgeon 99: 653–719, November 1946.

cation in their autopsy material which was, however, derived from fatal disseminated cases. Studying the primary disease in persons who, positive to coccidioidin, died of other causes, Butt and Hoffman [11] found calcified nodules interpreted as residua of healed or arrested coccidioidomycosis. Cox and Smith [12] identified arrested lesions, some of them calcified which had been mistaken for tuberculosis in roentgenograms and at autopsy, and, from one such calcified lesion, Smith [13] reported recovery of viable *Coccidioides*.

Precipitin test.—The precipitin test becomes positive within the first month of the disease, and, no matter what the course of the disease is, it becomes negative again in 3 months. Its value lies in establishing the fact that a given symptom picture represents the acute phase of coccidioidomycosis. In the presence of nonspecific symptoms and a positive cutaneous reaction to coccidioidin, a positive precipitin reaction would indicate that the patient has a recently acquired case of coccidioidomycosis. This test is of no prognostic significance.

Complement fixation test.—The complement fixation test is of both diagnostic and prognostic significance. Its titer rises with the severity of the infection, also beginning in the first month but continuing, and persisting possibly, for months or many years. In general, complement fixation in titers above 1–6 indicates disseminated disease. Except in a severe disseminated case with anergy, the complement fixation and precipitin tests will give negative results when the cutaneous reaction to coccidioidin is negative.

Erythrocyte sedimentation rate.—Elevation of the erythrocyte sedimentation rate in acute primary infection is of prognostic significance and useful in following the course of primary or disseminated coccidioidomycosis.

CLINICAL COURSE

The benign primary form of the disease may occur without symptoms, its only evidence being the change from a negative to a positive reaction to coccidioidin. The course of a clinically apparent but uncomplicated case of primary coccidioidomycosis varies from a mild picture resembling a cold to a moderately severe case of bronchopneumonia with fever, cough, chest pain, headache, generalized aching, and malaise. The duration is related to the severity and may be for 2 or 3 days, or may last for 4 or 5 weeks with low grade fever.

[11] Butt, E. M., and Hoffman, A. M.: Healed or Arrested Coccidioidomycosis; Correlation of Coccidioidin Skin Tests With Autopsy Findings. Am. J. Path. 21: 485–505, May 1945.

[12] Cox, A. J., and Smith, C. E.: Arrested Pulmonary Coccidioidal Granuloma. Arch. Path. 27: 717–735, 1939.

[13] Smith, C. E.: Parallelism of Coccidioidal and Tuberculous Infections. Radiology 38: 643–648, June 1942.

A number of complications may be associated with the primary phase, and these should not be confused with dissemination. Excavation may occur in a pneumonia area or, more frequently, may appear as a tension cavity with little surrounding infiltration. It does not have the worrisome connotation of a tuberculous cavity but usually heals in from 4 to 8 months with or without bed rest. Excavation, as observed for years, has not resulted in dissemination nor has it been a source of infection in others.[14] Hemorrhage may be associated with the cavity, and this is occasionally severe. A bronchopleural fistula may result from the cavity and this in turn may lead to empyema or pyopneumothorax. All of these may occur and the patient be quite ill but still with a *primary* coccidioidomycosis and with an excellent prognosis. If troublesome, these manifestations may be relieved by surgery.

Not until the disease passes through the hilar lymph glands and leaves the chest, most frequently causing an abscess in the left supraclavicular area, has dissemination occurred. When this happens, the prognosis has suddenly changed, and what was a benign disease with virtually no mortality has now become a malignant disease with a mortality of 50 percent for white patients and up to 85 percent in the dark-skinned races. Dissemination occurs in a little over 1 percent of the clinically diagnosed white patients, in from 3 to 4 percent of clinically diagnosed Spanish-American patients, from 12 to 14 percent of clinically diagnosed Negroes, and in almost all Filipinos clinically diagnosed.

The disseminated disease is protean in its manifestations. Abscesses may form anywhere in the body (fig. 15), including the subcutaneous tissues, muscle, bone, organs, and the central nervous system. The pericardium and the myocardium may be affected, and meningitis is a common cause of death. Bony lesions (fig. 16) are usually multiple and are cystlike, sharply circumscribed lesions with minimal surrounding reaction. They occur most commonly in the prominences of cancellous bones. In the long bones, they are more frequently formed near the ends of, and may extend into, the joints.

The course of disseminated coccidioidomycosis may be steadily and rapidly downhill with meningitis and death occurring in 3 to 4 months from the onset of the primary disease, or it may follow a very slow course with remissions and exacerbations (figs. 17 through 20). There may even be periods of a year or two when the disease is apparently gone, only to return with the opening up of a fistulous tract from some active bony lesion.

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[14] The possibility of spread from person to person cannot be completely dismissed in view of the demonstration, in a few postwar cases, of the mycelial form of *Coccidioides* in pulmonary cavities (see footnote 7, p. 55. Reported also by (1) Greer, S. J., Forsee, J. H., and Mahon, H. W.: Surgical Management of Pulmonary Coccidioidomycosis in Focalized Lesions. J. Thoracic Surg. 18: 589–601, October 1949; (2) Weisel, W., and Owen, G. C.: Pulmonary Resection for Coccidioidomycosis: Report of a Case. J. Thoracic Surg. 18: 678, October 1949). Nevertheless, Schwarz and Muth (Schwarz, J., and Muth, J.: Coccidioidomycosis: A Review. Am. J.M. Sc. 221: 89–107, January 1951), in their review, could still say "secondary infections in families of patients have never been demonstrated."

FIGURE 15.—Characteristic skin granulomata on the forehead. This patient also had a smaller skin lesion on the trunk and had roentgenographic evidence of pulmonary infiltration with hilar gland involvement.

The course may be associated with a minimum of temperature elevation or the temperature may be high. Increasing weakness, lassitude, anorexia, and loss of weight are typical. Individual abscesses may heal spontaneously in from 4 to 6 months or faster when irrigated, but new ones come. Bony lesions show healing and new bone formation, but new lesions form. Meningitis is like a tuberculous meningitis with the major

FIGURE 16.—Cystlike areas of destruction in the distal tibia, malleoli, and talus.
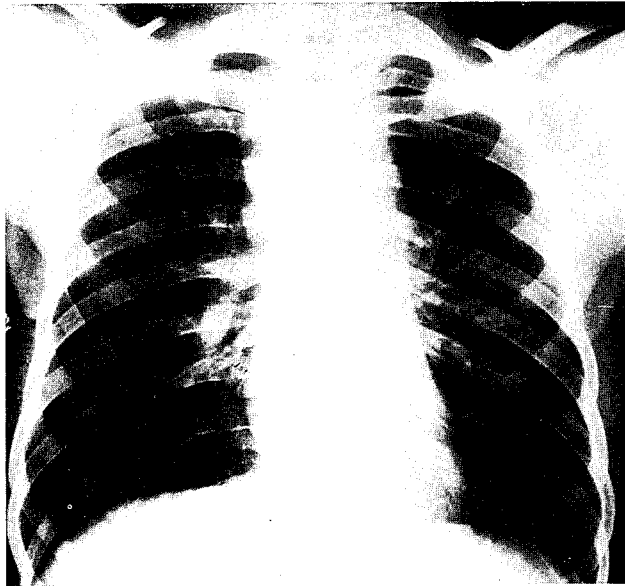
FIGURE 17.—Progressive coccidioidomycosis (coccidioidal granuloma). Massive mediastinal lymphadenopathy simulating lymphoblastoma. General dissemination with fatal termination 4 months after onset.
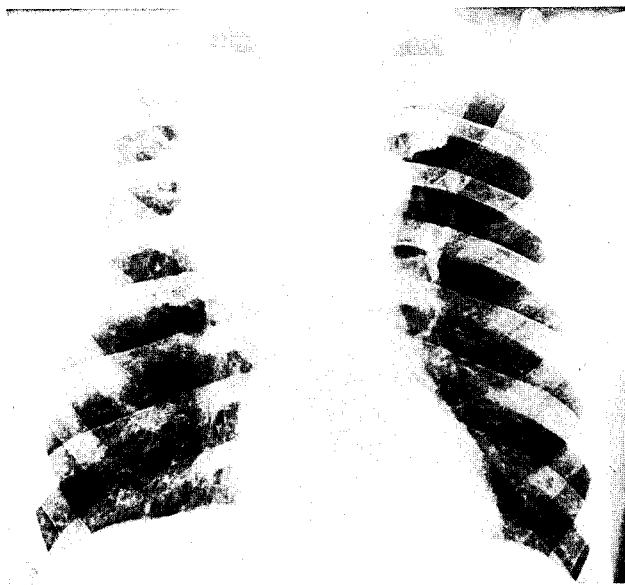
FIGURE 18.—Progressive coccidioidomycosis (coccidioidal granuloma). Dense shadow projecting from the right mediastinal border consisting of mediastinal lymphadenopathy with suppuration and associated parenchymal infiltration. Terminal miliary dissemination.
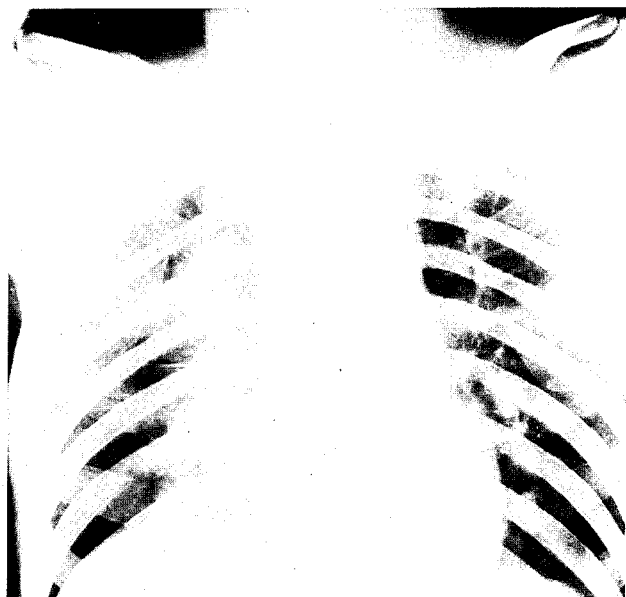
FIGURE 19.—Progressive coccidioidomycosis (coccidioidal granuloma). Diffuse pneumonia-like infiltration radiating from the right hilum. Broad mediastinum due to associated lymphadenopathy.

FIGURE 20.—Progressive coccidioidomycosis (coccidioidal granuloma). Extensive diffuse nodular infiltration through both lungs. Confluent zone of consolidation at the left apex. Mediastinal lymphadenopathy.

danger from loculation, obstruction, and increased intracranial pressure. It is almost always fatal.

The course of disseminated coccidioidomycosis is best followed by careful observation of the changing clinical picture and by the use of the complement fixation test, the latter being the best index of course and prognosis. A rising titer of complement fixation is definitely indicative of a spreading infection. A rising titer in the presence of a weakening coccidioidin skin reaction is a matter of very grave concern, usually followed by death in a month or two.

In Army experience, the disseminated phase, when it occurred, followed close upon the heels of the primary phase. A study [15] of the autopsy and biopsy material from cases in military personnel, including all fatal cases, suggested that the danger of dissemination (endogenous spread) would remain, long after the war, in persons who had been exposed in endemic areas. Clinical observations, however, confirmed by the passage of time, does not indicate that this danger exists in those who did not promptly show themselves, by dissemination, to be "immunologically defective" with respect to this disease.[16]

OBSERVATION AND EXPERIENCE

As knowledge of the disease gradually increased during some 50 years, roentgenographic studies lagged behind clinical investigation until the war provided opportunity to make serial studies of suitable patients in considerable numbers (figs. 21 through 30). It was generally agreed that the diagnosis could not be made from roentgenograms alone. Carter,[17] in 1931, noted that the pulmonary lesions might resemble tuberculosis or might even more closely resemble blastomycosis. Rosenberg and his associates,[18] in a study at the Mayo Clinic, Rochester, Minn., in 1942, noted that differential diagnosis between blastomycosis, coccidioidomycosis, and torulosis from roentgenographic appearances was difficult or, in some cases, impossible. Carter,[19] in 1942, commented, as follows:

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[15] See footnote 10, p. 55.

[16] "Army, experience * * * has indicated that dissemination occurs soon after the first infection * * * frequently within a matter of weeks and infrequently after months. It rarely occurs in the second year after infection * * *. Once dissemination ensues, the risk of continued dissemination is great though remission may occur. * * * none of our military coccidioidal patients, of whom we had records of thousands, has ever been reported to us as having undergone a postwar dissemination. * * * We have never seen dissemination occur in a patient with coccidioidal excavation. Recently Kurz and Loud have reported one [a postwar case, with recovery, of granulomatous cutaneous lesion developing at the site of a trauma, published in the 23 October 1947 issue of the New England Journal of Medicine], a very unusual case." (Cited from report by Smith and his associates, footnote 7, p. 55.)

[17] Carter, R. A.: Coccidioidal Granuloma: Roentgen Diagnosis. Am. J. Roentgenol. 25: 715–738, June 1931.

[18] Rosenberg, E. F., Dockerty, M. D., and Meyerding, H. W.: Coccidioidal Arthritis. Arch. Int. Med. 69: 238–250, February 1942.

[19] Carter, R. A.: Roentgen Diagnosis of Fungous Infections of Lungs With Special Reference to Coccidioidomycosis. Radiology 38: 639–659, June 1942.

Fungus diseases of the lungs share with tuberculosis the characteristics to be expected when there is organized cellular response to infection. These include involvement of the lymph nodes; persistent parenchymal lesions of many forms, massive, nodular and miliary; variously appearing diffuse infiltrations, none of them characteristic of any specific disease. The predilections of these differ somewhat from disease to disease.

Carter noted that cases showing in the late stage of dissemination a miliary lesion in the lungs associated with meningitis were especially likely to be mistaken for tuberculosis. Such late pulmonary involvement often occurred as a result of hematogenous spread.

The Army control program, with its coccidioidin tests and repeated roentgenographic examinations, discovered several hundred clinical and several thousand subclinical cases. Observation of cases in hospital showed the short, self-limited course in the majority, while a small percentage persisted for many weeks or months, and a few ended fatally. Colburn [20] studied 75 cases in Army personnel roentgenographically, with careful followup observations; the clinical details were reported by Goldstein and Louie.[21] The pulmonary changes cleared completely within 3 or 4 months, and all 75 patients were eventually returned to duty, although dissemination did occur in one case.[22] At the Regional Hospital, Santa Ana Army Air Base, Calif., to which most of the severe or prolonged cases were transferred, another study was made by Jamison [23] of 96 such cases observed closely in roentgenograms for periods of from 2 to 21 months.

Among these, there was a group of 23 cases with nodular parenchymal lesions, situated most frequently in the midpart of the lung, less often in the lower part, least often in the apical and subapical regions. In a second group of 35 cases, there were thin-walled, cystlike cavities, occurring less often in the upper than in the middle field of the lung and least often in the lower. In a third group, there was persistent pneumonitis, ranging from lesions occupying a third of the lung to small foci in the hilum. These were primary infections that had "failed to resolve or focalize as nodular or cystic lesions." In the 12 cases of disseminated disease, there was conspicuous involvement of lymph nodes and, finally, a rapidly developing miliary spread, becoming confluent. The roentgenographic appearances as described were often not dissimilar to tuberculosis but differed widely from tuberculosis in their clinical and epidemiologic significance.

Cavities, as has been noted, may go entirely unnoticed clinically, or may cause some inconvenience, but present no serious threat to life or to public health, persisting sometimes for months, or for years,[24] and finally

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[20] Colburn, J. R.: Roentgenological Types of Pulmonary Lesions in Primary Coccidioidomycosis. Am. J. Roentgenol. 51: 1–8, January 1944.

[21] Goldstein, D. M., and Louie, S.: Primary Pulmonary Coccidioidomycosis; Report of an Epidemic of 75 Cases. War Med. 4: 299–317, September 1943.

[22] Extended studies have shown a more favorable course in disseminations occurring at a considerable interval after the initial infection.

[23] Jamison, H. W.: A Roentgen Study of Chronic Pulmonary Coccidioidomycosis. Am. J. Roentgenol. 55: 396–412, April 1946.

[24] See footnote 7, p. 55.

FIGURE 21.—Primary coccidioidomycosis. Left hilar thickening. Slight prominence of right mediastinal border due to moderate lymphadenopathy.
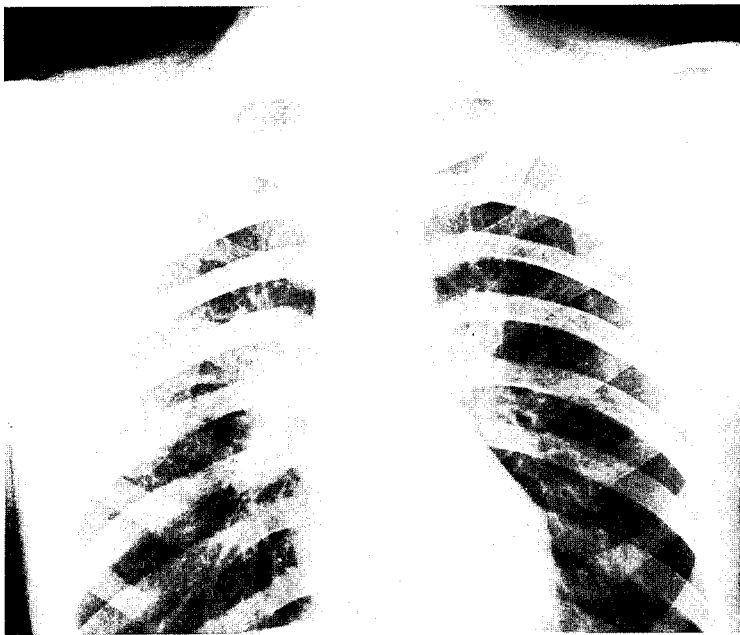
FIGURE 22.—Primary coccidioidomycosis. Fuzzy peribronchial right hilar thickening.
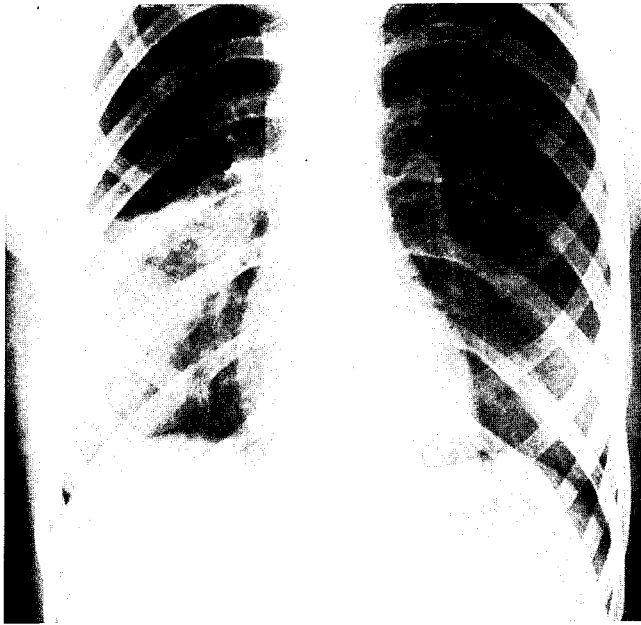
FIGURE 23.—Primary coccidioidomycosis. Pneumonia-like infiltration in the right lower lung field, which practically cleared after an interval of 1 week.
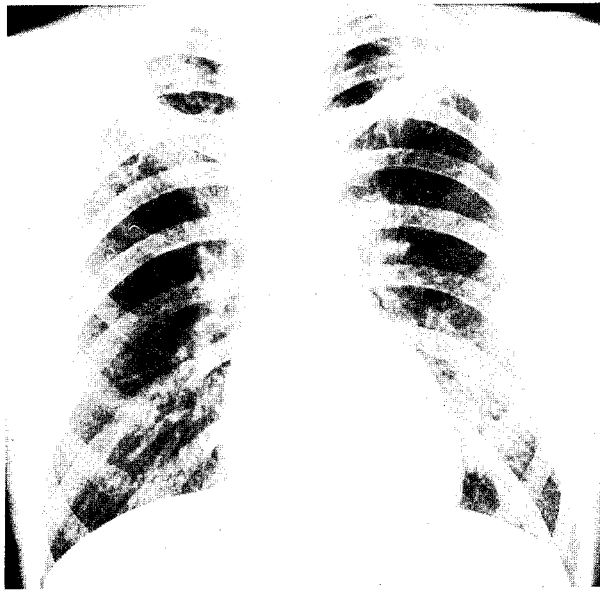
FIGURE 24.—Primary coccidioidomycosis. Patchy and strandlike infiltrations resembling tuberculosis at both apices and subapices. Note the thin-walled cavities just below the clavicles on each side.
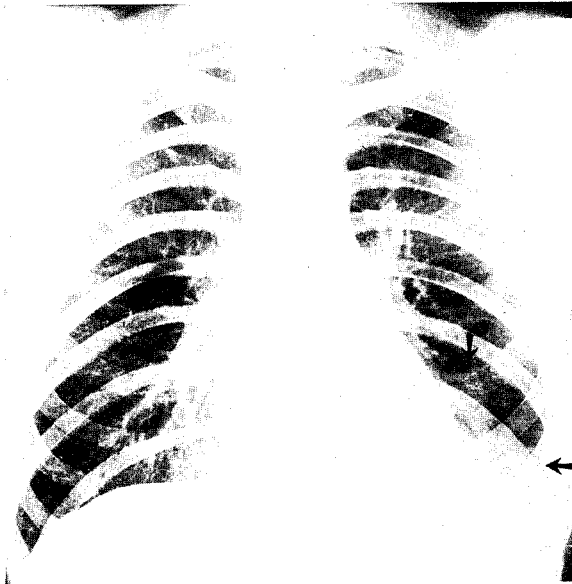
FIGURE 25.—Primary coccidioidomycosis. Small amount of infiltration at the left base associated with slight pleural effusion.
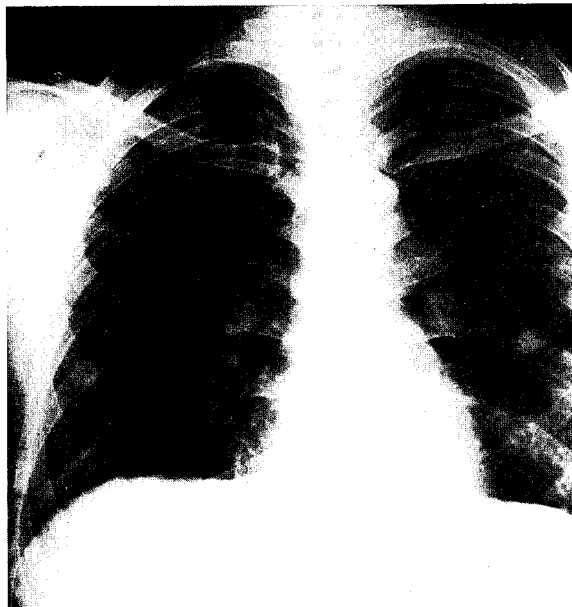
FIGURE 26.—Primary coccidioidomycosis. An unusual case, showing multiple nodular foci simulating metastatic carcinoma or multiple septic emboli. Central cavitation is visible in some of the nodules. The patient has shown progressive improvement both clinically and radiographically without evidence of extra thoracic dissemination.

FIGURE 27.—Primary coccidioidomycosis. The massive hilar and mediastinal lympha-
denopathy is unusual in primary infections. Observe the local zone of consolidation in
the right lower lobe and compare with figure 28.
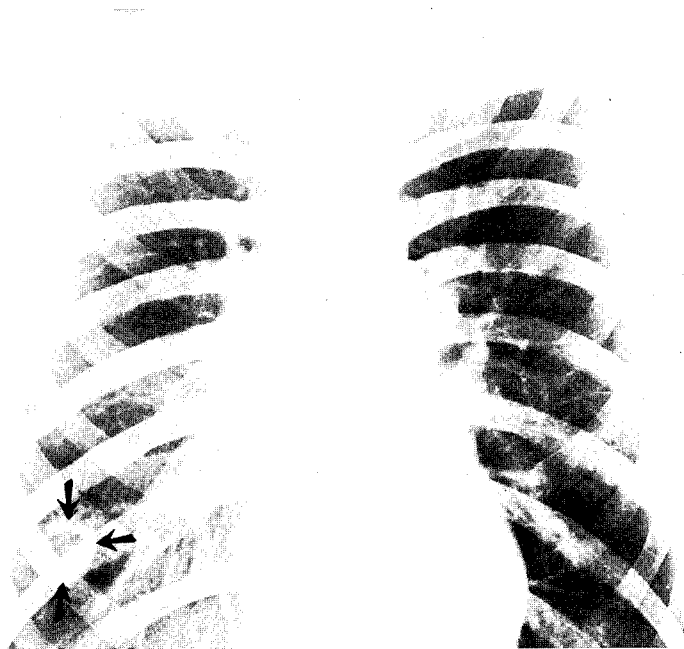
FIGURE 28.—Primary coccidioidomycosis. The mediastinal and hilar lymphadenopathy
shown in figure 27 has regressed after a period of 6 weeks; the local zone of infiltration at
the right base has been replaced by an isolated ringlike cavity.
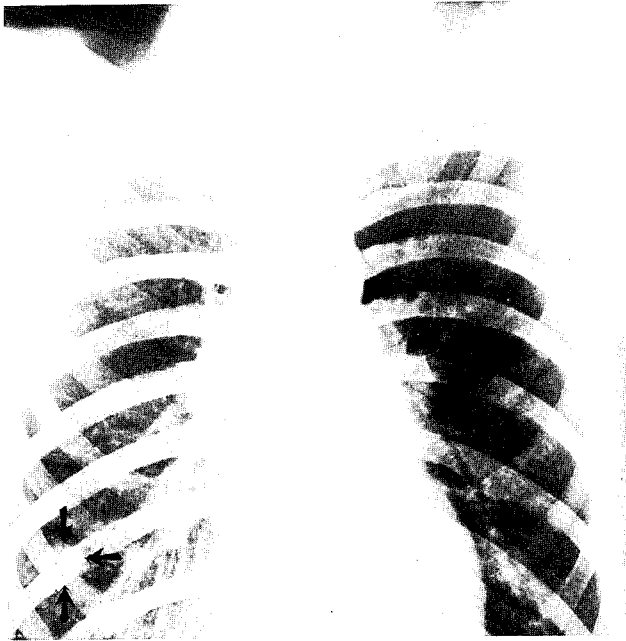
FIGURE 29.—Primary coccidioidomycosis. The mediastinal and hilar lymphadenopathy shown in figure 28 has further regressed after a period of 10 weeks; the cavity previously present has disappeared leaving a residual nodule.
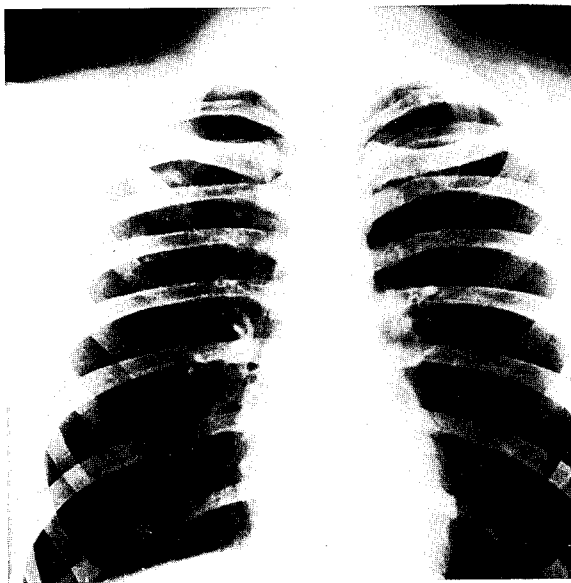
FIGURE 30.—Primary coccidioidomycosis. Ringlike cavity in the right subclavicular region simulating tuberculosis. The wall of the cavity became pencil thin after a 3 months' interval, resembling that of a congenital cyst. The outlines of this cystlike lesion then gradually "melted away" after a 6 months' interval.

closing without rest or other treatment. Some provoke cough and hemo-
ptysis, some are associated with chest pain or weakness, and in these
cases surgery may be done. Experience during and immediately following
World War II showed that there was no danger of endogenous spread
following surgery and that other complications can now be prevented by
the use of chemotherapy.[25] The typical coccidioidal cavity, repeatedly ob-
served in Army studies,[26] is thin walled, cystlike, not surrounded by in-
filtration, often fluctuating, sometimes widely. Cavities developing as
central excavation of nodular foci are smaller and their walls are thicker.

In studies of the bones and joints, it was again found difficult or im-
possible to make the diagnosis on the roentgenographic evidence alone
(fig. 31).[27] From the investigation at the Mayo Clinic are drawn the fol-
lowing comments on the arthritic changes observed in roentgenograms:

Early lesions are characterized by regions of destruction in articular surfaces, often
with evidence of swelling of overlying soft tissues. Cartilage may be destroyed and joint
spaces narrowed * * *. Later lesions in joints may cause complete disappearance of joint
spaces, more extensive zones of destruction in articular spaces and, in some instances,
ankylosis. These lesions have been commonly mistaken for those of tuberculous arthritis.
Carter pointed out that arthritis both in coccidioidal granuloma and in tuberculosis * * *
shows little tendency to heal by production of bone * * *. Taylor found the destructive
process in bones, as shown by roentgenograms, to be distinguished by an intensity and
rapidity of development not often noted in the presence of tuberculosis.

Such lesions, Rosenberg and his associates stated:

* * * are fairly commonly encountered [in the chronic granulomatous phase of cocci-
dioidomycosis]. Among 256 cases tabulated in the report of the California Department
of Public Health in 1931, involvement of joints was noted in 79 * * *. Often, several joints
are involved at one time. Affected joints have in this particular phase of the disease first
the appearance of acute, later of chronic, arthritis. Early, the joints are swollen and red;
later, fluctuation may appear. Nodular lesions may develop in the skin overlying affected
joints * * * may ulcerate and discharge pus containing *C. immitis*. McMaster and Gilfillan
expressed the opinion that joints may be primarily affected by direct involvement of the
synovial membrane or infection may extend to joints from adjacent foci of coccidioidal
osteomyelitis.

Similarly, in 1942, Benninghoven and Miller [28] described joint in-
volvement as of—

Two distinctly different types: (a) purely synovial, (b) synovial with subarticular
destruction indistinguishable from tuberculosis. Usually synovial involvement is seen as
a large swelling of the joint capsule. Occasionally there is periosteal new bone formation
on adjacent bone. This is thought to be a reactive rather than an infective process. In the

[25] See footnote 21, p. 62.

[26] (1) Winn, W. A.: Pulmonary Cavitation Associated With Coccidioidal Infection. Arch. Int. Med. 68:
1179–1214, 1941. (2) Winn, W. A., and Johnson, G. H.: Primary Coccidioidomycosis; Roentgenographic
Study of 40 Cases. Ann. Int. Med. 17: 407–422, September 1942. (3) Sweigert, C. F., Turner, J. W., and
Gillespie, J. B.: Clinical and Roentgenological Aspects of Coccidioidomycosis. Am. J.M. Sc. 212: 652–673,
December 1946.

[27] (1) Benninghoven, C. D., and Miller, E. R.: Coccidioidal Infection in Bone. Radiology 38: 663–668,
June 1942. (2) Carter, R. A.: Infectious Granulomas of Bones and Joints, With Special Reference to Cocci-
dioidal Granuloma. Radiology 23: 1–16, July 1934.

[28] See footnote 27 (1).
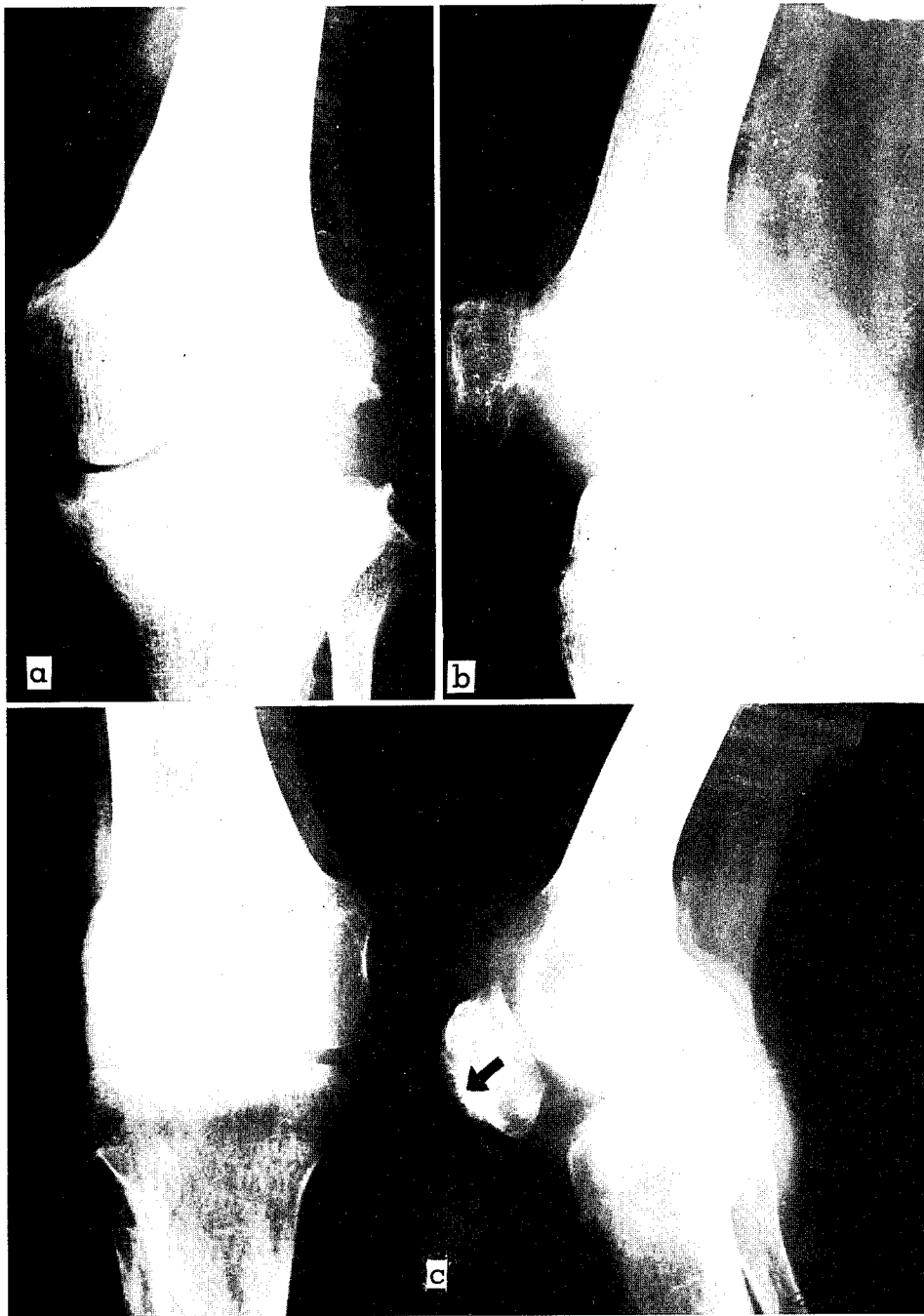
FIGURE 31.—Progressive coccidioidomycosis (coccidioidal granuloma). A and B. Destructive arthritis involving non-weight-bearing portions of joint. C. Proliferative periostitis at anterior surface of patella.

lesions that are indistinguishable from tuberculosis there is capsular swelling, marked periarticular osteoporosis, with cartilage and subarticular destruction of bone on both sides of the joint.

The investigators at the Mayo Clinic, turning to the benign primary disease, the "valley fever" of earlier writers, refer to its acute onset, with malaise, general aches and pains, "toxic erythema," sore throat, fever, and occasionally signs of bronchopneumonia. From 8 to 15 days after onset, at a time when there appears to be a general improvement of the patient's condition, lesions typical of erythema nodosum may appear, mainly on the shins, occasionally elsewhere. Roentgenographic examination of the thorax at this time usually discloses opaque regions that suggest the diagnosis of tuberculosis. Signs of acute arthritis develop in about one-third of these patients, usually appearing simultaneously with the erythema nodosum.[29] Joints are tender to pressure, painful on motion, and sometimes slightly swollen. Effusion and suppuration are not observed. Sometimes arthritis, conjunctivitis, and erythema nodosum appear together, persist about a month, and disappear at approximately the same time. In these cases, with their characteristically uneventful clearing, there is no residual damage or deformity of joints. Among older people, the arthritis was said to be more prolonged.

PATHOLOGY

Thus, knowledge of coccidioidomycosis, during little more than the half century since the problem was recognized, has necessarily been derived chiefly from clinical studies with, increasingly, roentgenographic observation. The anatomic changes seen in the severe disseminated form of the disease in material collected at the Army Institute of Pathology, Washington, D.C. (50 cases with autopsy, 45 with biopsy only), were reported and illustrated in detail at the close of World War II.[30] Anatomic changes in the mild uneventful case, or in the asymptomatic cases, could not be so studied except in the rarer event of observations made on persons known to have been positive to coccidioidin, negative to tuberculin (without tuberculous anergy), and coming to autopsy by reason of other causes.[31]

The pathologic picture of the primary coccidioidal infection as seen in infected animals is that of an interstitial pneumonia, and the response may be leukocytic. Disseminated coccidioidomycosis as seen in man at the autopsy table is as its earlier named indicated—a granulomatous disease, and strikingly similar to tuberculosis—with the spherule to be seen in the tubercle. The spread at first is probably lymphatic to the supraclavic-

[29] Faber, H. K., Smith, C. E., and Dickson, E. C.: Acute Coccidioidomycosis With Erythema Nodosum in Children. J. Pediat. 15: 153–171, August 1939.

[30] See footnote 10, p. 55.

[31] See footnote 11, p. 56.
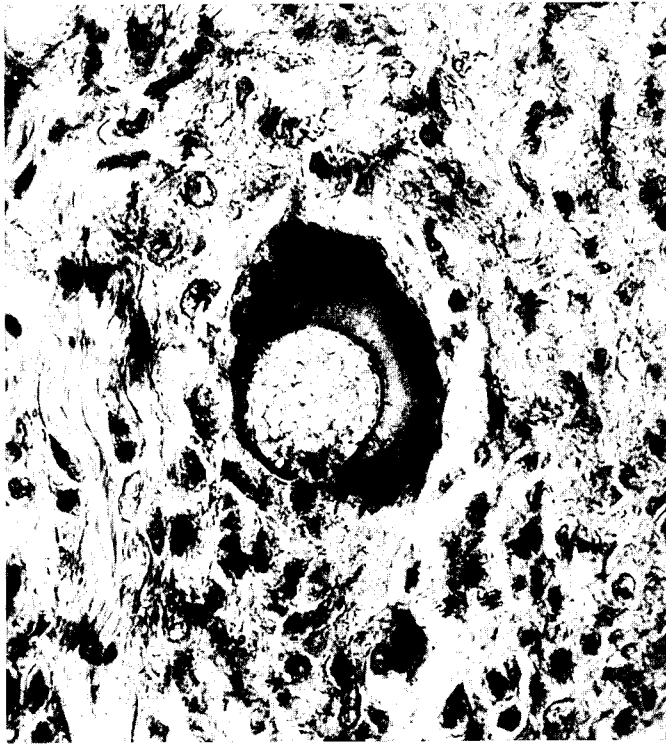
FIGURE 32.—Tissue section of coccidioidal granuloma showing a characteristic mature endosporulation spherule within a giant cell.

ular area, but after this first extrapulmonary abscess it spreads to the rest of the body through the bloodstream. No system, organ, or tissue seems immune, and the lesions are seen everywhere. Suppuration is characteristic of the bone involvement which otherwise resembles osteomyelitis. The typical elementary lesion of disseminated coccidioidomycosis is a small tubercle, granulomatous, with proliferation of epithelioid cells (fig. 32) and with giant cells containing spherules scattered in the caseous material. In the lungs, there may be areas of focal suppuration with thickening of the alveolar wall, together with fibroblastic proliferation, edema, and infiltration of plasma cells and neutrophiles in the interstitial tissues.

Diagnosis

The diagnosis of primary coccidioidomycosis is made on the basis of the clinical picture, following opportunity for infection, in conjunction with a changing (negative to positive) coccidioidin skin test and a positive precipitin test. Its corroboration depends on culturing *C. immitis* from

the sputum, gastric washings, or pleural fluid and by identifying the doubly refractile walled spherule in mice or guinea pigs inoculated with the culture.

The diagnosis of disseminated coccidioidomycosis depends on the development of its protean clinical picture *and* the increasing titer of complement fixation, 1–16 usually being taken as the differential point. In the disseminated disease, the fungus may be grown from sinus discharge, biopsies, pleural effusion, or spinal fluid. Roentgenographic evidence of bony or soft-tissue lesions are of definite assistance in making a diagnosis of disseminated disease. Pulmonary infiltrations of coccidioidomycosis cannot be differentiated from other diseases of the lungs by roentgenographic evidence alone.

Treatment

The treatment of primary coccidioidomycosis during World War II was essentially symptomatic, aspirin being the most useful single drug, but the possibility of dissemination was never forgotten and, if symptoms persisted or there was a rising complement fixation titer, conservative handling consisting primarily of bed rest and good diet was considered important. Temperature, leukocyte count, and sedimentation rates were useful guides in determining how much activity should be allowed. In general, with a slight elevation of temperature, an elevated white blood count, an elevated sedimentation rate, and a rising titer of complement fixation, the patient was kept in bed to lessen the possibility of dissemination.

Many methods of therapy have been hopefully instituted in an effort to cure disseminated coccidioidomycosis. Few have been of any specific value, until recently, in the treatment of this phase of the disease.[32] Of all, effective results have been obtained with one basic regimen; namely, bed rest and supportive measures—the only real treatment of tuberculosis of a few decades ago. Many are the patients who have seemed moribund, with complement fixation in titers about 1:256, with numerous draining sinuses, with continual elevations of temperature, and with extreme loss of weight, who on bed rest plus a high-protein, high-caloric diet, and supplemental vitamins have improved clinically and serologically and have left the hospital apparently cured.

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[32] The advent of the antibiotic Amphotericin B, related to streptomycin, and its effective use in the care of coccidioidomycosis patients, took place subsequent to submission of this chapter for publication. Amphotericin B is, apparently, the only effective drug thus far. Results are reported as excellent in early infections and encouraging even in chronic cases, although not as dramatic as those obtained in chronic blastomycosis with the drug.—A.L.A.

COCCIDIOIDOMYCOSIS IN THE ARMY AIR FORCES [33]

In 1940–41, the Army Air Forces began establishing airfields in the San Joaquin Valley as a first step in its training program. The high percentage of days with good flying weather and the unlimited space for emergency landing fields made this country very desirable for training. This region was part of the Ninth Corps Area (later the Ninth Service Command). Dr. Walter T. Harrison, the U.S. Public Health Service liaison officer in the Office of the Surgeon, Ninth Corps Area, alerted both the surgeon of the corps area and the headquarters staff of the West Coast Training Center to the environmental health hazard—coccidioidomycosis.

Dr. Smith, professor of public health at Stanford University School of Medicine, had just published (June 1940) in the *American Journal of Public Health* his study of the epidemiology of acute coccidioidomycosis with erythema nodosum in the San Joaquin Valley. This was a broad, 17-month study in Kern and Tulare Counties of 432 patients with the disease called San Joaquin Valley fever (with erythema nodosum), or valley fever, or desert rheumatism, and frequently confused with influenza, pneumonia, tuberculosis, measles, smallpox, poliomyelitis, typhoid fever, and syphilis. Dr. Smith observed that the incubation period was from 1 to 3 weeks, most frequently 2, and that coccidioidin sensitivity was established about 2 weeks after onset of symptoms with a variation of 2 to 17 days. He learned that erythema nodosum was associated with the hypersensitivity of a freshly acquired coccidioidin reaction and that this reaction, like tuberculin sensitivity, was of long duration. His study also indicated that the disease was acquired by inhalation of chlamydospores, that spherules or endospores did not pass the disease from host to host, and that the seasonal incidence of the disease was related to the climate and agricultural activities with a peak in the dusty windy fall and an ebb in the wet winter. The benign "valley fever," as measured by patients with erythema nodosum, was shown to be most common in white females while the coccidioidal granuloma, or disseminated form, was most common in dark-skinned males. Approximately 50 percent of patients acquiring the disease had lived in the Valley less than 1 year and only one-ninth over 10 years. This led to the conclusion that most residents of the region were infected eventually, with 5 percent or less developing erythema nodosum. Therefore, these 432 patients with erythema nodosum represent 8 to 10,000 patients with coccidioidomycosis.

Of the ecology of the micro-organism, little was known. It had been isolated from soil, though with difficulty, and it was known to be a bi-

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[33] For information to supplement the discussion of coccidioidomycosis in the Army Air Forces, Army Ground Forces (pp. 81–85), and prisoners of war (pp. 85–89), as presented in this volume, reference is made to Smith, Charles Edward: Coccidioidomycosis. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume IV. Communicable Diseases. Washington: U.S. Government Printing Office, 1958, pp. 285–316.

phasic fungus. The prevailing theory, based on animal trapping, considered rodents (particularly pocket mice and kangaroo rats) as the reservoir hosts of the disease.

The timely publication of this well-studied series helped to lessen the impact of the unfamiliar disease on the Armed Forces and provided a broad scientific basis for further study.

Because of his knowledge of the disease, Dr. Smith was brought into the problem as it concerned the command active in the area. A meeting was arranged for Dr. Smith to discuss the matter with the headquarters staff of the West Coast Training Center—Brig. Gen. Henry W. Harms, Commanding General; Lt. Col. (later Brig. Gen.) Charles R. Glenn, MC, Senior Flight Surgeon; and Maj. Otis B. Schreuder, MC. After consultation, it was decided that a detailed study, clinical and epidemiologic, should be made.

Early Planning

On 24 February 1941, Col. H. R. Beery, MC, Surgeon, Ninth Corps Area, wrote to Col. (later Brig. Gen.) Charles C. Hillman, MC, Assistant to The Surgeon General, enclosing a copy of Smith's paper on epidemiology. In his letter, Colonel Beery pointed out that the weather, which elsewhere had been bad for flying, was excellent where the San Joaquin Valley flying fields were being built. He further advised:

* * * J. P. Leake, Medical Director, U.S. Public Health, on duty in Office of The Surgeon General of that Service is familiar with the condition existing in the Valley. * * * Colonel [(later Brig. Gen.) Condon C.] McCornack, Surgeon 4th Army, is familiar with the situation and will see that no Army Maneuvers are held in the affected area * * *. The Board appointed by this headquarters for the purpose of locating new camp sites will leave the San Joaquin Valley out of the picture.

The Surgeon General's Office concurred in the thought that the Air Corps was justified in developing flying fields in the Valley and also with Colonel McCornack's decision not to hold Army maneuvers there.

At the same time that this problem was being approached and studied through the normal Army channels, it also became the subject of interest to the Commission on Epidemiological Survey, Board for the Investigation of Epidemic Diseases in the Army, Preventive Medicine Division, Office of The Surgeon General. This body, wisely created under the leadership of Dr. Francis Blake and Dr. Stanhope Bayne-Jones for the purposes that the name implies, established a division in the Ninth Corps Area with Dr. Edwin W. Schultz, as director, and Dr. Edward B. Shaw and Dr. Smith, as members. A program was planned that would minimize coccidioidal infection in the San Joaquin Valley and at the same time carry on research into its epidemiology. This plan of study was worked out by Drs. Smith, Bayne-Jones, and Blake and approved on

21 June 1941 by the Commission on Epidemiological Survey. Less orthodox channels, more sensitive to time and based on need and friendship, were also established between the Office of The Surgeon General (Col. (later Brig. Gen.) James S. Simmons, MC) and the West Coast Training Center.

Dr. Smith had been working on a grant from the Rosenberg Foundation. This grant was generously continued and supported the work at the airfields for the first 4 months, until more logical support could be obtained from the Army. Whether one wants to call this private injection into the great war machinery of the nation "pump priming" or "fusing," it served a great and helpful purpose and brought about a considerable speeding up of the work at a time when many decisions involving large masses of troops were being made every day.

It was planned through the coccidioidin test to learn who had or had not had the disease before coming to stations in the infected areas and, by repeated testing of "negatives" until they changed to "positives," to determine the proportion of those infected who really became ill with definite symptoms. The investigators expected to learn the variation in infection rate at different times of the year, and what influenced that rate. And it was hoped that they might evaluate the early and conservative treatment of the disease, and any other treatment that might shorten its course or save life in the disseminated disease. The study was in fact to throw important light on the meaning of the coccidioidin reaction and on the nature of resistance in this disease (pp. 54–56).

Institution of Program, West Coast Training Center

As this study got underway, it did so against a background familiar to most people going through Army training; namely, dust (four plus) or mud (four plus). When the program was started in July 1941 at Minter Field, Bakersfield, Calif., the background and the foreground were dust, with tents, informal equipment, and a frontier atmosphere of something great about to happen. The permanent staff of the Minter Field and the Gardner Field at Taft, Calif., was skin tested with coccidioidin, and 20 percent of those not already infected were found to convert from a negative to a positive reaction in the next 6 weeks.

It was soon apparent that the infection rate for coccidioidomycosis was highest at the two airfields nearest Bakersfield; namely, Gardner and Minter. (It is also apparent from the correspondence that more than one person in Washington, D.C., thought "Bakersfield" was yet another flying field.) The airfield at Lemoore, Calif., 50 miles to the north, had a lower rate, and the one at Merced in the northern part of the San Joaquin Valley, less than 150 miles from Gardner, had no coccidioidomycosis that was indubitably incurred at that field.

The study showed a seasonal variation in infection rate with a high in the latter part of the summer toward the end of the dry season and a low in the wet winter and spring. During the period when much building was in progress, the dust or mud was terrific, and in the dusty month of August 1941 over 5 percent of the susceptible personnel at Minter Field were infected. With the tapering off of construction, the planting of lawns, the paving of roads and airstrips, the change from field to aquatic sports and, of course, possible other factors, the incidence of coccidioidal infections was halved.

At a later period during the war, Dr. Smith noted one other possible factor influencing the infection rate; namely, that the 2 years with the highest incidence were preceded by the wettest winters. This extra rain, he thought, might help the growth of the fungus in nature (wherever that might be). Subsequent work would indicate that he was right.

On 20 October 1941, Dr. Smith wrote to Dr. Bayne-Jones, Department of Bacteriology, Yale University School of Medicine, New Haven, Conn., and director of the Commission on Epidemiological Survey, briefly outlining the progress of the coccidioidomycosis study up to that time. In this letter, as in others, Dr. Smith emphasized the intense interest and enthusiastic cooperation given the study by Colonel Glenn. Colonel Glenn, being a personal friend of Colonel Simmons, also was frequently able to shorten the line of communication without giving offense. Again, as in other letters, Dr. Smith spoke appreciatively of the great contributions made, both administratively and professionally, by Major Schreuder and by the flight surgeons of the two basic training centers (Maj. (later Lt. Col.) John E. Roberts, MC, and Maj. (later Lt. Col.) Robert R. Estill, MC) and their staffs, and praised the warm cooperation of the numerous doctors, aidmen, and others who made this work possible.

Dr. Smith reported that more than 2,000 men had been tested with coccidioidin. Handicapped by their irregular arrivals at camp and the frequent shifts of men from organization, the investigators concentrated on skin testing the recent arrivals. Until the population of the camps could be stabilized, it was thought useless to attempt to retest any who did not have clinical symptoms. Under these difficult conditions, some significant observations were nonetheless made as follows:

The men from the east and midwest are all negative to coccidioidin. Quite a few from central and western Texas, New Mexico, and Arizona and, of course, the San Joaquin Valley of California react to the material. Besides these areas we have had a few reactors from Nevada, Southern Utah, Idaho and Montana, indicating the possibility of these areas as previously unrecognized endemic foci. However, the numbers from these sparsely settled regions are still too small and only when we have the camps fully tested should we have a sufficiently large group from which to draw any deductions. Thus any comments at the present time on the distribution of the positive reactors of the "control" test would seem to me premature.

When we were down in the middle of September there had been a recent sharp increase in the number of cases of coccidioidal infection and during the week we saw ten

active cases at the Bakersfield Camp. As we hoped, the fact that the men had been tested with the coccidioidin proved a very great practical use in establishing diagnosis, for all that was necessary was to repeat the test and when it was positive, in view of previous negative record a copy of which is on file at the camp, a diagnosis was established.

The work of testing, tabulating, evaluating symptoms and treatment, and pointing up new areas of endemicity continued. This was not easy and was opportunist work as the Army moved personnel in and out. Dr. Smith continued to supply the coccidioidin and to perform the serology in his laboratory at Stanford University. In July 1942, the Commission on Epidemiological Survey took over the financial responsibility for the work being done by him and his coworkers under Contract W709 md–294.

On 2 January 1942, Dr. Schultz forwarded through Dr. Bayne-Jones, to Dr. Blake, President, Board for the Investigation of Epidemic Diseases, U.S. Army, a report prepared by Dr. Smith on the investigation of coccidioidomycosis in the Kern County, Calif., Air Corps Basic Flying Schools, West Coast Training Center, July through November 1941. In this complete report of the work so far accomplished, Dr. Smith brought out the method by which the coccidioidin-testing program was carried out, this being the basis for study of the epidemiology of this disease.

Following visits made solely for the purpose of educating medical officers on coccidioidomycosis, coccidioidin testing had been started on the Bakersfield group (Minter Field) on 13 July and on the Taft group (Gardner Field) on 20 July. The patients sick with the disease were seen in consultation. Lists of all nonreactors were kept at the station hospitals, and, if a man with a negative skin reaction appeared at sick call with specific symptoms, a retest with coccidioidin usually established the diagnosis (by a positive reaction) or ruled it out (by continued negative reaction). Skin-testing surveys being done for epidemiologic reasons thus became a very important part in the laboratory diagnosis of coccidioidomycosis.

The correlation between the positive skin reactions and residence at the time of entry into the Army indicated that Arizona and California had heavily infected populations, with Texas showing 12 percent of its men positive. In striking contrast were the consistently negative results found in men coming from the Eastern or Mideastern States, bearing out other evidence that the distribution of *C. immitis* is restricted to arid, dusty regions. The study also, and very importantly, indicated a high degree of specificity of the coccidioidin skin test, and, because relatively few reactors could recall any specific illness suggesting their primary infection, it brought out the relative infrequency with which the infection is recognized. The diagnosis of primary coccidioidomycosis was made in 66 cases, of which 44 required hospitalization with an average stay of 14 days.

Because it was still not feasible to do repeat testing in an organized way, it was thought that many "converters" were missed, having changed over without being sick. October was the peak of the season and with the onset of winter rains the incidence dropped very markedly. Over half of

those who became ill with the disease had been in camp less than 2 months. Smith suggested that, because of the immunity conferred by a single infection, the personnel in these endemic areas be stabilized, including the medical personnel for the additional purpose that they become increasingly expert in recognizing and handling the disease. He recommended that the disease be treated with respect because of the possibility of dissemination. He reiterated that except for the Air Corps training fields large concentrations of soldiers should avoid the San Joaquin Valley and finally advised that Dr. Harrison (p. 73) should continue to be consulted regarding any plans or problems that might have to do with coccidioidomycosis.

On 6 February 1942, Colonel Simmons, through Lt. (later Lt. Col.) Douglass W. Walker, MC, asked Dr. Smith if he could furnish more up-to-date information concerning the areas of endemicity of coccidioidomycosis and what hazards there might be in having concentrations of troops stationed in such areas, particularly in California, Arizona, New Mexico, and Texas.

On 2 March 1942, Dr. Smith answered that coccidioidomycosis was present in the southern half of the San Joaquin Valley and in Stanislaus, Merced, Madera, San Benito, Fresno, Kings, Tulare, and Kern Counties— being most intense in the last three (the south end of the San Joaquin Valley). He stated further that coccidioidin testing at the San Joaquin Valley airfields had shown occasional cases from the eastern half of Monterey, San Luis Obispo, Santa Barbara, and Ventura Counties, and further south and east in the northern part of Los Angeles County and in San Bernardino, Riverside, Imperial, and San Diego Counties. With reference to all the endemic areas he recommended that except for aviation training, which made the need very great, the following areas should be avoided for large encampments: (1) The San Joaquin Valley of California, (2) the southern half of Arizona, (3) the southern tip of Nevada, (4) the vicinity of St. George, Utah, (5) the southern half of New Mexico, and (6) Texas, the region from San Angelo, west and south. He ended his letter by saying: "We are still in quest of why the fungus is found where it is, what restricts its distribution and where it actually grows in nature."

The Syllabus

During the summer of 1942, a syllabus on coccidioidomycosis was prepared. It was published and distributed by Headquarters, West Coast Army Air Forces Training Center, in October of that year. It was revised in September 1943, and in March 1944 the publication of a third edition was made possible by the Josiah Macy, Jr. Foundation. Originally prepared by the surgeon of the command (Colonel Glenn and later Col. Michael G. Healey, MC), it was enlarged in scope and detail by Maj. (later Lt. Col.) Norman Nixon, MC. It was well illustrated by plates showing cultural

characteristics of the fungus and by roentgenograms credited to Dr. R. A. Carter at the Los Angeles County Hospital, Los Angeles, Calif., and to Maj. Horace W. Jamison, MC. A map showed endemic areas. A graph indicated seasonal incidence. There was an extensive bibliography.

In substance, the syllabus was an excellent handbook on the disease, covering symptoms, diagnostic procedures, course, and criteria for discharge from hospital. It also pointed out the military significance of coccidioidomycosis; namely, that the total number of deaths would be low, the morbidity would be high, and the period of hospitalization, rather prolonged. All enlisted personnel and officers were to be tested with coccidioidin on their arrival at a station and twice yearly thereafter, and the reactions recorded on the individual's service record and his immunization register MD Form 81. The responsibility for reporting and control was placed on the medical officer specifically assigned to the coccidioidomycosis problem at each of the fields, and he in turn was to be responsible to the coccidioidomycosis control officer of the West Coast Army Air Forces Training Center, at the Santa Ana Air Base. By the time of issue of the second edition, the term "Coccidioidomycosis Control Officer" was as generally accepted in the endemic areas as "V. D. Control Officer."

The authors described the two clinical forms as (1) *primary coccidioidomycosis,* the acute, benign, self-limited respiratory infection and (2) *progressive coccidioidomycosis,* the chronic, disseminated, usually fatal illness, manifested by cutaneous, subcutaneous, visceral, and osseous lesions, occurring in certain individuals as one continuous progressive disease, although the serious form may not be recognized as such until several weeks or months have elapsed. Continued spread of infiltration suggests the progressive form, and the discovery of extrapulmonary foci confirms it. Death usually occurs in such cases after a course of many weeks' to 6 months' duration. Rarely, a patient will focalize his disseminating disease, usually after prolonged rest in bed, and make a complete recovery. The great majority of primary infiltrations, however, do not go on to dissemination but will disappear completely in 5 or 6 weeks. In some of these cases, residual cavities will persist, but the benign nature of these is indicated by their clinical course and low sedimentation rate.

They noted, on the other hand, the high susceptibility of dark-skinned persons to disseminating disease, advising against the use of Negro troops. They noted how infection is acquired by inhalation of dust containing the tiny live chlamydospores coming from the soil in endemic areas, and that some 90 percent of persons who have been resident in heavily endemic regions will react to coccidioidin. They summarized the important points, from the point of view of the military surgeon, to be (1) the recognition of the disease, (2) the prompt hospitalization of all clinical cases until the sedimentation rate becomes normal, and (3) the ability to distinguish this condition from tuberculosis, which it so closely resembles.

There are many aids to differentiation from tuberculosis once the essential differences have been clearly established. First is the difference in epidemiology as this disease spreads from environment to man rather than from man to man. There is the striking immunologic difference in that the initial infection with the fungus confers permanent resistance against subsequent infection. Although people living in endemic areas (the San Joaquin Valley and southern Arizona) are repeatedly exposed to contaminated dust throughout their lives, the incidence of serious disease is low, probably not more than 1 case of the progressive form to 500 of the benign primary form.

By March 1943, there had been 253 clinical cases of coccidioidomycosis at the Minter, Gardner, and Lemoore Fields. There had been none at Merced. There were 125 cases in personnel of the Air Forces at Minter between July 1941 and March 1943, 61 at Gardner, and 67 at Lemoore. There were three cases of disseminated coccidioidomycosis with two deaths. The big months for coccidioidomycosis were from June through November with the emphasis in September and October. The infection rate at the three fields was approximately 20 percent per year, Minter and Gardner having the highest. It was observed that recruits from Merced County rarely showed evidence of having had coccidioidal infection; no clinical infections occurred at Merced Army Air Field and only seven changeovers.

Dr. Smith gave great credit to the persistence and cooperation of the following medical officers in carrying out the coccidioidomycosis-control program—Lt. Col. John E. Roberts, Lt. Col. A. L. Jennings, and Maj. Edward C. Donohoe, all successively at Minter Field; Lt. Col. Robert R. Estill, Lt. Col. Albert Phillips, successively at Gardner Field; Lt. Col. Edward Padden, at Lemoore; Lt. Col. M. U. Prescott and Lt. Col. Neil Johnson, at Merced. The designated coccidioidomycosis-control officers who took a leading part in the program were Maj. Russell W. Mapes, at Minter; Lt. David L. Thurman, at Gardner; Maj. J. Murray Kinsman, at Lemoore; and Capt. Harvey A. Woods, at Merced. All these medical officers, themselves subject to rapid turnover, were quick to grasp the problems before them and persistent in carrying out the work.

Again on 1 June 1943, Maj. Forrest M. Willet, MC, chief of the medical service at the Station Hospital, March Field, near Riverside, Calif., replying, through the Air Surgeon, to an inquiry from the Office of The Surgeon General, told of a recent increase in cases in connection with construction of an airfield at Banning, Calif., where Company B of the 856th Engineer Battalion (Aviation) had joined Company C on 24 April. These were Negro troops. Three weeks later, several patients with clinical coccidioidomycosis were admitted to the station hospital. The medical staff thereupon tested all members of the 856th Engineer Battalion with coccidioidin, finding a large number of positive reactors, all of whom had been in endemic areas before coming to March Field.

A number of soldiers from Company B who had failed to react to coccidioidin entered the hospital later with the clinical disease. Company A of that battalion did not go to Banning and coccidioidomycosis developed in only one of its personnel, a man who had gone to Banning on a visit. A new outfit, 198 soldiers, moved in to replace the 856th Engineers. They were given the cutaneous test and there were three positive reactors, all of whom had previously been in endemic areas. It was planned to repeat such skin tests twice for the purpose of definitely proving Banning an endemic area.

With so much interest, widened by the experience of the Army, in a disease local by nature, many papers appeared in medical journals. These various publications [34] helped alert the physicians of the country to the disease—its epidemiology, diagnosis, clinical course, and hazards.

COCCIDIOIDOMYCOSIS IN THE ARMY GROUND FORCES

Early Cases

On 1 December 1941, a report was forwarded to the Office of The Surgeon General through channels from Camp Roberts, Calif. It was written by Lt. Robert M. Shelton, MC, and later formed the basis of an excellent paper.[35] The first case had been discovered in April 1941 among the troops there, whose training was in large part carried on in the area east of U.S. Highway 101, which included some of the rather dry country of the Coast Range. A number of other cases were seen in the Station Hospital, and a skin-testing survey was begun in June 1941. In all, 888 men were tested; 3 months later 736 of the negative reactors were retested, and of these 14 were found to react to coccidioidin. Allowing for those who might have been exposed elsewhere, the result pointed to an annual incidence of approximately 6 or 8 percent, indicating that 1,000 men would become infected annually at Camp Roberts. This report prompted a continuation of the survey.

During 1942 and the first half of 1943, coccidioidomycosis appeared sporadically in ground force units bordering the endemic areas and most

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[34] Many of these reports and studies have been cited in this chapter. Among others appearing in 1943–44 were (1) Smith, C. E.: Coccidioidomycosis. M. Clin. North America 27: 790–807, May 1943; (2) Colburn, J. R.: Roentgenological Types of Pulmonary Lesions in Primary Coccidioidomycosis. Am. J. Roentgenol. 51: 1-8, January 1944; (3) Goldstein, D. M., and McDonald, J. B.: Primary Pulmonary Coccidioidomycosis; Follow-Up of 75 Cases, With 10 More Cases From New Endemic Areas. J.A.M.A. 124: 557–561, 26 Feb. 1944; (4) Lee, R. V.: Coccidioidomycosis in Western Flying Training Command. California & West. Med. 61: 133–134, September 1944; (5) Quill, L. M., and Burch, J. C.: Surgical Manifestations of Coccidioidomycosis. Ann. Surg. 120: 670–679, October 1944; and (6) Denenholz, E. J., and Cheney, G.: Diagnosis and Treatment of Chronic Coccidioidomycosis. Arch. Int. Med. 74: 311–330, November 1944.

In July 1943, Colonel Bayne-Jones prepared an excellent chapter on "Coccidioidomycosis" for General Simmons' revision of "Laboratory Methods of the United States Army." This chapter included exposition of the initial or primary infection, the progressive or disseminated infection, the distribution, and the mode of spread, with fairly detailed laboratory instructions covering techniques from the growth of the fungus to the preparation of coccidioidin and the performance of the precipitin and complement fixation tests.

[35] Shelton, R. M.: Survey of Coccidioidomycosis at Camp Roberts, California. J.A.M.A. 118: 1186–1190, 4 Apr. 1942.

probably associated with travel through them by individuals or small groups.

Desert Training

In the latter part of 1942 and early 1943, a desert training center was created for the purpose of preparing troops for the terrain and the extremes of heat and dryness which they might encounter if fighting continued in North Africa. This area was a large one in the lower Mojave Desert west of Blythe and northeast of the Salton Sea. It included the Pallen Mountains, the Granite Mountains, and the Iron Mountains, and all the dry springs and dry lake beds in an area 3 or 4 thousand square miles in extent. With such an assignment and such country, the trainees were really put through their paces. As more and more troops came in, ultimately reaching 80,000 and including at least one Negro division, it was obvious to those interested in coccidioidomycosis that parts of this region were highly endemic for the disease, particularly certain camps near Yuma and the area near Pallen Pass west of Blythe. The distribution would indeed seem to be very spotty but intense where it existed, thus offering opportunities to avoid small heavily infested areas.

On 26 March 1943, the following communication went from the Office of The Surgeon General to the Surgeon, Army Ground Forces:

1. This office has recently been informed that a number of cases of acute coccidioidomycosis (Valley Fever) have recently occurred in troops maneuvering in the Desert Training area in Southern California. This area is somewhat beyond the highly endemic San Joaquin Valley, and while cases have been reported in this region, it has not hitherto been considered that coccidioidomycosis constitutes a serious threat to persons living within this area.

2. In view of the above, it is requested that full information as to the extent of any recent outbreak of coccidioidomycosis among troops in this area be obtained. It is believed that Major Roswell K. Brown, M.C., Desert Warfare Board, Camp Young, California, is acquainted with this situation.

The first action in this was apparently taken in December of that year, according to a memorandum for file on a conference with the Ground Surgeon, Col. William E. Shambora, MC, on 23 December 1943, to determine the policy of his office with respect to coccidioidomycosis control in Ground Forces organizations. For the conferees, including Maj. (later Lt. Col.) Aims C. McGuinness, MC, Colonel Shambora obtained the following information from Col. Frank S. Matlack, Surgeon, Headquarters, Communications Zone, California-Arizona Maneuver Area, Banning, Calif.:

a. All pertinent information furnished the Ground Surgeon by the S.G.O. has been forwarded to units maneuvering in the endemic regions.

b. A meeting of all battalion and regimental surgeons, and hospital medical officers of troops on maneuvers in this region was held. Full details on the endemicity and recognition of coccidioidomycosis were present at this meeting. The services of Dr. Charles E. Smith have been utilized.

c. Information about the disease has also been furnished to line officers.

d. A large number of cases of coccidioidomycosis have recently occurred in troops in the vicinity of Yuma, Arizona. Efforts are being made to locate this source of infection more accurately.

e. Commanding officers responsible for the selection of maneuvers sites will be advised concerning the avoidance of endemic regions. There is no doubt that such advice will be followed so far as it is consistent with military necessity.

It was agreed that an exchange of all pertinent information on this subject reaching either the Surgeon General's Office or the Ground Surgeon's office should be kept up.

Coccidioidomycosis-control programs were instituted in the Communications Zone of the California-Arizona Maneuver Area in the summer of 1943, but efforts to institute it in the real desert training center were refused, and, except for the information given physicians in this area, no real cooperation was established.

Coccidioidomycosis was picked up from New Jersey to the western Pacific in troops who had been in this area. One of the most significant reports came from Fort Bragg, N.C., in the following letter from Dr. Theodore J. Abernathy to Dr. Smith, in early 1944:

Recently, a case of coccidioidomycosis was discovered on the wards of the Station Hospital at Fort Bragg. This patient was suffering from the primary form of the disease, characterized by a circumscribed pneumonic lesion in which cavitation was demonstrated roentgenographically. A skin test with Coccidioidin, 1–100 dilution, done at the height of the disease, was positive. * * * [Other tests not completed.]

Checking back on this patient's army experience it was learned that he was one of a group of Field Artillery trainees, recruited largely from Michigan, Ohio and Illinois, who had spent three months (22 August to 24 November) at Camp Iron Mountain, California, participating in desert maneuvers. Further investigation of 35 additional patients from this same group, now stationed at Fort Bragg and admitted within the past week because of various medical and surgical complaints, has disclosed five positive reactors to Coccidioidin (14.2 percent). One patient who gave the strongest positive reaction was admitted with a presumptive diagnosis of rheumatic fever, and the test was exceedingly valuable in pointing toward the true nature of the disease.

Available information which we have at our disposal is that Camp Iron Mountain is located in the extreme south-easterly portion of California close to the Arizona border. According to the syllabus on coccidioidomycosis (AAFWFTC), this area is in close proximity to an endemic focus of the disease in Arizona. Do you have any reports indicating that cases of coccidioidomycosis may have originated in Camp Iron Mountain or in the desert maneuver area? Have you any information regarding a control program in this camp and the results of same, if attempted?

We are considering enlarging the present study to include the skin testing of a large number of men who were at Camp Iron Mountain * * *.

Cases were picked up also at Camp Dix, N.J., in Hawaii, and in the western Pacific in members of the 77th Infantry Division who had gone through the desert maneuvers. Further testing reported in a later letter from Dr. Abernathy showed that over 15 percent of 555 men from one field artillery battalion coming from the desert maneuver area reacted positively to coccidioidin. By 16 March, Dr. Abernathy reported to Colonel

(later Brigadier General) Bayne-Jones on cavalry units that had been stationed in the California-Arizona Maneuver Area at Camp Hyder (halfway between Yuma and Phoenix), Camp Laguna (27 miles north of Yuma), and Camp Pilot Knob. Positive skin reactors in these groups were as follows: 28.6 percent of 70 men in the 11th Group; 23.8 percent of 736 men in the 36th Squadron; and 20.6 percent of 786 men of the 44th Squadron. Plans to examine by roentgenogram the 337 positive reactors dissolved when the three organizations were sent to four different places.

A letter from Maj. (later Lt. Col.) George A. Young, Jr., MC, Consultant, Headquarters, Communications Zone, California-Arizona Maneuver Area, to Dr. Smith is quoted at length as indicating the efforts so many of us made for months and years to open the ears of the fire-eating trainers to our message.

Your letter of 12 Jan. 44 to Lt. Col. Manjos has been forwarded to this headquarters for reply. Following my letter to you of 29 July 43, we initiated a program for the study of coccidioidomycosis in the Desert Training Center * * *. Unfortunately this headquarters has jurisdiction only over Communications Zone installations and when we attempted to extend the program to the entire desert we were informed by the Desert Training Center that: "1. Not favorably considered. 2. There is not sufficient data to indicate an urgent need of this work and with the present shortage of Medical Officers in DTC it is not considered that this diversion of personnel is practical. 3. If research and investigation of special problems in DTC are indicated, it should be done under the direction of the Surgeon General by especially trained and assigned personnel." The foregoing required us to continue our project in an unofficial status and limit our activities to the Communications Zone. Within the past month we succeeded in convincing the DTC as to the importance of the problem of coccidioidomycosis and it will now be possible to more thoroughly approach the problem. What factual information we have accumulated from the present study was forwarded to the Army Ground Forces, 3 Jan 44 * * *. To this can be added the following statements which are considered to be sound, but which are, as yet, unsupported by sufficient factual data:

a. The maneuver area proper, indicated on map * * *, is highly endemic. Supporting this statement is the fact that a division of Negro troops was stationed at Camp Clipper for three (3) months without experiencing significant coccidioidal infection; then, beginning three weeks after they participated in exercises in the maneuver area proper thirty (30) cases of coccidioidomycosis were admitted to one of our hospitals. These soldiers were acutely ill and were admitted with transfer diagnoses such as atypical pneumonia, lobar pneumonia, bronchitis, etc. Obviously many hundreds of milder cases are going unrecognized. It would appear most reasonable that the cases described by Dr. Abernathy represent troops recently in the formal maneuver area, and that the maneuver area and not their camp site was the endemic region. It is my personal belief that a great many soldiers are leaving this area with unrecognized smouldering infections which become manifest at a new station. Not every medical installation will be as alert as the Ft. Bragg group and recognize the disease.

b. The entire area between Yuma and Hyder, Arizona is heavily endemic. Over two hundred cases of the disease occurred in troops stationed at Camp Hyder. These cases were diagnosed by the 32nd Evacuation Hospital; but because they were a combat zone unit, we received no data and could not include them in any official report. * * * [however there is] a more satisfactory liaison now established between the two zones * * *. Incidentally eight (8) nurses of the 32d Evacuation Hospital developed coccidioidomycosis. The hospital was located between Horn and Hyder, Arizona.

c. Pomona, Camp Young, Thermal and San Bernardino are areas of very low or no endemicity. This statement is based on the absence of changeovers after serial skin tests (3, 6, 9, and 12 weeks) and is supported by the absence of any proven cases from the areas noted.

d. Supporting the belief that Desert Center, Granite, Coxcomb, and Camp Young are innocuous areas is the experience of the Station Hospital SCU 1925 which hospitalized soldiers from the areas mentioned during the period 15 July 42 to 15 Feb 43. After receipt of some coccidioidin we requested from you, Capt. Elmer Brock, our radiologist, skin tested in all cases showing pulmonary pathology—no positive reactions were demonstrated.

At the present time our general hospitals are functioning under a 45 day evacuation policy, this has necessitated the evacuation of coccidioidomycosis patients to hospitals outside of our supervision. In an attempt to centralize these patients, we have established a policy wherein all such cases are evacuated to the Camp Haan [Calif.] Station Hospital. Reports from your laboratory are then forwarded to Camp Haan. Dr. Rutherford and Mr. Copper from USC visited us frequently in Banning collecting rodents and plants from the area of Banning airstrip. A recent conversation with Dr. Kessel indicates as yet they have grown no coccidioides. It is Dr. Rutherford's plan to carry out his rodent survey in all proven endemic areas.

The preceding paragraphs contain the pertinent data and impressions we have obtained. I feel certain that much of this is unknown to the Surgeon General's Office; however any official communication by us is precluded [by the disapproval by the Desert Training Center] * * *.

* * * This office will continue to supervise the program which, however, it is felt will now continue under its own momentum. We have purposely made each hospital and laboratory feel this was their program and that all data at this office are available to them. I believe that many will publish articles on the subject. We have requested an informal summary from each general hospital and the mobile laboratory, a copy of which will be furnished you.

It is my belief that the medico-military aspects of coccidioidomycosis in this area are now obvious and appropriate steps should soon follow. It would appear wise to consider the transition of this study into State Health channels as it is possible that the present laboratory facilities will not always exist * * *.

May I express the deep appreciation we all feel for the generous manner in which you have aided us. We regret exceedingly that the suggestions included in your letter of July could not be carried out for the entire desert. I feel that we have finally hacked out some data instead of obtaining the clean cut results that might have been accomplished.

A plan was projected for continuation of the work if necessary by the use of mobile laboratories, but none were to be assigned to the Communications Zone, as the whole desert training program was being given up and the area was to be completely evacuated by 1 May 1944.

COCCIDIOIDOMYCOSIS IN PRISONERS OF WAR

In a report dated 4 February 1944, Col. Verne R. Mason, MC, medical consultant to the Ninth Service Command, brought to The Surgeon General's attention the fact that there was a large number of patients with coccidioidomycosis among the prisoners of war at Florence, Ariz. He noted, in part, as follows:

There are 89 patients with tuberculosis in the hospital. Of these, 2 are Japanese, a number are German, and the remainder are Italian. In addition to these patients, there

are a large number with primary pulmonary coccidioidomycosis. A number of patients have both active tuberculosis and coccidioidomycosis. Some have developed coccidioidomycosis of pulmonary type while in the hospital under treatment for active tuberculosis. A recent survey of 557 enlisted men of this SCU [Service Command Unit] was made. Of this number 54 percent had a positive coccidioidin test. The percent with positive tests varies directly with the length of time at this camp. The effects of co-incidental or contemporary coccidioidomycosis on the course of active tuberculosis may be studied well at this station. At present one Italian prisoner has the rapidly fatal acute disseminating type of coccidioidomycosis with miliary pulmonary lesions and pustular dermal lesions.

By 23 February, Dr. Smith was in Florence, at the request of the Preventive Medicine Service of the Surgeon General's Office, and, on 3 March 1944, made a report to The Surgeon General through Colonel Bayne-Jones. After careful study of the patients in the Station Hospital at Florence and a review of the many relevant factors, he made the following comments and recommendations:

Probably two-thirds to three-quarters of new arrivals from non-endemic areas can be expected to become infected during a year. Had this fact been realized prior to the location of the Camp, another choice might have been made. However, * * * my personal recommendation would be to continue the Camp but to develop a Control Program based upon repeated coccidioidin testing, detection of clinical coccidioidomycosis and prompt treatment. This is the plan which was developed as part of the work of the Commission on Epidemiological Survey in the San Joaquin Valley and which was expanded and applied by the entire Western Flying Training Command. The plan has been discussed with Lieutenant Colonel Bernadine and his medical personnel and they will welcome it * * *. The Station Hospital laboratory is already prepared to carry on its part, with sedimentation tests * * * culturing * * * and proper collection of blood specimens * * * in case of diagnostic doubt. Arrangements have been made to send us positive cultures for animal confirmation as well as blood for the serological testing. It is most important that sufficient medical personnel be available so the Camp Surgeon can designate one man to be in charge of the Program. It should not take more than one-third of his time * * *. The Camp Hospital is developing into an important tuberculosis sanitarium with enthusiastic chest specialists experienced in survey work * * *.

[It seems not improbable, and because of the climate not illogical] that the Florence Station Hospital is destined to be made the tuberculosis sanitarium for Prisoners-of-war. However, coccidioidomycosis poses two complicating considerations. First, can people acquire coccidioidomycosis when merely staying indoors in the hospital ward? Second, if they should acquire a coccidioidal infection, would it adversely affect their "cure" for tuberculosis?

The decision made shortly thereafter in the Office of The Surgeon General was announced in a memorandum from the Medicine Division to the Hospital Division, on 24 March 1944, as follows:

A conference was called by Brigadier Generals Bayne-Jones and Morgan for the purpose of considering the removal of the tuberculosis center for prisoners-of-war from the Station Hospital at Florence, Arizona, to another location. Evidence has been acquired recently which indicates that the incidence of coccidioidal infection at Florence, Arizona, is high. It has been shown that patients in the Station Hospital there have acquired the infection in residence. It was agreed that prisoner-of-war patients with tuberculosis should be protected from this additional health hazard. Therefore, the conference unanimously recommends that the tuberculosis center for prisoners-of-war be moved from the Florence, Arizona, Station Hospital and located elsewhere.

In May 1945, the incidence of coccidioidomycosis at Camp Cooke, Prisoner of War Center (San Luis Obispo County, Calif.), began to rise, 162 cases occurring. In the subsequent 3 months, investigation by Dr. Smith for the Surgeon General's Office, and by others, determined that these cases were incurred by prisoners working near Shafter in the San Joaquin Valley in one of the subsidiary prisoner-of-war camps. These prisoners and those at Lamont were digging potatoes and working cotton and other crops. Similar conditions obtained at some of the subsidiary camps around Florence. Dr. Smith, consulted from the field, explained the difficulty and the amount of personnel necessary to set up a coccidioidomycosis-control program among these scattered installations. When it was pointed out to the commanding officers of the prisoner-of-war camps that the rate at Camp Cooke alone was higher than for all the rest of the Army, the prisoners of war were withdrawn from work in the Shafter and Lamont areas.

The war was now drawing to a close and with it the immediate concern of the Army with this disease of arid regions. The time was approaching when we could all "go back to hoeing our own potatoes" and allow the search for a living to bring fresh divisions of civilians into the endemic areas—but of their own volition.

On 31 August 1944, Capt. Louis Schneider, MC, radiologist at the Separation Center, Fort Dix, N.J., wrote Dr. Smith a letter which is a good preamble to the conclusion of the story of coccidioidomycosis in World War II. The letter follows.

As you know, routine chest films will be taken on all service men and women who will be demobilized through these centers. In the course of these examinations, we have come across and will continue to come across soldiers who months ago recovered from a case of Primary Coccidioidomycosis and now have residual pulmonary lesions which are undoubtedly not active, and though they have not regressed by comparison of serial roentgenograms, the pulmonary shadows have neither broken down or extended. From my present knowledge it would appear safe to discharge these individuals, appreciating that they may therefore go out into any civil employment with little fear of reactivation. Of course it would be wise, it seems to me, to follow these cases with serial chest radiographs at Veterans Hospitals' out-patient departments much as we do with arrested cases of pulmonary tuberculosis. In this connection, your advice and comment in regard to the handling and after-handling of such separatees will be appreciated.

This letter, as concerned with a matter of policy regarding the separation of Army personnel with roentgenographic evidence of residual coccidioidal lesions, was referred by Dr. Smith to Generals Morgan and Bayne-Jones of the Office of The Surgeon General, and to Dr. Blake as President of the Board for the Investigation of Epidemic Diseases, U.S. Army. In his reply of 6 September 1944 to Captain Schneider, Dr. Smith gave his personal opinion, as follows:

First, may I express great pleasure and congratulate you upon your discernment in your evaluation of the pathogenesis of coccidioidal infection. Unfortunately, even in the newly revised edition of Cecil's text the opinion is expressed that many soldiers who acquired coccidioidomycosis in the Service will break down with a disseminated infection

in civilian life. Such an expression is ill founded and very damaging. As you indicated, even with coccidioidal nummular lesions remaining, men can be discharged without fear of disseminating coccidioidal infection. There does remain the very slight possibility of a cavity developing. This complication is so rare, generally developing within a few months after the infection, while the nummular lesions may continue so long (many years), that it would be impractical to continue the man in the Service until the roentgenogram is clear. The one safeguard I would recommend is that suggested by you, serial chest roentgenograms at Veterans Hospitals, say every six months. There should be no question of compensation or pension, as these lesions are not incapacitating. Particular pains should be taken to reassure these men not only for their peace of mind but also to keep them out of the hands of shyster lawyers or even misinformed medical men who * * * may try to make invalids out of these utterly healthy veterans. If any specific problems arise, please feel free to write me. I do feel quite certain that the Fort Dix separatees will be handled wisely.

General Bayne-Jones referred Dr. Smith's letter with its enclosures to Col. Esmond R. Long, MC, Deputy Chief, Professional Service, Office of The Surgeon General. Colonel Long, visiting the Fort Dix separation center, primarily to look over the chest X-ray work, spent some time with Captain Schneider, who again raised the same question. Colonel Long concurred in the general opinion that no public health problem was involved and was inclined to think also that the medical problem would not be serious. "The Army is not going to discharge men with active coccidioidomycosis, and men with scarred lesions are not likely to break down." He observed that the Army could not insure followup examinations although each separatee, being informed of his right to medical care under the Veterans' Administration, might be advised to have periodic checkups for appropriate conditions, of which coccidioidomycosis was only one in several.

On that sensible note, the experience of the Army with coccidioidomycosis was brought to a close. There remains only to summarize statistics before bringing to its close this historical sketch. During the years 1942–45, the admission rate per 1,000 troops per year (based on the total number of cases reported in the Army in the continental United States and the strength of the Ninth Service Command) ranged from 0.2 to 2.8 per month, being greater than 1 in 22 months and greater than 2 in 6 months of the span of 37 months. The Marines, in the small detachments scattered through the endemic areas, and specifically those reported by Lt. Cdr. E. F. Pfanner, MC, USNR, at Mojave, Calif., and by the U.S. Navy, in some of its inland installations, such as Inyokern, Calif., encountered the disease but in numbers insufficient to warrant very active countermeasures.

We have thus again one of the few unequivocally good things that sometimes come out of modern war, more knowledge of a disease process. In this instance, a gradual accumulation of knowledge, accelerated by work done shortly before the war, was further accelerated as a medical problem of local interest affecting the Army. It has been suggested [36] that general interest may continue as the modern habit of travel brings into endemic

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[36] Jamison, H. W., and Carter, R. A.: Roentgen Findings in Early Coccidioidomycosis. Radiology 48: 323–332, April 1947.

regions increasing numbers of people who, like the young soldiers negative to coccidioidin, are highly susceptible. However that may be, better understanding has been achieved of one of the diseases that attack the lungs, with the immediate gain of increased clinical competence and with wider implications for comparative research.

CHAPTER III

Schistosomiasis Japonica

Frederik B. Bang, M.D., and
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INTRODUCTION ON LEYTE

Life Cycle of the Parasite

Schistosomiasis japonica, a disease due to a parasitic worm, *Schistosoma japonicum,* is found in large areas of China, in a few foci in Japan, and on four of the larger islands of the Philippines. A strain, apparently of low pathogenicity for man, is present on Formosa, and there is at least one small focus in the Celebes. When the cercariae (larval forms) escape from infected snails into fresh water, as in ricefields, swamps, or ponds, they seek a susceptible host and either penetrate this host or die in from 24 to 48 hours. If the water drains into a river, the cercariae may be swept down the stream and in its course find their susceptible host. After burrowing through the skin, and migrating through the bloodstream and the lungs, they lodge at a later stage of development in the liver. By crawling down the portal venous system, they arrive at the branches of the vessels leading from the large intestine or rectum. After fertilization of the female by the male which carries her in a groove of his body, the female deposits clumps of eggs within the terminal branches of the vessels or in the liver. The embryo develops to a miracidium inside the eggshell. If this egg works its way through the intestinal mucosa, it is extruded in the feces and the miracidium hatches. The miracidium penetrates susceptible snails (if available) and in several weeks develops into a cystlike stage which has within it many cercariae. Thus, an increase in eggs takes place in the definitive host (man, dog, or other appropriate animal), and an increase in the cercariae occurs within the snail.[1]

Recognition, Incidence, Epidemiology

Before World War II, American experience with acute schistosomiasis japonica was limited. Most knowledge of the disease had been derived from

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[1] (1) Faust, E. C., and Meleney, H. E.: Studies on Schistosomiasis Japonica. Am. J. Hyg. Monographic Series, No. 3, 1924. (2) Faust, E. C.: Schistosomiasis Japonica: Its Development and Recognition. Ann. Int. Med. 25: 585–600, October 1946. (3) War Department Technical Bulletin (TB MED) 167, June 1945.

chronic infections in native populations living in endemic areas and from occasional acute outbreaks among small numbers of foreigners visiting or resident in these areas.[2]

When the campaign to recapture the Philippine Islands was planned, it was known that schistosomiasis japonica was endemic in the eastern part of Leyte Island, but its intensity and potential danger were not generally realized. A number of preventive and educational measures were undertaken, as described in detail elsewhere,[3] and, among the officers of many of the hospital units that followed up the invasion, there was some academic discussion of the disease and the possibility of encountering it. Nevertheless, the picture left in the minds of many was hazy.

It is not surprising, therefore, that schistosomiasis japonica burst very suddenly upon a relatively uninformed Medical Department early in the Leyte campaign, in December 1944. The invasion of Leyte had occurred on 20 October 1944. During the invasion, many soldiers had frequent contact with fresh water. Combat troops, patrols, and engineers occupied in building bridges and airports and in repairing roads were frequently in freshwater swamps and streams for short or long periods of time. The value of protective clothing was not appreciated. The troops were inadequately informed concerning the dangers of contact with fresh water, and, when actual fighting died down, many soldiers bathed, washed clothes and vehicles, and swam in infested waters.

Late in November and during December, U.S. soldiers were admitted to hospitals with symptoms that were sometimes suspected as being due to schistosomiasis, but for the most part the disease was not recognized. Ova of *S. japonicum* were first found in stools of a soldier on Leyte Island, on 30 December 1944, by Lt. Walter L. Barksdale, SnC, who was on detached service with the 36th Evacuation Hospital from the 19th Medical General Laboratory, Hollandia, New Guinea. The patient was under the care of Capt. David P. Gage, MC, on temporary duty with the 36th Evacuation Hospital from the 49th General Hospital, who had suspected the diagnosis and had encouraged a search for the ova. It is of interest that on 28 December 1944 in the 132d General Hospital on Biak Island the diagnosis of schistosomiasis had also been made from a liver biopsy by Capt. Morris Goldberg, MC. The patient was a soldier who had been evacuated from Leyte with unexplained fever and marked enlargement and tenderness of the liver.

On Leyte during the last week in December 1944, at least 16 patients who were subsequently found to have schistosomiasis were admitted to hospitals. Most of these patients came from two organizations—the 51st Portable Surgical Hospital and the 50th Engineer Combat Battalion. During the months of January and February 1945, slightly more than 300 additional

[2] Egan, C. H.: Outbreak of Schistosomiasis Japonica. J. Roy. Nav. M. Serv. 22: 6–18, January 1936.

[3] Ferguson, M. S., Graham, O. H., Bang, F. B., and Hairston, N. G.: Studies on Schistosomiasis Japonica. V. Protection Experiments Against Schistosomiasis Japonica. Am. J. Hyg. 44: 367–378, November 1946.

cases of schistosomiasis were diagnosed in hospitals on Leyte.[4] These soldiers were from all types of units but combat troops, engineers, and artillerymen predominated.

The occurrence of schistosomiasis in the 50th Engineer Combat Battalion provided a unique opportunity, which was taken by Lt. Col. Ralph R. Sullivan, MC, and Capt. Malcolm S. Ferguson, SnC,[5] to study the epidemiology of the disease. This battalion, numbering 534 soldiers, was employed to a large extent in building bridges, but the occupations and opportunities for exposure varied from company to company and among the different platoons. The incidence of cases in the battalion was thoroughly investigated and correlated with the battalion's job roster to determine the amount of exposure to fresh surface water of the individual companies, platoons, and personnel. A paragraph of this paper may be quoted here:

The attack rate for the battalion was 19.6 percent (102 cases as of 31 May 1945) which may be compared with an estimated XXIV Corps rate of 0.73 percent. The rates increase to 27 and 33 percent respectively as B and C companies, engaged in bridge construction, are considered separately. Moreover, the attack rate increases to the range of 41–53 percent as attention is focused on the specific platoons engaged in bridge construction. Finally as the rates are computed for the water-exposed bridge-workers themselves, these range from 71–89 percent in the various platoons of B and C Companies. Actually in dealing with the water-exposed bridge-workers it becomes a matter of trying to explain why 100 percent of them were not infected. Since a number were unfortunately not hospitalized or were not diagnosed because typical ova could not be demonstrated, the possibility of 100 percent infection in this group cannot be eliminated.

Another interesting, circumscribed episode of infection occurred among men of the 51st Portable Surgical Hospital. On 16 November 1945, nine members of this unit, including two medical officers, left their bivouac at Dulag for Abuyog to obtain medical supplies. As a bridge over a stream later recognized as infested with cercariae of S. japonicum was under construction, they could proceed no further and decided upon a swim. It is worthy of note that the medical officers commented before entering the water on the possibility of contracting schistosomiasis but only jokingly, and they decided to risk it. The stream in question is slow moving, and these officers were under the impression that the danger in moving water was minimal. Two officers and six enlisted men went in for approximately 30 minutes; one enlisted man did not enter the water. In the eight who were in the water, symptoms of schistosomiasis developed 4 to 5 weeks later; the one who remained on the bank escaped. No other cases of schistosomiasis developed among personnel of the 51st Portable Surgical Hospital. No snails (Oncomelania quadrasi) were found in this area, but higher up the stream snails were found.

Another noncombat unit, in which many became infected with S. japonicum, was the 118th General Hospital, Tolosa, Leyte. Although the

[4] Essential Technical Medical Data, U.S. Army Forces, Far East, for January and February 1945.

[5] Sullivan, R. R., and Ferguson, M. S.: Studies on Schistosomiasis Japonica. III. An Epidemiological Study of Schistosomiasis Japonica. Am. J. Hyg. 44: 324–347, November 1946.

medical officers of this unit were aware of the existence of schistosomiasis on Leyte, they had no idea of the very real danger of infection from streams in the immediate vicinity of the hospital. Surveys of the area in question had been made for snails, and when none were found an unjustified feeling of confidence in the freedom of the water from cercariae pervaded the unit. The stream is one which runs between Tanuan to the north and Tolosa to the south. Of a medical detachment consisting of approximately 500 enlisted men, 164 admitted contact with this fresh water or with swamps draining into it. By 30 April 1945, 75 of these men had been found to have schistosomiasis by the demonstration of ova in their stools. Others may have been found to have the disease at a later date, or may have remained undiagnosed.

Hospital admissions on Leyte Island, for the period January–May 1945, due to schistosomiasis were listed as follows: [6]

	Number of cases
January	69
February	305
March	313
April	197
May	78
Total	962

A breakdown of a random 575 of these cases shows the occurrence by various types of units to be as follows:

Unit:

	Number of cases
Infantry	189
Engineer	203
Field Artillery	54
Antiaircraft	61
Cavalry and reconnaissance	10
Medical	12
Quartermaster	4
Signal	15
Tank	10
Ordnance	12
Chemical	4
Special Service	1

By February 1946, a total of approximately 1,300 cases of schistosomiasis japonica had been diagnosed in American troops infected on Leyte Island. Comparatively few cases were diagnosed on Leyte after the last of May 1945, but other cases were found, as follows:

1. Among units that had been exposed to infested water and had moved on to more advanced bases before the onset of symptoms. An example [7] of this is a survey of an engineer battalion, moved from Leyte to Okinawa, in

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[6] Essential Technical Medical Data, U.S. Army Forces, Pacific, for July 1945.

[7] Essential Technical Medical Data, U.S. Army Forces, Pacific, for September 1945. Appendix E thereto.

which 19 of 206 men examined were found to have ova of *S. japonicum* in their feces. Of these patients, 12 gave a history of symptoms. They had all been away from Leyte approximately 4 months at the time of the survey.

2. Among soldiers evacuated from Leyte through medical channels for diseases other than schistosomiasis.

3. Among personnel who had been infected immediately before returning home on rotation and whose symptoms first occurred either in transit or in the United States.

Disposition of Patients Infected on Leyte

As has been indicated, the theater was not fully prepared to handle efficiently a sudden outbreak of acute schistosomiasis japonica among American troops on Leyte. At first, the criteria for diagnosis, the method of treatment, and the final disposition of these cases were somewhat haphazard and were decided for the most part by individual hospitals. Some patients with schistosomiasis were evacuated as soon as the diagnosis was made. Others were treated and then evacuated, while still others were treated and held for observation.

Finally, a disposition policy, based on suggestions from the Surgeon General's Office, was announced,[8] as follows:

Seriously ill cases and those with present evidence of involvement of the central nervous system should be evacuated to the United States without delay. Other patients who after a course of treatment have persistent clinical signs or positive laboratory findings should also be evacuated. Mild cases which appear to have been cured and have regained their previous state of health may be returned to duty where they can be given periodic examinations of their general conditions and of the blood and stool specimens in accordance with instructions contained in letter from Headquarters, USAFFE, 5 March 1945, FEMD 710, Subject: Aftercare of Patients with Schistosomiasis Japonica.

The Surgeon General, in a letter to the Theater Surgeon, USAFFE (U.S. Army Forces, Far East), dated 26 March 1945, had suggested that all patients in whom a diagnosis of schistosomiasis japonica had been made be evacuated to the United States, after a course of treatment, for further observation and treatment in the centers designated for the care of tropical diseases—Moore General Hospital, Swannanoa, N.C., and Harmon General Hospital, Longview, Tex. This stand was taken by The Surgeon General because it was known that followup of these patients was both important and time consuming (by many months) and that treatment in many cases would have to be repeated. It was thought that the number of patients who would have to be evacuated for this cause was not large enough to affect the military strength significantly.

The theater surgeon replied to this letter by endorsement, dated 14 April 1945, reiterating the policy of retaining in the theater mild cases for followup. Many difficulties, however, were encountered both in administra-

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[8] Technical Memorandum No. 5, Office of the Theater Surgeon, U.S. Army Forces, Far East, 31 Mar. 1945.

tion and in clinical evaluation to determine which patients to keep and which to send home. For this reason, in a letter to section and base surgeons dated at Headquarters, USAFWESPAC (U.S. Army Forces, Western Pacific), 18 July 1945, the theater surgeon directed that all patients with a diagnosis of schistosomiasis japonica be evacuated to the Zone of Interior. It was emphasized in this letter that the period of treatment and observation in the theater should not exceed 120 days and that any soldiers with schistosomiasis, who had already been sent to limited duty under previously existing directives, should be rehospitalized and evacuated to the United States.

Actually, after February 1945, very few patients ill with schistosomiasis were seen.[9] The majority admitted to hospitals thereafter had mild or asymptomatic cases, diagnosed by routine examinations of stools during unit surveys or during hospitalization for other causes.

Postscript from Mindanao

In the early part of December 1945, it was brought to the attention of the Office of The Surgeon General, by the Walter Reed General Hospital, Washington, D.C., that the chief of the Tropical Disease Section at that hospital, Capt. Joseph H. Burchenal, MC, had made a definite diagnosis of schistosomiasis japonica in five soldiers whose only possible common source of infection had been at the Davao Penal Colony, 51 kilometers north-northeast of Davao, Mindanao, Philippine Islands. Actual exposure to infection was believed to have occurred in the Mactan ricefields, 8 kilometers east of the penal colony. These soldiers had been prisoners of war, following the surrender of the Philippine Islands to the Japanese. Some 600 soldiers and sailors were reported by officers imprisoned there to have survived to return to the United States. Of these, it was possible to follow up approximately 50, all of whom were given thorough tests for schistosomiasis, including examinations of the stools. The diagnosis was made in approximately 30 of them. It is possible that other individuals among these 600 men had schistosomiasis which remained undiagnosed.

THE DISEASE PICTURE

The course of schistosomiasis japonica in all three of its stages has been discussed in textbooks of tropical medicine. A full description of the early manifestations of the disease is justified here, however, by the extensive experience with American troops infected during the Leyte campaign, affording an unusual opportunity to make numerous observations on the early phase of the disease. Hitherto, the repeatedly infected, chronically ill populations of endemic regions were the principal subjects available for

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[9] See footnote 6, p. 94.

large-scale study, with, on occasion, much smaller groups of Americans and Europeans exposed to the same environment.[10]

As the three stages into which it is customary to divide the course of the disease are continuous, the clinical phenomena attributed to them usually overlap. The first stage includes the period from the penetration of the body by the cercariae to the settling of the paired worms in the mesenteric venules. The second stage is initiated when eggs are deposited by the female worms in the small vessels of the intestinal wall, the liver, or ocasionally elsewhere. Allergic manifestations are common at this time. The third stage is characterized by proliferation and repair of damaged tissue and by continued heavy deposition of eggs. The present review will be largely concerned with the second stage, when the acute manifestations occur.

It should be reemphasized that this division into stages is purely for the sake of convenience. Experience with American troops with acute schistosomiasis japonica on Leyte showed that, in clinically severe and moderately severe cases, the onset of symptoms was directly associated with the maturation of worms and the deposition of ova. In some clinically mild cases, the onset of symptoms was noted shortly after the ova had been found in the stools and, in some cases, diagnosed only by the demonstration of ova in the stools, maturation of worms and deposition of ova caused no symptoms.[11] It seems probable that the severity of symptoms is a measure of the severity of the infection.

Billings and his associates, in their clinical study of 337 cases of acute schistosomiasis japonica in American troops, including a detailed analysis of 75 of them, discussed at length the interval of time between exposure to infection and the occurrence of symptoms. In 12 cases in which the exact time of the only exposure to infection was known, symptoms first occurred from 26 to 58 days after exposure, an average of 42 days. In the remaining 63 cases, it was more difficult to estimate this latent period because the time of exposure varied from several days to several weeks, and penetration of the skin by cercariae could have occurred on any one or all of the days on which the individual was in contact with fresh water. However, even when contact with infested water covered a period up to 14 days, the latent period was fairly uniform. In 14 of the 75 cases analyzed in detail, there was a close correlation between the onset of symptoms and the appearance of ova in the stools, and there was definite indication that the infection was asymptomatic during the period of development of the schistosomes.

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[10] See footnote 1 (1) and (2), p. 91.

[11] Billings, F. T., Winkenwerder, W. L., and Hunninen, A. V.: Studies on Acute Schistosomiasis in Philippine Islands: Clinical Study of 337 Cases With Preliminary Report on Results of Treatment With Fuadin in 110 Cases. Bull. Johns Hopkins Hosp. 78: 21–56, January 1946.

SYMPTOMS, PHYSICAL FINDINGS, AND
EARLY COURSE

The manifestations and early course of the acute phase of the disease as it appeared among American troops who took part in the invasion of Leyte Island are described in the study by Billings and his associates and in several other papers.[12]

Symptoms

"Swimmers' itch," symptomatically the first possible indication, occurs very soon after exposure to water infested with cercariae. Its incidence is apparently highly variable. On Leyte, three groups [13] of patients were carefully questioned about itching immediately after contact with fresh water, and the incidence varied as follows: 1 in 42, 4 in 41, and 9 in 75. Thus, it occurred in 8.8 percent of these 158 patients. The extensive recent work on swimmers' itch, which is due to schistosomes, usually in newly infected men in whom sensitization plays a large role, should be related to these data.

Following an asymptomatic latent period during which the parasite developed to adulthood, the onset of symptoms was usually abrupt with headache, chills, feverishness, cough, urticaria, aches, and anorexia of varying severity. In some cases, the onset was insidious, and the symptoms in some of these remained mild throughout the symptomatic phase and in others were intensified after several days. In a few instances, the onset was not only abrupt but severe or fulminating in character. Lastly, the disease sometimes had an asymptomatic course; such cases were detected through group surveys. On the basis of the intensity and severity of symptoms and the height of the temperature and the duration of the fever, the series of 337 cases cited (p. 97) were divided into four groups, as follows: Severe, 21 cases; moderately severe, 123 cases; mild, 168 cases; and asymptomatic, 25 cases. The incidence of the chief symptoms as shown in table 13, however, is based on 75 cases subjected to detailed analysis. It should be stated that this classification is made on clinical grounds only, and it is not known whether the severity of symptoms is necessarily correlated with the degree of infection.

Moderately severe cases.—Since these cases present the most common symptomatology, they are discussed first. The symptoms usually began suddenly with fever, chills, headache, generalized aches and pains, soreness and stiffness of the neck, discomfort in the upper part of the abdomen accompanied by anorexia, urticaria, and an irritating dry hacking cough, all or

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[12] (1) Thomas, H. M., and Gage, D. P.: Symptomatology of Early Schistosomiasis Japonica. Bull. U.S. Army M. Dept. 4:197–202, August 1945. (2) Johnson, A. S., Jr., and Berry, M. G.: Asiatic Schistosomiasis; Clinical Features, Sigmoidoscopic Picture and Treatment of Early Infections. War Med. 8: 156–162, September 1945. (3) Thomas, H. M., Bracken, M. M., and Bang, F. B.: Clinical and Pathological Picture of Early Acute Schistosomiasis Japonica. Tr. A. Am. Physicians 59: 75–81, 1946.

[13] See footnote 11, p. 97, and footnote 12(1) and (2).

some of which lasted from 1 to 8 weeks. The clinical course of schistosomiasis, acute, moderately severe, is shown in figures 33 and 34.

TABLE 13.—*Incidence of symptoms in 75 patients with acute schistosomiasis japonica*

Symptoms	Patients affected	
	Number	Percent
Fever	75	100.0
Headache	69	92.0
Weight loss	69	92.0
Malaise	67	89.3
Anorexia	66	88.0
Pain in upper quadrant of abdomen	60	80.0
Stiff neck	57	67.0
Abdominal cramps	52	65.0
Cough	48	64.0
Generalized aches, backaches, and arthralgia	45	60.0
Urticaria and angioneurotic edema	39	52.0
Chills	37	49.0
Diarrhea	21	28.0
Constipation	18	24.0
Pain in chest	17	22.0
Itching (after exposure to infested water)	9	12.0
Testicular aching	9	12.0
Neurologic complications	7	9.3
Nausea and vomiting	6	8.0
Asthma	6	8.0

In 14 cases, 8 of which presented the shorter latent periods, the acute febrile illness, considered as ushering in the symptomatic phase of the disease, subsided partially or entirely in from 2 to 8 days; thereafter, the symptoms persisted in mild form, or remained completely in abeyance for a week or two, and then recurred, gradually or sharply. This initial acute illness often suggested dengue, atypical forms of which occurred on Leyte. Typical skin eruptions of dengue were never noted in these cases, however, in which the acute febrile period may represent the host reaction to the initial dissemination of the ova of S. *japonicum*.

The first chief complaints in many cases were fever, chills, headache, cough, and urticaria with or without angioneurotic edema; in several cases, the first manifestations were limited to this type of skin lesion. Later, within a few days to 2 weeks, the urticaria and cough subsided in most cases, but pain or discomfort in the upper quadrants of the abdomen, anorexia, loss of weight, headache, fatigue toward evening, stiff neck, and varied myalgic and arthralgic pains persisted, though fluctuating from day to day.

The febrile stage lasted from 1 to 8 weeks; the fever was remittent and of the saw-toothed type, with the temperature rising sharply to 102° to
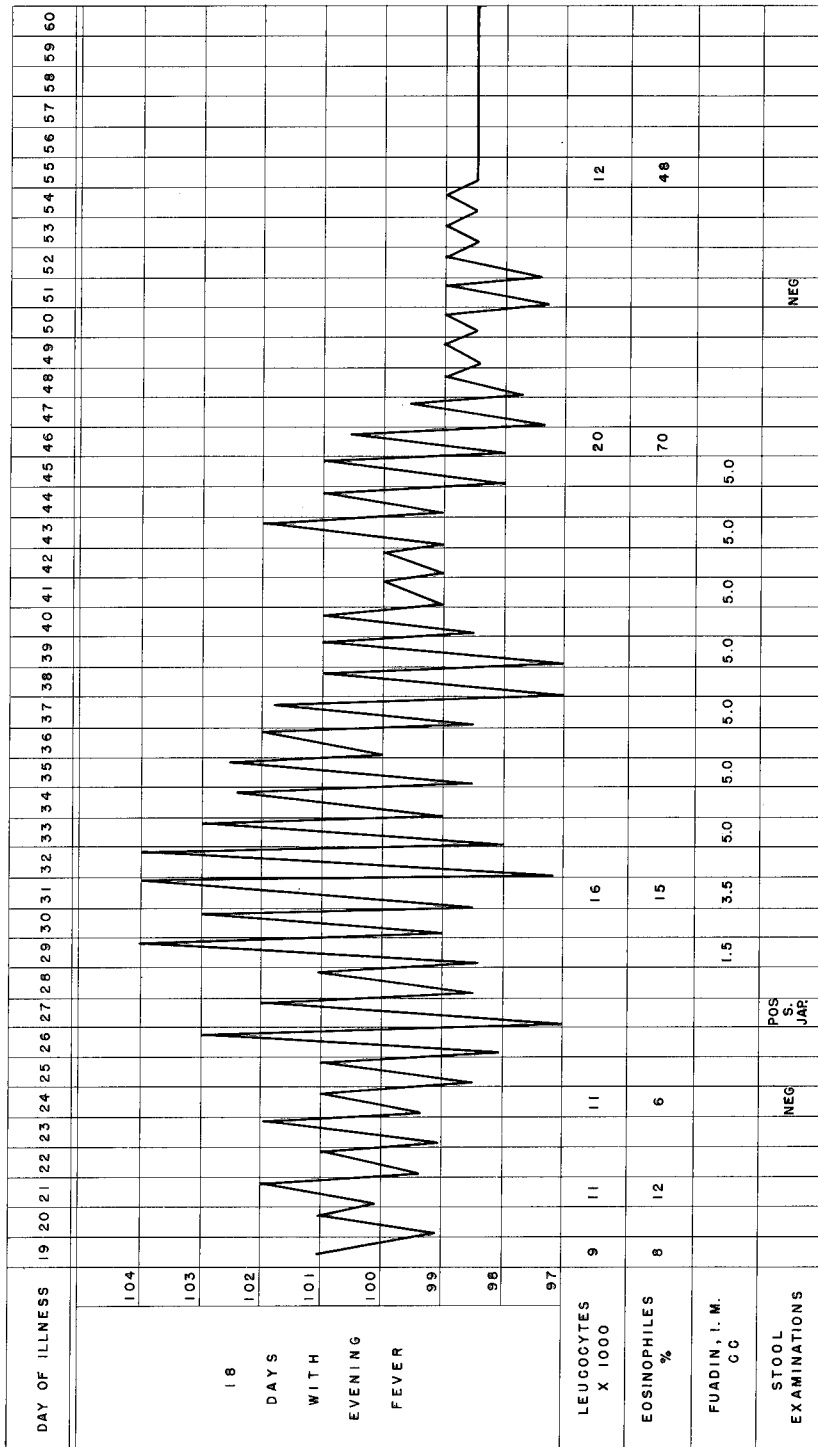
FIGURE 33.—Clinical course of schistosomiasis japonica, acute, moderately severe, in 20-year-old white male. This patient was admitted to hospital on 25 January 1945. Trivalent antimony compounds, at that time, were being given in amounts inadequate for most effective treatment. Patient, asymptomatic on 1 March 1945, subsequently relapsed.
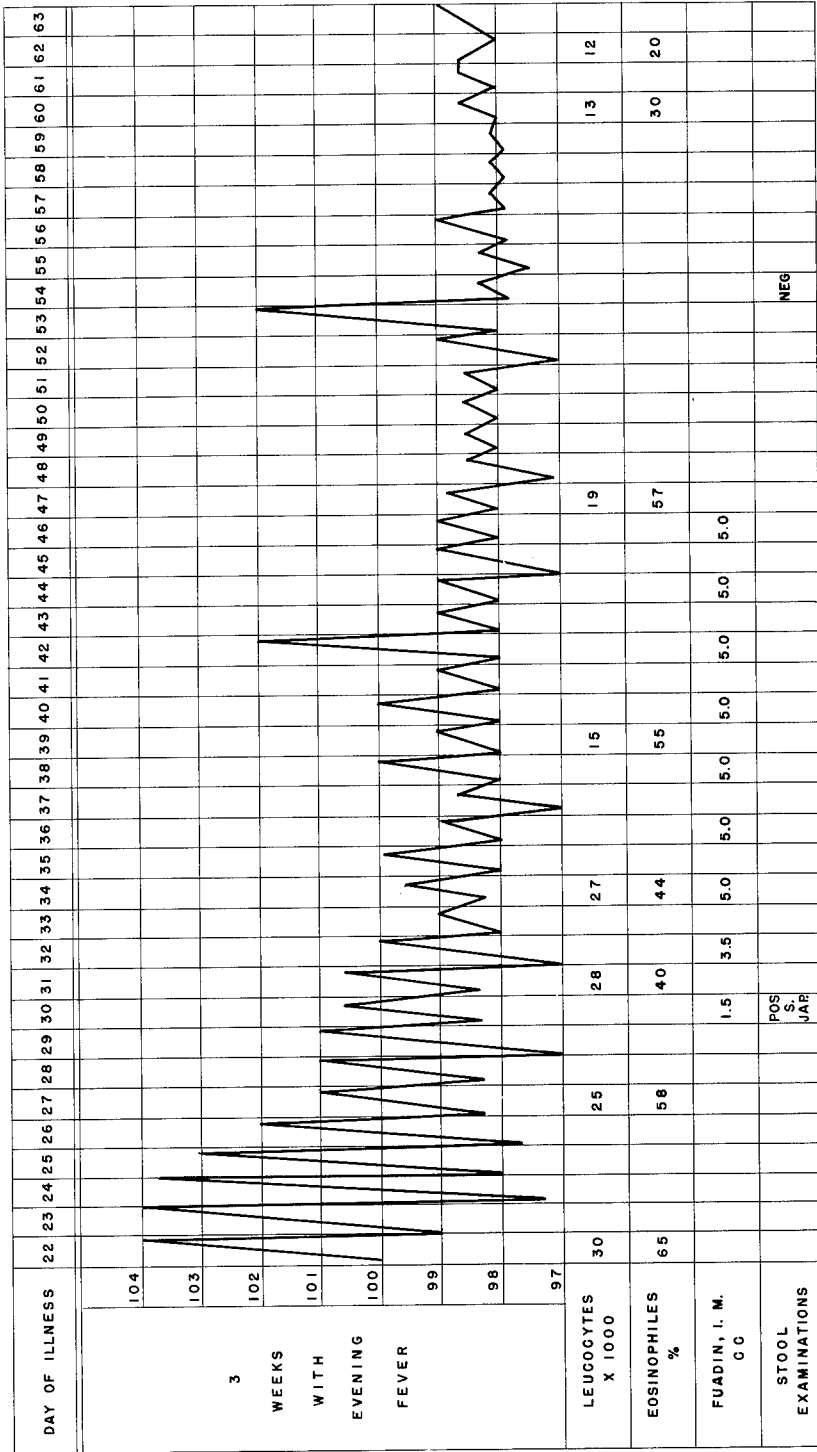
FIGURE 34.—Clinical course of schistosomiasis japonica, acute, moderately severe, in 22-year-old white male. This patient was admitted to hospital on 6 January 1945. Treated with small amounts of Fuadin, the patient made rapid progress and felt well when evacuated on 18 February 1945.

104° F. in the evening and, with rare exceptions, returning to normal or below normal in the morning. Likewise, there was diurnal variation in the intensity of symptoms; the majority of patients felt better or "tolerably" well in the morning but worse in the afternoon and evening, when all symptoms were characteristically intensified.

Urticaria or angioneurotic edema, which was noted in 52 percent of the patients, varied from an occasional small and fleeting wheal to lesions of tremendous size. The lesions were indolent and persistent. They were not strikingly responsive to adrenalin. Swelling of the posterior half of the tongue was noted in one patient, but edema of the fauces and larynx was not seen.

A very common symptom was soreness and stiffness of the neck. In this series of 75 patients, 57 had this complaint and in some it was striking. Usually, it developed suddenly and lasted from 24 to 48 hours, then subsided only to recur in several days' time. In one patient, the head was held rigid, incapable of any movement, for a period of 2 weeks. Lateral rotation was especially restricted and, less commonly, flexion. This symptom is probably not due to involvement of the meninges, but is more likely myalgic in origin, as soreness of the trapezius and sternocleidomastoid muscles was elicited on palpation. Meningitis was occasionally suspected, but examinations of the spinal fluid revealed no abnormalities.

In association with anorexia and discomfort in the upper quadrants of the abdomen, abdominal cramps were frequent, but diarrhea occurred in only 21 patients (28 percent), and then it was not clear whether it was due to the disease or to an intercurrent infection, as attacks of diarrhea were fairly common among persons on Leyte. More frequently, the bowel movements were normal or were constipated, sometimes severely so as the disease progressed. Blood in the stools was found rarely and only in the occult form. Anorexia and loss of weight, which in cases of long standing may amount to as much as 40 pounds, were prominent features.

A nonproductive cough was sometimes accompanied by moist rales or scattered areas of consolidation, especially at the bases of the lungs, or by diffuse signs characteristic of acute asthmatic bronchitis, which occasionally dominated the clinical picture at first. In some cases of the latter type, the true nature of the disease was not suspected until more characteristic symptoms appeared.

Alopecia, which was noted by Hunt[14] in several of a series of 18 patients who contracted the disease on the adjacent island of Samar, was not seen in this series. Lesions of the skin in which ova of *S. japonicum* were demonstrated (fig. 35) were reported in one case of the disease among American troops on Leyte.[15]

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[14] Hunt, A. R.: Schistosomiasis in Naval Personnel, a Report of 16 Cases. U.S. Nav. M. Bull. 45: 407–419, September 1945.

[15] Fishbon, H. M.: Case in Which Eggs of *Schistosoma japonicum* Were Demonstrated in Multiple Lesions. Am. J. Trop. Med. 26: 319–326, May 1946.

Mild cases.—The symptoms and physical findings in this form of the disease were often minimal. In many cases, patients complained toward evening of occasional cough, slight feverishness, malaise, headache, fatigability, and anorexia. Occasionally, they had mild discomfort in the upper quadrants of the abdomen, transitory scattered aches and pains, and at times they complained of a "crick" in the neck. They did not seek medical
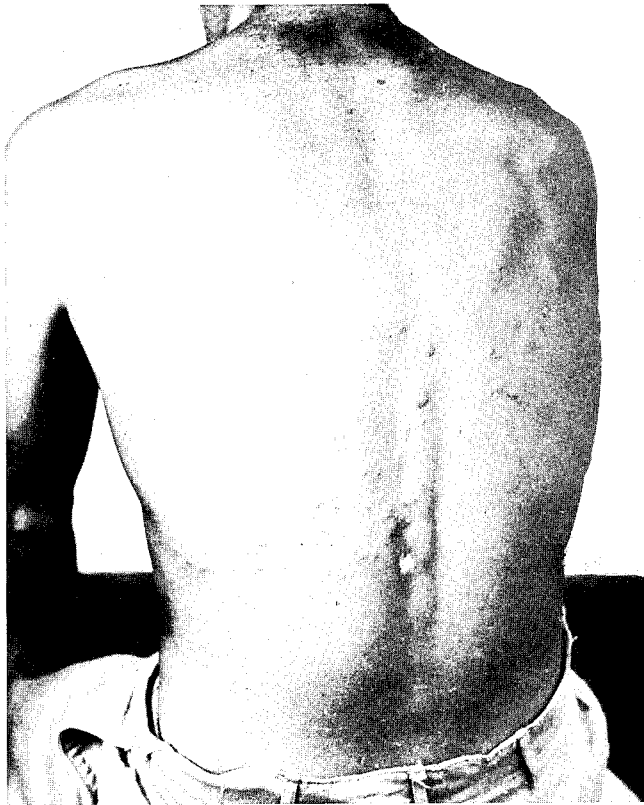

FIGURE 35.—Schistosome dermatitis—papular eruption on back.

attention for days or even weeks, but attributed their symptoms merely to the unaccustomed tropical environment. When a patient reported to sick call in the morning, as a rule his temperature was normal and he felt well, so that the infection was easily overlooked. In fact, such vague and variable symptoms led to the diagnosis of psychoneurosis in several patients before schistosomiasis was discovered.

Physical examination in many cases of this type revealed loss of weight, enlargement of the posterior cervical lymph nodes, tenderness in the epigastrium and right upper quadrant of the abdomen, and a slightly en-
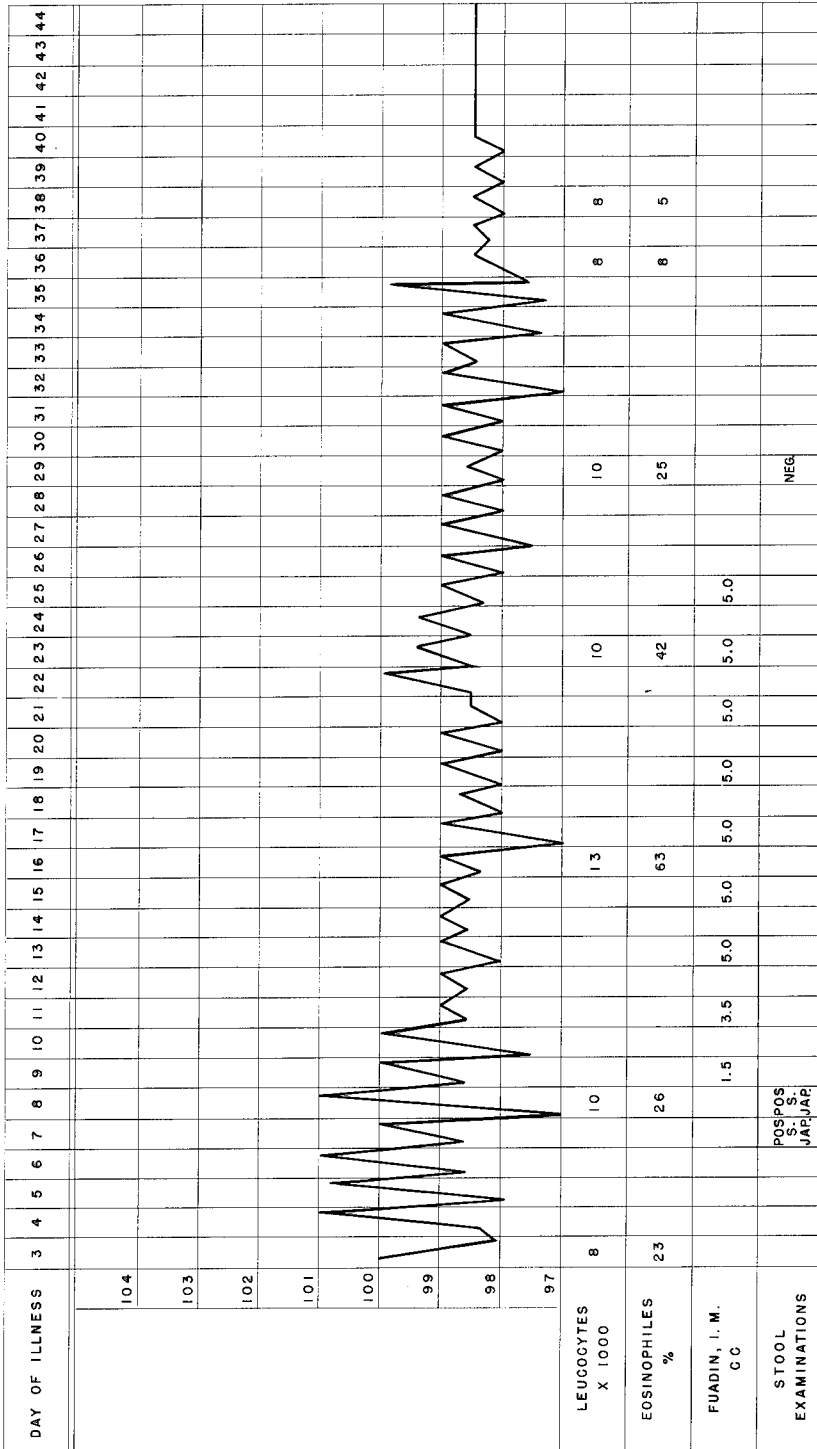
FIGURE 36.—Clinical course of schistosomiasis japonica, mild, in 29-year-old white male. This patient was admitted to hospital on 12 January 1945 and was evacuated on 18 February 1945. Treated with small amounts of Fuadin, the patient improved rapidly.
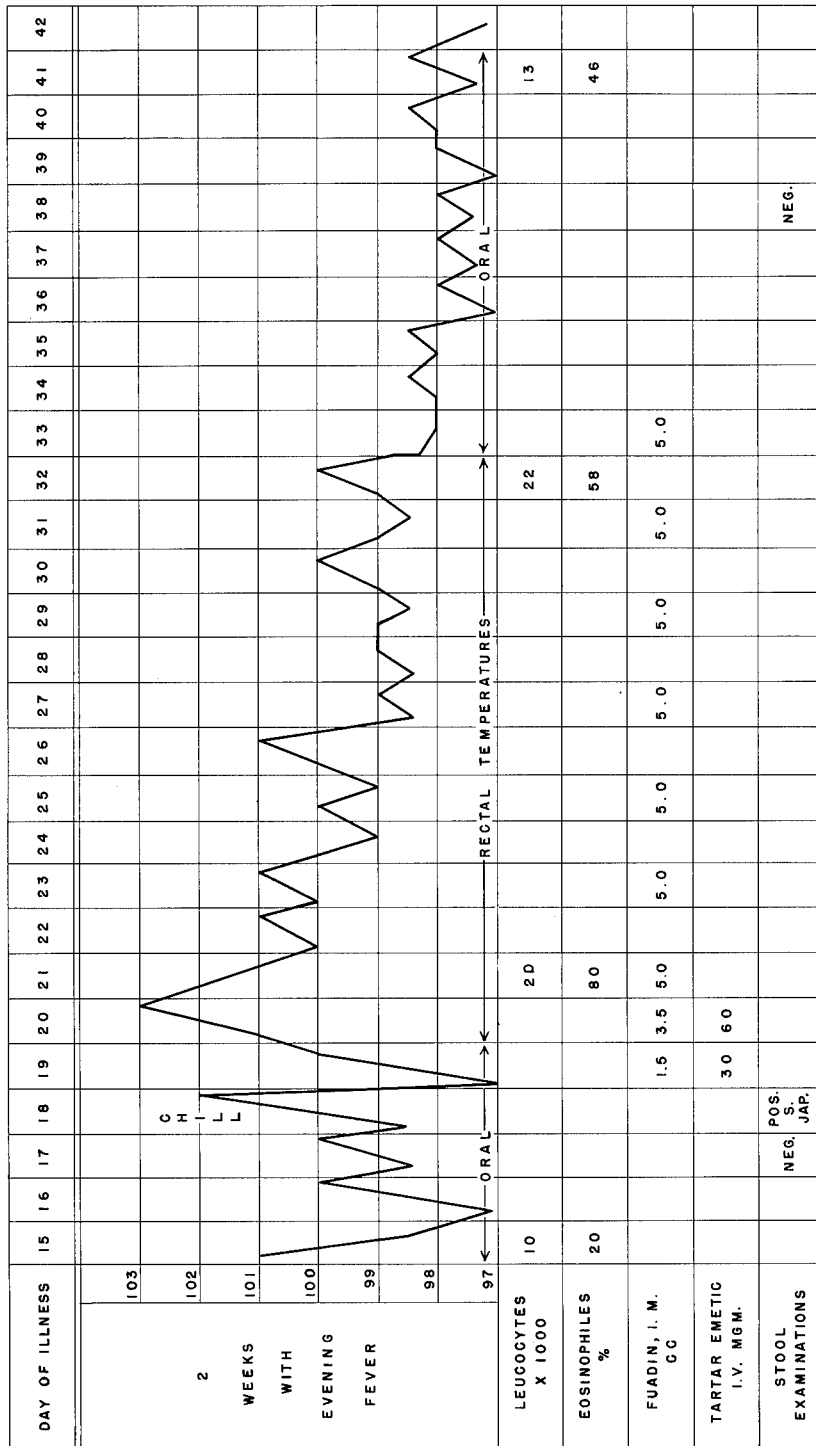
FIGURE 37.—Clinical course of schistosomiasis japonica, acute, severe, with involvement of the central nervous system, in a 21-year-old white male. This patient was admitted to hospital on 3 February 1945 and treated with Fuadin and tartar emetic to 21 February. Two months later, eosinophilia was still found, but repeated stool examinations were negative, and peripheral neurologic signs were minimal. Patient was evacuated to the Zone of Interior on 11 April 1945.

larged liver. The spleen was seldom palpable. Figure 36 illustrates such a mild case with a short episode of low grade fever and minimal abnormal physical findings.

Severe cases.—In 21 of the series of 337 patients, the symptoms and the clinical course were sufficiently severe to justify this classification. Figure 37 illustrates the clinical course of the disease in one patient of this group. The patients were often prostrated and semicomatose; the temperature was high and spiking; and the headaches, generalized aches and pains, cough, and anorexia were severe. Enlargement and tenderness of the liver were more pronounced, and the spleen was uniformly enlarged. In a few patients in this series, mild anemia was observed. Several in the group of severe cases had neurologic manifestations which are described later (p. 108).

Asymptomatic cases.—In 25 patients of the 337 studied, the disease developed without symptoms; no such cases were included among the 75 studied in detail. Schistosomiasis was suspected in this group because of known exposure to infested water or because of the discovery of eosinophilia, either during a routine survey of military units in which other members were known to have schistosomiasis or during hospitalization for another disease. The incidence of this type of the disease among troops who were stationed in endemic areas was impossible to estimate and could only be determined by extensive surveys of such units.

Physical Findings

Table 14 presents a list of the most frequent physical findings in the 75 cases of acute schistosomiasis japonica studied in detail. The discussion will be limited to the patients with schistosomiasis of moderate severity. These patients usually appeared thin, the degree depending, however, on the duration of symptoms. They were sallow and appeared chronically rather than acutely ill. In the absence of urticaria, the skin was normal. Enlargement of the posterior cervical lymph nodes, and less often a mild general enlargement of all the lymph nodes, was found. The mucous membranes in some patients were pale. The eyes, ears, nose, mouth, and throat were normal. Since cough was a frequent complaint, one might have expected changes in the lungs, but in most patients abnormal pulmonary signs were not elicited. Only five patients in this series had objective pulmonary changes. These were seen in roentgenograms as scattered areas of infiltration and patchy consolidation at the base of one or the other lung. In most instances, the abnormal findings disappeared after 1 or 2 weeks. In one severe case observed on Leyte, typical miliary seeding (pseudotubercles) of the lungs was demonstrated roentgenographically.

The heart and blood pressure were normal; the pulse varied directly with the temperature. The abdomen was usually flat but occasionally some-

TABLE 14.—*Incidence of important physical findings in 75 patients with acute schistosomiasis japonica*

Physical findings	Patients affected	
	Number	Percent
Enlargement or tenderness of liver	69	92
Tenderness of epigastric region	63	84
Enlargement of spleen	51	67
Enlargement of posterior cervical lymph nodes	27	36
General enlargement of lymph nodes	25	33
Objective pulmonary changes	5	6
Objective neurologic changes	3	4

what distended. There was often mild generalized tenderness, usually limited to the upper quadrants of the abdomen and especially to the midepigastrium where tenderness to palpation and percussion was sometimes exquisite. The liver was tender and palpably enlarged in 92 percent of the 75 patients. It extended as much as 5 cm. below the costal margin in some instances, but in many patients the enlargement was demonstrable only as a widening of the area of dullness. Even in these patients, there was tenderness to deep palpation below the right costal margin and to percussion over the lower costal area. The spleen was enlarged 67 percent. It occasionally extended as much as 4 cm. below the costal margin, but in many instances enlargement was indicated only by increased dullness over the splenic area. The spleen was slightly or not at all tender. Although testicular pain was complained of by several patients, the genitalia appeared normal.

Sigmoidoscopic Examination

The important sigmoidoscopic studies by Johnson and Berry[16] of patients with acute schistosomiasis japonica are a significant contribution to observation of the disease. They examined the lower part of the large intestine of 63 patients. The following excerpt from their report describes their findings:

* * * characteristic multiple, firm, yellow nodules, 1 to 3 mm. in diameter, occurring in clusters of from 3 to 25 were seen beneath the mucosa. They were most abundant at the rectosigmoid junction, but were also present above in the lower sigmoid. In many cases the nodules were found 4 to 5 cm. below the rectosigmoid junction. There was no ulceration, and definite relationship to the visible blood vessels was not apparent. The mucosa showed no inflammatory or vascular changes. On biopsy of these lesions many ova were present in the tissue removed. All were beneath the mucosa. Some were not as mature as the ova seen in stool examination but could be identified easily.

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[16] See footnote 12 (2), p. 98.

Following these observations, the examination of the lower part of the large intestine by means of a sigmoidoscope became a routine procedure in all hospitals caring for patients with schistosomiasis japonica and in the tropical disease centers in the United States. This examination was especially valuable as an aid to definite diagnosis of the disease in cases in which difficulty was encountered in finding ova in the stools. It was also particularly helpful as an aid to determining whether treatment of the disease had been effective. The appearance of characteristic nodules in the intestinal mucosa after a course of treatment was completed was highly suggestive of the persistence of live worms in the portal system. A biopsy of such a nodule in which ova with live miracidia could be demonstrated furnished proof that a cure had not been obtained, and further treatment was instituted.

Later observations enlarged on the findings of Johnson and Berry. At the 118th General Hospital, small ulcerations were demonstrated, scrapings of which yielded ova. At Harmon General Hospital, 300 patients were examined by proctoscope.[17] In only three were lesions demonstrated. These were described as "single, flat, oval, moderately indurated granulomata, 0.5 to 2.0 cm. in their longest diameter. These were 7, 10, and 15 cm., respectively, from the anus. They were well demarcated and the low grade inflammatory appearance did not extend to the surrounding normal mucosa." These lesions were described as bleeding easily with the traumata of the proctoscope, and ova were demonstrated in biopsies of them. In 46 sigmoidoscopic examinations at Moore General Hospital,[18] 33 patients were found "abnormal," but only 1 had a polyp and 1 a small nodule, both containing ova of S. japonicum.

Neurologic Manifestations

During the period from the invasion of Leyte on 20 October 1944 to March 1946, groups of U.S. Army medical officers reported 33 new cases of schistosomiasis japonica of the central nervous system among Americans who were on that island.[19] These and other cases are fully summarized in a review of a large number of patients with neurologic signs and symptoms by Kane and Most.[20] It is possible that other cases of this type appeared

[17] Mason, P. K., Daniels, W. B., Paddock, F. K., and Gordon, H. H.: Schistosomiasis Japonica; Diagnosis and Treatment in American Soldiers. New England J. Med. 235: 179–182, 8 Aug. 1946.

[18] Most, H., Kane, C. A., Lavietes, P. H., Schroeder, E. F., Behm, A., Blum, L., Katzin, B., and Hayman, J. M., Jr.: Schistosomiasis Japonica in American Military Personnel: Clinical Studies of 600 Cases During the First Year After Infection. Am. J. Trop. Med. 30: 239–299, March 1950.

[19] (1) See footnote 11, p. 97, and footnote 12(1), p. 98. (2) Tillman, A. J. B.: Cerebral Manifestations of Schistosomiasis Japonica. Bull. U.S. Army M. Dept. 4: 492, November 1945. (3) Carroll, D. G.: Cerebral Involvement in Schistosomiasis Japonica. Bull. Johns Hopkins Hosp. 78: 219–234, April 1946. (4) Cutler, J. G.: Schistosomiasis of the Central Nervous System. J. Nerv. & Ment. Dis. 104: 425–431, October 1945. (5) Watson, C. W., Murphy, F., and Little, S. C.: Schistosomiasis of the Brain Due to Schistosoma japonicum; Report of Case. Arch. Neurol. & Psychiat. 57: 199–210, February 1947.

[20] Kane, C. A., and Most, H.: Schistosomiasis of the Central Nervous System; Experiences in World War II and Review of the Literature. Arch. Neurol. & Psychiat. 59: 141–183, February 1948.

from time to time as later manifestations of the disease, but certainly they were few, and it may be said that, among almost 1,300 cases of the disease diagnosed, neurologic involvement occurred in approximately 2.5 percent.

Nevertheless, further details and observations relating to the neurologic picture associated with schistosomiasis japonica as it appeared among American troops seem worthy of consideration and discussion. Data from the review of this subject by Kane and Most and from the studies of Billings and his associates have been drawn upon heavily in the preparation of this discussion and description.

Previous workers have well established the fact that the neurologic manifestations are probably due to the presence of ova of *S. japonicum* in the substance of the central nervous system.[21] No new light has been thrown on the subject of how these ova arrive there. Although Shimidzu refers to the fact that a second Japanese investigator, Fujinami, found worms in the cerebral veins of monkeys exposed to a very heavy concentration of cercariae, no reports have been found in which worms have been observed in operative or autopsy material from human brains. This does not preclude the possibility that adult forms may be present in cerebral blood vessels at some distance from the main pathological process incited by the ova. Although some ova may filter through the liver-lung barrier from the portal system and reach the central nervous system, it is difficult to explain the occurrence of "nests" of eggs within the brain by the deposition of eggs in areas other than the cerebral veins. It should be emphasized that the discovery of adult worms in thrombosed veins at post mortem is difficult if the veins are full of blood.

Many of the gross and microscopic findings from localization of these ova in the central nervous system had been described before the experience with the disease in American troops in World War II. Suffice it to say that the ova have now been demonstrated in practically all areas of the brain but seem to have been found in greater abundance in the pia-arachnoid, the cortex, the subcortex, the basal ganglia, the internal capsules, and the chorioid plexuses of the lateral ventricles.

With such a wide distribution of the ova, it is not surprising that, when the central nervous system is involved, the neurologic symptoms and other manifestations are protean.

Clinically, a striking feature of the complication is the suddenness of the onset regardless of whether the neurologic signs and symptoms occur in association with the first acute stage of the disease or as a later manifestation. Kane and Most, analyzing 18 neurologic cases, found that the average interval from the time of first potential exposure to the onset of neurologic manifestations was 14 weeks with a range of from 6 to 36 weeks. The average interval from the time of appearance of the first recognized general

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[21] (1) See footnote 1 (1), p. 91. (2) Shimidzu, K.: Ein Operationsfall von Schistosomiasis cerebi. Arch. f. klin. Chir. 182: 401–407, 1935.

systemic symptoms to the occurrence of signs and symptoms referable to the central nervous system was 5.3 weeks with a range of from 3 days to 24 weeks. The neurologic manifestations were the presenting features of the disease in two of their cases.

The intervals from first exposure to manifest involvement of the central nervous system were as follows:

Time interval (weeks):

	Number of cases
0–5	0
6–10	9
11–15	3
16–20	1
21–25	4
26	1

It is thus apparent that neurologic complications of schistosomiasis may appear as late as 6 months after exposure to the disease, and there is no reason to believe that they may not appear even later, depending on the location of the ova in the brain, the number present, and the rate of development and repression of the inflammatory process.

In addition to the usual indications of infection with *S. japonicum*, patients with involvement of the nervous system may exhibit a variety of other symptoms. Kane and Most tabulated the significant symptoms occurring in their cases of neurologic schistosomiasis (table 15) and discuss the significance of the most outstanding. Although headache was experienced by all the patients on whom they report, they found that for the most part it was either transitory or intermittent in character and of little value in localizing the lesion. In a few of their patients, it was a severe and persistent complaint, and, in three out of four patients on whom an operation was eventually performed for a brain lesion the headache was located over the area where the pathological process was found.

There were disturbances of the sensorium at some time during the course of illness in all of the 18 patients. This varied from momentary periods of confusion resembling petit mal attacks to prolonged periods of unconsciousness lasting hours, especially in those with convulsive seizures. Disorientation and confusion was a striking feature and in six patients lasted as long as 2 weeks. Many of this group of patients were listless and apathetic for several weeks but four showed marked restlessness, at times bordering mania. Of the four patients operated upon, all experienced convulsions of one type or another with coma lasting up to 12 hours. All types of seizures were noted—sensory, motor (Jacksonian, tonic-clonic, adversive, atypical), and psychomotor—and these were associated with a variety of transient sequelae—motor aphasia, cranial nerve and visual field defects, alexia, micropsia, plus pyramidal tract defects usually consisting of hemiparesis or hemiplegia.

TABLE 15.—*Incidence of symptoms in 18 patients with schistosomiasis japonica, involving the central nervous system*

Symptoms	Patients affected	
	Number	Percent
Headache	18	100
Disturbance of sensorium	18	100
Weakness of extremities	18	100
Incontinence	10	55
Visual disturbance	10	55
Speech disturbance	10	55
Apraxia	9	50
Ataxia	7	38
Sensory disturbance	4	22
Tinnitus	3	17
Vertigo	2	11
Deafness	1	5

Visual disturbances were found in 10 of the 18 patients. These disturbances represented cortical involvement of the higher centers of sight, and visual field defects were noted in a few patients who were found at operation to have granulomatous tumors.

Disturbance of the higher speech centers was noted in 10 of the 18 patients. These were usually transitory in nature and varied from slight inability to use the right words or slurring to true motor aphasia.

Weakness in one or more extremity was observed in all 18 patients. The onset of this phenomenon was usually sudden, and the type of paralysis consisted in the different cases of hemiplegia, quadraplegia, hemiparesis, or paralysis of one extremity. In some patients, the paralysis was flaccid; in others, spastic; and, in one, it was mixed, the patient having spastic paralysis of the upper extremities and flaccid paralysis of the lower extremities.

Kane and Most conclude on the basis of the neurologic findings that in practically all their cases there was diffuse encephalitis and involvement of the pyramidal tracts. In several of them, the nuclei of some of the cranial nerves seemed to be involved, and in others there appeared to be changes in the cerebellum. In those patients on whom operations for brain tumor were performed, lesions were chiefly found in the left parietotemporal or occipital lobes.

LABORATORY FINDINGS

Stool Examinations

Final diagnosis of schistosomiasis japonica depended on the demonstration of the characteristic ova of the parasite either in the stools or in the

tissues of the patient. In the great majority of cases seen during the outbreak among American troops on Leyte, ova were found in the stools before a diagnosis was definitely made and treatment begun. It was the general policy both overseas and in the hospitals in the United States to withhold treatment until ova had been demonstrated, except in severe cases requiring immediate treatment. This was considered a sound policy because other parasitic infections were extremely prevalent, and sometimes mimicked acute schistosomiasis. It was thought that in almost every case of schistosomiasis, ova could be demonstrated if enough stools were examined by trained personnel and if routine proctoscopic examinations were made.

The following difficulties were, however, encountered in the demonstration of ova, especially during earlier days of the outbreak:

1. In many cases, especially the mild ones, ova were present in the stool in relatively few numbers. However, in some mild cases, ova were demonstrated in the first stool examined, while in occasional severe cases as many as 15 to 20 stool specimens were examined before ova were found.

2. Many laboratory officers were not familiar with the appearance of the ova of *S. japonicum* in all its stages of development, and confusion arose between identification of vegetable cells and maturing and degenerating ova. Vogel [22] had described the ova of *S. japonicum* in all stages. In addition, a manual based on a series of studies in locally infected dogs was written and illustrated by Lt. N. G. Hairston, reproduced locally, and distributed by the Office of the Surgeon, USAFFE. These publications were of great assistance in the training of laboratory officers. Where immature ova were present in a stool, mature ova could also be found, and it was safer and less likely to be confusing to base a definite diagnosis of the disease on mature ova containing miracidia.

3. The technique used to find ova in stools was tedious and necessitated painstaking and thorough adherence to procedure. Many laboratory officers were not familiar with the best technique, and faced with hundreds of suspected cases the problem of careful stool examinations on all of them was in many instances overwhelming. Varied techniques were employed reflecting the diversity of training and differences of opinion among laboratory officers as to the most efficient method.

It soon became clear that, in addition to the direct examination of any bloody mucous that might be present in the stool, some method of concentrating the eggs from a larger portion of the stool was worthwhile, and a number of techniques were compared. A method originally described by Hunninen [23] was frequently used. Baroody and Most [24] at the Moore General Hospital concluded that among a variety of techniques, including acid ether,

[22] Vogel, H.: Ueber Entwicklung, Lebensdauer und Tod der Eier von Bilharzia japonica im Wirtsgewebe. Deutsche tropenmed. Ztschr. 46: 57–69, 1 Feb. 1942; 81–89, 15 Feb. 1942.

[23] See footnote 11, p. 97.

[24] Baroody, B. J., and Most, H.: Relative Efficiency of Water Centrifugal Sedimentation and Other Methods of Stool Examination for Diagnosis of Schistosomiasis Japonica. J. Lab. & Clin. Med. 31: 815–823, July 1946.

zinc sulphate, brine flotation, and niter centrifugal sedimentation, the last was the best. It has the advantage of simplicity for field usage. However, in general diagnostic laboratories, other techniques have subsequently replaced it, and for the relative advantages of each the standard texts such as the "Clinical Parasitology" by Craig and Faust may be consulted.

Hematological Findings

Leukocytes and eosinophils.—It had been known for some time that leukocytosis and eosinophilia are characteristic of acute schistosomiasis japonica. This was confirmed in the clinical studies of the disease as it occurred among American troops.

In addition, it was found that there was a tendency for the counts to rise as the acute phase of the disease progressed. There appeared to be no constantly direct relationship between the degree of leukocytosis and eosinophilia and the severity of symptoms; rather the counts often fluctuated irregularly from day to day and from week to week. Many mild or asymptomatic cases were found to have leukocytes and eosinophils that remained within normal numerical limits throughout observation of the acute phase.

As intensive treatment was instituted and the acute phase subsided, there was definite evidence that the number of leukocytes and eosinophils declined. At both Moore [25] and Harmon [26] General Hospitals, it was observed that, in the later stages of the disease, the degree of leukocytosis and eosinophilia could in general be used as an indication of whether treatment had been successful. Occasional eosinophilia could not be taken to mean failure of treatment, but persistent eosinophilia was a useful warning indicating that repeated careful search of the stools might reveal the ova of *S. japonicum*. In the final analysis, however, the presence or absence of ova in the stool was the only reliable criterion for evaluation of treatment.

Erythrocytes.—Mild anemia occurred rarely in the acute cases of schistosomiasis japonica seen among American troops. By the time these soldiers reached hospitals in the Zone of Interior, the erythrocytes were normal in number.

Roentgenographic Findings

Significant findings by roentgenogram were limited to the chest. In clinical reports [27] dealing with the acute phase of the disease, it was mentioned that signs of scattered pulmonary infiltrations were demonstrable at the time of physical examination. Abnormalities were visible in roent-

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[25] See footnote 18, p. 108.

[26] (1) Mason, P. K., Daniels, W. B., Paddock, F. K., and Gordon, H. H.: Latent Phases of Asiatic Schistosomiasis. Arch. Int. Med. 78: 662–678, December 1946. (2) See footnote 17, p. 108.

[27] See footnote 12(2) and (3), p. 98, and footnote 22, p. 112.

genograms of the lungs [28] and occurred five times in 75 cases analyzed in detail by Billings and his associates. For the most part, these abnormal findings were present for only a short time, a matter of 1 or 2 weeks, and only in the severe or moderately severe cases.

Tests of Liver Function

Since many of the eggs of *S. japonicum* are scattered into the liver after they have been deposited in the small vessels of the portal system, it would have been of interest to know the effect of this seeding upon that organ. Unfortunately, however, no studies were reported relating to hepatic function in the acute phase of the disease. On the other hand, Lippincott and his associates,[29] at Harmon General Hospital, studied the hepatic function of patients with schistosomiasis japonica who had been evacuated to the United States after the acute phase. In this study, they used several tests including determinations of Bromsulphalein (sulfobromophthalein) retention, galactose tolerance, hippuric acid excretion, icterus index, serum bilirubin, formol-gel reaction, and urinary urobilinogen in serial dilutions. They found that diminution of hepatic function was minimal and were inclined to attribute the abnormal findings to the antimony used in treatment.

Spinal Fluid Examinations

Lumbar punctures and examinations of the spinal fluid were carried out only in those cases in which the central nervous system was apparently damaged. In the acute stage overseas, abnormal findings were limited to an increased cellular content of the fluid in a few cases. In by far the greatest number of examinations, the spinal fluid was normal. The amounts of globulin and protein and the patterns of colloidal gold curves were not reported. There was an increase in the protein and globulin content of the spinal fluid in a few of the neurologic cases studied in the United States, and a midzonal type of reaction to colloidal gold was observed in a very few cases.[30]

PICTURE OF THE DISEASE IN PATIENTS EVACUATED TO ZONE OF INTERIOR

Following diagnosis and preliminary treatment in oversea hospitals, patients with schistosomiasis japonica were evacuated to the Zone of In-

[28] Weinberg, H. B., and Tillinghast, A. J.: Pulmonary Manifestations of Schistosomiasis Caused by *Schistosoma japonicum*. Am. J. Trop. Med. 26: 801–809, November 1946.

[29] Lippincott, S. W., Paddock, F. K., Rhees, M. C., Hesselbrok, W. B., and Ellerbrook, L. D.: Tests of Liver Function in Schistosomiasis Japonica, With Particular Reference to Antimony Treatment and With Report of 2 Autopsies. Arch. Int. Med. 79: 62–76, January 1947.

[30] See footnote 21 (2), p. 109.

terior. On reaching the United States, they were sent to one or the other of two centers for the study of tropical diseases in the Army, Moore General Hospital or Harmon General Hospital. Each hospital received approximately 600–650 patients with this diagnosis. Three very complete reports of the disease as observed following the acute stage, in the so-called latent stage, at these hospitals were prepared for publication by Most and his associates (p. 108) and by Mason and his associates (pp. 108 and 113). From Harmon General Hospital, a thorough evaluation of the clinical status at the time of initial examination and during followup of 300 patients [31] diagnosed and treated overseas was reported. These patients appear to be a representative cross section of all those received at the two tropical disease centers, although it should be noted that they were probably as a group more severely infected than those patients received from overseas at a later date, who not only had less severe acute manifestations of the disease but had been treated more extensively before evacuation to the Zone of Interior. Suffice it to say that these 300 patients received at Harmon General Hospital were in strikingly good physical condition. None were acutely ill, although 255 (85 percent) had a combination of residual complaints of relatively mild degree, such as abdominal discomfort (155), weakness (75), and headache, myalgia, and nervousness (186); positive stools were obtained in 76 (30 percent) of the 255 patients. Of 46 (15 percent) patients with no complaints, positive stools were obtained in 17 (38 percent). The liver and spleen were palpable in 32 and 4 patients, respectively. All patients had lost weight. The general condition of the 300 patients was such that for only 6 did furlough have to be delayed beyond the initial 2-week period of evaluation. All of these had neurologic complications.

The abdominal complaints present in 155 of the 300 soldiers were limited to the upper quadrants of the abdomen and varied from an indefinite awareness of soreness to intermittent mild to moderate cramping pain in the region of either the epigastrium or the liver.

It is interesting to note, in the same report from Harmon General Hospital, the observation that, although moderate and marked leukocytosis was a common feature of the acute phase of the disease, in the latent phase after evacuation to the Zone of Interior positive stools were no more common in those with leukocytosis than in those with normal numbers of white blood cells. Marked eosinophilia was also more characteristic of the acute than of the latent phase, although there seemed to be some correlation between the level of the eosinophilia and the likelihood of finding ova in the stool.

Proctoscopic examinations of these 300 patients resulted in the demonstration of lesions due to schistosomiasis in only 3. This is in striking contrast to the high incidence of lesions of the lower bowel in the acute phase.

Involvement of the central nervous system was manifested as often in the latent phase seen in the Zone of Interior as in the acute phase of the

[31] See footnote 26 (1), p. 113.

disease observed overseas. This may be accounted for by the fact that very few of the neurologic complications cleared up before evacuation to the United States, and in addition several cases were reported in which signs referable to the central nervous system developed as a late manifestation (p. 110). The general prognosis for patients with schistosomiasis japonica of the central nervous system does not seem to be favorable as far as complete recovery is concerned, though marked improvement of function has been observed in most cases.

TREATMENT AND RESULTS

Methods

Before experience with schistosomiasis japonica in American troops, no opportunity had presented itself to study various methods of treatment of this disease in large numbers of acutely infected individuals. Observations had for the most part been limited to patients chronically infected and reinfected, living in endemic areas where adequate followup studies were impossible, and one could not be sure of the duration of the disease before treatment nor of the amount of reinfection occurring during and after treatment. In a few isolated instances where small numbers of individuals were infected by brief exposure to infested water, adequate followup studies on the efficacy of the treatment employed were not reported. The epidemic of schistosomiasis on Leyte brought the Army Medical Department face to face with the challenging problem of determining what the best method of treatment was. If the known methods of therapy were not effective, new ones would have to be evolved.

The drugs accepted as most useful in treating this infection before World War II were the trivalent antimony compounds, Fuadin (stibophen) and tartar emetic, which contain 13.6 percent and 36 percent antimony, respectively. Emetine and Anthiomaline (lithium antimony and thiomalate) were quickly shown to be ineffective. The data to be presented deal with the use of Fuadin and tartar emetic.

Before the epidemic on Leyte, little was known by the Army Medical Corps about the toxicity to man of large amounts of trivalent antimony or about its parasiticidal properties against *S. japonicum*. It was used carefully and, as it turned out later, too sparingly in the beginning. No complete studies are available regarding the results of treatment overseas, for the most part with amounts of antimony now known to be much less than adequate for a complete cure. It is significant, however, that of 300 patients diagnosed as being infected with *S. japonicum* in oversea hospitals, in the large majority on the basis of positive stool examinations, only 31 percent were found to have positive stools on arrival at Harmon General Hospital. At Moore General Hospital, closer to 45 percent of such patients had stools

positive for the ova. All of these patients had been treated overseas, and it is safe to say that, inadequate as their treatment now seems, it must have been effective in some instances. Table 16 presents a summary of most of the treatment schedules used, especially in the United States, with results of treatment.

TABLE 16.—*Treatment schedule and results of treatment of patients infected with* S. japonicum, *using increasing amounts of trivalent antimony compounds*

Treatment schedule [1]	Trivalent antimony compound		Gram of antimony	Number of patients treated	Treatment failures		Where treated
	Fuadin (6.4 percent solution)	Tartar emetic (0.5 percent solution)			Number	Percent	
	Cc.	Cc.					
1	40	--------	0.35	165	[2] 55	33	Overseas.
2	65	--------	.57	44	38	85	Harmon General Hospital.
3	65	--------	.57	15	15	100	Harmon General Hospital followed at Moore General Hospital.
4	70	--------	.61	44	34	77	Moore General Hospital.
5	100	--------	.87	32	8	32	Do.
6	105	--------	.91	15	6	40	Harmon General Hospital followed at Moore General Hospital.
7	--------	290	.52	51	26	51	Moore General Hospital.
8	--------	320	.58	59	11	19	Harmon General Hospital.
9	--------	320	.58	18	10	55	Harmon General Hospital followed at Moore General Hospital.
10	--------	360	.65	100	20	20	Moore General Hospital.
11	--------	416	.75	44	3	7	Do.
12	--------	416	.75	41	7	17	Harmon General Hospital followed at Moore General Hospital.

[1] See text (p. 118) for discussion.
[2] Only observed from 4 to 28 weeks after treatment.

Winkenwerder and his associates,[32] while still on Leyte, reported results of treatment of 184 patients with comparatively small amounts of Fuadin. These results are not conclusive because the followup period was not long enough, but the data serve to emphasize that this method of treatment in the early days of the epidemic was not effective. One-third of the patients suffered a relapse before evacuation to the United States interrupted observations. These unsatisfactory results with the doses of trivalent

[32] Winkenwerder, W. L., Hunninen, A. V., Harrison, T., Billings, F. T., Carroll, D. G., and Maier, J.: Studies on Schistosomiasis Japonica; Analysis of 364 Cases of Acute Schistosomiasis With Report of Results of Treatment With Fuadin in 184 Cases. Bull. Johns Hopkins Hosp. 79: 406–435, December 1946.

antimony recommended in the early days of the epidemic were confirmed at the Army tropical disease centers. A final report on 72 cases treated with tartar emetic was published by Carroll and Hunninen.[33]

It soon became apparent that if the trivalent antimony compounds were to be effective at all, they would have to be given in larger doses. Consequently, several methods of treatment were used, employing one or the other of the two drugs, Fuadin and tartar emetic, and gradually increasing the amounts administered to each patient as more and more was learned of the individual's tolerance to the drug and the parasite's resistance to its effects.

The following were treatment schedules used (see table 16) :

1. Fuadin (6.4 percent solution) intramuscular injections on alternate days of 1.5 and 3.5 cc., then 5.0 cc. for 7 doses to a total of 40 cc. in 17 days.

2 and 3. Fuadin (6.4 percent solution) intramuscular injections on 5 successive days of 1.5, 3.5, 5.0, 5.0, and 5.0 cc., then on alternate days 5.0 cc. for 9 doses to a total of 65 cc. in 23 days.

4. Fuadin (6.4 percent solution) intramuscular injections on 3 successive days of 1.5, 3.5, and 5.0 cc., then on alternate days 5.0 cc. for 12 doses to a total of 70 cc. in 27 days.

5. Fuadin (6.4 percent solution) daily intramuscular injections of 2, 4, 6 cc., then 8 cc. for 11 doses to a total of 100 cc. in 14 days.

6. Fuadin (6.4 percent solution) intramuscular injections on alternate days of 5.0 cc. to a total of 105 cc.

7. Tartar emetic (0.5 percent solution) intravenous injections on alternate days of 5, 10, and 15 cc., then 20 cc. for 13 doses to a total of 290 cc. in 31 days.

8 and 9. Tartar emetic (0.5 percent solution) intravenous injections on alternate days of 8, 12, 16, and 20 cc., then 24 cc. for 11 doses to a total of 320 cc. in 29 days.

10. Tartar emetic (0.5 percent solution) intravenous injections on alternate days of 10 and 20 cc., then 30 cc. for 11 doses to a total of 360 cc. in 25 days.

11 and 12. Tartar emetic (0.5 percent solution) intravenous injections on alternate days of 8, 12, 16, 20, and 24 cc., then 28 cc. for 12 doses to a total of 416 cc. in 33 days.

Some interesting considerations as to the results of treatment are suggested by table 17. In the first place, as has been indicated, the observations on patients treated by the first method were terminated too soon by evacuation to the United States, and more than 33 percent undoubtedly relapsed. This conclusion is based on the fact that a much higher percentage of patients relapsed at the tropical disease centers even though they received 65–70 cc. of Fuadin.

[33] Carroll, D. G., and Hunninen, A. V.: Studies on Schistosomiasis Japonica in Philippine Islands; Clinical Study of 72 Cases Treated With Tartar Emetic. Bull. Johns Hopkins Hosp. 82: 366–372, March 1948.

In the second place, it can be definitely stated that tartar emetic is a more effective drug in the treatment of schistosomiasis japonica than is Fuadin under the conditions described here. This conclusion is based on the fact that, by methods 2 and 3 and 8 and 9, approximately the same amount of antimony is administered to the patients yet a higher percentage suffered a relapse in the group receiving Fuadin than in the group taking tartar emetic. There is some discrepancy in the results of treatment by methods 8 and 9, although these methods are identical. This may be accounted for by the fact that the patients under method 8 were treated and followed at Harmon General Hospital, while those under method 9 were treated at Harmon General Hospital and followed at Moore General Hospital. All stools at Moore General Hospital were examined by the concentration method, whereas many at Harmon General Hospital were examined by direct smear alone.

Thirdly, it is of great interest to note that the most effective schedule of treatment was the one that employed the largest amounts of tartar emetic; that is, 416 cc. or 0.75 gm. of antimony. The use of Fuadin, even when as much as 0.91 gm. of antimony was administered, was not so effective. However, relative toxicities are not known.

TABLE 17.—*Incidence of minor toxic symptoms of trivalent antimony compounds in patients with schistosomiasis japonica*

Trivalent antimony compound	Number of patients treated	Cough		Nausea	Vomiting	Joint and muscle pain	
		Occasional	Frequent			Occasional	Frequent
Tartar emetic:		*Percent*	*Percent*	*Percent*	*Percent*	*Percent*	*Percent*
Fresh (320 cc.)	36	69	33	17	6	81	
Commercial (320 cc.)	33	58	30	15	6	52	3
Fresh (416 cc.)	17	76	24	18	6	24	65
Commercial (416 cc.)	16	81	19	13		13	81
Fuadin:							
First course (65 cc.)	33					6	3
Second course (55 cc.)	25			4	4	28	28
Sixth course (105 cc.)	15						100

Results of Treatment; Relapses

It was the experience of all observers that trivalent antimony, whether as Fuadin or tartar emetic, even in the early insufficient doses altered the course of the disease as was indicated by subsidence of symptoms, return of the temperature to normal or more nearly so, decrease in the number of leukocytes and eosinophils, and disappearance of ova from the stools, at least temporarily.

Relapses, when they occurred, were detected in all but very rare cases only by the reappearance of ova in the stools. In a few instances, clinical signs and symptoms recurred, and more frequently the eosinophils again increased in number. In relapses, ova reappeared in the stools in from 4 to 11 weeks after cessation of therapy. Both Moore and Harmon General Hospitals arbitrarily set a 3-month followup period as sufficient time to allow for the reappearance of ova. This time limit was fixed after many patients had been followed without relapse for much longer periods of time. It is possible that further followup of these patients by the Veterans' Administration will indicate that relapse can occur months after the completion of a course of treatment. Numerous very careful and very exhaustive examinations of concentrated specimens of stool are necessary before it can be stated that a patient has been cured of this disease.

Toxicity of Fuadin and Tartar Emetic

A striking fact that has been emphasized by the administration of large amounts of trivalent antimony, either as Fuadin or tartar emetic, to large numbers of patients is that neither of these drugs is as toxic as it was once thought to be. At Harmon General Hospital, 2,100 injections of 0.5 percent solution of tartar emetic in 5 percent glucose and saline were given to 102 patients and the toxic manifestations summarized.[34] There were no serious reactions. Table 17 presents the types of reactions that were encountered while using tartar emetic and Fuadin. Transient electrocardiographic changes persisting several days after termination of a course of treatment have been described by Tarr [35] at Moore General Hospital and by Schroeder and his associates [36] at Harmon General Hospital. The latter analyzed 315 electrocardiograms of 100 patients during various stages of treatment with Fuadin and tartar emetic. They observed increase in the amplitude of P waves in 11 percent of the patients; fusion of ST segment and T waves, in 45 percent; in 99 percent, varying degrees of decrease in amplitude of T waves in all leads resulting in deep inversion in many cases; and in 27 percent, prolongation of the QT interval. They concluded that, since in all cases the changes were transient, they were probably not indicative of cardiac damage nor of serious impairment of cardiac function.

SUMMARY

Approximately 1,300 cases of acute schistosomiasis japonica resulting from exposure to the parasites on Leyte, Philippine Islands, were diagnosed

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[34] See footnote 26 (1), p. 113.

[35] Tarr, L.: Effect of Antimony Compounds, Fuadin and Tartar Emetic, on Electrocardiogram; Preliminary Report. Bull. U.S. Army M. Dept. 5: 336–339, March 1946.

[36] Schroeder, E. F., Rose, F. A., and Most, H.: Effect of Antimony on the Electrocardiogram. Am. J.M. Sc. 212: 697–706, December 1946.

and treated by members of the U.S. Army Medical Department. An opportunity was taken for careful study of the disease in its early stages, and advances were made in methods of diagnosis and treatment.

CHAPTER IV

Filariasis

Joseph M. Hayman, Jr., M.D.

Filariasis became a problem of importance in American or other military forces for the first time in history during World War II. In fact, the epidemic occurrence of the disease in the American military forces apparently represents the first such to be reported in medical literature, although, of course, its endemic presence in certain areas was well known. There were two principal reasons for these epidemics and for the importance which they assumed in the military and the logistic planning. These were the assignment of previously unexposed troops to endemic areas without adequate protection and the ignorance of the majority of medical officers of the early symptoms, the diagnosis, and the course of the disease.

HISTORICAL NOTE

Filariasis, contrary to common opinion, has not been unknown in the United States. The first demonstrated cases of filariasis indigenous in the United States were reported by John Guitéras in 1886.[1] Though sporadic cases were reported from time to time from Florida, Alabama, and Virginia, the region around Charleston, S.C., was the only known focus of any consequence in the United States. In 1915, Johnson reported finding microfilariae in 19 percent of 400 hospital admissions within a year.[2] By 1940, however, filariasis indigenous in the United States had practically disappeared, even from Charleston. This disease was probably brought to the West Indies and the Americas with the importation of African slaves.[3] The absence of the disease on the Pacific coast, even in tropical America, in contrast to its wide geographic range on the Atlantic coast, supports this view, as does the fact that there is no mention of so striking a condition as elephantiasis in the early accounts of the Barbados where later it was so common that it was known as "Barbados leg." The vast majority of medical officers had no knowledge of the early symptoms or manifestations of filariasis, and their only concept of the infection was that of incapacitating elephantiasis, relatively rare even in endemic foci. The symptoms and course of filariasis in an endemic area, where exposure begins in childhood, are very different

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[1] Guitéras, J.: The Filaria Sanguinis-Hominis in the United States. M. News (Philadelphia) 48: 399, 1886.

[2] Johnson, F. B.: Filarial Infection. South. M.J. 8: 630, 1915.

[3] Smith, A. J.: Filariasis in the Americas. *In* Proceedings of Second Pan American Scientific Congress, 1917, vol. 9, sec. 8, pt. 1, pp. 49–76.

from the manifestations of early infection in previously nonexposed adults. Medical literature contains only meager descriptions of the latter, and American medical officers had practically no knowledge of this aspect of the disease.

DEFINITION

Filariasis is the term applied to infection of man and animals by certain nematodes (round worms) of the superfamily Filarioidea. Only one genus, *Wuchereria,* was of any military importance. This genus contains two closely related species, *Wuchereria bancrofti* and *Wuchereria malayi.* The latter is endemic in Malaya and is present in many of the islands in the Far East, as well as in parts of China and India. Few infections with this parasite were recognized in troops. *Wuchereria malayi* has the same life history as *W. bancrofti* but is believed to produce milder symptoms and not to lead to the development of elephantiasis. It will not be considered separately from *W. bancrofti* in this chapter.

CAUSATIVE AGENT

The adult *W. bancrofti* are white hairlike translucent worms measuring from 25 to 100 mm. in length and about 0.01 mm. in breadth. Adult male and female worms live coiled together in the dilated lymphatics, mainly in those of the pelvic region. Occasionally, adult worms, including gravid females, are found in peripheral lymphatics and lymph nodes. The gravid female discharges sheathed embryos, periodically, which reach the bloodstream and circulate there. There is no evidence that the embryos themselves produce any symptoms. These microfilarial embryos measure about 360 by 7 microns, including sheath. The microfilariae do not develop further nor multiply in the bloodstream. Further development occurs only in the intermediate host, the mosquito. When a suitable mosquito feeds on a person with microfilariae in the peripheral blood, the embryos are taken in and enter the stomach. Here, the embryos escape from their sheaths and enter the thoracic muscles of the mosquito. In the thoracic muscles, fuller development, including one or more molts, takes place. After 10 or more days, the infective microfilariae or filariform larvae, now measuring from 1.5 to 2 mm. in length, migrate to the proboscis. When the mosquito next feeds on a person, the larvae escape and enter through the puncture wound made by the mosquito, or through abrasions in the skin, and find their way into the peripheral lymphatics and thence into the systemic circulation. It should be noted that there is no multiplication of the larvae in the insect; the larvae taken in at the time of feeding simply grow and mature into the infective stage. The time from the entry of the mature larvae to the appear-

ance of microfilariae in the blood of the host is usually stated to be about 1 year.

In most endemic areas, the microfilariae exhibit a nocturnal periodicity; that is, they are present in the peripheral blood in much greater numbers during the night than during the day, reaching a maximum between 2100 and 0200 hours. This is not true of filariasis in Samoa, Fiji, and some other Pacific islands. The reasons for this nocturnal periodicity are not known.

GEOGRAPHIC DISTRIBUTION

Filariasis is endemic throughout most of the moist and warm regions of the world between latitudes 30° N. and 32° S. In Europe, it is apparently confined to Spain (Barcelona), Hungary, and Turkey. It is present along the southern shore of the Mediterranean and is common throughout the whole central tropical belt of Africa. In the Far East, it extends along the coast of India, through Malaya, French Indochina, southern China, Korea and Japan, the Philippines, and Borneo. It is sparsely present in northern Australia. In the western world, it is common along the eastern coast of Central and South America from about central Mexico to Argentina, although it has not been reported from the west coast. It is common in the Greater and Lesser Antilles. It was formerly present in the neighborhood of Charleston (p. 123). It is endemic in the population of all major island groups in the Pacific Ocean from a latitude which would bisect the islands of Japan to one that would cross Australia just south of Brisbane, with the exception of New Zealand and the Hawaiian Islands. Throughout this filarial belt, the prevalence of the disease is spotty, large variations in incidence often being noted in adjacent villages, and is related to the flight range of the local vector.

TRANSMISSION

Epidemic filariasis occurred only in troops in the South and Central Pacific Islands where microfilariae among the natives were "non-periodic" (diurnal), where the vector was an *Aedes* species day-biting mosquito which was present in considerable numbers, and where there was intimate intermingling of infected natives and of troops. In contrast, filariasis occurred only sporadically in other Pacific islands, such as the New Hebrides, Solomons, and New Guinea where the parasite is nocturnal. Maj. James I. Knott, MC, who was assigned to investigate filariasis in the Pacific area in March 1944,[4] indicated, in his series of reports,[5] that the islands where American troops had been infected were Tongareva (Penryhn), Bora-Bora

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[4] Memorandum, Maj. O. R. McCoy, MC, Tropical Disease Control Division, to Chief, Personnel Service, The Surgeon General's Office, 21 Feb. 1944, subject: Assignment of Medical Officer for Filariasis Study.

[5] Reports on Filariasis Bancrofti in American Forces in the Pacific Area, April 1944–January 1945, by Maj. James I. Knott, MC.

(Society), Aitutaki (Cook), Wallis, Tutuila (American Samoa), Upolu (British Samoa), Tongatabu (Tonga), and Fiji. He believed that reports of infection from Apamama (Gilberts), the Solomons, Bismarck, and New Guinea were doubtful and probably in error.

Throughout the filarial belt, some 50 species of mosquitoes, including species of *Aedes, Anopheles, Culex,* and *Mansonia,* have been reported as possible vectors. About half are known to transmit the disease naturally, while the others have been shown experimentally to permit the development of the parasite and hence are potential vectors. The majority are more active night biters, and, therefore, the disease is probably transmitted chiefly at night. But in some areas, such as Samoa,[6] the principal vector is a day biter, *Aedes scutellaris* var. *pseudoscutellaris.* This one factor was probably as much responsible as any other for the large number of cases in the Samoan Defense Area. The troops in this area were instructed in preventive measures and were provided with means to prevent contact with night biters, but the importance of day feeders was not known. It should be noted, however, that many night biters will actively feed during dark days, in the jungle and in quarters.

<div align="center">COURSE</div>

Symptoms and Signs in Natives

To appreciate the problem presented by the epidemics of filariasis in the Armed Forces, it is necessary to point out the difference in the manifestation and course of the disease among natives in an endemic area and among adults heavily exposed for the first time. In an endemic area, children begin to be infected in infancy and presumably develop a certain degree of immunity. Iyengar[7] found that the incidence of microfilariae in the peripheral blood increased from childhood up to the age oi 20, and then remained constant, while the incidence of filarial disease, as manifested by symptoms, increased steadily up to the age of 45. That is, microfilariae were less apt to be found in the blood of those showing symptoms than in those symptom free. A similar decrease in the presence of microfilariae with age was found in Puerto Rico, by Bercovitz and Shwachman,[8] where 5.03 percent of men between 18 and 20 years of age, but only 0.92 percent of men between 36 and 38 years of age, were positive. Of 460 men showing microfilariae in their blood, only 11 gave any history suggestive of filarial disease. Thus, in endemic areas, it appears that only a few of those infected develop symptoms, and then after some years of microfilaremia.

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[6] Byrd, E. E., St. Amant, L. S., and Bromberg, L.: Studies on Filariasis in the Samoan Area. U.S. Nav. M. Bull. 44: 1–20, January 1945.

[7] Iyengar, M. O. T.: Studies on the Epidemiology of Filariasis in Tranvancore. Indian Medical Research Memoir No. 30, Supplemental Series to Indian J. M. Research, 1938.

[8] Professional History of Internal Medicine in World War II, The Antilles Department, pp. 131–135. [Official record.]

In a certain number of infected persons, symptoms due to obstruction of lymphatics by adult worms develop. These early symptoms—often called those of the acute stage—consist of recurring lymphangitis, adenitis, and scrotal swelling often accompanied by fever and lasting from several days to 2 weeks. Gradually, the attacks become less severe and come at longer intervals. These bouts are called elephantoid fever in some places; agua, in Barbados; mumu, in Samoa; and wanganga, in Fiji. Secondary bacterial, streptococcal or staphylococcal, infection or trauma has been held necessary for the development of these attacks. However, O'Connor,[9] in 1933, showed that the presence of bacteria is not necessary for the occurrence of most of the pathological and all of the inflammatory attacks associated with filariasis. This conclusion has been amply verified by Wartman [10] and by others [11] from the study of cases among the Armed Forces. The role of possible toxic secretions from adult worms (uterine fluid), of products from disintegrated microfilariae caught and destroyed in lymph nodes, or of an allergic reaction in the production of these recurrent attacks has not been determined.

After the first few attacks of lymphangitis and adenitis, or of funiculitis and scrotal swelling, the limb or genitalia may return to its previous size. But, in continually reinfected natives, increasing lymphatic obstruction takes place, so that in the course of time each attack leaves a slight permanent increase in the size of the limb. "At first there is ordinary pitting edema, then swelling becomes harder and does not pit; later the whole limb becomes massive, 'brawny,' harsh and dry, the folds and cracks appear; finally these become infected with septic organisms and ulceration occurs." [12] This is filarial elephantiasis, which develops most commonly in the arms, the forearms, the legs, the feet, and the scrotum. Manson-Bahr [13] has pointed out that it must not be thought that lymphatic elephantiasis is solely due to filarial infection. Lymphatic elephantiasis may be congenital or familial (Milroy's or Meige's disease); it may be the result of streptococcic infection, secondary to venous thrombosis; or it may be due to obstruction from tuberculous glands or malignant growths. Other manifestations of the chronic stage of filariasis are lymph varices (most common in the groin), lymph scrotum, chyluria, chylous ascites, arthritis, and filarial abscess. These conditions are seen almost exclusively in natives of endemic areas or in persons who have lived for many years in such areas and have had repeated reinfections.

[9] O'Connor, F. W., cited by Lane, C.: Mechanical Basis of Periodicity in *Wuchereria bancrofti* Infection. Lancet 2: 399–404, 19 Aug. 1933.

[10] Wartman, W. B.: Lesions of Lymphatic System in Early Filariasis. Am. J. Trop. Med. 24: 299–313, September 1944.

[11] (1) Dickson, J. G., Huntington, R. W., Jr., and Eichold, S.: Filariasis in Defense Force, Samoan Group; Preliminary Report. U.S. Nav. M. Bull. 41: 1240–1251, September 1943. (2) Zuckerman, S. S., and Hibbard, J. S.: Clinicopathologic Study of Early Filariasis. With Lymph Node Biopsies. U.S. Nav. M. Bull. 44: 27–36, January 1945.

[12] Napier, L. Everard: The Principles and Practice of Tropical Medicine. New York: The MacMillan Co., 1946, p. 674.

[13] Mason-Bahr, Philip H.: Tropical Diseases, 11th edition. Baltimore: Williams & Wilkins Co., 1942, p. 759.

Symptoms and Signs in Military Personnel

The picture of filariasis as it occurred in the Armed Forces was quite different. Symptoms usually began to appear from 5 to 18 months after first possible exposure and consisted of pain, swelling, or redness of an arm or a leg, or pain and swelling in the scrotal region. Constitutional symptoms, such as chills, fever, malaise, or headache, were rarely reported. A few cases developed symptoms as early as 3 months after the first possible exposure.[14] In this regard, the case of O'Connor's assistant who developed epitrochlear adenitis 43 days after being bitten by a filariated mosquito is pertinent.[15] Dickson, Huntington, and Eichold [16] described a case in which adult worms were recovered 5½ months after the first possible exposure to filariasis.

The observations on different groups of infected men were described in a number of reports to The Surgeon General and later published in the literature. These have been reviewed by Wartman [17] who gives an extensive bibliography. Many men were only exposed in an endemic area for 1 to 2 months, so that symptoms did not develop until their removal to a non-endemic area. In other groups, symptoms began to develop while the troops were still in the endemic area. No relation was noted between season and onset of symptoms, nor to time of day.

When the reports of different observers are combined, symptoms referable to the genitalia were the most common initial complaint, although varying from 11 [18] to 97 percent [19] in different reports. The commonest complaint was of heaviness or mild pain in the scrotum, less often in the groin, frequently first noticed after severe exertion and usually made worse by exercise. On examination, edema of the spermatic cord was the most constant finding.[20] This might be present alone; however, it was frequently accompanied by the swelling of the epididymis or the testicle and by the presence of a hydrocele or scrotal edema. Absence of the cremasteric reflex on the affected side, attributed to edema of the cremasteric muscle, was thought a helpful early diagnostic sign in some cases.[21] The left spermatic

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[14] (1) King, B. G.: Early Filariasis Diagnosis and Clinical Findings; Report of 268 Cases in American Troops. Am. J. Trop. Med. 24: 285–298, September 1944. (2) Burhans, R. A., Camp, J. D., Butt, H. R., and Cragg, R. W.: Lymphangitis of Suspected Filarial Origin; Preliminary Report Concerning Its Treatment. U.S. Nav. M. Bull. 42: 336–340, February 1944.

[15] O'Connor, F. W., and Hulse, C. R.: Some Pathological Changes Associated With *Wuchereria* [Filaria] *bancrofti* Infection. Tr. Roy. Soc. Trop. Med. & Hyg. 25: 445–454, May 1932.

[16] See footnote 11 (1), p. 127.

[17] Wartman, W. B.: Filariasis in American Armed Forces in World War II. Medicine 26: 333–394, December 1947.

[18] Smith, F. R., Jr.: Filariasis; Study of 737 Patients So Diagnosed. U.S. Nav. M. Bull. 44: 719–725, April 1945.

[19] Johnson, P. A. G.: Filariasis; Clinical Findings in 189 Cases. U.S. Nav. M. Bull. 43: 950–954, November 1944.

[20] Hodge, I. G., Denhoff, E., and Vander Veer, J. B.: Early Filariasis (Bancrofti) in American Soldiers. Am. J.M. Sc. 210: 207–223, August 1945.

[21] Saphir, W.: Filariasis; Early Clinical Manifestations; Analysis of 35 Cases. J.A.M.A. 128: 1142–1144, 18 Aug. 1945.

cord was involved more frequently than the right. Bilateral involvement was not uncommon.

The entire cord from the internal ring to its junction with the epididymis might be involved. In some cases, there was only slight thickening of one side as compared with the other, or the entire cord would be enlarged from two to five times its normal size. The swollen cord was usually rubbery in consistency, but sometimes nodular. The pain varied from slight discomfort to exquisite pain, similar to that resulting from a blow to the scrotum. The funiculitis was descending or retrograde, similar to the lymphangitis seen in the extremities. Fogel and Huntington [22] were able to follow the development of the lesion in three hospital corpsmen. The onset consisted of lower abdominal pain at which time the spermatic cords were normal on palpation. The authors noted, as follows:

Within 12 hours there was palpable swelling high up in the inguinal canal. The examining finger could be inserted through the external inguinal ring without causing much discomfort to the patient. As the hours passed the progress of the swelling could be palpated as it moved down the cord. Within 24 hours that part of the cord lying within the inguinal canal was greatly swollen and tender. It was difficult to pass the palpating finger through the external ring because of the swelling and tenderness of the cord. In the succeeding 24 hours a scrotal mass was visible and palpable.

Such observations leave little doubt that the acute funiculitis was an acute lymphangitis of the spermatic cord. As with other filarial lesions, the swelling of the cord subsided in a few days to 2 weeks, often to recur one or more times at varying intervals. Frequently, especially after several attacks, slight painless enlargement of the cord persisted and was probably the most permanent of all physical findings.[23]

According to King,[24] the globus major was most frequently involved, and the body and globus minor only infrequently. In most instances, the lesion subsided completely, but in some cases thickening and palpable nodules remained. Some attached considerable significance to the presence of a small, shotlike lymph node, located where the vas deferens becomes distinctly palpable from the epididymis, which might persist for many months.

Acute orchitis, unilateral or bilateral, occurred in from 14 to 54 percent of reported cases. Symptoms consisted of pain, swelling, and tenderness. The pain might radiate up to the spermatic cord, or it might appear first in the lower quadrant of the abdomen and radiate downward to the spermatic cord and the testicle. Pain was usually not severe. Aspiration in a few cases yielded a small amount of fluid similar to that obtained from an ordinary hydrocele. Inflammation of the scrotal skin was not uncommon, usually in the most dependent portion of the scrotum, and was not related

[22] Fogel, R. H., and Huntington, R. W., Jr.: Genital Manifestations of Early Filariasis. U.S. Nav. M. Bull. 43: 263–270, August 1944.

[23] Leede, W. E., and Josey, A. I.: Early Diagnosis of Filariasis and Certain Suggestions Relative to the Cause of Symptoms. Ann. Int. Med. 23: 816–822, November 1945.

[24] See footnote 14 (1), p. 128.

to the degree of swelling of the cord. Microfilariae were not found in aspirated hydrocele fluid. Varicocele was reported by a number of observers, usually on the left side, but its relationship to filariasis was not determined and certainly is open to serious question.[25]

Acute lymphangitis was the most striking and characteristic physical finding in acute filariasis, and the one most helpful in making the clinical diagnosis. It occurred in the arm, the leg, the buttock, the groin, the abdomen, or the neck. Regardless of location, retrograde spread was characteristic, often starting from a palpable lymph node. It was about twice as common in the arms as in the legs in all series reported from the Pacific islands. This is the reverse of Grace's [26] report from British New Guinea where four-fifths of the patients showed involvement of the legs first. The lymphangitis of the arms occurred most commonly along the course of the brachial vessels or on the volar surface of the forearm. It took one of three forms—as a red streak of varying length, often with an underlying firm, irregular cord; as a patch of subcutaneous edema and overlying redness, irregular in outline and of varying size, most commonly occurring on the inner anterior surface of the forearm, just below the elbow; or as a diffuse edema and erythema of the upper part of the arm or the forearm. With erythema, there was local heat, but again tenderness was only mild or moderate. The red streaks were usually shorter, broader, and more diffuse than in bacterial lymphangitis. The characteristic retrograde progression, in contrast to the centripetal progression of bacterial infection, should be stressed. Lymphangitis of the extremities progressed from the axilla down the arm to the elbow, from the antecubital region down the forearm to the wrist, or from the inguinal region either down the inner aspect of the thigh or around the lateral aspect of the thigh, above the greater trochanter, to the gluteal region.

Hodge, Denhoff, and Vander Veer [27] believed that involvement of the deep lymph vessels of the abdomen should be considered in the presence of pain in the flank or the abdomen, with radiation to the genitalia or the thigh, and tenderness of the abdomen on the affected side. It is obvious that other causes of these symptoms, such as appendicitis and renal, ureteral, and retroperitoneal pathological conditions, should be excluded before considering filariasis as the explanation of the symptoms. An attack of lymphangitis often began to fade in 24 hours, and lasted from a few days to 2 weeks. Recurrences were common and characteristic. Chronic lymphangitis, however, was rare.[28] Persistent lymph edema was also rare.[29]

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[25] See footnote 17, p. 128.

[26] Grace, A. W.: Tropical Lymphangitis and Abscesses. J.A.M.A. 123: 462–466, 23 Oct. 1943.

[27] See footnote 20, p. 128.

[28] Behm, A. W., and Hayman, J. M., Jr.: Course of Filariasis After Removal From Endemic Area. Am. J.M. Sc. 211: 385–394, April 1946.

[29] Coggeshall, L. T.: Lymphadenopathy and Filariasis. (Abstract) Bull. U.S. Army M. Dept. 5: 250, 1946.

Enlarged, slightly tender, discrete lymph nodes without attachment to the skin or without suppuration were described by all authors and constituted the commonest symptom attributable to filariasis. Most critical medical officers found it difficult to judge the significance of enlarged nodes, particularly when the enlargement was slight, nontender, and in the more common sites for palpable nodes, such as the axilla and the groin. Among marines at Klamath Falls, Ore., Coggeshall[30] found enlarged nodes in 60 percent of 200 men diagnosed as filariasis, in 57 percent of 271 men evacuated for malaria, and in 50 percent of 98 controls who had never been overseas. Adenopathy was more suggestive of filariasis when the enlargement came on acutely without ascribable cause and when it occurred in places where enlarged nodes are not usually palpable, such as the antecubital area, the epitrochlear region, particularly above the site of the common epitrochlear node, the intercostal region, the popliteal space, in the back, the wrist, the tip of the ilium, or in the region of the teres and serratus muscles.

Transient or fugitive swellings, believed to be evidence of hypersensitivity to filarial products, were described in arms, legs, hands, feet, torso, eyelids, and forehead. According to Burhans, Camp, Butt, and Cragg,[31] the swellings developed along the path of lymphatic vessels or at the edges of muscles. Fogel and Huntington (p. 129) observed them in areolar tissue. These swellings were raised, usually slightly tender, and sometimes resembled erythema multiforme. They lasted from a few days to 2 weeks and disappeared without residua. No worms were found in biopsies from such swellings.

Filarial abscess, or abscess or suppurating nodes attributed to filariasis, was extremely rare. Glauser[32] reported three cases and Englehorn and Wellman[33] two cases. No worms or filariae were found in the pus.

The initial attack lasted from 3 to 5 days to 2 weeks, occasionally as long as a month. King[34] recorded fever in 53 (19.7 percent) of 268 cases. Usually, the temperature did not exceed 99° or 100° F., but in a few cases it reached 102° or 104° F. A striking feature of these attacks was the lack of severe constitutional symptoms. The patients did not feel sick, and the local lesions were not extraordinarily painful. In no instance did there seem to be danger to life. From the military standpoint, the attacks were most important because the lesions were incompatible with full field duty. The average hospital stay in King's series was 15.9 days.

Recurrences of adenopathy, lymphangitis, and scrotal swelling were common and characteristic. They occurred at intervals of a few days to

[30] Coggeshall, L. T.: Filariasis in Serviceman; Retrospect and Prospect. J.A.M.A. 131: 8–12, 4 May 1946.
[31] Burhans, R. A., Camp, J. D., Butt, H. R., and Cragg, R. W.: Lymphangitis of Suspected Filarial Origin: Preliminary Report Concerning Its Treatment. U.S. Nav. M. Bull. 42: 336–340, February 1944.
[32] Glauser, F.: Filariasis in Returning Marines. U.S. Nav. M. Bull. 44: 21–26, January 1945.
[33] Englehorn, T. D., and Wellman, W. E.: Filariasis in Soldiers on Island in South Pacific. Am. J.M. Sc. 209: 141–152, February 1945.
[34] See footnote 14 (1), p. 128.

several months. Relapses became less frequent and severe with the passage of time, but during the first 12 to 18 months this was not always true, and not infrequently a relapse would be more severe than the initial attack. Relapse was observed as long as 2 years after the initial attack.[35] The frequency of relapse diminished rapidly after evacuation to the United States. Complaints of subjective symptoms were far more common than objective findings. Coggeshall (p. 131) commented that men assigned to tasks they liked did not complain; men on the football and basketball teams did not experience any difficulty, while men on guard duty or police detail would complain bitterly. Behm and Hayman [36] believed that complaints of pain unaccompanied by recurrence or increase in swelling of nodes, scrotal contents, or lymphangitis should not be regarded as due to filariasis but rather should be more properly interpreted as due to muscle strain, fatigue, arthritis, or some other cause. Nearly all observers believed that relapses were prone to be precipitated by severe physical exertion.[37] Coggeshall, however, was unable to precipitate a recurrence by exhausting exercise in 10 marines after their return to Klamath Falls. Behm and Hayman reported from a study of 408 men, diagnosed to have filariasis, who had been in a hyperendemic area for 1 year and then observed for 14 months after removal, that the number of attacks varied from 1 to 13, as follows:

Number of attacks	Number of men
1	139
2	99
3	76
4	53
5	21
6	10
7–13	10

No attacks were observed in this group later than 13 months after removal from the endemic area. A number of other reports noted the rapid disappearance of signs and symptoms after return to the United States.[38]

Laboratory Examinations

Routine laboratory examinations were of little value in diagnosis.[39] No abnormalities of the urine attributable to filariasis were described. From the reported data, the total white blood cell count averaged about 9,000, with extremes of 3,600 and 19,000 per cubic millimeter. There was no significant alteration in the number or the form of neutrophils, lymphocytes,

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[35] Coggeshall, L. T.: Malaria and Filariasis in Returning Serviceman; Ninth Charles Franklin Craig Lecture. Am. J. Trop. Med. 25: 177–184, May 1945.

[36] See footnote 28, p. 130.

[37] (1) Brown, Maj. T. McP., Stifler, Capt. W. C., and Bethea, Capt. R. W., Jr.: Supplementary Report From the 118th General Hospital on 536 Officers and Enlisted Men From 134th Field Artillery Battalion, 31 July 1944. (2) See footnote 28, p. 130, and footnote 23, p. 129.

[38] (1) See footnote 32, p. 131, and footnotes 18 and 19, p. 128. (2) Zeligs, M. A.: Psychomatic Aspects of Filariasis; Present Day Evaluation. J.A.M.A. 128: 1139–1142, 18 Aug. 1945.

[39] See footnote 17, p. 128.

or mononuclear cells. In his review, Wartman observed: "Eosinophilia occurred in one-half to two-thirds of the cases, the average being about 850 cells per cu. mm. Most authors thought the presence of eosinophilia was not helpful in diagnosis." Eosinophilia was not observed in Leede and Josey's patients. On the other hand, King, and Hodge, Denhoff, and Vander Veer found that the incidence of eosinophilia (9 percent or above) was significantly greater in soldiers exposed to filariasis. Among exposed troops with signs of filariasis, the incidence of eosinophilia was greater than in those with no evidence of the disease but was twice as great in those with slight or doubtful findings, as in those with frank clinical filariasis. No significant changes were found in red blood cell counts, hemoglobin, or sedimentation rate. Bacterial cultures of biopsy material, blood, aspirated fluid from lymph nodes, and hydroceles showed no pathogens.

Despite many thousands of blood examinations, by all known methods, at all times of the day and night, microfilariae were only found in the blood of approximately 20 cases. Since some of these men had served in Puerto Rico, the source of infection could not always be established. Flynn [40] found 8 positive blood or lymph node aspiration material in 125 patients. Hodge, Denhoff, and Vander Veer (p. 128) found a single microfilaria in 2 blood samples among over 2,000 taken from 266 soldiers. Leede and Josey found microfilariae once in an individual who had lived for years in an endemic zone in childhood. Goodman, Weinberger, Lippincott, Marble, and Wright [41] reported finding microfilariae on one occasion in each of 2 soldiers among 145 examined on 7 nights and 3 days by the Knott concentration method. In other large groups of men, including those reported by King and by Behm and Hayman, no microfilariae were found despite careful and repeated study by Knott's method as well as by thick smears.

The "new" disease which was epidemic among troops in certain Pacific areas was first definitely established as filariasis by the demonstration of adult worms and microfilariae in biopsied lymph nodes and lymphatics. Wartman (p. 127), Michael,[42] Hartz,[43] and Rifkin and Thompson[44] described the pathological findings in biopsy material, and Wartman (p. 128) summarized all the material available in the Army Institute of Pathology. As a result of these studies, Wartman concluded that it was clear that the adult filaria worms in the lymphatic system might cause a granulomatous inflammatory reaction. When in lymph nodes, the changes were often not confined to the immediate vicinity of the worms but were present throughout

[40] Flynn, P. D.: Filariasis Suspects; Review of Cases Admitted. U.S. Nav. M. Bull. 42: 1075–1079, May 1944.

[41] Goodman, A. A., Weinberger, E. M., Lippincott, S. W., Marble, A., and Wright, H. W.: Studies of Filariasis in Soldiers Evacuated From South Pacific. Ann. Int. Med. 23: 823–836, November 1945.

[42] Michael, P.: Filariasis: Histopathologic Study. U.S. Nav. M. Bull. 45: 225–236, August 1945.

[43] Hartz, P. H.: Contribution to Histopathology of Filariasis. Am. J. Clin. Path. 14: 34–43, January 1944.

[44] Rifkin, H., and Thompson, K. J.: Structural Changes in Early Filariasis. Arch. Path. 40: 220–224, October 1945.

the node. Michael believed that the sex of the infecting worm influenced the histological changes, male worms degenerating somewhat earlier and faster than females, and fertilized females still more slowly. Many of the changes found in worm-infested nodes were also observed in tissues in which no parasites were discovered, even in serial sections. Biopsies of such nodes at the height of enlargement showed marked hyperplasia, infiltration with eosinophils, and distention of lymphatic sinuses. Changes in lymph vessels consisted of dilatation, lymph thrombosis, and acute lymphangitis which was sometimes necrotizing. In some, these changes appeared reversible, but in others fibrosis and obstruction of the affected lymphatic vessel had ensued. No difference could be detected in the changes associated with the presence of living or dead worms. From his failure to find parasites in genital lesions, Michael speculated that many genital enlargements were toxic or allergic in nature, and not due to direct invasion of the organs by parasites, and that therefore the changes could be presumed to be reversible. In a study of 58 biopsies from the Pacific area, Wartman found adult worms in 8 (13.8 percent) and microfilariae in 3 (5.1 percent) and regarded the histological picture in 24 (51.0 percent) of the biopsies that showed no parasites as characteristic of the disease. Michael reported finding adult worms in 30 percent of 120 biopsies. He also pointed out that, if a cut node is placed in saline solution, the adult worm may be found in the ambient fluid in 24 to 48 hours, thus saving the labor of serial sections. While the demonstration of adult worms or microfilariae is satisfactory proof of the diagnosis, biopsies should not be undertaken lightly or routinely. Biopsies from the inguinal and femoral region are usually unsatisfactory and frequently lead to prolonged disability. Excision of lymph nodes or other tissue while acute symptoms are present may be followed by severe exacerbation of symptoms. An epitrochlear or other unusually enlarged node, or a palpable lymphatic cord, taken as an attack subsides is apparently the most profitable site for biopsy.

Because of the failure to demonstrate microfilariae in the blood and the difficulty in making a reasonable clinical diagnosis of filariasis, numerous attempts were made to develop a satisfactory laboratory test. Older observations had shown that there is in the filariids a common group reacting factor capable of eliciting an intradermal response in persons harboring filarial infection and that antigens prepared from these filariids could also be used in serologic tests. Because of the impracticality of obtaining adult *W. bancrofti*, most workers had used a related filariid, especially the dog heartworm, *Dirofilaria immitis*. Taliaferro and Hoffman [45] had originally used a 1:200 dilution of saline extract of the dog heartworm, while Fairley [46] found that a 1:1,000 dilution gave fewer false positive reactions.

[45] Taliaferro, W. H., and Hoffman, W. A.: Skin Reactions to *Dirofilaria immitis* in Persons Infected With *Wuchereria bancrofti*. J. Prev. Med. 4: 261–280, July 1930.

[46] Fairley, N. H.: The Skin Test and Complement Fixation Reaction in Filariasis. Tr. Roy. Soc. Trop. Med. & Hyg. 25: 220, 1932.

Since no prepared antigen was available from supply, oversea units prepared their own antigens from *D. immitis* procured locally. King [47] showed that even minor differences in the method of preparation made significant differences not only in patients but in controls. The results of these studies, both overseas and in the United States, are summarized by Wartman. In general, antigens prepared from *D. immitis* gave false positive reactions in 5 to 14 percent of men who had never been in an endemic area and in 83 to 91 percent of those showing clinical symptoms that might be filariasis. A finding that made the interpretation of these skin tests particularly difficult was the increased incidence of positive reactions in men who had tropical service in a nonfilarial area or in one of very low endemicity, as well as among those who had served in an endemic area but had never had symptoms. The former was as high as 27 percent in some series. The latter might be attributed to a "biological" rather than a "clinical" infection; that is, to an infection sufficient to produce skin sensitization but no symptoms, comparable to that observed in certain individuals who give a positive reaction to *Trichinella* antigen. Huntington's [48] conclusions that while the skin test is helpful in the general study of the incidence and epidemiology of filariasis, it is not particularly helpful in the diagnosis of individual cases, would be echoed by most observers. Both immediate and delayed reactions were observed; the immediate being apparently the more sensitive, the delayed giving fewer false positive reactions. The use of other filariid antigens (*Setaria equina*, Litomosoides carinii) gave similar results. The presence of intestinal helminths apparently made no significant difference in the incidence of positive reactions. Bozicevich and Hutter [49] believed that the test was made more specific by use of a 1:8,000 dilution of antigen. Complement fixation and precipitin reactions were not found to be particularly useful.

With this brief review of filariasis, as described in most textbooks of medicine, and of the symptoms and findings in acute epidemic filariasis as encountered among military personnel in World War II, it is hoped that the description of the experience in different units (p. 138) and in the various theaters can be appreciated.

INCIDENCE

When the marines went into the Samoan area early in 1942, there was extreme military necessity of getting under cover as quickly as possible. The native villages were the most available sites. As a result, there was intimate contact between troops and the heavily infected native population.

[47] See footnote 14 (1), p. 128.

[48] Huntington, R. W., Jr.: Skin Reactions to *Dirofilaria immitis* Extract. U.S. Nav. M. Bull. 44: 707–717, April 1945.

[49] Bozicevich, J., and Hutter, A. M.: Intradermal and Serological Tests With *Dirofilaria immitis* Antigen in Cases of Human Filariasis. Am. J. Trop. Med. 24: 203–208, May 1944.

The possibility that the troops might become infected with filariasis was not seriously considered, for the region had been occupied by white men for a number of years without evidence of infection. Indeed, some believed that the white man was not susceptible. Previous white residents of the area had lived apart from native villages and in screened quarters. Moreover, while the men were equipped with mosquito nets, it was not recognized that the important vector of filariasis in this area was the day-biting *A. scutellaris* var. *pseudoscutellaris* and that the microfilariae in this area were nonperiodic. As a consequence of living in and near native villages and of a day-biting vector, these men were subjected to a large number of infected bites in a relatively short time. In all of the Pacific islands, a high incidence of infection among troops occurred only where these two conditions existed.

It is difficult to get precise data on the number of men infected. Coggeshall (p. 131) estimated that 38,300 men of the U.S. Navy and the U.S. Marine Corps were exposed, and a filarial registry showed 10,421 diagnosed cases. Many of these were erroneous diagnoses, but on the other hand there were many cases in which the diagnosis of filariasis was not entered on the health record.

The approximate number of primary admissions for filariasis in the years 1942–45 is shown in table 18. One death was recorded in an oversea theater in 1944.

TABLE 18.—*Admissions for filariasis in the U.S. Army, by area and year, 1942–45*

Area	Number of cases				
	1942–45	1942	1943	1944	1945
Continental United States	481			391	90
Overseas:					
Europe					
Mediterranean [1]	9		8	1	
Middle East	1			1	
China-Burma-India	2		1	1	
Southwest Pacific	323		70	233	20
Central and South Pacific	1,348		557	741	50
North America [2]	1		1		
Latin America	307	3	18	216	70
Total overseas	[3] 2,002	3	660	1,194	145
Total Army	[3] 2,483	3	660	1,585	235

[1] Includes North Africa.
[2] Includes Alaska and Iceland.
[3] Includes admissions on transports.

The admissions tabulated as from continental United States represent infections acquired overseas. The marked decrease in 1945 as compared with 1944 was due to the movement of the war away from hyperendemic areas, as well as to better mosquito control, and to the separation of troops and natives. The average number of days lost per man in 1943 was 112, while in 1945 it was 66. The annual admission rate for filariasis per 1,000 mean strength in the Central and South Pacific Area was 1.91 in 1943 and 1.69 in 1944. A few cases were reported in Puerto Rican troops who had probably been infected in Puerto Rico before military service. The chief sources of infection in Army units were Bora Bora, Aitutaki, Tongareva, Fiji, and Tongatabu Islands (pp. 125–126).

DISCUSSION OF EPIDEMIC

Full consideration must be given to the fact that the military activities in the Pacific areas early in the war were such that the tactical situation had highest priority. In commenting on the epidemic in Samoa, Wallis, and Aitutaki, Knott reported [50] that recommendations by medical officers that natives be removed from camp areas raised objections from island governments and were vetoed by area commanders. Many medical officers could not believe that the lymphangitis observed in troops was filarial. No one was to speak or write of filariasis. To combat rumors, Knott reported, the area commander put out the famous order that no case was to be called filariasis because "this disease does not affect white men." The men themselves, however, believed the natives. Shortly after this order, the diagnosis was settled by finding worms in biopsy material. Knott commented further:

The army units in the Central Pacific Area were not warned officially that filariasis had broken out in the marines on Samoa and Wallis when it first broke out, but the medical officers promptly passed the word along to the others. Officers from the Army islands visited Samoa and learned what they could. But here again the information was gotten after the units had already been infected. And again, the medical officers could not convince the island commanders that they should exclude the natives from the camp areas. Perhaps the area commanders would have listened to the medical officers if they had had scientific data to prove the danger of the situation. But there were no epidemiologic mosquito survey, nor mosquito control units in the area.

The men who had seen examples of filariasis among the natives were extremely fearful of the diagnosis, believing that they would suffer similar disfigurement and particularly that they would be sterile. The obvious ignorance of medical officers of the disease only seemed to increase this apprehension, lower morale, and lead to the conviction of the men that they had been afflicted with a serious and incurable disease about which nobody knew anything. Examples of the ignorance of the disease are the remark of a (Navy) consultant who when shown sections of worms in biopsied glands said that this couldn't be filariasis, since no microfilariae were found in

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[50] See footnote 5, p. 125.

peripheral blood but must be a new disease,[51] and by the action of a post medical inspector who, in recording the admission of 108 patients diagnosed filariasis, reported as follows:

> Immediate and rigid precautions were taken to isolate patients by restriction of the patients to the ward several hours before dusk; by careful, complete screening of the building in which they were housed; by spraying of the screens and doors several times during the day and night. * * * blood smears were taken during day and night in an attempt to detect the presence of microfilariae. However, these smears were entirely negative.[52]

The impact of such treatment on the emotional reaction of the men and their families can well be imagined.

Another example of ignorance of the disease was noted in a report [53] which contained the following statement:

> It is known that the microfilaria cannot reproduce themselves asexually. It takes a number of months for the microfilaria to develop into the adult macrofilaria. We have seen adult macrofilaria in the human from 15 to 18 months after exposure and so know that the adult forms can develop in this time; * * *. It is necessary to have an adult male and female macrofilaria in close harmony to produce sexually mature microfilaria.

It is hard to believe that the writer, who was making the diagnosis of filariasis and talking to patients, knew even the life cycle of the parasite!

That the disease was filariasis was recognized officially in a directive from the Surgeon General of the Navy, dated 23 May 1943. The directive clarified the administrative handling of filariasis and directed that those so diagnosed be transferred to the nearest U.S. naval hospital in the United States to be hospitalized until free from symptoms and not to be sent again into endemic areas. The presence of microfilariae did not restrict movement. No such definite evacuation policy was established by the Army.[54] War Department Circular No. 189, 21 August 1943, specified that filariasis was disqualifying for service in tropical areas; War Department Circular No. 293, 11 November 1943, provided that men suffering from filariasis would not be dispatched overseas; and War Department Technical Bulletin (TB MED) 142, "Filariasis (Wuchereria) With Special Reference to Early Stages," appeared in February 1945, but by this time the epidemic overseas was past.

UNIT HISTORIES

The history of two Army units illustrates the difficulty in diagnosis, the results of indecision, and the loss in manpower caused by filariasis. The 134th Field Artillery Battalion and the 404th Combat Engineer Company (Separate) were dispatched overseas in April 1942 and were stationed

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[51] Personal experience.—J. M. H., Jr.

[52] Monthly Sanitary Report for Month of July, Halloran General Hospital, 3 Aug. 1943.

[53] Essential Technical Medical Data, South Pacific Base Command, for February 1945, dated 12 Mar. 1945.

[54] To the best of my knowledge.—J. M. H., Jr.

on Tongatabu, where the nonperiodic form of filariasis was highly endemic, from May 1942 to May 1943. No symptoms recognized as due to filariasis developed during this time. These units left Tongatabu in May 1943, stopped at New Caledonia and in Townsville, Australia, and then were stationed on Woodlark Island, southeast of New Guinea, until January 1944. While Woodlark Island is in the filarial zone, the endemicity is extremely low, if any. An Australian mine superintendent who had lived on the island for 30 years reported that he had never seen evidence of the disease among natives, and physical examinations and blood smears on 100 natives showed no evidence of filariasis.[55] In addition to the men who had been on Tongatabu, 145 replacements were with them on Woodlark. Recurrent lymphangitis, scrotal swelling, and adenopathy began to develop in the Tonga group about August 1943. Many men who complained of pain and discomfort showed no significant physical findings. Similar symptoms developed *at the same time* among the replacements who had never been on Tongatabu. Because of the number of men exhibiting symptoms, the uncertainty of the actual number infected, and the loss of morale and efficiency, the units were transferred to Sydney, Australia, and examined by the staff of the 118th General Hospital.[56] In addition to history, physical examination, and blood studies, skin tests were done with a 1 : 1,000 extract of *D. immitis*. The results of these skin tests are shown in table 19.

TABLE 19.—*Results of skin tests for filariasis, 118th General Hospital, 1944*

Group tested	Number of tests	Positive reaction	
		Number	Percent
Tonga	502	368	73.3
Non-Tonga	143	35	24.5
Control [1]	72	13	18.1
No tropical service	100	11	11.0

[1] Personnel of 118th General Hospital.

On the basis of history, examination, and skin tests, it was concluded that 494 of 526 men who had been on Tonga and 17 of the 144 who had only been on Woodlark showed evidence of filariasis. The commanding officer of the Sixth U.S. Army recommended that these units be returned to the United States because (1) their combat efficiency had been seriously impaired, (2) rehabilitation would extend over a long period, (3) their future combat value was highly doubtful, and (4) replacement of all individuals

[55] Letter, Maj. Albert M. Dashiell, Headquarters, Sixth Army, to Surgeon, Sixth U.S. Army, 11 Nov. 1943, subject: Filariasis.

[56] Brown, Maj. T. McP., Stifler, Capt. W. C., Jr., and Bethea, Capt. W. R., Jr.: Preliminary Report of Filariasis Survey of 501 Men From 134th Field Artillery Battalion and 171 Men From 404th Combat Engineer Company (S), 10 Mar. 1944.

showing evidence of filariasis would result in a state of training far below that required for efficient combat.[57]

The personnel of the organizations returned to the United States as patients in July 1944. When they reached Moore General Hospital, Swannanoa, N.C., the troops had been overseas 27 months, had never been in combat, and had been hospitalized for 7 months. The men were confused, apprehensive, and discouraged. They had, many of them, seen some of the late sequelae of filariasis, had been conscious of the concern and indecision of the medical officers who had examined them, and commonly believed that they were afflicted with an incurable, progressive, and eventually disfiguring and incapacitating disease. This was borne out by the men's own opinion of their ability to do duty. Of the 134th Field Artillery who had been on Tonga, 24 percent thought they were fit for full duty, 70 percent that they were fit only for limited duty, and 6 percent that they were completely incapacitated. After thorough study and from 2 to 10 months' observation, 196 (36.8 percent) of those who had been on Tonga were diagnosed as filariasis. Of these, three were separated from the service because of filariasis, one with persistent lymph edema of both legs, one with a lymph scrotum, and one with recurrent lymphangitis; the others were returned to duty in the Zone of Interior in accordance with current directives. No microfilariae were demonstrated on repeated search. The number of recurrent attacks of lymphangitis, adenopathy, or scrotal swelling was difficult to estimate, since many more were recounted by the men than were documented in medical records or observed by a medical officer. On the basis of histories of 408 men, 139 stated that they had had a single attack; 99, two attacks; 76, three; 53, four; 10, six; and only 10, more than 10 recurrences. No evidence of recurrence of physical findings that could be attributed to filariasis was observed later than 25 months after removal from the endemic area. Of 308 men returned to duty as nonfilarial and followed for an additional 8 months, 3 presented sufficiently characteristic symptoms of recurrent adenopathy to justify a change in diagnosis to

TABLE 20.—*Comparison of results of skin tests for filariasis, with* D. immitis *antigen, overseas (February–March 1944) and Zone of Interior (September 1944)*

Group tested	Percent positive with antigen dilution of—	
	1 : 1,000 (February–March 1944)	1 : 8,000 (September 1944)
Tonga	73.3	57.7
Woodlark	24.5	18.3
Control		6.0

[57] Letter, Lt. Gen. Walter Krueger, Headquarters, Sixth U.S. Army, to Commanding General, U.S. Army Forces, Far East, 8 Apr. 1944, subject: Return of 134th Field Artillery Battalion and 404th Engineer Company (C) (Separate) to the United States,

filariasis. The entire group was skin tested according to the technique of Bozicevich and Hutter, using a 1 : 8,000 dilution of antigen. The results of these tests in comparison with those done overseas are shown in table 20.

Of the men discharged because of filariasis, 79.5 percent had a positive skin test while 42.0 percent of the "not filariasis" Tonga group and 19.1 percent of the Woodlark group did also. The former might be thought of as due to a "biological" rather than "clinical" infection; that is, to an infection sufficient to produce skin sensitivity but no symptoms, comparable to that observed in certain individuals who give a positive reaction to *Trichinella* antigen. But it is hard to apply this explanation to the Woodlark group where the possibility of infection was very problematical. This obviously makes the skin test of less value in the individual case than would be desirable.

The history of these two units has been given in some detail because they were the most carefully studied of Army units and because the experience in other groups of men exposed in hyperendemic areas was similar. The amount of physical incapacity was slight in proportion to that produced by fear, anxiety, and uncertainty. Zeligs [58] presented factual data which showed that these fears were groundless. The longer the period of inactivity because of a diagnosis of filariasis, the more difficult it was to return men to duty. When presented with evidence of their ability to lead normal lives and with the demonstration that they could exercise without producing symptoms, most men ceased to be concerned. Those with a past history of psychoneurotic behavior, or where the element of secondary gain was prominent, frequently used filarial symptoms to help solve preexisting emotional problems or to escape unpleasant situations. The ignorance of most medical officers of the disease led to a diagnosis of filariasis in men who had never been in an endemic area or who suffered from angioneurotic edema, thrombophlebitis, lymphogranuloma venereum, and epididymitis secondary to a urethritis.

DIAGNOSIS

The diagnosis of early filariasis is not easy. Demonstration of microfilariae in the peripheral blood or of adult worms in biopsy material is the only proof. Care should be taken with blood smears to prevent contamination with filarial-like structures.[59] Usually, the diagnosis must be made on history and clinical findings. History of exposure in an endemic area is of prime importance; the diagnosis should not be entertained without it. History of lymphangitis, adenopathy, or scrotal pain is unreliable. An acute attack of retrograde lymphangitis, adenopathy, particularly in

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[58] See footnote 38 (2), p. 132.

[59] Manson-Bahr, P.: A Spurious Blood Parasite From Fiji. Tr. Roy. Soc. Trop. Med. & Hyg. 45: 12, 1951.

unusual locations, funiculitis, epididymitis, or orchitis should be observed. All other discoverable causes for the symptoms should be excluded. The skin test is helpful in surveys but is not reliable in the individual. Exercise tests are of value where they precipitate acute attacks.[60]

PREVENTIVE MEASURES

Prevention of infection in troops depends upon information on the presence of microfilariae among natives, whether the parasite is diurnal or periodic, and on the important local vectors. The greatest danger is where the parasite is diurnal and the vector a day biter. Under such conditions, separation of troops and natives is essential. Studies by Byrd, St. Amant, and Bromberg[61] showed that, while 25 percent of *Aedes scutellaris* collected in the center of a native village might be infected, the infection rate dropped to zero at 200 yards. Thus, while this mosquito has a short flight range, other vectors have a longer range. Where the tactical situation permits, troop areas should be at least 1 mile from native villages, or the latter moved. All methods for mosquito control should be instituted. Where the vector is a day biter, preventive measures, such as the wearing of long sleeves and full-length trousers and the frequent application of repellent, should be enforced.

The value of observing the principles of military sanitation was shown by Lt. Gen. Thomas E. Watson, U.S. Marine Corps,[62] on the island of Upolu. About 90 percent of the troops were in a camp around an airfield. Natives were excluded from the camp, and mosquito-control measures were carried out in the area. Only rare cases of filariasis developed, and these may not have been acquired in the area. The other 10 percent of troops, stationed in the town of Apia, intermingled with natives and a number acquired filariasis.

When the presence of filariasis among troops was recognized, measures were taken not only to prevent further infection, but to minimize the possibility of development of late complications from prolonged exposure. Filariasis was designated as disqualifying for duty in tropical areas, and later for any oversea assignment (p. 138).

Another problem arose late in the war with the transfer of prisoners of war from heavily infected Pacific islands to Hawaii and continental United States where possible vectors existed.[63] Between June 1945 and the end of hostilities, over 4,000 prisoners from Okinawa were received

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[60] War Department Technical Bulletin (TB MED) 142, February 1945.

[61] See footnote 6, p. 126.

[62] See footnote 5, p. 125.

[63] (1) Newton, W. L., Wright, W. H., and Pratt, I.: Experiments to Determine Potential Mosquito Vectors of *Wuchereria bancrofti* in Continental United States. Am. J. Trop. Med. 25: 253–261, May 1945. (2) Scott, O. K., Richards, C. S., and Seaman, E. A.: Experimental Infection of Southern California Mosquitoes With *Wuchereria bancrofti*. J. Parasitol. 31: 195–197, June 1945.

in the Hawaiian Islands, 16 percent of whom showed microfilariae.[64] It was promptly recommended that these men be returned to one of the islands of the western Pacific or to relatively uninhabited islands where introduction of the disease would be of small consequence.[65]

CONCLUSIONS

A valuable, though expensive, lesson can be learned from the experience with filariasis in World War II. Medical officers should be given all the information available about the diseases in the area into which they go. As information is obtained from one service or area, it should be passed on rapidly, at least as information bulletins, to other officers. While "a little knowledge is a dangerous thing," it is better than none. The War Department technical bulletin on filariasis (p. 138) did not appear until the epidemic was over. The importance of a knowledge of military sanitation for every medical officer in the field, no matter how high his other professional qualifications, was demonstrated again. To this might be added the ineffectiveness of such knowledge unless commanders can be convinced of its importance.

It is highly improbable that any number of men infected overseas will have symptoms or incapacity attributable to filariasis in the future. A few may develop an asymptomatic microfilaremia. A few such cases have been reported.[66] This is consistent with Neumann's observations that microfilariae are not commonly found in the peripheral blood before the seventh year after infection. If no longer exposed to reinfection, such microfilariae may persist for 15 years, which apparently is the average life of the worms.[67] Such cases, even should they occur, would be so scattered that the chance of establishing a focus of the disease in the United States is negligible.

There is no specific treatment for the acute attacks of filariasis. The sulfonamides and antibiotics are without effect unless bacterial infection is superimposed. Rest and administration of mild analgesics, such as acetylsalicylic acid, during the presence of acute symptoms are all that is required. Of a large number of drugs studied for effect on microfilariae,

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[64] History of Preventive Medicine, Headquarters, U.S. Army Forces, Middle Pacific, ch. 34. [Official record.]

[65] Swartzwelder, J. C.: Filariasis Bancrofti. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume VII. Washington: U.S. Government Printing Office, 1964.

[66] (1) Eyles, D. E., Hunter, G. W. III, and Warren, V. G.: Periodicity of Microfilariae in 2 Patients With Filariasis Acquired in South Pacific. Am. J. Trop. Med. 27: 203–209, March 1947. (2) Conn, H. C., and Greenslit, F. S.: Filariasis Residuals in Veterans With Report of Case of Microfilaremia. Am. J. Trop. Med. 1: 474–476, May 1952.

[67] Neumann, H.: Filariasis in White Man. J. Trop. Med. 47: 25–28, June–July 1944.

diethylcarbamazine (Hetrazan) is the most promising.[68] It is quite effective in reducing or abolishing microfilaremia. Its effect on adult worms is less definitive.

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[68] (1) Santiago-Stevenson, D., Oliver-Gonzalez, J., and Hewitt, R. I.: Treatment of Filariasis Bancrofti With 1-Diethylcarbamyl, 4-Methylpiperazine Hydrochloride ("Hetrazan"). J.A.M.A. 135: 708–712, 15 Nov. 1947. (2) Kessel, J. F., Thooris, G. C., and Bambridge, B.: Use of Diethylcarbamazine (Hetrazan or Notezine) in Tahiti as an Aid in Control of Filariasis. Am. J. Trop. Med. 2: 1050–1061, November 1953.

CHAPTER V

Helminthiasis

Harry Most, M.D.

Helminthic infections [1] were acquired by a relatively large number of military personnel during World War II. The parasites discussed in this section may be classified as follows: (1) Those that enter the body as larvae via the skin or mucous membrane (hookworm and *Strongyloides stercoralis*) and (2) those that enter the body via the gastrointestinal tract (*Ascaris lumbricoides, Trichuris trichiura, Trichinella spiralis, Enterobius vermicularis,* and tapeworms).

Particularly in the Pacific islands, every possible condition existed to facilitate the dissemination of intestinal parasites. Infection in native and enemy troop populations was high, troops frequently operated in terrain containing human feces; facilities for fecal disposal were limited or nonexistent; and facilities for washing hands, bodies, clothing, and mess equipment were either limited or absent.

Table 21, compiled from data from seven surveys,[2] shows the high incidence of parasitism in the various groups of natives and prisoners in areas where the U.S. Army operated under military conditions. The unsanitary living conditions made the acquisition of many of the parasitic infections almost inevitable.

Table 22, which represents the results of surveys done overseas and in the United States,[3] shows the extent of infections in troops in the United States. The incidence was at least twice as great in troops who served in the Pacific as in those who served in the continental United States only; in general, probably, the incidence of infection overseas was actually greater than is indicated in the table. Examinations of single specimens of stool by direct smear only were frequent. Troops surveyed after returning to the United States may previously have had courses of treatment. Higher percentages were discovered in small groups who were not treated previously and in those in whom several stools were examined by concentration techniques.

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[1] Schistosomiasis and filariasis which are discussed in chapters 3 and 4, respectively, are excluded from the discussion in this chapter.

[2] The various sources from which the data were compiled are listed in table 21.

[3] The various sources from which the data were compiled are listed in table 22.

TABLE 21.—*Prevalence of parasitism in various groups of natives and prisoners, in tropical areas*

Group surveyed	Number examined	Percent parasites recovered									
		Hookworm	Strongyloides stercoralis	Trichuris trichiura	Ascaris lumbricoides	Schistosoma japonicum	Schistosoma mansoni	Entamoeba histolytica	Clonorchis sinensis	Tapeworm	Enterobius vermicularis
(1) Leyte civilians	2,576	57.0	0.4	68.0	80.0	10.0	____	0.1	____	____	____
(2) Filipinos (employed in messhalls)	89	40.4	1.1	13.5	30.3	____	____	1.1	____	.	____
(2) Formosan prisoners	244	81.9	.4	63.1	50.4	____	____	10.2	____	____	____
(3) Japanese orphans	62	68.0	64.0	45.0	8.0	____	____	17.7	____	____	____
(4) Japanese prisoners (Gilbert Islands)	83	26.5	2.4	6.0	1.2	____	____	14.4	____	____	____
(4) Civilians (Marshall Islands)	140	.7	.7	.7	____	____	____	____	____	____	____
(4) Korean civilians (Makin Islands)	244	34.4	____	28.7	1.2	____	____	8.6	3.3	6.2	____
(4) Civilians (Gilbert Islands)	50	____	____	____	____	____	____	30.0	____	____	____
(4) Puerto Ricans (Oahu)	209	26.7	10.5	51.6	1.9	____	4.3	7.6	____	____	____
(5) Puerto Ricans	1,046	20.5	____	52.9	5.0	____	8.6	32.2	____	____	____
(6) Children (Panama)	618	23.8	5.9	20.8	33.7	____	____	____	____	____	15.7
(7) Civilians (India)	1,000	28.0	____	____	____	____	____	____	____	____	____

NOTE.—Figures in parentheses identify source of data.

Source: (1) Essential Technical Medical Data, U.S. Army Forces, Far East, for January and February 1945, dated 20 Apr. 1945.

(2) Quarterly Report, 30th Malaria Survey Detachment, dated 30 June 1945.

(3) Report, 217th Malaria Survey Detachment (undated).

(4) History of Internal Medicine in the Central Pacific in World War II. [Official record.]

(5) Report, G. H. Houck, P. L. Burlingame, M. S. M. Watts, and J. T. Marcones, 4th AA Command, San Francisco, Calif., 5 Aug. 1945, subject: Report of Disinfestation Program in 762d and 891st AAA Gun Bns.

(6) Einhorn, N. H., and Miller, J. F.: Intestinal Helminthiasis: Clinical Survey of 618 Cases of Infection With Common Intestinal Helminths in Children. Am. J. Trop. Med. 26: 497–515, July 1946.

(7) Blumgart, H. L., and Pike, G. M.: History of Internal Medicine in India-Burma Theater. [Official record.]

HOOKWORM INFECTIONS

Incidence

The incidence of hookworm infections varied in different areas and frequently was related to the branch of service (being highest in the infantry) and to the duration of combat or to the length of residence in the area. A total of 800 cases were discovered among 2,000 Australian troops who had been in combat in New Guinea for periods of several weeks to months; 97 percent of one brigade was infected. In American troops serving in the Pacific, the prevalence was from 10 to 15 percent, according to several large surveys. After campaigns in the Solomon and Philippine Islands, as many as 20 to 40 percent infected might be found among those surveyed.

TABLE 22.—*Prevalence of parasitism in U.S. Army troops, oversea service and service in continental United States only*

Area of service and of survey	Number of troops examined	Percent parasites recovered					
		Hook-worm	*Strongy-loides stercoralis*	*Trichuris trichiura*	*Ascaris lumbri-coides*	*Entamoeba histo-lytica*	*Schisto-soma japonicum*
(1) Solomon Islands	1,000	23.6					
(2) South Pacific	4,624	5.2				18.7	
(3) South Pacific	2,300	10.4	0.9	1.7	0.8	5.8	
(4) Manila	630	14.1	.3	10.7	17.8	8.1	
(5) Leyte	206	39.8			34.4	15.0	9.2
(6) Leyte [1]	463	16.4	2.2	11.4	3.2	3.5	
(6) Pacific [1]	1,261	10.8	1.0	3.3	1.3	1.0	
(6) European and Mediterranean [1]	535	5.0	.2	1.3	.7	.4	
(7) Pacific [1]	342	10.2				11.7	
(7) European [1]	310	12.9				13.8	
(7) United States [2]	398	6.8				7.0	
(8) Pacific [1]	2,500	11.5					
(8) United States [2]	4,300	6.2					

[1] Area of service; the survey was conducted in the United States.

[2] Service in continental United States only.

NOTE.—Figures in parentheses identify source of data.

Source: (1) Essential Technical Medical Data, U.S. Army Forces, South Pacific Area, for February 1944, dated 7 Mar. 1944.

(2) Essential Technical Medical Data, South Pacific Base Command, for March 1945, dated 15 Apr. 1945.

(3) Essential Technical Medical Data, South Pacific Base Command, for April 1945, dated 15 May 1945.

(4) Essential Technical Medical Data, U.S. Army Forces, Pacific, for October 1945.

(5) Medical Bulletin No. 19, Office of the Surgeon, Headquarters, Army Service Command I, Okinawa, 17 Sept. 1945.

(6) Hesselbrock, W. B., Lippincott, S. W., and Palmer, E. D.: Large-Scale Routine Examinations of Stool for Parasites; Practical Experience in a General Hospital in the Zone of Interior. Am. J. Clin. Path. 16: 264–269, April 1946.

(7) Report, Fourth Service Command Laboratory, 3 Mar. 1946.

(8) Most, H., Hayman, J. M., Jr., and Wilson, T. B.: Hookworm Infections in Troops Returning From the Pacific. Am. J.M. Sc. 212: 347–350, September 1946.

Some infections disappeared spontaneously with the passage of time and many were eradicated by repeated courses of treatment, reducing the figure to about 10 percent by the time surveys were conducted in the United States.

Only about 5 percent of the troops who served in the European and Mediterranean theaters had hookworm. This was similar to the findings in men who served in the United States only, with the exception of one survey [4] which was conducted at a separation center in the southern part of the United States, where the incidence of infection was notably higher (12.9 percent of those examined). Sanitary and combat conditions in the European and Mediterranean areas were often favorable to the acquisition of parasites. That infection did not occur more frequently may have been

[4] Report, Fourth Service Command Laboratory, 3 Mar. 1946.

due to low native and enemy troop infection in those areas, to particular combat conditions, or to insufficient time or temperatures for development of infecting larvae. Generally speaking, the infections discovered in men returning from the European and Mediterranean theaters were regarded as having been acquired in the United States before military service, although some may have been the result of local conditions overseas.

Hookworm infection in troops who saw no oversea duty was about 5 percent and was a reflection of the existence of hookworm in various southern States. A small number of infections due to *Necator americanus* may have been acquired during maneuvers in hookworm areas in the United States.

Nature and Severity of Infections

Few attempts were made overseas to recover adult hookworms after treatment, and few egg counts were done. At the 39th General Hospital, Auckland, New Zealand,[5] stool egg counts in 39 patients varied from 350 to 71,000 per gram of feces, the majority being between 1,000 and 5,000. A total of 602 worms, all *Ancylostoma duodenale,* were recovered from 11 patients, 411 of the worms from the patient having the 71,000 stool count. The same parasite was recovered from 3 patients treated at the 8th General Hospital, Dumbea Valley, New Caledonia,[6] and from 8 of 14 patients reported from India.[7] The series from India included also two patients with *Necator* parasites and four with both varieties. The number of worms in the 14 cases in India varied from 8 to 100. These scattered figures indicate that *Ancylostoma* was responsible for a considerable number of mild infections.

Further studies in the United States have confirmed this impression. In one general hospital,[8] out of 169 patients from whom adult worms were recovered after treatment, 87 had *Ancylostoma,* 69 had *Necator,* and 13 had both. The majority of hookworm infections acquired overseas were *Ancylostoma,* although a few men from northern nonhookworm areas picked up *Necator* (which is the variety endemic in southern United States), and some already infected with *Necator* acquired *Ancylostoma* as well.

On the whole, hookworm infections were not heavy. The number of worms recovered per patient in all but 14 of the 169 patients just mentioned was 25 or less. The maximum number of *Necator* was 86 and of *Ancylostoma,* 112. The average stool count for *Necator* infections was 1,900 (range 100 to 9,100) and for *Ancylostoma,* 2,295 (range 200 to 9,800). All

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[5] Essential Technical Medical Data, U.S. Army Forces, South Pacific Area, for June 1944, dated 5 July 1944.

[6] Essential Technical Medical Data, South Pacific Base Command, for April 1945, dated 15 May 1945.

[7] Essential Technical Medical Data, U.S. Army Forces, India-Burma Theater, for June 1945, dated 1 Aug. 1945. Enclosure 4 thereto.

[8] Most, H., Hayman, J. M., Jr., and Wilson, T. B.: Hookworm Infections in Troops Returning From the Pacific. Am. J. M. Sc. 212: 347–350, September 1946.

169 patients had had previous courses of treatment, but in another group not previously treated the average stool counts for *Necator* and *Ancylostoma* were 2,400 and 3,200, respectively. It is pertinent to recall here that *A. duodenale* lays almost twice as many eggs a day as *N. americanus*. Stool counts of the same order of magnitude have been reported in other series.

Whether *Ancylostoma* will become established in the United States, time will tell.[9] Persisting infections will, presumably, be extremely light. An attempt was made to survey troops overseas and to treat the positives before they left. The pressure of demobilization, however, was so great that it was impossible to carry out this program.

Effect of Infection on the Host

As a rule, several hundred hookworms are necessary to produce symptoms. Since less than 25 worms were present in 90 percent of Army cases, it is not surprising that hookworm disease was a very uncommon manifestation of hookworm infection. Anemia was infrequent and usually mild, but leukocytosis and eosinophilia were common. Numerous courses of treatment were often required to eliminate all worms, resulting in prolonged hospitalization of patients. In occasional cases, clinical symptoms were disabling, and the basis for acute or chronic vague complaints was obscure until hookworm infection was discovered. These factors are discussed briefly.

Anemia.—Severe anemia did not occur in U.S. troops, and much of the mild anemia observed may have been due to tropical and military conditions rather than to hookworm infection. In one report,[10] 15 percent of 907 men without hookworm had erythrocyte counts below 4 million and 37 percent had a hemoglobin of less than 80 percent. Only 20 percent of 93 men with hookworm had erythrocyte counts below 4 million and 34 percent had hemoglobins less than 80 percent. The difference in the two groups is not significant. In one study [11] of 74 patients with hookworm, 48 of whom had gastrointestinal symptoms, only 3 had anemia (hemoglobin 11 to 13 gm.). In another series,[12] 3 of 39 patients had anemia (red blood cells 2.9 to 3.8 million, hemoglobin 56 to 76 percent). In a general hospital in the United States, among 100 men who had hookworm as an incidental finding,[13] there was none with anemia attributed to this infection.

White blood cells.—Leukocytosis and eosinophilia commonly occurred early in the course of hookworm infection. The persistence of the latter for many months was used in estimating the probable rate of hookworm infec-

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[9] Up to 1953, no case of this parasite acquired in the United States has been reported.

[10] Essential Technical Medical Data, U.S. Army Forces, South Pacific Area, dated 1 Feb. 1944.

[11] Hodes, P. J., and Keefer, G. P.: Hookworm Disease; A Small Intestinal Study. Am. J. Roentgenol. 54: 728–742, December 1945.

[12] See footnote 5, p. 148.

[13] See footnote 8, p. 148.

tion in the 43d Infantry Division.[14] When compared to positive stool counts, however, eosinophilia did not prove to be a very reliable criterion. Examination of one or two stools by brine flotation in judiciously sampled, representative small groups is a more satisfactory method. Eosinophilia occurred most frequently in infantry combat outfits and was directly related to the duration of combat or to the length of residence in the endemic area. The peak occurred 3 or 4 months after the greatest exposure and fell in a little over 8 weeks' observation. The highest eosinophilia observed was 68 percent and the greatest leukocytosis, 28,000. Eosinophilia, ranging from 10 to 70 percent, was found in other groups of patients with hookworm in India.[15] An average eosinophilia of 10.2 percent in a group of 100 men in the United States,[16] with hookworm as the only parasitic infection, attests to the persistence of this sign.

Clinical findings.—Hookworm disease was evident in only 5 of a series of 600 patients with hookworm infection.[17] However, various clinical signs and symptoms were observed that were attributed to the infection. In India, abdominal pain and tenderness, nausea, vomiting and diarrhea, and eosinophilia in some patients were not explained until hookworm eggs were found in the stools. In 50 selected cases of apparently recent hookworm infection,[18] the onset of symptoms was often acute, simulating gastroenteritis. The signs and symptoms noted in this group are as follows:

Signs and symptoms:

	Incidence
Diffuse abdominal pain, after meals and during the night_____percent____	86
"Foxhole" cough without coryza or sore throat, appearing 1 to 2 weeks after ground itch and lasting 3 weeks_____percent____	70
Abdominal tenderness_____percent____	66
Diarrhea (average 6 stools per 24 hours) without blood or pus__percent____	52
Ground itch 4 to 6 weeks before onset of abdominal symptoms__percent____	28
Anorexia and weight loss_____	Common
Low grade fever_____	Occasional

The leukocytes numbered as many as 41,000 per milliliter, averaging 13,700 per milliliter. The maximum percentage of eosinophiles was 70 percent, averaging 34 percent. Eggs were found in a single direct smear examination of the stools in 21 percent and in 57 percent after repeated examinations. When concentration methods were used, 86 percent of first examinations were positive, and all were positive with three examinations. From 8 to 100 adult worms per patient were collected from 14 cases.

Treatment completely relieved 20 percent of the 50 patients of symptoms, improved 55 percent, and produced no change in 25 percent. Stools were positive after two courses of treatment in 63 percent of the men.

[14] Liebow, A. A., and Hannum, C. A.: Eosinophilia, Ancylostomiasis, and Strongyloidosis in the South Pacific Area. Yale J. Biol. & Med. 18: 381–403, May 1946.
[15] See footnotes 7, p. 148; 10, p. 149; and 11, p. 149.
[16] See footnote 8, p. 148.
[17] See footnote 14.
[18] See footnote 7, p. 148.

Complete gastrointestinal studies were conducted in a general hospital in Burma [19] on 74 patients whose symptoms appeared several weeks after their arrival in that country. Of the 74 patients, 48 were hospitalized because of abdominal symptoms and the rest, for other reasons. The majority of the 48 patients complained of dull, cramping, or gnawing intermittent abdominal pain, most marked in the epigastrium or the midabdomen. In some patients, the onset was acute, marked by nausea, vomiting, pain and diarrhea, and occasionally fever with a temperature of about 100° F. Anorexia and bloating were common. The clinical diagnosis at onset was frequently peptic ulcer. Change from field rations to bland hospital diet brought no relief. In 54 acute cases, eosinophilia was between 10 and 70 percent, half being over 30 percent. The erythrocyte count and hemoglobin values were normal in all but three patients.

Roentgenographic studies.—Roentgenographically, the intestines of the 54 patients showed the following:

Distal duodenum.—No disturbance in tone or rugal pattern in mild infections. Moderate to marked thickening and prominence of mucous membrane in 26 patients. Irritability. Tenderness on palpation frequent.

Jejunum.—Tenderness on palpation in most cases. Rugal abnormalities, from slight prominence of the valvulae conniventes to severe coarsening of the mucosal folds in 60 percent of patients. Serrations between folds and height and contour of rugae variable. Normal intestinal tone in half the patients; increased tone in half, with narrowing of lumen and shortening of loops. Irritability.

Ileum.—Rugal prominence in contour similar to ileum but to a lesser degree. Normal mobility in majority; delayed mobility in 30 percent. Normal tone in half the patients; increased tone in half, producing bolus formation and segmentation.

These changes, which are those of a disordered motor function, appeared first in the proximal jejunum, then in the distal duodenum and distal jejunum, and finally in the entire ileum in severe cases. It was suggested that they resulted from disturbance in the intramural nervous mechanism of the myenteric and submucosal plexuses. Edema and cellular changes in the wall of the intestine associated with the presence of adult hookworms were of secondary importance. In a fatal case of scrub typhus, 260 *Ancylostoma* were found in the small intestine. Small erosions of the mucosa, edema, ecchymosis, and occasional worms in the submucosa were observed. After one or more courses of treatment, improvement was manifested by loss of tenderness to palpation, loss of hypermotility and irritability, and restoration of normal tone. Recovery was complete in mild cases within a few weeks after treatment, but X-ray changes sometimes persisted for months.

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[19] See footnote 11, p. 149.

Treatment

It was a disappointment to find that tetrachloroethylene was frequently unsuccessful in eliminating all hookworms. In one oversea hospital,[20] only 46 percent were cured after a course of 4.0 ml. tetrachloroethylene, 74 percent after three courses, and one patient required seven courses before stools became negative. In a series of 50 in India,[21] 63 percent of the men had positive stools after two courses, while in another oversea area[22] only 50 percent of 600 men were reported free of infection after 1 to 14 courses.

The unexpected failure of tetrachloroethylene was shown[23] to be due to the relative refractoriness of *Ancylostoma* to the drug as compared to *Necator*. Stools were examined from patients with untreated hookworm before, and a week after, treatment, and the results correlated with the species of adult recovered. Only 25 percent of 35 patients with proved *Ancylostoma* infections were cured after one course of 4.0 ml. tetrachloro-ethylene, and 55 percent after two courses. This contrasts with 66 percent of 24 patients with *Necator* cured after one course of treatment and 85 percent after two courses. Since *Ancylostoma* accounted for three-fourths of hookworm acquired overseas, the resistance of this species explains the poor results obtained. Drug deterioration in the Tropics was not responsible since use of fresh drugs in the United States gave no better results. Of 100 men previously treated overseas, 42 percent were cured by one course of treatment in the United States, 79 percent were cured after three treatments, and 98 percent after six treatments. It is probable that *Necator* infections were largely eliminated by prior treatment and failures were due to the persistence of *Ancylostoma*. Increase of dosage of tetrachloroethylene to 5.0 ml. did not improve its efficacy.

No striking toxicity was observed after from 3.0 to 5.0 ml. doses in thousands of men. A combination of tetrachloroethylene and oil of cheno-podium was not thoroughly tested. Hexylresorcinol apparently was rela-tively ineffective in eliminating hookworm infections, but no detailed studies were conducted.

Military Aspects of Hookworm Infections

Since the vast majority of hookworm infections were light, producing no anemia or symptoms, the military efficiency of U.S. troops was not im-paired by such infections. Severe infections resulted in hospitalization of a small number of men, but for the most part hookworm infections were discovered incidentally in the course of surveys or hospitalization for other causes.

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[20] See footnote 5, p. 148.
[21] See footnote 7, p. 148.
[22] See footnote 14, p. 150.
[23] See footnote 8, p. 148.

Failure of treatment often resulted in needlessly prolonged hospitalization of men who were clinically well but still had hookworm eggs in the stools or prolonged eosinophilia. At Fort Bragg, N.C., for example, 61 patients, in whom hookworm was discovered incidentally, lost an average of 14.4 days per man (longest 48 days) because of repeated courses of treatment.[24] It was recommended from that station that 2 days on quarters' status was sufficient for treatment. A similar recommendation to minimize time lost from duty was made by an antiaircraft medical officer.[25] Because most infections were subclinical and because *Ancylostoma* was often not eliminated by tetrachloroethylene, it was officially recommended in 1945 [26] that treatment be limited to two courses.

OTHER PARASITIC INFECTIONS

Ascariasis

Infections due to *Ascaris lumbricoides* did not constitute a clinical or military problem. Ascariasis was discovered in relatively few troops (1 to 3 percent) after their return from overseas. This is probably due to the short lifespan of this parasite and to the fact that hexylresorcinol, which is fairly effective against *Ascaris,* was frequently used in treating hookworm infections. However, *Ascaris* infection was rather prevalent in certain Pacific areas in which the local incidence was very high. It was found in 18 percent of 630 American troops in the vicinity of Manila and in 34.4 percent of 206 men in an engineer group on Leyte. Infections were not symptomatic and were easily eliminated with hexylresorcinol.[27] Prolonged hospitalization was rare.

Strongyloidiasis

The incidence of strongyloidiasis in troops from the Pacific was from 1 to 3 percent. *Strongyloides stercoralis* were often found in patients who had hookworm. In 633 stools that were positive for hookworm or *Strongyloides* or both, 7.4 percent had *Strongyloides.*[28] No reports of significant clinical symptoms caused by *S. stercoralis* are available, although severe diarrhea has been observed. Eosinophilia was common. No cases of chronic

[24] Williams, A. F., and Kinsman, J. M.: Management of Subclinical Hookworm Infestation in the Army. [Professional paper.]

[25] Report, G. H. Houck, P. L. Burlingame, M. S. M. Watts, and J. I. Marcones, 4th AA Command, San Francisco, Calif., 5 Aug. 1945, subject: Report of Disinfestation Program in 762d and 891st AAA Gun Battalions.

[26] The Management of Hookworm Infection. Bull. U.S. Army M. Dept. 4: 660–661, December 1945.

[27] Studies subsequent to the close of hostilities have shown the therapeutic value of piperazine hexahydrate (Antepar) in ascariasis. With daily administration of 50 to 75 mg. per kilogram for 5 days, the cure rate has been well above that observed following a single course of hexylresorcinol. Piperazine is also the drug of choice in treating pinworm infections.

[28] See footnote 14, p. 150.

infection or of pulmonary involvement have been reported. Discovery of this parasite in the stools or in material drained from the duodenum occasionally accounted for the existence of prolonged eosinophilia. Frequent failure of standard treatment with gentian violet medicinal (96 tablets, 0.03 gm. during 16 days) led to prolonged hospitalization. Intensive treatment via duodenal tube or gradual increase in daily dosage to the maximum tolerance (18 tablets daily) produced cures in one hospital. Differential diagnosis of strongyloidiasis and schistosomiasis japonica could often be facilitated by examination of liquid postcathartic stools or duodenal fluid.[29]

Trichuriasis

The incidence of trichuriasis in men from the Pacific was from 10 to 15 percent and closely paralleled the incidence of hookworm. *Trichuris trichiura* produced no symptoms or signs other than slight eosinophilia. One case of epileptiform convulsions, probably due to sensitivity to the protein of the adult worm, was observed by the author. Large amounts of anticonvulsant drugs were required for control, but after the elimination of worms with two courses of leche de higuerón, convulsions ceased and did not return when anticonvulsants were omitted. Examination of stools for *T. trichiura* frequently led to discovery of other potentially more severe infections *(Entamoeba histolytica)*. Common anthelmintics were not effective in eliminating whipworms, but, since these parasites were of no clinical significance, treatment was not attempted and hence prolongation of hospitalization did not ensue.

Creeping Eruption

A total of 19 cases of cutaneous infection with *Ancylostoma braziliense* larvae were reported from Camp Rucker, Ala., over a period of 2½ years.[30] The average time lost from duty was 27 days; the maximum, 77 days. Local freezing with ethyl chloride spray controlled the infection. Associated eosinophilia and pulmonary infiltration have been reported. The infrequency of this infection is somewhat surprising in view of the probability of exposure to terrain soiled by cat and dog feces.

Tapeworm

For the years for which this information is available, a total of 14 cases of infections due to larvae of *Taenia solium* (cysticercosis) or *Echino-*

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[29] Baroody, B. J., and Most, H.: The Relative Efficiency of Water Centrifugal Sedimentation and Other Methods of Stool Examination for Diagnosis of Schistosomiasis Japonica. J. Lab. & Clin. Med. 31: 815–823, July 1946.
[30] Annual Report, Camp Rucker, Ala., for 1944, dated 13 Jan. 1945.

coccus granulosus (hydatid disease) were reported in military personnel.[31]

A small number of cases of dwarf tapeworm infections *(Hymenolepis nana)* were discovered incidentally to routine stool examination. Their origin may or may not have antedated military service. There were no clinical manifestations, and the infection was readily eliminated by several courses of oleoresin of aspidium. Dwarf tapeworms were present in some men who were on prolonged quinacrine suppression. This drug has been said to inhibit the development of a related parasite *(Hymenolepis fraterna)* in the mouse. Beef tapeworms *(Taenia saginata)* were very rarely found, possibly because of the use of federally inspected meat and, overseas, of large amounts of processed beef.

Trichinosis

During World War II, a total of 285 admissions for trichinosis were reported in the U.S. Army. Of this total, 77 occurred outside the continental United States, giving an average rate of 0.01 per 1,000 average strength per year; the 208 admissions reported in the continental United States produced the same rate.

In May 1941, before the United States had entered World War II, a small outbreak of trichinosis occurred at Camp Edwards, Mass.,[32] resulting in the hospitalization of 13 acutely ill soldiers. Diagnosis was proved in four cases by muscle biopsy. These patients were hospitalized for from 31 to 33 days. Skin tests were positive in 28 percent of the other 129 members of the same company who ate in the same mess. Thirty percent of these men also had eosinophilia above 10 percent, indicating that subclinical trichinosis may have been present in 25 percent of the company.

SUMMARY

Parasitic infections occurred fairly extensively in World War II. This was principally due to operations in the Pacific islands where, with a high incidence among natives and enemy troops, living conditions and type of military operations presented a perfect background for infection.

Hookworm was the most common of the pathogenic helminths. In U.S. troops returning from the Pacific, the incidence of hookworm was at least twice that found in men who had served only in the United States or in Europe. *Ancylostoma duodenale* was responsible for the majority of infections. Infection was generally light, and hookworm disease was rare.

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[31] According to sample tabulations of individual medical records, there were 13 admissions for echinococcus infection during 1942–45 reported among U.S. Army personnel, and 1 admission for cysticercosis in 1944 (none in 1945; data not available for 1942–43). Data on secondary cases, available only for the years 1944 and 1945, showed no cases for these diseases during the 2 years. All but one of the echinococcosis cases were admitted in the Zone of Interior; one in Hawaii. The cysticercosis case was admitted in the Mediterranean theater.

[32] Marble, A., Skoog, A. P., and Bucholz, D. J.: Trichinosis: Report of an Outbreak at Camp Edwards, Massachusetts. Mil. Surgeon 90: 636–643, 1942.

Tetrachloroethylene was not very effective in treating hookworm, particularly *A. duodenale*. Prolonged hospitalization of men without clinical symptoms, because of persistence of eggs in the stools, resulted in many days lost from duty. Military efficiency of U.S. troops was not impaired, but it is conceivable that a prolonged war in severely infected areas might result in heavy *Ancylostoma* infections of a more serious type.

Other common intestinal parasites were also prevalent, but these did not constitute an important medical or military problem.

Clothing and skin protection against larvae of hookworm or of *Strongyloides*, possible soil treatment for destruction of larvae or eggs, and development of more effective drugs for the treatment of *Ancylostoma, Trichuris,* and *Strongyloides,* remain to be achieved.

CHAPTER VI

Bullis Fever

John C. Woodland, M.D.

During World War II, early in the spring of 1942, medical officers on duty in the Contagious Disease Section, Brooke General Hospital, Fort Sam Houston, Tex., first recognized that a disease entity [1] with which they were dealing defied definite identification. There were several outstanding clinical features characterizing the illness: An initial chill followed by fever, an unusually low leukocyte count with an associated neutropenia, a severe postorbital and occipital headache, and lymphadenopathy. In all cases, there was evidence of multiple tick bites. All the patients comprising this group were soldiers of the Army Ground Forces of Fort Sam Houston who had been on maneuvers at Camp Bullis, Tex., a training area located some 20 miles from San Antonio.

When it became apparent that a condition existed presenting a problem in diagnosis, The Surgeon General was requested to furnish consultants especially qualified in that field of medicine which was related to the problem. In response to the request, three members of the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army arrived at Fort Sam Houston on 8 July 1942. After examining a number of the patients in the hospital suffering from the disease and after a minute scrutiny of the clinical records of those who had been under observation and treatment, the consultants agreed that this was a definite disease found only in those soldiers who had been on duty at Camp Bullis and who had been bitten by ticks.[2] It was the Board's opinion that the epidemiological evidence associating this illness with the bite of the tick was highly suggestive but that the causative agent had not been conclusively identified nor could it be definitely shown at that time that the disease was transmitted to man through the tick as vector.

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[1] It is not often that a new disease entity, including the causative infectious agent, and its insect vector are revealed with such clarity and in such short space of time. Consequently, this account of the discovery of "Bullis Fever," and the research studies conducted, will be read with intense interest. The author, Dr. John C. Woodland, in collaboration with Drs. M. M. McDowell and J. T. Richards, wrote the original article (see footnote 3, p. 158), calling attention to the new disease, while Army medical officers stationed at Brooke General Hospital, Fort Sam Houston, Tex., in 1943.—A. L. A.

[2] Letter, Kenneth F. Maxcy, M.D., Consultant to the Secretary of War, to The Surgeon General, 10 Aug. 1942, enclosure thereto, subject: Investigation of Cases of the Typhus-Spotted Fever Group, Station Hospital, Fort Sam Houston, Texas, July 18–25, 1942.

CLINICAL MANIFESTATIONS

Woodland, McDowell, and Richards, in the original article on Bullis fever,[3] described it briefly, as follows:

The illness was usually ushered in with an initial chill or a chilly sensation, which was soon followed by fever, the temperature ranging from 102° to 105° F. A great majority of the patients complained of severe headache located in the postorbital and occipital regions. Pronounced lassitude, prostration, anorexia, and general weakness were noted during the febrile stage of the disease, and occasionally there was nausea and vomiting. The fever lasted from 4 to 14 days and subsided by lysis. In the average case, the temperature remained elevated for 5 days. Convalescence was protracted, especially in the more severe cases. Loss of weight was observed in many of the patients, one patient losing as much as 20 pounds (9 kg.) within a fortnight. It has been established that the incubation period in Bullis fever is from 7 to 10 days.

PHYSICAL FINDINGS

There was usually a paucity of physical findings in patients with Bullis fever; however, enlargement of the lymph glands was characteristic. At times, only a regional group of glands were involved, but commonly there was general lymphadenopathy. The glandular involvement persisted throughout the acute stage of the illness and disappeared rather promptly with the clearing of the symptoms. The throat at times was slightly red and injected, but symptoms referable to the respiratory tract were notably absent. In the more severe forms of the disease, a maculopapular rash, involving the trunk and, later, the extremities, appeared during the febrile stage and usually disappeared completely within 48 hours. This fleeting eruption was similar to the rash seen in endemic typhus. In all instances, examination revealed multiple tick bites. Enlargement of the spleen was also noted in the more severe forms of the disease. Subconjunctival hemorrhage was found in the more seriously ill patients.

LABORATORY FINDINGS

A constant laboratory finding was a definite leukopenia occurring on or about the second or third day of illness, the leukocyte count dropping to 3,000 cells per cubic millimeter or less. With the abrupt drop in the total number of leukocytes, there was an associated neutropenia, the differential count showing polymorphonuclears as low as 23 percent. During the period

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[3] Woodland, J. C., McDowell, M. M., and Richards, J. T.: Bullis Fever (Lone Star Fever—Tick Fever). An Endemic Disease Observed at Brooke General Hospital, Fort Sam Houston, Tex. J.A.M.A. 122: 1156–1160, 21 Aug. 1943.

of convalescence, the leukopenia gradually disappeared and the differential count approached normal. All other laboratory procedures commonly performed showed no abnormal findings in Bullis fever. Complement fixation tests for Q fever, Rocky Mountain spotted fever, and endemic typhus fever yielded negative results. The Weil-Felix test, using *Proteus* X–19, X–2, and OX–K, was consistently negative. Agglutination determinations were uniformly negative for undulant fever, tularemia, typhoid fever, and paratyphoid fever. The heterophile antibody reaction was negative. Cultures of the blood were sterile. The spinal fluid was normal. Biopsy of enlarged lymph glands disclosed only lymphoid hyperplasia.

CLINICAL COURSE

The disease is self-limited in nature and varies from a mild febrile illness of short duration to a severe, debilitating, prolonged disease with a protracted convalescence. There have been two deaths attributed to Bullis fever. No form of therapy appears to affect the duration or severity of the illness. The sulfonamide drugs and penicillin have been used in a number of cases without apparent benefit.

EXPERIMENTAL LABORATORY STUDIES

During the spring and summer of 1943, about 485 cases of Bullis fever were observed at Brooke General Hospital. Livesay and Pollard,[4] after exhaustive laboratory investigation of the disease, concluded—

1. That the clinical syndrome referred to as "Bullis Fever" has no immunological relationship to Rocky Mountain Spotted Fever.

2. That the disease does not appear to be typhus, based on guinea pig reactions, Weil-Felix reactions, and complement-fixation tests; nor "Q" fever, based on clinical syndrome and complement-fixation tests.

3. That a Rickettsia-like agent from clinical cases has thus far been passaged through three and five series of guinea pigs, inducing mild febrile reactions on the ninth to twelfth days, without orchitis.

4. That Rickettsia-like bodies have been observed in hyperplastic lymph nodes from men ill with this disease, and in guinea pigs killed during the febrile stage of the reaction.

5. That "Bullis Fever" is a previously undescribed syndrome in which Rickettsiae appear to be the etiological agent, without the development of a significant Weil-Felix reaction.

6. That it may be associated with an arthropod vector, the tick or *Trombicular*, in the Camp Bullis area.

7. Epidemiologically it appears that this disease is more severe and more prevalent in 1943 than in 1942. This may be interpreted with qualifications as follows:

a. Either the agent is increasing in virulence as a result of repeated passage, or,

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[4] Livesay, J. R., and Pollard, M.: Laboratory Report on a Clinical Syndrome Referred to as "Bullis Fever." Am. J. Trop. Med. 23: 475–479, September 1943.

b. The human population being exposed to this disease is more susceptible: in the past the troops occupying this area have been largely local troops who perhaps had developed some degree of immunity. The latest exposures, and those in whom the disease has been rather severe and highly prevalent, are new troops, for the most part originating in relatively tick-free parts of the country such as Chicago or New York.

Shortly after this, Anigstein and Bader, working in their laboratories at the University of Texas, in Galveston, Tex., recovered a rickettsialike micro-organism from guinea pigs inoculated with Lone Star ticks (*Amblyomma americanum*) that had been collected at Camp Bullis.[5] This micro-organism resembled the one found in patients by Livesay and Pollard, with regard to morphology, cultural characteristics, and behavior in laboratory animals.

The next laboratory work of importance which aided in establishing Bullis fever as a distinct entity was accomplished by Livesay and Pollard in the spring and summer of 1944.[6] In this work, they attempted the serologic identification of Bullis fever and its differentiation from some of the known rickettsial agents. The lack of relationship between the agents of Bullis fever and those of Rocky Mountain spotted fever had already been demonstrated by a guinea pig challenge experiment. A suggestion of similarity in the clinical picture between Bullis fever and Q fever was then investigated and was not confirmed.

Serum specimens were collected from patients in whom the clinical diagnosis of Bullis fever was made. In addition, specimens of serum were collected from cases of unrelated diseases and from normal individuals as controls. Several species of animals from Camp Bullis were killed and serum specimens collected for examination. These included 40 deer, 7 rabbits, 2 raccoons, and 1 armadillo. All serum specimens were tested for Weil-Felix agglutination reaction and by the complement fixation test for endemic typhus, American Q fever, and Bullis fever. The antigen for Bullis fever was prepared by triturating with sand enlarged spleens of mice that had been infected experimentally with a strain of the micro-organism isolated from a patient.

Of 192 specimens collected from soldiers who had recovered from illness diagnosed clinically as Bullis fever, 76 percent gave positive complement fixation for this disease. So also did 4 of the 40 deer specimens and 2 of the 7 rabbits. All of 29 specimens of normal human serum, 4 of endemic typhus, 3 of Rocky Mountain spotted fever, 4 of scrub typhus, and 2 of Q fever were negative in complement fixation tests with the Bullis fever antigen. This work established the specificity of the antigen and further confirmed the original opinion that Bullis fever was a distinct entity. It was the conclusion of the authors:

[5] Anigstein, L., and Bader, M. N.: Investigations on Rickettsial Diseases in Texas. Part 4. Experimental Study of Bullis Fever. Texas Rep. Biol. & Med. 1: 389–409, 1943.

[6] Livesay, H. R., and Pollard, M.: Serological Studies of Bullis Fever. Am. J. Trop. Med. 24: 281–284, September 1944.

1. The Bullis fever syndrome is not characterized by a significant *Proteus* OX–19, OX–K, or OX–2 agglutination reaction.

2. There does not appear to be any serological relationship between the rickettsia-like agent of Bullis fever and the rickettsia of American Q fever by the complement fixation tests.

3. From the results obtained, there does appear to be some significant serological relationship between the agent isolated from a human case of Bullis fever and the serums of convalescent cases.

Following the publication of this work, two more articles appeared, one on the specificity of Bullis fever rickettsia, by Bader and Anigstein,[7] and the other by Blair and Bader, on experimental Bullis fever in man.[8] Blair and Bader summarized their observations, as follows:

Two strains of the infectious agent recovered from human patients and from ticks of the Camp Bullis area were used for human experiments. Both strains had been maintained in guinea pig passage for a number of generations. Fresh or lyophilic material was used for the inoculum. All of the patients save one inoculated with these strains showed the syndrome of Bullis fever as described by Woodland and associates; however, most were of a mild nature. Patients inoculated with material isolated from ticks (*A. americanum*) showed the same reaction as those inoculated with the BH [Bullis human] strain. These results offer further evidence that the rickettsiae isolated from human patients (Livesay and Pollard, 1943) and from ticks (Anigstein and Bader, 1943) are specific for the disease diagnosed as Bullis fever.

During the summer of 1945, further experimental studies[9] were conducted by Maj. M. Pollard, VC, Col. H. R. Livesay, MC, Capt. D. J. Wilson, MC, and Col. J. C. Woodland, MC, on duty at Fort Sam Houston. This experimental work was done with a view to acquiring further information about the nature of the Bullis fever syndrome, its etiology, mode of transmission, and immunologic relationship to other virus and rickettsial diseases. Human male volunteers were inoculated with various types of inoculum, as follows:

1. Whole blood from natural cases of the disease.

2. An agent derived from the blood of a natural human case of Bullis fever and propagated on chick embryo.

3. An agent, propagated on chick embryo, that was derived from emulsion of ticks (*A. americanum*) collected from deer at Camp Bullis.

4. Agents, both of human and of tick origin, to determine their immunologic relationship.

5. Laboratory strains of the agent of Bullis fever, to challenge the immunity of natural cases of the disease.

6. The agent of Colorado tick fever, to study the immunologic relationship to Bullis fever.

[7] Bader, M. N., and Anigstein, L.: Specificity of Bullis Fever Rickettsia. Texas Rep. Biol. & Med. 2: 405–412, 1944.

[8] Blair, R. K., and Bader, M. N.: Observations on Experimental Bullis Fever in Man. Texas Rep. Biol. & Med. 3: 105–111, 1945.

[9] Pollard, M., Livesay, H. R., Wilson, D. J., and Woodland, J. C.: Experimental Studies With Bullis Fever. Am. J. Trop. Med. 26: 175–187, March 1946.

On the basis of the information obtained from these experimental studies, it was established that Bullis fever is a transmissible clinical syndrome which can be reproduced by transferring blood from a patient with the disease to a normal individual and that it can be maintained in series. It was also established that a syndrome was produced from the agent obtained from ticks (A. americanum) gathered at Camp Bullis that was indistinguishable from the syndrome in naturally acquired cases of Bullis fever and in the disease experimentally produced by a strain of human origin.

The critical phase of the problem was to determine the response of a convalescent case of the disease, acquired naturally, to the Bullis fever strain, propagated on chick embryo. Convalescent cases were challenged with the chick embryo material and were found immune. Controls developed the disease. It was thus established that a distinct immunologic relationship exists between the agent isolated from ticks and from human cases and the agent in naturally acquired cases of Bullis fever.

Since no relationship could be detected between Bullis fever and other known rickettsial diseases, attention was directed toward Colorado tick fever, as a disease similarly transmitted by ticks and characterized by a low leukocyte count. Challenge experiments with a known strain of Colorado tick fever agent [10] in human volunteers immune to Bullis fever (acquired naturally and induced experimentally) failed to demonstrate any relationship between these two diseases.

The results of this work, and the conclusions drawn from it, may be summarized as follows:

1. The Bullis fever syndrome is a distinct clinical entity which may be reproduced in human subjects by the inoculation of blood from febrile cases of the disease.

2. The Bullis fever agent from the blood of febrile cases has been propagated on the yolk sac of the developing chick embryo. After 20 serial transfers on yolk sac, the agent so propagated reproduced the Bullis fever syndrome in human subjects.

3. The Bullis fever agent has been isolated from emulsion of ticks (A. americanum) from Camp Bullis and has been propagated on the yolk sac of the developing chick embryo. After propagation for 12 generations, the agent reproduced the Bullis fever syndrome in human subjects.

4. The same immunologic responses are induced by the agent from these several sources.

5. There is no immunologic relationship between the agent of Bullis fever and the agent of Colorado tick fever.

During the months of November and December 1945, further ex-

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[10] Obtained through the courtesy and cooperation of Dr. Edward R. Mugrage and Dr. Lloyd Floria, University of Colorado School of Medicine, Denver, Colo.

perimental work was accomplished by medical officers [11] of Fort Sam Houston in an effort to distinguish between the Bullis fever syndrome and dengue fever. On the basis of a challenge experiment in human volunteers, no relationship between Bullis fever and dengue fever could be demonstrated.[12] Some clinical similarity has been noted to the anicteric form of leptospirosis; further serologic studies should therefore be made to confirm or deny the possibility that a leptospiral infection is responsible.

Whatever doubt still remains about the causative agent, the evidence appears definite that the tick is the vector. It is the opinion of all those familiar with Bullis fever that future studies will show that this syndrome is not confined to one small geographic area in Texas but that it will be observed elsewhere in the United States, in regions where the tick *A. americanum* abounds; namely, the Mississippi Valley and many eastern States.

[11] Col. H. R. Livesay, MC, Maj. M. Pollard, VC, Maj. Donald J. Wilson, MC, Maj. Choice B. Matthews, MC, and Capt. Sidney M. Cohen, MC.

[12] Livesay, H. R., Wilson, D. J., Pollard, M., and Woodland, J. C.: Experimental Studies of Bullis Fever and Dengue Fever. Am. J. Trop. Med. 26: 379–381, July 1946.

CHAPTER VII

Sarcoidosis

Max Michael, Jr., M.D.

Sarcoidosis was uncommon among U.S. military personnel during World War II; only some 300 cases were diagnosed. However, this disease, though infrequent, resulted in a good deal of lost time because of the inherent difficulties of diagnosis and decision concerning ultimate disposition. The multiple systemic involvement with many bizarre and seemingly unrelated symptoms, the extreme variations in its clinical course, and the utter confusion of opinion as to its management made it a stimulating challenge to the many medical officers who invariably studied each patient. Much was learned about sarcoidosis from this experience, and this information was augmented by further study of many of these patients after discharge from the service.[1]

CLINICAL PICTURE

A comprehensive review of sarcoidosis, with a description of the clinical features and the diagnostic difficulties encountered in 28 patients, was made by McCort and his associates.[2] Individual case reports called attention to unusual manifestations, such as sarcoidosis of the stomach.[3] This patient had a filling defect on the greater curvature of the stomach, and the lesion, when resected, had all the histological features of sarcoidosis. There were no other clinical evidences of sarcoidosis at that time or in subsequent followup examinations. Klinefelter and Salley described one patient with renal insufficiency resulting from sarcoidosis.[4] The extreme hypercalcemia rather than the postulated sarcoid renal infiltrates was most likely responsible for the uremia.

Since military personnel are often apt to seek medical attention quite early in the course of their illness, it is not surprising that the

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[1] The clinical records of all personnel have been made available for a study undertaken with the support of the Veterans' Administration through their Committee on Veterans Medical Problems of the National Research Council. Only those cases that had the histological picture and clinical features compatible with sarcoidosis were studied. The pathological sections were all reviewed by the Army Institute of Pathology, Washington, D.C.

[2] McCort, J. J., Wood, R. H., Hamilton, J. B., and Ehrlich, D. E.: Sarcoidosis; Clinical and Roentgenologic Study of 28 Proved Cases. Arch. Int. Med. 80: 293–321, September 1947.

[3] Gore, L., and McCarthy, A. M.: Boeck's Sarcoid: Case Involving Stomach. Surgery 16: 865–873, December 1944.

[4] Klinefelter, H. F., Jr., and Salley, S. M.: Sarcoidosis Simulating Glomerulonephritis. Bull. Johns Hopkins Hosp. 79: 333–341, November 1946.

complaints occasioning admission to the hospital differed somewhat from those encountered in civilian practice. The incidence of signs and symptoms in a group of 297 patients analyzed by the author is recorded in the tabulation which is to follow. Of this group of patients, 21 percent had no complaints.

Complaints referable to—

	Percent
Chest	31
Peripheral nodes	17
Eyes	11
Skin	3
Other systems	17

Complaints referable to the chest consisted of cough, dyspnea, pain, and wheezing. The surprisingly large percentage who sought medical attention because of lymphadenopathy probably reflects a not unusual concern with the body and the bodily functions while under the stress of military duty. Other less frequent presenting complaints were of considerable medical interest. Two patients developed symptoms related to the hypercalcemia of sarcoidosis, six had joint pains not unlike those of rheumatoid arthritis, and another patient had a severe generalized itching in the absence of demonstrable skin lesions.

The patients with no complaints (21 percent) are particularly interesting. Sarcoidosis was discovered in most of these men when roentgenograms of the chest made at separation from the service showed pulmonary infiltrations or hilar adenopathy or both. The men were completely asymptomatic at that time.[5] Diagnosis of the disease in a few of the patients in this group was made while the men were hospitalized for other medical causes, such as trauma. It is safe to say that in many patients sarcoidosis would have caused no symptoms and would never have been recognized if roentgenograms had not been made at the time of separation from the service. The frequency of incidence of sarcoidosis is not generally recognized, no doubt because of the number of cases with minimal or no symptomatology in whom the lesions clear completely. These lesions go undetected unless roentgenograms of the chest are made routinely.

Sarcoidosis is usually, but not invariably, a disease with a benign outlook. Twenty-two patients diagnosed as having sarcoidosis died during the period of Army hospitalization. However, when Ricker and Clark [6] analyzed these records, they showed that these 22 deaths did not reflect the true mortality of the disease. It was the cause or contributing cause of death in only six of these patients, including two with disseminated

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[5] In early followup studies in the Veterans' Administration, most of these patients had vague subjective complaints, the assessment of which was extremely difficult since many of the men were receiving compensations for their disease.

[6] Ricker, W., and Clark, M.: Sarcoidosis; Clinico-Pathologic Review of 300 Cases, Including 22 Autopsies. Am. J. Clin. Path. 19: 725–749, August 1949.

tuberculosis and sarcoidosis. Two other patients were later shown to have histoplasmosis with a sarcoid tissue reaction.[7] In eight cases of sudden violent death and in six patients dying of other diseases, sarcoidosis was an incidental finding at necropsy.

DIAGNOSIS

Many of these patients were seen in several hospitals in the chain of evacuation before a definitive diagnosis was made, but a high index of suspicion and a diligent search for lymph nodes usually facilitated diagnosis. Actually, a major cause of delay in diagnosis was the conflicting reports of the pathologists with their differences of interpretation of the histological changes found in tissues.

Considerable confusion existed about the relation, if any, between sarcoidosis and tuberculosis. Sarcoidosis has often been considered a manifestation of tuberculosis, but recent evidence does not confirm such a relation. This confusion was evident in the handling of many military patients. Not infrequently, the roentgenograms of the chest were interpreted as revealing tuberculosis, and the biopsies of lymph nodes were regarded as characteristic of this disease. Indeed, several patients were transferred to special hospitals for management of tuberculosis.

Occasionally other diagnostic difficulties were encountered, based on the fact that the sarcoid tubercle with all of its histological features can be produced by various viral, mycotic, parasitic, bacterial, and metallic agents as well as by neoplastic tissue. One patient diagnosed as having sarcoidosis (with a typical clinical and histological picture) had worked for a number of years before induction in a fluorescent lamp factory. The exposure to beryllium fumes was quite heavy, and the incidence of delayed chemical pneumonitis was high in workers in the plant.[8] Without a specific test for sarcoidosis, it is difficult to say which disease the patient had, although epidemiological features would indicate berylliosis rather than sarcoidosis.

It is probable that there are other patients among the military cases, as well as in all series of cases of sarcoidosis, who actually have responded with the sarcoid picture to a variety of other agents.[9]

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[7] Pinkerton, H., and Iverson, L.: Histoplasmosis; 3 Fatal Cases With Disseminated Sarcoid-Like Lesions, A.M.A. Arch. Int. Med. 90: 456–467, October 1952.

[8] Hardy, H.: Personal communication.

[9] A recent report of the findings of *Histoplasma capsulatum* in sections of two patients who had all the clinical and histological features of sarcoidosis and who were so diagnosed is of interest (see footnote 7).

A review of the sections demonstrated *H. capsulatum* in various "sarcoid lesions." Both patients had caseous adrenals which caused confusion whether this was tuberculosis, though no acid-fast organisms were demonstrable. These patients were carried as sarcoidosis in the Army files and are included in studies of this series. They further underline the need for clean-cut criteria for the diagnosis of the Boeck's sarcoidosis.

TREATMENT AND DISPOSITION

The therapeutic problem was often frustrating, and during World War II it was the general practice to recommend prolonged bed rest which was usually carried out. Other modes of therapy included radiation with ultraviolet and roentgen rays. It is fair to state that no beneficial effect was accomplished by any therapeutic regimen.

Any disease occurring during military duty poses the problem of loss of time and its effect on military forces. Although sarcoidosis occurred infrequently among military personnel, it accounted for a considerable loss of time. The duration of hospitalization was in terms of months rather than weeks; much time was consumed in transportation through the chain of evacuation and in diagnostic workups, often rather slowly accomplished. With the exception of very few men, all were given certificates of disability for discharge when the diagnosis was established, and many were transferred directly to Veterans' Administration hospitals for further care.

FOLLOWUP STUDIES

Followup studies of certain medical problems encountered among military personnel during World War II by the CVMP (Committee on Veterans Medical Problems) of the National Research Council under the sponsorship of the Veterans' Administration have been a farsighted and fruitful endeavor. Sarcoidosis was one of the diseases chosen for such study. Dr. John Ransmeier, who at that time was secretary of the CVMP, felt that some unique epidemiological features of the military cases warranted further study. Accordingly, more thorough epidemiological and clinical analysis of the cases was undertaken, the results of which have appeared elsewhere.[10] While such a retrospective study cannot be said to have contributed to an understanding of the illness during World War II, nevertheless it has certain far-reaching implications that seem to warrant a brief résumé in this report.

Some doubt has been cast on the validity of the findings, summarized in the paragraphs which follow, with the implication that the preinduction medical screening in one part of the country was not as adequate as it was in other parts. This seems improbable, since physicians at the various induction stations came from all over the country, not merely from the region where induction occurred.

1. The disease was more prevalent in inductees from the Southeastern United States, more particularly among those from the Gulf and the At-

[10] (1) Michael, M., Jr., Cole, R. M., Beeson, P. B., and Olson, B. J.: Sarcoidosis: Preliminary Report on Study of 350 Cases With Special Reference to Epidemiology. Am. Rev. Tuberc. 62: 403–407, October 1950. (2) Gentry, J. T., Nitowsky, H. M., and Michael, M., Jr.: Studies on the Epidemiology of Sarcoidosis in the United States: The Relationship to Soil Areas and to Urban-Rural Residence. J. Clin. Invest. 34: 1839, 1955.

lantic Coastal Plain areas. The attack rates per 100,000 inductees are indicated in table 23.

2. Sarcoidosis occurred with a greater frequency in Negroes than in whites.

3. A majority of the inductees were born in rural rather than in urban areas.

TABLE 23.—*Attack rates for sarcoidosis for World War II servicemen, by race, and region of induction (residence)*

[Attack rate expressed as number of cases per 100,000 inductees]

Region of induction [1] (residence)	White		Negro		Total		Ratio (Negro : white)
	Number of cases	Attack rate	Number of cases	Attack rate	Number of cases	Attack rate	
I	29	1.3	156	23.5	185	6.3	18:1
II	25	.6	38	13.3	63	1.5	22:1
III	31	.5	18	8.3	49	.7	17:1
Total	85	0.7	212	18.2	297	2.1	

[1] Roman numerals indicate region of greatest incidence (I), region of next greatest incidence (II), and region of lowest incidence (III).

NOTE.—Ratio of rates for regions:
    I : III—Total, 9 : 1; white, 3 : 1; Negro, 3 : 1.
    I : II—Total, 4 : 1; white, 2 : 1; Negro, 2 : 1.

4. The birthplaces appeared to be concentrated within certain soil areas. Speculation on the significance of this epidemiological pattern is warranted. This is not the epidemiology of tuberculosis, an argument against sarcoidosis being caused by the tubercle bacillus. The heavy concentration of cases in the Southeast is explained in part, but by no means in toto, by the heavy Negro population. Various ecologic factors that have been explored have not yet proved fruitful. One would suggest that either (1) there is a concentration of the etiological agent (or agents) in this area or (2) its propagation is favored by climatic, geologic, or environmental conditions in this area; or (3) that people in this region react differently because of environmental factors to the agent or agents.

It is of interest to compare the birthplace of the patients with sarcoidosis with those in the military service during the same time who had Hodgkin's disease. As shown in table 24, the rates for Hodgkin's disease are quite constant, region by region, in contrast to the heavy concentration of sarcoidosis in one region.

Whether servicemen from parts of the country removed from the "endemic area" would acquire sarcoidosis when exposed to these regions is a matter of interesting speculation. Hundreds of thousands of such

TABLE 24.—*Comparison of attack rates [1] of sarcoidosis with those of Hodgkin's disease*

Region of induction [2]	Sarcoidosis		Hodgkin's disease	
	Number of total cases	Attack rate	Number of total cases	Attack rate
I	223	7.4	61	2.0
II	36	.85	122	2.8
III	31	.44	190	2.7
Total	290	2.0	373	2.6

[1] Calculations are based on birthplace rather than on residence in region of induction.

[2] Roman numerals indicate region of greatest sarcoidosis incidence (I), region of next greatest incidence (II), and region of lowest incidence (III).

servicemen were so exposed in the many large military installations, such as Fort Bragg, N.C., Fort Benning, Ga., and Fort Jackson, S.C., located in the endemic area. A recent study [11] seems to indicate that after 10 years no striking general increase of sarcoidosis has occurred in men under these conditions. Since the incubation of sarcoidosis is unknown but is assumed to be many years, perhaps no definite answer to this problem can be given for another decade. Even though hundreds of thousands of men were exposed to the endemic area, it is entirely possible that their contact with the "agent or agents" was too brief or too remote to result in sarcoidosis. Certainly, no major outbreak of sarcoidosis attributable to military service has yet been uncovered.

[11] Cummings, M. M., Dunner, E., Schmidt, R. H., Jr., and Barnwell, J. B.: Concepts of Epidemiology of Sarcoidosis: Preliminary Report of 1,194 Cases Reviewed With Special Reference to Geographic Ecology. Postgrad. Med. 19: 437–446, May 1956.

CHAPTER VIII

Allergy

Walter L. Winkenwerder, M.D.

Definitive studies of the impact of allergic diseases on the U.S. Army were not described during or immediately after the First World War, and it was not until 1941 that Vaughan [1] summarized the data on asthma observed during the World War I period. Vaughan emphasized asthma's importance as a cause of rejection and disability and its cost to the Government for pensions eventually granted to personnel retired from military service. Asthma was then the only allergic condition particularized in the diagnostic classification of diseases; hay fever, when so reported, was coded to a residual category of lung conditions, but if reported as any form of rhinitis it would have been classified as "rhinitis (cause not stated)."

During World War II, allergic diseases, especially asthma, caused a significant amount of disability in the Army. Knowledge concerning these diseases had accumulated rapidly between the two conflicts, and soon after mobilization many hospitals formed allergy clinics and promptly instituted formal instruction in examination, diagnosis, and therapy; these hospitals and, later, those in oversea areas submitted studies and reports on various allergic disturbances. An analysis of these data and of the comprehensive statistics compiled by the Medical Statistics Division, Office of The Surgeon General, form the basis of this chapter. The statistics illustrate the total load the allergic diseases imposed on the Military Establishment. The diseases include asthma, allergic rhinitis, dermatitis venenata, eczema, angioneurotic edema, urticaria, allergic dermatitis, and certain other allergic disorders.

STATISTICAL DATA

Disqualifications of Selective Service Registrants for Military Service Because of Allergic Diseases

Statistics on disqualifications for military service because of allergic diseases are presented in tables 25 and 26. They were taken from several studies [2] and relate to World War II experience.

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[1] Vaughan, W. T.: Problems of Allergy in Wartime. Mil. Surgeon 89: 737–746, November 1941.

[2] (1) Hyde, R. W., and Kingsley, L. V.: Distribution of Allergic States in Selectees. J. Allergy 14: 386–392, July 1943. (2) Rowntree, L. G., McGill, K. H., and Edwards, T. I.: Causes of Rejection and the Incidence of Defects Among 18 and 19 Year Old Selective Service Registrants. J.A.M.A. 123: 181–185, 1943. (3) Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, U.S. Army.

TABLE 25.—*Disqualifications for military service due to allergic diseases, World War II*

[Rate expressed as number disqualified per 1,000 examined registrants]

Source of data	Total allergic diseases	Asthma	Hay fever	Other
Hyde and Kingsley:[1]				
Primary disqualifying cause	6.6	5.9	0.4	0.3
Primary and secondary disqualifying cause	8.2	7.3	.5	.4
Rowntree, McGill, and Edwards:[2]				
Primary disqualifying cause	4.5	3.7	.8	--------
Karpinos:[3]				
Primary disqualifying cause	5.6	5.3	.2	.1
Prevalence of disqualifying cause	6.6	6.2	.4	.1

[1] Hyde, R. W., and Kingsley, L. V.: Distribution of Allergic States in Selectees. J. Allergy 14: 386–392, July 1943. (Note that the rates are not given in the study. They were derived from the specified number of disqualified, by diagnosis, and the number examined.)

[2] Rowntree, L. G., McGill, K. H., and Edwards, T. I.: Causes of Rejections and the Incidence of Defects Among 18 and 19 Year Old Selective Service Registrants. J.A.M.A. 123: 181–185, 1943.

[3] Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, U.S. Army.

TABLE 26.—*Disqualifications for military service due to allergic diseases, and prevalence of these disqualifying diseases by age, World War II, (November 1943 through December 1944)*

[Rate expressed as number per 1,000 examined registrants, by age]

Diagnosis	All ages (18-37)	18-19	20-24	25-29	30-34	35-37
Principal disqualifying cause:						
Asthma	5.34	3.90	5.01	5.88	6.23	6.65
Hay fever	.24	.16	.26	.21	.35	.33
Other	.04	.02	.02	.03	.06	.05
Total	5.62	4.08	5.29	6.12	6.64	7.03
Prevalence of disqualifying disease:						
Asthma	6.18	4.35	5.72	6.71	7.38	8.13
Hay fever	.41	.25	.30	.43	.58	.63
Other	.05	.03	.03	.06	.09	.08
Total	6.64	4.63	6.05	7.20	8.05	8.84

Source: Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, U.S. Army.

The data by Hyde and Kingsley (table 25) deal with disqualifications for allergic diseases among the first 60,000 selective service registrants examined at the Boston Recruiting and Induction Station during the winter, spring, and summer of 1942. The age range was from 21 through 24 for the first 6,000 examinees and from 21 through 44 for the remaining

examinees. These data indicate that allergic diseases were the primary (or sole) cause of disqualifications for 6.6 per 1,000 examinees, with asthma being the main cause (5.9 per 1,000 examinees). In some cases, the allergic disease was the secondary cause of disqualification, implying that the disease was of sufficient severity to disqualify the examinee were it not for a more serious defect that was taken as the primary cause. As shown in the table, 8.2 per 1,000 examinees had a disqualifying allergic disease (primary and secondary cause). The corresponding disqualification rate for asthma was 7.3 per 1,000 examinees. It should be noted that these total rates include certain diseases (for example, allergic dermatitis and atopic eczema) which were not included among the allergic diseases in the other studies. The disqualifications for these additional diagnoses, however, were negligible.

Hyde and Kingsley were primarily interested in relating the disqualifications for allergic diseases to socioeconomic factors. They found on the basis of their "desirability" factors, such as medical care, education, and population density, that the prevalence of allergic diseases was constant in many socioeconomic backgrounds, although a relatively higher rate was noted for semirural communities and a relatively lower rate for tenement districts.

The study by Rowntree, McGill, and Edwards (table 25) deals with causes of disqualification among 18- and 19-year old selective service registrants. It covers a 3-month period, from December 1942 through February 1943. It was a sample study which included some 45,600 physical examination forms. The disqualification rates were computed by the authors as 4.5 per 1,000 examinees for all allergic diseases and as 3.7 for asthma alone. These rates are lower than those reported by Hyde and Kingsley because the study by Rowntree and his associates comprised a younger population. (Compare these rates with those given in table 26 for the 18–19 age group.)

The study by Karpinos (tables 25 and 26) covers a 14-month period, from November 1943 through December 1944. It was also a sample study which included some 147,000 physical examination forms of medically disqualified registrants. (It comprised altogether 384,000 physical examination forms, by including those of qualified examinees.)

When limited to the primary disqualification cause, Karpinos indicates that the disqualification rate for allergic diseases was 5.6 per 1,000 examinees, with asthma having a rate of 5.3. The total prevalence of disqualifying allergic diseases (including both primary and secondary diagnoses) was computed as 6.6, and that for asthma as 6.2, per 1,000 examinees. (Rowntree and his coworkers report a total prevalence of 10.6 for allergic diseases: For asthma 5.3 and for vasomotor rhinitis 5.3. These rates, however, include both disqualifying and nondisqualifying

diseases. In other words, the rates include men accepted with allergic diseases.)

As indicated in table 26, disqualification and prevalence rates increase with age. The disqualification rate was 4.1 for the youngest (18–19) age group and 7.0 for the oldest (35–37) age group. The prevalence rate was about twice as high in the 35–37 age group as it was in the 18–19 age group; 4.6 for the youngest age group versus 8.8 for the oldest age group.

To summarize statistically, the World War II data indicate the following:

1. About 6 per 1,000 examinees were disqualified for allergic diseases and about 7 per 1,000 examinees had a disqualifying allergic disease, asthma being the main disqualifying cause.[3] That many registrants with allergic diseases were knowingly taken into the military service, while others with allergic disease were apparently not properly screened out (representing about 1 percent of 1,000 examined), presented a problem in the Army, as reflected later by aggravation or recurrence of allergic diseases, notably asthma, as is brought out in the succeeding section.

2. The disqualifications for allergic diseases represented a relatively small percentage of the disqualifications for all causes: 1.8 percent of the disqualification for all causes (total disqualification rate 358.0 per 1,000 examinees), as reported by Hyde and Kingsley; 1.8 percent (total disqualification rate 253.3 per 1,000 examinees), as reported by Rowntree and his associates; and 1.6 percent (total disqualification rate 353.6 per 1,000 examinees), as reported by Karpinos.

Hospital Admissions for Allergic Conditions

The number of admissions to hospitals and quarters for allergic conditions for the years 1942–45, inclusive, is given in table 27 and for each year in the 4-year period (1942, 1943, 1944, and 1945) in tables 28, 29, 30, and 31, respectively. During this 4-year period, 248,680 patients with allergic conditions were admitted to hospitals in the United States and in oversea theaters, in order of frequency as follows: With asthma, 87,630; with dermatitis venenata, 75,371; with urticaria, 29,811; with allergic dermatitis and other allergic disorders, 28,259; with hay fever, 15,254; with angioneurotic edema, 7,154; and with eczema, 5,201. All the allergic states were comparatively more frequent in the United States than in oversea areas, but the relative incidence overseas increased sharply after 1942 in the four major oversea areas—the European theater, the Mediterranean theater, the Southwest Pacific Area, and the Pacific Ocean Area.

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[3] These disqualification rates might have been higher if examining physicians had adhered strictly to the provisions of MR (Mobilization Regulations) 1–9, "Standards of Physical Examination During Mobilization," 15 October 1942, as applied to allergic states.

TABLE 27.—*Admissions to hospitals and quarters for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]

Area or theater	Total allergic diseases	Asthma	Hay fever	Dermatitis venenata	Eczema	Edema, angio-neurotic	Urticaria	Allergic dermatitis and certain other allergic disorders [1]
Continental United States	162,980	61,785	10,084	59,452	2,231	3,868	16,649	8,911
Overseas:								
Europe	22,868	8,014	2,004	2,843	784	980	4,494	3,749
Mediterranean	10,924	3,839	933	1,457	362	437	2,345	1,551
Middle East	1,147	419	51	99	20	84	301	173
China-Burma-India	5,108	1,377	232	1,362	248	187	852	850
Southwest Pacific	24,435	4,737	912	5,147	833	720	2,232	9,854
Pacific Ocean Area	14,969	5,361	807	3,761	474	588	1,525	2,453
North America	1,988	634	35	385	59	110	505	260
Latin America	3,355	1,240	194	683	114	146	658	320
Total overseas [2]	85,700	25,845	5,170	15,919	2,970	3,286	13,162	19,348
Total Army	248,680	87,630	15,254	75,371	5,201	7,154	29,811	28,259

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

This trend is consistent with the relatively increased number of troops serving overseas during 1943–45 and with the well-recognized frequency with which allergic states developed or were aggravated during oversea duty. Asthma and dermatitis venenata represented the chief causes for hospitalization throughout the war period, except for the marked increase in the category "Allergic Dermatitis and Certain Other Allergic Disorders" during 1944 and 1945.

The number of admissions for urticaria seems high in view of its relatively low incidence noted in the individual studies on allergic diseases reported both in the United States and from oversea theaters (see p. 192). Allergic dermatitis and the miscellaneous allergic conditions included in the residual category increased sharply during and after 1944 while dermatitis venenata decreased, especially in 1945. These shifts may, in part, be related to changes in coding procedures and codes which were introduced beginning with the 1944 coding.

The rate of admissions per year per 1,000 average strength for allergic conditions in the Army for the years 1942–45, inclusive, is given in table 32; for each of the years in the 4-year period (1942, 1943, 1944, and

TABLE 28.—*Admissions to hospitals and quarters for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1942*

[Preliminary data based on sample tabulations of individual medical records]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	28,600	10,418	673	12,686	363	670	3,177	613
Overseas:								
Europe_____	433	233	16	34	28	20	49	53
Mediterranean_____	79	48	1	8	6	2	13	1
Middle East_____	61	25	_____	15	1	5	13	2
China-Burma-India_____	60	25	1	13	4	3	11	3
Southwest Pacific_____	565	246	27	117	18	31	107	19
Pacific Ocean Area_____	1,331	730	52	285	31	56	144	33
North America_____	475	179	2	93	12	23	150	16
Latin America_____	882	352	27	191	27	48	208	30
Total overseas [2]_____	3,962	1,871	127	770	129	192	713	160
Total Army_____	32,562	12,289	800	13,456	492	862	3,890	773

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

1945), the admission-rate data are given in tables 33, 34, 35, and 36 respectively. Asthma, dermatitis venenata, and urticaria represent the highest rates, in the order given. The higher rates in tropical theaters, namely, the China-Burma-India and the Pacific Ocean and Southwest Pacific Areas, probably reflect the unfavorable effect of tropical environment on allergic conditions. It is of interest, however, that the rate for asthma in the Latin American theater closely approximates that for the tropical areas mentioned and that the highest rates for hay fever were in the Pacific Ocean Area and in the Mediterranean theater and for angioneurotic edema in the Middle East. Definitive studies on asthma were not reported from the Latin American theater to explain its high rate; in North Africa, dust and pollen were prevalent and the considerable daily alterations in temperature, with warm days and cool nights, were reported to be of etiological importance. Why the Middle East had the highest rates for urticaria and angioneurotic edema is not explained by statistics nor by individual studies on allergic states reported from this theater. Again, the high rate for allergic dermatitis in the Southwest

TABLE 29.—*Admissions to hospitals and quarters for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1943*

[Preliminary data based on sample tabulations of individual medical records]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma- titis venenata	Eczema	Edema, angio- neurotic	Urti- caria	Allergic derma- titis and certain other allergic disorders [1]
Continental United States	60,685	25,000	3,700	23,310	670	1,400	5,335	1,270
Overseas:								
Europe	1,504	707	94	179	162	61	235	66
Mediterranean	2,904	1,468	279	260	91	137	584	85
Middle East	441	213	25	30	9	31	115	18
China-Burma-India	516	217	21	123	24	19	100	12
Southwest Pacific	2,440	893	86	933	71	92	304	61
Pacific Ocean Area	3,576	1,670	166	1,120	114	126	318	62
North America	718	272	10	143	18	33	174	68
Latin America	987	375	63	243	37	48	185	36
Total overseas [2]	13,224	5,890	745	3,055	529	551	2,041	413
Total Army	73,909	30,890	4,445	26,365	1,199	1,951	7,376	1,683

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

Pacific probably represents the effect of tropical environment with its high humidity.

Disposition of Allergic Patients

Table 37 presents the total numbers and the rates, per year per 1,000 average strength, of disability separations and retirements due to allergic diseases for the years 1942–45, inclusive.

During the 4-year period, a total of 46,607 allergic patients were discharged or retired for disability. Asthma accounted for 38,575 (82.7 percent) of the total number; hay fever and allergic dermatitis and certain other allergic disorders, combined, for 12.9 percent; and the other categories, only insignificant totals. It is surprising how few disability discharges were caused by dermatitis venenata, considering the large number of cases (75,371) observed over the war period.

A comparison of admissions and disability separations, for selected allergic diseases in the U.S. Army for the period 1942–45, inclusive, is shown in table 38. Of the total number of admissions, 18.7 percent were

TABLE 30.—*Admissions to hospitals and quarters for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1944*

[Preliminary data based on sample tabulations of individual medical records]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma- titis venenata	Eczema	Edema, angio- neurotic	Urti- caria	Allergic derma- titis and certain other allergic disorders [1]
Continental United States_____	43,125	15,647	2,766	15,831	673	1,083	4,527	2,598
Overseas:								
Europe_____	7,636	3,304	544	1,050	289	379	1,205	855
Mediterranean_____	5,046	1,658	458	759	155	198	978	840
Middle East_____	415	116	21	34	5	38	118	83
China-Burma-India_____	2,157	650	100	571	110	105	336	285
Southwest Pacific_____	8,415	1,638	334	2,717	289	247	691	2,499
Pacific Ocean Area_____	5,222	1,576	254	1,681	174	206	518	813
North America_____	540	133	23	104	19	39	131	91
Latin America_____	776	279	49	144	20	25	135	124
Total overseas [2]_____	30,464	9,409	1,793	7,144	1,072	1,248	4,183	5,615
Total Army_____	73,589	25,056	4,559	22,975	1,745	2,331	8,710	8,213

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

discharged or retired and 81.3 percent were returned to duty (how many to full or to limited status is not known).

That 38,575 patients, representing 44 percent of admissions to hospital for asthma, received disability separations strikingly illustrates the importance of the disease in the Army. Of 15,254 admitted for hay fever, 1,938 or 12.7 percent were given disability discharges. What percentage of the hay fever was due to seasonal or to the more serious perennial form of allergic rhinitis is unknown. That only 454 (0.6 percent) of the 75,371 admissions for dermatitis venenata were separated from service illustrates the benign nature of this form of contact dermatitis; whereas, allergic dermatitis and certain other allergic disorders combined were second only to asthma as the basis for disability separations from the service.

CLINICAL DATA

The statistical material just presented conveys, only insofar as statistics can, some concept of the total "load" that the allergic diseases imposed

TABLE 31.—*Admissions to hospitals and quarters for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1945*

[Preliminary data based on sample tabulations of individual medical records]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	30,570	10,720	2,945	7,625	525	715	3,610	4,430
Overseas:								
Europe_____	13,295	3,770	1,340	1,580	305	520	3,005	2,775
Mediterranean_____	2,895	665	195	430	110	100	770	625
Middle East_____	230	65	5	20	5	10	55	70
China-Burma-India_____	2,375	485	110	655	110	60	405	550
Southwest Pacific_____	13,015	1,960	465	1,380	455	350	1,130	7,275
Pacific Ocean Area_____	4,840	1,385	335	675	155	200	545	1,545
North America_____	255	50	_____	45	10	15	50	85
Latin America_____	710	235	55	105	30	25	130	130
Total overseas [2]_____	38,050	8,675	2,505	4,950	1,240	1,295	6,225	13,160
Total Army_____	68,620	19,395	5,450	12,575	1,765	2,010	9,835	17,590

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

upon all branches of the military service, including the Medical Corps. A series of clinical reports by medical officers supplements the statistical data, in many instances specifying the etiology, the results of treatment, and the disposition in selected series of patients.

All reports emphasize that—

1. Of all persons with asthma and hay fever, observed in clinic or hospital or both, at least 50 percent gave an appropriate history or actually had symptoms at the time of entering the military service.

2. Many persons giving a history or having mild symptoms of asthma or hay fever on entry into the service were able, with or without appropriate treatment, to remain on duty in the United States, although aggravation of symptoms frequently developed when such persons were sent to oversea theaters.

3. Desensitization of extrinsic asthma and allergic rhinitis when indicated was relatively more successful in the United States than in oversea areas, where retention of only a small percentage of patients so treated was found possible.

TABLE 32.—*Admission rates for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]

[Rate expressed as number per year per 1,000 average strength]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders[1]
Continental United States_____	11.05	4.20	0.68	4.03	0.15	0.26	1.13	0.60
Overseas:								
Europe_____	5.20	1.82	0.46	0.65	0.18	0.22	1.02	0.85
Mediterranean_____	7.37	2.60	.63	.98	.24	.29	1.58	1.05
Middle East_____	7.85	2.87	.35	.68	.14	.57	2.06	1.18
China-Burma-India_____	11.65	3.13	.53	3.11	.57	.43	1.94	1.94
Southwest Pacific_____	13.31	2.58	.50	2.80	.45	.39	1.22	5.37
Pacific Ocean Area_____	11.91	4.27	.64	2.99	.38	.47	1.21	1.95
North America_____	4.04	1.29	.07	.78	.12	.22	1.03	.53
Latin America_____	8.80	3.25	.51	1.79	.30	.38	1.73	.84
Total overseas [2]_____	7.98	2.40	0.48	1.48	0.28	0.31	1.23	1.80
Total Army_____	9.76	3.44	0.60	2.96	0.20	0.28	1.17	1.11

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

4. Allergic states other than asthma, dermatitis venenata, and hay fever, namely, atopic eczema, urticaria, and angioneurotic edema, were relatively unimportant causes of disability.

During the period of partial mobilization before war was declared, special clinics or services for allergic conditions were not available in either station or general hospitals, and medical officers experienced in allergy were scarce. The need became evident with the rapid increase of the Armed Forces. In the Fourth Service Command, the organization of comprehensive facilities for the diagnosis and treatment of allergic diseases under the supervision of Col. Sanford W. French, MC, was started in March 1942. Formal instruction for medical officers was organized, and a central laboratory was established. At this laboratory, extracts for skin testing and desensitization were prepared and dispensed to the 89 individual allergy clinics eventually organized in this command and, subsequently, to many station and general hospitals in the other eight service commands.

TABLE 33.—*Admission rates for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1942*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number per year per 1,000 average strength]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	10.76	3.92	0.25	4.77	0.14	0.25	1.20	0.23
Overseas:								
Europe_____	5.22	2.81	0.19	0.41	0.34	0.24	0.59	0.64
Mediterranean_____	3.45	2.10	.04	.35	.26	.09	.57	.04
Middle East_____	10.09	4.13	0	2.48	.17	.83	2.15	.33
China-Burma-India_____	6.87	2.86	.11	1.49	.46	.34	1.26	.34
Southwest Pacific_____	7.93	3.45	.38	1.64	.25	.44	1.50	.27
Pacific Ocean Area_____	8.82	4.84	.34	1.89	.21	.37	.95	.22
North America_____	4.72	1.78	.02	.92	.12	.23	1.49	.16
Latin America_____	8.65	3.45	.26	1.87	.26	.47	2.05	.29
Total overseas [2]_____	6.76	3.19	0.22	1.31	0.22	0.33	1.22	0.27
Total Army_____	10.04	3.79	0.25	4.14	0.15	0.27	1.20	0.24

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.
[2] Includes admissions on transports.

French and Halpin,[4] in 1944, compiled data from 67 of the 89 clinics (including 28 Army Air Force hospitals) for the period of one year ending in November 1943. These data provide an excellent picture of the high incidence of allergic diseases in personnel stationed in the United States. Among the 32,046 allergic patients in all 89 clinics at this time, there were 6,842 with dermatitis venenata. In the 67 clinics selected for study, because they had been in operation longer than the rest, there were 25,204 allergic patients, of whom 1,785 were civilian dependents of servicemen. Among them, there were 4,573 with uncomplicated seasonal hay fever, of whom an estimated 85 percent were under desensitization therapy. The diagnosis of seasonal bronchial asthma was made in 946 patients; of seasonal hay fever accompanied by asthma, in 1,384 patients. Of the 7,261 patients with perennial bronchial asthma, 1,903 exhibited seasonal aggravation due to pollen. Perennial allergic rhinitis accounted for 3,831 patients, of whom 1,105 noted increased severity of symptoms during the pollen seasons. In

[4] French, S. W., and Halpin, L. J.: Army Allergy: Fourth Service Command, 1943. Ann. Allergy 2: 365–379, September-October 1944. [Includes discussion by L. E. Leider, p. 374.]

TABLE 34.—*Admission rates for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1943*

[Preliminary data based on sample tabulations of individual medical records]

[Rate expressed as number per year per 1,000 average strength]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	11.71	4.82	0.71	4.50	0.13	0.27	1.03	0.25
Overseas:								
Europe_____	5.64	2.65	0.35	0.67	0.61	0.23	0.88	0.25
Mediterranean_____	6.36	3.21	.61	.57	.20	.30	1.28	.19
Middle East_____	8.31	4.01	.47	.57	.17	.58	2.17	.34
China-Burma-India_____	13.02	5.48	.53	3.10	.61	.48	2.52	.30
Southwest Pacific_____	12.85	4.71	.45	4.92	.37	.48	1.60	.32
Pacific Ocean Area_____	12.27	5.71	.57	3.84	.39	.43	1.09	.21
North America_____	3.69	1.40	.05	.74	.09	.17	.89	.35
Latin America_____	8.17	3.10	.52	2.01	.31	.40	1.53	.30
Total overseas [2]_____	7.83	3.49	0.44	1.81	0.31	0.33	1.21	0.24
Total Army_____	10.76	4.51	0.65	3.84	0.17	0.28	1.07	0.24

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

these few figures, covering a 1-year period, it thus appears that pollen sensitivity, manifested by rhinitis or asthma or both involved 9,911 of 25,204 patients. Considering the geographic location of the Fourth Service Command, ragweed pollen, as would be anticipated, was the most important of the antigens; dust, feathers, and other environmental antigens were less important. Infection of the respiratory tract, including the paranasal sinuses, was a minor factor in ambulatory patients but was more evident in hospitals that received the more persistent and refractory cases of asthma and rhinitis. Urticaria of the acute and chronic type was noted in 1,644 cases in the 67 clinics. Gastrointestinal allergy was noted in 255 and food allergy in 1,565 patients.

Information derived from detailed studies made in Army installations has been summarized for presentation in the paragraphs which are to follow.

Asthma

History.—Careful study of clinical records revealed that at least 50 percent of the patients observed in hospitals or dispensaries had symptoms

TABLE 35.—*Admission rates for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1944*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number per year per 1,000 average strength]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	10.86	3.94	0.70	3.99	0.17	0.27	1.14	0.65
Overseas:								
Europe_____	4.55	1.96	0.33	0.63	0.17	0.23	0.72	0.51
Mediterranean_____	7.77	2.55	.71	1.17	.24	.30	1.51	1.29
Middle East_____	8.98	2.51	.45	·.74	.11	.82	2.55	1.80
China-Burma-India_____	12.79	3.86	.59	3.39	.65	.62	1.99	1.69
Southwest Pacific_____	15.60	3.04	.62	5.03	.54	.46	1.28	4.63
Pacific Ocean Area_____	11.90	3.59	.58	3.83	.40	.47	1.18	1.85
North America_____	4.18	1.04	.18	.80	.15	.30	1.01	.70
Latin America_____	9.04	3.25	.57	1.68	.23	.29	1.57	1.45
Total overseas [2]_____	7.98	2.46	0.47	1.87	0.28	0.33	1.10	1.47
Total Army_____	9.45	3.22	0.59	2.95	0.22	0.30	1.12	1.05

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neurogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

or gave a history of asthma on entering the military service.[5] Recurrence in many individuals developed comparatively soon thereafter. Gold and Bazemore [6] reported in 1942 that in their series 65 percent of men discharged for asthma had had less than 6 months' service and 21 percent, less than 30 days' service. All reports stressed that more adequate preinduction examinations would have resulted in disqualifying the majority of such persons who later in service were discharged or retired for disability.

Etiology.—A summary of the several studies on asthma observed in the United States and in oversea theaters indicated that pollens, dust and other environmental antigens, infections of the respiratory tract, and, in the Tropics, high humidity were the major factors responsible for chronic symptoms or recurring attacks.

[5] Rudolph, J. A.: Study of Bronchial Asthma in General Hospital, With Statistical Report of 200 Cases. Ann. Allergy 3: 258–270, July-August 1945.

[6] Gold, E. M., and Bazemore, J. M.: Significance of Allergy in Military Medicine: Report of Incidence of Allergic Diseases in Large Station Hospital, and Method of Preinduction Evaluation of Allergic State. J. Allergy 15: 279–282, July 1944.

TABLE 36.—*Admission rates for selected diagnostic categories of allergic conditions in the U.S. Army, by area or theater and year, 1945*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number per year per 1,000 average strength]

Area or theater	Total allergic diseases	Asthma	Hay fever	Derma-titis venenata	Eczema	Edema, angio-neurotic	Urti-caria	Allergic derma-titis and certain other allergic disorders [1]
Continental United States_____	10.43	3.67	1.00	2.60	0.18	0.24	1.23	1.51
Overseas:								
Europe_____	5.60	1.58	0.56	0.67	0.13	0.22	1.27	1.17
Mediterranean_____	8.18	1.88	.55	1.22	.31	.28	2.17	1.77
Middle East_____	5.62	1.59	.12	.49	.12	.24	1.35	1.71
China-Burma-India_____	10.73	2.19	.50	2.96	.50	.27	1.83	2.48
Southwest Pacific_____	12.56	1.89	.45	1.33	.44	.34	1.09	7.02
Pacific Ocean Area_____	12.88	3.69	.89	1.80	.41	.53	1.45	4.11
North America_____	3.75	.73	0	.66	.15	.22	.73	1.26
Latin America_____	9.75	3.24	.76	1.44	.41	.34	1.78	1.78
Total overseas [2]_____	8.19	1.87	0.54	1.07	0.27	0.28	1.34	2.82
Total Army_____	9.06	2.56	0.72	1.66	0.23	0.27	1.30	2.32

[1] About four-fifths of the admissions shown in this category were classified as "allergic dermatitis," which included cases reported as "atopic dermatitis," "atopic eczema," "eczematoid dermatitis," "impetiginous eczema," and "neu-rogenic dermatitis"; the remainder were admissions reported as due to "allergic conjunctivitis," "chronic allergy," unspecified allergy, and other allergic reactions.

[2] Includes admissions on transports.

TABLE 37.—*Disability separations and retirements due to selected allergic disorders, U.S. Army, 1942–45* [1]

[Preliminary data based on tabulations of individual medical records]
[Rate expressed as number per year per 1,000 average strength]

Cause of separation	1942–45		1942		1943		1944		1945	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Asthma_____	38,575	1.51	3,162	.97	16,111	2.35	8,482	1.09	10,820	1.47
Hay fever_____	1,938	.08	47	.01	786	.11	364	.05	741	.10
Dermatitis venenata_____	454	.02	1	[2].00	57	.01	145	.02	251	.03
Eczema_____	448	.02	26	.01	125	.02	128	.02	169	.02
Edema, angioneurotic_____	388	.02	24	.01	153	.02	89	.01	122	.02
Urticaria_____	948	.04	32	.01	264	.04	248	.03	404	.05
Allergic dermatitis and certain other allergic disorders_____	3,856	.15	53	.02	238	.03	566	.07	2,999	.40
Total_____	46,607	1.84	3,345	1.03	17,734	2.58	10,022	1.29	15,506	2.09

[1] Year shown is year of separation for disability.
[2] Indicates a rate of more than zero but less than 0.005.

TABLE 38.—*Comparison of admissions and disability separations, for selected allergic diseases, U.S. Army, 1942–45, inclusive*

Cause of admission or separation	Number of admissions	Disability separations	
		Number	Percent
Asthma	87,630	38,575	44.0
Hay fever	15,254	1,938	12.7
Dermatitis venenata	75,371	454	.6
Eczema	5,201	448	8.6
Angioneurotic edema	7,154	388	5.4
Urticaria	29,811	948	3.2
Allergic dermatitis and certain other allergic disorders	28,259	3,856	13.6
Total	248,680	46,607	18.7

Studies on asthma originating or aggravated in tropical areas revealed that aggravation or recurrence developed usually in a shorter period of time, in terms of tropical service, than the initial or primary attack in individuals who had no previous history of asthma.[7] Leopold,[8] in his report, questioned the significance of pollens and molds in the causation of asthma in the Tropics. He had studied 200 asthmatic patients of whom 91.5 percent had served in the Tropics, mostly in the Pacific Ocean Area. In this series of cases, the onset of initial attacks (occurring in 31.5 percent) was ascribed to factors of climate in 79.5 percent, to exposure to dust in 16 percent, and to infection in 4.5 percent. In recurrent attacks, climate, alone or in combination, was a precipitating factor in 88 percent; dust, alone or in combination, in 84 percent; and infections of the respiratory tract, in 24 percent. The botanist O. C. Durham, having been consulted, observed that tropical areas do not have the flora nor the climate conducive to the development or spread of airborne pollen and fungus. Others might object that molds grow luxuriantly in tropical islands or suggest[9] that the pollens of grasses, rice, and sugarcane sometimes play a part. Leopold concluded that the hot humid climate of the Tropics was the principal determining factor in his cases. At all events, irrespective of the cause or causes, tropical service appears to be contraindicated for individuals giving a history or presenting symptoms of asthma.

Infections of the respiratory tract were reported by several authors as important factors precipitating acute attacks of asthma or as being

[7] Young, C. T., Cook, W. R., and Kawasake, I. A.: Allergic Rhinitis and Asthma in Hawaii. War Med. 3: 282–290, March 1943.
[8] Leopold, H. C.: Study of Asthmatics Returned From Overseas. J. Allergy 16: 30–43, January 1945.
[9] Rosen, F. L.: Bronchial Asthma in Young Male Adult: Study of 50 Patients Returned From Tropics for Bronchial Asthma, as Compared to 50 Asthmatics Stationed in United States. Ann. Allergy 4: 391–396, September-October 1946.

present in chronic form in many of the patients with persistent symptoms.[10] Actually, the incidence of infection varied considerably. In Leopold's series of 200 patients, 25 were subjected to bronchoscopic examination, but only 2 showed findings that could be interpreted as evidence of infection; a comparatively low percentage in any group of unselected patients with asthma. By contrast, Zoss [11] and his coworkers, who were primarily interested in infection, reported on the bronchoscopic findings in 250 patients with asthma studied at the Finney General Hospital, Ga. Of the 250 patients, 206 had seen active duty overseas. Of the oversea group, 71 had developed asthma in the oversea area, and in 117 symptoms were intensified while overseas. Of the 250 cases, 20 percent were considered to be the extrinsic type, due to environmental and atmospheric antigens; 40 percent were considered to be the intrinsic type; and in 40 percent, the etiology was obscure. Of the total number of patients, 50 percent had chronic sinus infection. Bronchoscopic examination revealed evidence of chronic bronchitis in 220, suppurative in 123, and nonsuppurative in 97. Only in four were the mucosal changes considered typically allergic in appearance. The incidence of infection both in the sinuses and in the bronchial tree, considering the comparative youth of this series, is rather high.

Study of the cause of asthma based on bronchoscopic findings may, however, be inaccurate and misleading. The observations cited might well have had a different interpretation by other observers, for it is known that changes in the bronchial mucosa in many alleged infective asthmatic patients may be due primarily to hypersensitivity to inhaled allergens, such as dust and pollen, upon which the changes related to infection are merely superimposed. Hampton and Rand,[12] however, also found a rather high incidence of infection at the Army Air Forces Regional Hospital of the San Antonio Aviation Cadet Center. Of 186 patients with asthma, chronic infection alone or in combination with inhalant or food hypersensitivity or both was found in 141; acute infections precipitated attacks in 50. That the incidence of infection varied in different theaters is illustrated in a series of 209 cases of asthma studied in a general hospital in Australia,[13] of which only 14 percent were considered related to infection. Furthermore, in a series of 192 cases reported by Young, Cook, and Kawasake [14] at the Tripler General Hospital in Hawaii, the great majority of cases were considered to be due to pollen and dust, with infection a minor factor.

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[10] Rosen, F. L.: Bronchial Asthma in Young Male Adult; Study of 100 Hospitalized Patients in Army General Hospital, With Special Reference to Nasal Symptoms and Findings. Ann. Allergy 4: 247–260, July-August 1946.

[11] Zoss, A.; Neidlinger, W. J., and Read, H. S.: Survey of Bronchial Asthma in Soldiers; Bronchoscopic Findings and Incidence of Respiratory Infection. J. Allergy 17: 87–96, March 1946.

[12] Hampton, S. F., and Rand, H.: Problem of Allergy at Army Air Forces Hospital; Respiratory Allergy (Hay Fever, Vasomotor Rhinitis and Bronchial Asthma). J. Allergy 15: 355–368, September 1944.

[13] Winkenwerder, W. L.: Asthma—As Observed in Overseas General Hospital in Southwest Pacific Area—With Special Reference to Relationship of Tropical Service to Onset and Recurrence. Bull. Johns Hopkins Hosp. 78: 78–95, February 1946.

[14] See footnote 7, p. 185.

The question of the importance of psychosomatic elements in the etiology of asthma was emphasized by Fishman [15] in a study of 100 patients returned from the European theater. Prolonged exposure to dampness and dust, to undue exertion and fatigue, and to infections were cited as significant causes. "Few patients would admit that fear was a precipitating or aggravating factor, but many felt that worry facilitated the onset of symptoms." A special group of 16 patients, 4 officers and 12 enlisted personnel, none of whom had had asthma before going overseas, was returned to the United States with the diagnosis of asthma plus neuropsychiatric disease. The latter diagnosis had been made in each case by the neuropsychiatric consultant. In the 16 patients, pollen and other inhalant antigens and undue fatigue could not be related to their attacks; in only 3, did dust play a role. None developed symptoms during combat; nearly all did, however, exhibit symptoms during the period of precombat preparation. In three patients, asthma developed as part of a generalized functional disorder after specific mental insults. All 16 patients improved on return to the United States.

In contrast, Leopold (p. 185), in his report, stated: "The importance of the rôle of psychogenic factors in the etiology of asthma was considered. Many of these patients were in actual combat, underwent air bombardment, slept in wet clothes in wet foxholes, and faced the hardships of service in the jungles." The patients in his series manifesting anxiety symptoms were studied by the psychiatrist and in no instance were emotional factors found to be of significance. Other observers, including the author of this chapter, would disagree with such an all-inclusive denial that the psyche modifies the asthmatic state; the anxiety symptoms studied in Leopold's series of patients may not represent the peculiar emotional stress recognized by many authorities as aggravating asthma. Zanfagna,[16] in a study of 100 cases in a station hospital, concluded that psychic factors play an important part in the production of attacks in predisposed persons. On the other hand, Rosen [17] points out that the asthmatic patient is sometimes unjustly tagged as being psychoneurotic.

Disposition of patients.—Of the several series of patients with asthma studied in detail, varying percentages were discharged from service or assigned to duty, usually of a limited nature, in the United States and in oversea areas. Of the series reported by French and Halpin (p. 181) from the Fourth Service Command, 8,139 (32.3 percent) were admitted to hospital during a 12-month period. Of these, only 602 had uncomplicated hay fever; 5,447 had bronchial asthma. Among 3,742 allergic patients discharged for disability, 3,231 had bronchial asthma. A total of 10,573 patients with various other allergies were retained in the service—appropriate

[15] Fishman, A. P.: Etiologic Evaluation of Asthma in 100 Cases Returned From Overseas. J. Allergy 18: 115–124, March 1947.

[16] Zanfagna, P. E.: Perennial Bronchial Asthma; Analysis of 100 Cases. Bull. U.S. Army M. Dept. (No. 87): 100–103, April 1945.

[17] See footnote 10, p. 186.

treatment, including drugs, elimination or control of infection, and desensitization therapy, was considered responsible in great part for returning this number to duty. The overwhelming majority of patients with asthma originating or aggravated overseas were eventually returned to the United States. In a general hospital in Australia,[18] a total of 352 cases of asthma were admitted to the hospital. These represented 1.2 percent of total admissions over a 2-year period ending July 1944. Of the 352 cases, 209 were analyzed in detail, and it was found that total disability represented by time spent in the hospital was 12,260 days, an average of 58.6 days per patient. Of 2,980 patients returned to the United States by this hospital, asthma represented 9.1 percent and was, next to the psychiatric group, the largest single cause for evacuation. Treatment of the asthmatics, including desensitization, instituted in the hope of retaining men overseas even for limited service, was relatively unsuccessful—only 13 of 38 patients so treated were returned to duty status; 339 of the 352 were eventually evacuated to the United States.

There are conflicting data on the clinical course and the disposition of patients with asthma after their return to the Zone of Interior. The great majority of such patients after periods of observation and treatment were discharged from service, although Alford[19] and Leider[20] emphasized that in their series patients with asthma originating or aggravated overseas improved rapidly after evacuation to the United States and that the majority of them were returned to duty. In Leopold's series of 200, on the other hand, 176 patients including 125 whose symptoms improved were eventually given disability discharges.

The question of the frequency of recurrence in military service of childhood asthma with a history of remission for some years was commented on only by Alford. In his series, relapse of childhood asthma was infrequent. Patients with chronic or recurrent asthma, whether beginning in childhood or in later years, were all separated from service.

Allergic Rhinitis

Seasonal hay fever.—Seasonal hay fever observed in the United States was reported by several investigators.[21] Most of the patients were studied and treated in dispensaries. The specific pollens implicated depend on geo-

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[18] See footnote 13, p. 186.

[19] Alford, R. I.: Disposition of Soldiers With Bronchial Asthma. J. Allergy 15: 196–202, May 1944.

[20] See footnote 4, p. 181.

[21] (1) Blank, P.: Military Aspects of Allergy. J. Lab. & Clin. Med. 38: 609–618, February 1943. (2) Blank, P.: Survey of Allergy in Station Hospital. Mil. Surgeon 92: 419–423, April 1943. (3) Blank, P., and Levitt, H.: Military Aspects of Allergic Rhinitis. M. Bull. North African Theat. Op. (No. 4) 2: 96, October 1944; also Ann. Allergy 3: 113–122, March-April 1945. (4) Edwards, W. M.: Diagnostic Test for Atopic Sensitivity. Mil. Surgeon 95: 222–224, September 1944. (5) See footnotes 4, p. 181; and 6, p. 183. (6) Goltz, H. H., and Kalisch, A. C.: A Monograph on the Diseases of Allergy in the Mediterranean Theater of Operations, U.S. Army. [Official record.] (7) Gutmann, M. J.: Urticaria Caused by Chlorinated Drinking Water. J. Allergy 15: 395–398, November 1944.

graphic location, ragweed and grass pollen in that order being the more important agents in the United States. A summary of pollen distribution throughout the world was given by Blank and Levitt.[22] Desensitization treatment was reported to be feasible and effective in the United States,[23] but actual statistical data to support this statement are not available. Desensitization overseas was rarely practicable, owing to frequent change of station and lack of appropriate facilities. Even in fixed installations in rear areas, such treatment was relatively ineffective, although a few patients so treated were maintained on duty status.[24] It was well known that large numbers of men in various oversea areas experienced mild symptoms of hay fever but were not disabled thereby and served throughout the war. It was the general opinion of most authors that, unless symptoms were severe and prolonged, seasonal hay fever was not incompatible with military service in the United States where adequate observation was possible and treatment was readily available, but assignment to duty overseas, especially in tropical areas where, as in cases of asthma, aggravation or recurrence was frequent, was considered inadvisable. Furthermore, service in combat units may be very hazardous not only to the person with hay fever but also to others in the unit. Golz and Kalisch,[25] in a statistical analysis of allergic diseases observed at several station and general hospitals in the Mediterranean theater, cited an instance where the presence of men on secret night maneuvers was made known to enemy troops by the irrepressible sneezing of one soldier, resulting in prompt enemy fire.[26]

The question of the effects of flying and of the accompanying atmospheric pressure changes on allergic rhinitis (hay fever) was commented on in the study by Hampton and Rand (p. 186) of allergic diseases at the Army Air Forces Regional Hospital in San Antonio. Although adequately controlled experiments were not carried out, it was the general opinion of several observers that rapid changes in atmospheric pressure did not aggravate symptoms of allergic rhinitis nor induce aerosinusitis or pain in the middle ear. This view received some support in the field; for example, Golz and Kalisch cite the experience of the 5th Bomb Wing of the Fifteenth U.S. Army Air Force. Of approximately 4,256 aviators, 43 had hay fever during the months of April, May, and June 1944, while serving in the Mediterranean theater. Flying status was not modified, and symptoms actually subsided during flight.

Perennial allergic rhinitis.—Perennial allergic rhinitis due to environmental antigens other than pollens was not reported on in detail. French and

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[22] See footnote 21 (3), p. 188.

[23] See footnotes 21 (2), p. 188, and 4, p. 181.

[24] See footnote 13, p. 186.

[25] See footnote 21 (6), p. 188.

[26] A similar instance was called to my attention. The nocturnal sneezing and wheezing of one of our men occupying a foxhole with two comrades on a tropical island in the South Pacific disclosed their position and brought on an enemy attack. The soldier's friends very promptly sent him to the rear with orders not to return.—W. L. W.

Halpin (p. 181) reported 3,831 patients with this diagnosis in their series of a total of 25,204 persons with allergic diseases and, of these, 1,105 noted increased severity of symptoms during the pollen seasons. Specific antigens other than pollen were not mentioned.

In Australia, the author personally observed and studied, in some detail, 82 unreported cases of perennial allergic rhinitis. Of these, 40 had developed before entry into service. Based on history and positive skin reactions to significant antigens, 38 were considered to be allergic in origin, 20 were associated with infection, and in 24 possible causes were not definable. Nine cases developed symptoms in the Tropics; preexisting symptoms in 18 were aggravated by tropical duty and in 4, were not. Nasal polyps were found in five, sinusitis in four, and adenoidal infection in three; significant positive skin reactions in this group were obtained in only 33 percent as compared to almost 100 percent of the allergic group. Headaches, attributed to edema of the nasal mucosa and sinuses, were frequent complications in both the infective and allergic types and occurred in 18 cases, particularly in the Tropics; in several instances, this was the chief basis for admission to hospital. All were returned to the Zone of Interior except 10 of the allergic group, who were desensitized with apparent success; of these, 4 were eventually assigned to limited nontropical service and the others to full duty.

That allergic rhinitis per se does not predispose to the development of aerosinusitis or aero-otitis media makes it important to differentiate chronic or recurring rhinitis due to allergic factors from rhinitis associated with infection in the upper respiratory tract, in the sinuses, and, particularly, in adenoid tissue of the nasopharynx which frequently impinges on and causes obstruction of the eustachian tubes. Symptoms of such a condition may closely simulate chronic allergic rhinitis, but specific therapy differs in the two conditions and depends primarily on an accurate diagnosis. On the basis of prewar studies, Crowe and Baylor [27] instituted the principle of radon therapy for chronic adenoidal infection not amenable to surgical excision. This method of treatment was introduced by Bordley [28] in the South Pacific Area in 1942 for the treatment of aero-otitis media, occurring frequently in aviators in whom such infections were found on nasopharyngoscopic examination. Eventually, this form of treatment was employed by the Army Air Forces in other theaters of operations.

Atopic Eczema

Although eczema of the atopic type was referred to by several authors, the question of etiology in such cases was not commented on and an analysis

[27] Crowe, S. J., and Baylor, J. W.: Prevention of Deafness. J.A.M.A. 112: 585–590, 1939.

[28] Bordley, John: Personal and Special Communication to Chief Surgeon, Air Corps, U.S. Army, 7 Feb. 1943, subject: Proposal for the Treatment of Aero-otitis Media With Radon.

of this form of hypersensitivity is not possible based on the published reports, which were primarily statistical.

Urticaria and Angioneurotic Edema

Again, comprehensive etiologic studies of urticaria and angioneurotic edema were not reported. The acute and chronic type of urticaria was noted in 1,644 patients of the series of 25,204 allergic patients reported by French and Halpin (p. 181). Etiology was not specified other than by general reference to the possibility that the broad immunization program instituted by the military service was the inciting stimulus in many instances. Golz and Kalisch (p. 189) list 91 patients with urticaria and angioneurotic edema observed in the Mediterranean theater in 1944, but in only 3 of these cases was etiology referred to. These authors described three penicillin reactions resembling states like serum disease marked by urticaria and dermatitis, this being the only reference to penicillin hypersensitivity reactions in the various studies and reports analyzed herein. Gutmann [29] reported one patient in whom the urticaria was presumably due to drinking chlorinated water, and Golz [30] studied one soldier in whom urticaria was associated with recurrent tertian malarial infection, the lesions recurring subsequently a year later when relapse of infection developed. Although the causal relationship in the latter instance is very suggestive because of cyclic attacks at 48-hour intervals and remission of lesions coincident with Atabrine (quinacrine hydrochloride) therapy, actual sensitivity to malarial antigen was not demonstrated.[31] It is of interest that urticaria and angioneurotic edema were relatively common in the acute phase of schistosomiasis [32] but did not occur in early filariasis [33] although sensitization to specific antigen develops and has been demonstrated in both diseases. Considering the large number of soldiers serving in tropical areas in World War II, one would have anticipated more than one report of a single instance of heat allergy manifested by urticaria. Peters and Silverman [34] studied one soldier in whom the lesions were brought out by elevated environmental temperature and exercise, and on the basis of considerable experimentation they postulated that the mechanism was more related to some abnormal response of both acetylcholine and histamine rather than to

[29] See footnote 21 (7), p. 188.

[30] Golz, H. H.: Malaria and Urticaria. Ann. Allergy 4: 293–294, July-August 1946; also, M. Bull. North African Theat. Op. (No. 2) 2: 27–28, August 1944.

[31] If hypersensitivity to malarial parasitic antigen was the cause of urticaria in this soldier, it was a rare occurrence, for descriptions of reactions similar to that reported by Golz have not been reported nor called to my attention despite the thousands of cases of malarial infection observed during the war.—W. L. W.

[32] Billings, F. T., Winkenwerder, W. L., and Hunninen, A. V.: Studies on Acute Schistosomiasis Japonica in Philippine Islands; Clinical Study of 337 Cases With Preliminary Report on Results of Treatment With Fuadin in 110 Cases. Bull. Johns Hopkins Hosp. 78: 21–56, January 1946.

[33] Brown, T. M., Stifler, W. C., Jr., and Bethea, W. R., Jr.: Early Filariasis. Bull. Johns Hopkins Hosp. 78: 126–154, March 1946.

[34] Peters, G. A., and Silverman, J. J.: Role of Histamine and Acetylcholine in Mechanism of Heat Allergy; Report of Studies on Soldier. Arch. Int. Med. 77: 526–543, May 1946.

the latter alone. The reviewer observed one case related to heat intolerance which developed in the Tropics, but no experimental studies were possible. In general, the total data on urticaria and angioneurotic edema are meager and scanty, considering the large number of hospital admissions (1,336) resulting from this particular allergic syndrome (table 38).

Dermatitis Venenata

Dermatitis of the contact type has been included in the statistics on allergic diseases by the Medical Statistics Division, Office of The Surgeon General. As an allergic manifestation, it ranked next to asthma in number of hospital admissions (table 38), but contrary to asthma, 99.4 percent of admissions were returned to duty, indicating in general a self-limited condition, responding favorably to treatment.

SUMMARY AND CONCLUSIONS

Of the allergic diseases, asthma, hay fever (vasomotor rhinitis) and allergic dermatitis and certain other allergic disorders were important causes of disability in World War II.

Disqualifications.—Data on disqualifications of selective service registrants for military service in World War II indicate that some 6 per 1,000 examinees were disqualified for allergic diseases. The main diagnosis was asthma; about 5 per 1,000 examinees were disqualified for this disease. In World War II, the disqualifications for allergic diseases comprised about 1.6 percent of the disqualifications for all causes—administrative, mental, and medical.

Admissions to hospital.—There were 248,680 admissions for allergic diseases in the U.S. Army for the years 1942–45, inclusive, as follows: For asthma, 87,630; for dermatitis venenata, 75,371; for urticaria, 29,811; for hay fever, 15,254; for angioneurotic edema, 7,154; for eczema, 5,201; and for allergic dermatitis and certain other allergic disorders, 28,259. The admission rate for allergic conditions in the total Army varied from 9.06 to 10.76 per year per 1,000 average strength during the 4 years. The rate was slightly but definitely higher in the China-Burma-India, the Southwest Pacific, and the Pacific Ocean Area theaters.

Disposition.—Of patients admitted to hospitals for allergic conditions, 81.3 percent were returned to duty, and 18.7 percent were given disability discharges or were retired. In the second category, a total of 46,607 persons were released from the Army for disability due to allergic disorders during 1942–45, inclusive: For asthma, 38,575, or 1.51 per year per 1,000 average strength; for hay fever, 1,938, or 0.08 per 1,000; for dermatitis venenata, 454, or 0.02 per 1,000; for eczema, 448, or 0.02 per 1,000; for angioneurotic edema, 388, or 0.02 per 1,000; for urticaria, 948, or 0.04 per 1,000; and for

allergic dermatitis and certain other allergic disorders, 3,856, or 0.15 per 1,000 average strength.

Reports and special studies by medical officers of allergic conditions observed in hospitals in the United States and oversea theaters indicate that—

1. At least 50 percent of the allergic conditions, notably asthma and hay fever, observed in military service existed before entry into the service.

2. The relapse rate of asthma was high, particularly in personnel serving overseas and especially in tropical areas where dust, high humidity, and infection were considered the chief aggravating conditions.

3. Allergic rhinitis is not disqualifying for military service, but it should disqualify the individual soldier for combat duty.

4. The disability resulting from allergic diseases other than asthma, allergic rhinitis, dermatitis venenata, and allergic dermatitis was insignificant, and unless the condition is severe and protracted, military service is not contraindicated.

5. Contrary to MR (Mobilization Regulations) 1–9, October 1942, selective service registrants presenting asthma or a history of asthma were accepted for military service. The difficult question confronting medical examiners in induction centers was how to assess the severity of the particular allergic syndrome presented or, if evidence of disease was lacking, how much significance to give to a history of allergic symptoms such as hay fever and asthma. Frequently, this history was not supported by adequate records or, if symptoms and signs of asthma and hay fever were in remission, many young men intentionally omitted mention of them in order to enter the military services. In many instances, however, selectees and volunteers presenting mild symptoms or signs of asthma, not disturbing in their civilian environment, were accepted for service. The number of potential candidates for disability discharges or retirements for allergic diseases, in particular for asthma, the most important allergic syndrome, could be appreciably reduced in the future by more adequate examinations and by stricter adherence to regulations prescribing standards for physical fitness.

CHAPTER IX

Heat Casualty

Ludwig M. Eichna, M.D.

The global nature of World War II required men to live, work, and fight in climatic extremes far in excess of any to which most of them had ever before been exposed.[1] This was particularly true of the hot climates, and troops were stationed in many of the hottest regions on earth. Lay opinion had long maintained the traditional belief that the white men could not endure very hot climates. The natives of these areas were believed to have gained, over the centuries, special adaptations to life in such environmental extremes. It was said of certain hot regions that their climate, and endemic diseases, proved a more dangerous adversary than the enemy. How did the soldier fare and perform in such hot climates? The answer is: "Well—*after* he had learned several fundamental rules."

The experience of the military forces in hot climates, and the lessons learned, can be briefly summarized. When troops first entered a hot region, regardless of whether it was in the United States or overseas—in the arid desert or the humid jungle—a considerable number of heat casualties were encountered. Accumulation of knowledge and experience led to effective preventive measures, so that the problem of heat casualty was greatly reduced. In the last years of the war, it was concluded that, although environmental heat constituted an added handicap to troops, hot climates were well tolerated and did not prevent effective military operations. Military experience demonstrated, from the physiological standpoint, that hot climates are not the exclusive domain of their natives and that the white man, once he has learned, can live healthfully and work efficiently in extreme heat.

ENVIRONMENTAL TEMPERATURE

Although a discussion of the environmental features of the hot climates cannot be undertaken here, some data indicating the heat loads imposed upon troops by the climates of representative hot areas will be presented. Adequate climatic data are scarce, and the only systematic meteorological data were collected by the Army Air Forces. Other reports, in which air

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[1] The discussion in this chapter deals solely with those effects of heat as a physical agent imposing a thermal load which man must dissipate. His inability to maintain the required compensatory adjustments leads to systemic changes which render him a casualty, hereafter termed "heat casualty," "casualty from heat," "ill effects of heat," "heat disability," or "adverse effects of heat."

temperature is mentioned secondarily, present data obtained under many varying conditions and usually only the highest readings are recorded. As a rule, the dry bulb temperatures [2] were obtained, and the more important wet bulb temperatures or dewpoint readings are lacking. With these limitations, table 39 indicates the climatic conditions for representative hot areas occupied by U.S. troops.

TABLE 39.—*Climatic conditions in representative hot areas where U.S. troops were stationed*

Area	Air (dry bulb) temperatures	Approximate relative humidity [1]
	°F.	Percent
Desert:		
Southwestern United States	110–122	10–15
Iran	112–126	10–15
Semidesert:		
India (dry monsoon)	98–118	20–30
Tropical:		
Burma	98–110	50–65
Southwest Pacific Islands	93–112	50–65
Semitropical:		
Southeastern United States	93–108	35–50

[1] Estimated representative humidity during hot season in each area. At peak dry bulb temperatures, humidities are often lower.

These temperatures give only a partial picture. They are based on observations made near fixed installations usually constructed in clearings and often near the seacoast with its moderating winds. Few data are available from areas deep within the jungle or the desert or from foxholes, caves, dugouts, tents, and other combat positions. Additional heat loads were also imposed upon men in closed spaces; for example in "buttoned" tanks, in truck cabs, in grounded planes, in ships and ships' holds, in storehouses, and in kitchens. The environment in such spaces may be much more rigorous than that of the outside air (table 40).[3]

Finally, the heat stress of an environment cannot be defined correctly by individual temperature readings without considering the duration of elevated temperatures and of humidities. Moderately high temperatures, continued throughout the day and night, subject personnel to greater physiological stresses than do much higher temperatures in the daytime, followed by relatively milder nights. The desert areas and small islands thus impose

[2] A thermometer in air, shielded from the sun, measures the air, "dry bulb," temperature; when the bulb of the thermometer is covered with a wetted wick and the thermometer is swung in air, a lower, "wet bulb," temperature is obtained, because of the evaporative cooling from the wick. The degree of lowering of the temperature is a function of the moisture content of the air.

[3] Adolph, E. F.: Tolerance to Heat. Report No. 1, Contract No. OEM-cmr 483, for Committee on Medical Research, Office of Scientific Research and Development, 1 Feb. 1945.

TABLE 40.—*Maximal climatic conditions of installation in representative areas, by location and closed spaces*

Location	Temperature		Rela-tive humid-ity	Installation	Temperature		Rela-tive humid-ity
	Dry bulb	Wet bulb			Dry bulb	Wet bulb	
	°F.	°F.	Percent		°F.	°F.	Percent
Iran	120	------	------	Tent	137	------	------
Louisiana	97	76.5	------	Buttoned tank after 4-hour run	123	91	------
Philippine Islands:							
Luzon	91	79	59	Turret of stationary buttoned tank	98	93	84
Do	88	80	70	Loaded transport plane before takeoff	97	88	70
Offshore	90	80	65	Tank deck (landing ship, tank)	109	90	48

Source: (1) Data for Iran and its installation: History of Medical Section, U.S. Army Forces in the Middle East, September 1941 to September 1945. [Official record.]

(2) Data for other locations and installations: Personal observations of the author, 1944 and 1945.

a somewhat lesser heat stress and inland tropical areas a greater stress than their peak temperatures would indicate.

INCIDENCE

The incidence of heat casualty in World War II is not accurately determinable, for the following reasons: (1) The confusion regarding diagnosis, largely because medical officers were not familiar with the ill effects of heat; (2) the coexistence of other conditions, particularly wounds and injuries on which attention was focused primarily; and (3) the difficulties of recordkeeping on a global scale. With these shortcomings in mind, tables 41, 42, 43, and 44 present statistics on heat casualty in the U.S. Army in World War II.[4] The data include admissions for heatstroke, heat exhaustion, and certain other ill effects of heat during 1942–44.

Tables 41, 42, and 43 indicate that, in terms of admission rates per 1,000 average strength per year, heat casualty never became a major medical problem for the Army at any time during the war. Thus, for the total Army, the admissions per 1,000 average strength per year were as follows: For 1942, 2.03; for 1943, 2.54; and for 1944, 0.88. These data are to be compared with the peacetime (1940) rates of 0.5 for the Army in the United States, 1.4 for the Army in Panama, and 1.3 for the Army in the Philippines. The wartime increase in the admission rates for heat

[4] Unless otherwise indicated, the statistical analysis of the ill effects of heat in the U.S. Army in World War II is based on data compiled by the Medical Statistics Division, Office of The Surgeon General, Department of the Army.

TABLE 41.—*Admissions for ill effects of heat (excluding sunburn and burns), in the U.S. Army, by area and month, 1942*

[Rate expressed as number of admissions per annum per 1,000 average strength]

[Preliminary data based on sample tabulations of individual medical records]

Area	Total number of admissions	Rate												
		Total	January	February	March	April	May	June	July	August	September	October	November	December
Continental United States	5,852	2.20	0.03	0.01	0.10	0.27	1.30	4.13	12.49	5.80	2.29	0.25	0.06	0.03
Overseas:														
Europe	4	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00
Mediterranean [1]	2	.09	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	.00	.13
Middle East	35	5.78	(2)	(2)	(2)	(2)	(2)	22.22	9.52	15.02	15.45	4.66	4.58	.94
China-Burma-India	92	10.52	(2)	(2)	7.55	.00	10.97	70.80	42.86	8.71	1.77	2.66	.00	.00
Southwest Pacific	122	1.72	6.38	3.64	2.95	.24	.17	.44	.13	.83	.97	1.62	2.52	5.85
Central and South Pacific	174	1.15	.43	.85	3.41	1.60	.88	1.49	.75	.66	.62	.40	1.09	2.23
North America [3]	8	.08	.00	.00	.00	.00	.00	.00	.72	.09	.00	.00	.00	.00
Latin America	114	1.12	.99	1.60	2.03	1.54	.86	.58	.75	.43	1.60	1.16	.96	1.18
Total overseas [4]	727	1.24	0.94	1.55	2.34	0.95	3.92	1.64	1.15	0.70	0.85	0.59	0.72	1.33
Total Army	6,579	2.03	0.13	0.20	0.40	0.38	1.74	3.69	10.32	4.78	2.00	0.31	0.20	0.28

[1] Includes North Africa.
[2] Few or no troops in area.
[3] Includes Alaska and Iceland.

[4] Includes admissions (176) on transports.

NOTE.—The 0.00 indicates a rate of less than 0.005.

TABLE 42.—*Admissions for ill effects of heat (excluding sunburn and burns), in the U.S. Army, by area and month, 1943* [1]

[Rate expressed as number of admissions per annum per 1,000 average strength]

[Preliminary data based on sample tabulations of individual medical records]

Area	Total number of admissions	Rate												
		Total	January	February	March	April	May	June	July	August	September	October	November	December
Continental United States	14,470	2.79	0.05	0.10	0.07	0.41	1.75	7.28	11.15	8.92	1.83	0.16	0.01	0.06
Overseas:														
Europe	8	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.14	0.08	0.00	0.02	0.00
Mediterranean [2]	713	1.56	.05	.00	.00	.41	1.67	3.63	5.84	3.42	1.95	.06	.00	.02
Middle East	1,103	20.80	.73	.00	1.43	1.15	15.41	17.30	57.45	88.59	21.91	2.40	.00	.00
China-Burma-India	92	2.32	.00	.66	1.08	.44	8.91	6.56	6.18	1.57	4.80	.62	.50	.00
Southwest Pacific	386	2.03	3.36	3.59	2.69	1.57	1.02	.50	.93	1.28	1.20	2.75	2.58	3.04
Central and South Pacific	460	1.58	2.80	3.25	1.46	1.31	1.23	.26	1.00	.68	3.07	1.37	1.48	1.55
North America [3]	4	.02	.00	.00	.00	.00	.00	.00	.15	.00	.00	.00	.00	.00
Latin America	97	.80	1.48	.82	1.13	.69	.37	.60	1.06	.96	.50	1.02	.52	.34
Total overseas [4]	2,934	1.74	1.13	1.29	0.77	0.65	1.76	2.06	4.45	4.61	2.07	0.72	0.61	0.61
Total Army	17,404	2.54	0.26	0.33	0.20	0.46	1.76	6.12	9.52	7.82	1.89	0.32	0.19	0.24

[1] Excludes 4 admissions characterized as battle injuries, for which the monthly distribution is not available.
[2] Includes North Africa.
[3] Includes Alaska and Iceland.
[4] Includes admissions (71) on transports.

NOTE.—The 0.00 indicates a rate of less than 0.005.

TABLE 43.—*Admissions for ill effects of heat (excluding sunburn and burns), in the U.S. Army, by area and month, 1944* [1]

[Rate expressed as number of admissions per annum per 1,000 average strength]

[Preliminary data based on sample tabulations of individual medical records]

Area	Total number of admissions	Rate												
		Total	January	February	March	April	May	June	July	August	September	October	November	December
Continental United States	4,299	1.08	0.01	0.05	0.06	0.14	1.04	3.58	3.82	2.84	1.27	0.05	0.01	0.00
Overseas:														
Europe	75	0.04	0.00	0.00	0.05	0.05	0.12	0.00	0.11	0.19	0.03	0.00	0.00	0.00
Mediterranean [2]	196	.30	.02	.06	.06	.07	.23	.64	1.19	.97	.04	.11	.00	.00
Middle East	158	3.41	1.20	.26	.00	1.37	3.02	15.76	14.37	4.87	.27	.49	.00	.00
China-Burma-India	525	3.11	.00	.00	.40	2.77	13.31	13.21	3.57	2.79	.67	.28	.17	.15
Southwest Pacific	1,061	1.97	3.21	2.59	2.49	1.97	2.40	2.17	1.03	1.08	1.28	3.54	1.99	1.01
Central and South Pacific	391	.89	1.48	.73	.89	.59	.74	1.64	1.05	.70	.71	.68	.75	.80
North America [3]	4	.03	.00	.00	.00	.00	.00	.28	.10	.00	.00	.00	.00	.00
Latin America	31	.36	.72	.53	.37	.13	.13	.72	.14	.15	.62	.60	.00	.15
Total overseas [4]	2,535	0.67	0.66	0.53	0.52	0.52	1.19	1.45	0.89	0.71	0.35	0.66	0.40	0.25
Total Army	6,834	0.88	0.24	0.24	0.25	0.31	1.11	2.55	2.36	1.75	0.78	0.39	0.23	0.15

[1] Excludes 107 admissions characterized as battle injuries, for which the monthly distribution is not available.

[2] Includes North Africa.

[3] Includes Alaska and Iceland.

[4] Includes admissions (94) on transports.

NOTE.—The 0.00 indicates a rate of less than 0.005.

TABLE 44.—*Summary of heat casualties in the United States, by area, installation, and unit, 1942–43*

Area and installation	Unit	Date	Heat casualties			Remarks
			Total number	Number hospi-talized	Number of deaths	
Southeastern United States. [1]	Fourth Service Command.	1 Jan.–26 Aug. 1942.	1,307	378	13	Data compiled from 21 stations (see table 48).
Fort Eustis, Va. [2]	Station Hospital.	1942	------	49	------	Fifth in frequency of hospital admissions.
Fort Eustis, Va. [3]	----do--------	Summer of 1943.	273	------	2	Major medical problem in the summer.
Camp McCain, Miss. [4]	87th Infantry Division.	July and August 1943.	------	164	3	
Camp Van Dorn, Miss. [5]	99th Infantry Division.	6 Apr.–11 Sept. 1943.	300	------	2	
Desert Training Center, southern California. [6]	77th Infantry Division.	1943	649	183	------	
Desert Training Center, southern California. [7]	----do--------	8 Apr.–23 Sept. 1943.	409	25	------	
Desert Training Center, southern California. [7]	----do--------	8 and 9 June 1943.	73	------	------	Fell out during marching in heat.
Desert Training Center, southern California. [7]	----do--------	26–29 June 1943.	68	------	------	Strict water discipline.
Desert Training Center, Indio, California. [8]	7th Armored Division.	26 June–15 July 1943.	51	44	------	On maneuvers for 20 days.

[1] Letter, Headquarters, Fourth Service Command, to The Surgeon General, 26 Aug. 1942, subject: Report of Cases of Heat Stroke and Heat Exhaustion.

[2] Annual Report, Station Hospital, Fort Eustis, Va., for 1942.

[3] Annual Report, Station Hospital, Fort Eustis, Va., for 1943.

[4] Annual Report, 87th Infantry Division, for 1943.

[5] Annual Report, 99th Infantry Division, for 1943.

[6] Letter, Office of the Division Surgeon, Headquarters, 77th Infantry Division, to Commanding General, 77th Infantry Division, 3 Aug. 1943, subject: Summary of Medical Experiences and Problems on Desert Maneuvers.

[7] Sneidman, G. I.: Exhaustion and High Temperatures as Experienced in Desert Operations. [Professional paper.]

[8] Annual Report, 7th Armored Division, for 1943.

TABLE 45.—*Deaths due to environmental heat, in the U.S. Army, by area and cause of death, 1942-45*

[Rate expressed as number of deaths per annum per 100,000 average strength]

[Preliminary data based on complete files of individual medical records]

Area and cause of death	1942-45		1942		1943		1944		1945	
	Number of deaths	Rate	Number of deaths	Rate	Number of deaths	Rate	Number of deaths	Rate	Number of deaths	Rate
Continental United States:										
Heatstroke	153	1.04	46	1.73	82	1.58	15	0.38	10	0.34
Heat exhaustion	25	.17	6	.23	12	.23	7	.18	------	0
Other	24	.16	6	.22	17	.33	1	.02	------	0
Total	202	1.37	58	2.18	111	2.14	23	0.58	10	0.34
Overseas:										
Heatstroke	17	0.16	1	0.17	7	0.41	[1] 6	0.16	3	0.06
Heat exhaustion	11	.10	------	0	3	.18	5	.13	3	.07
Sunburn	1	.01	------	0	------	0	1	.03	------	0
Other	8	.08	2	.34	4	.24	2	.05	------	0
Total	37	0.35	3	0.51	14	0.83	[1] 14	0.37	6	0.13
Combined continental United States and overseas:										
Heatstroke	170	0.67	47	1.45	89	1.29	21	0.27	13	0.17
Heat exhaustion	36	.14	6	.18	15	.22	12	.15	3	.04
Sunburn	1	[2] .00	------	0	------	0	1	.01	------	0
Other	32	.13	8	.25	21	.31	3	.04	------	0
Grand total	239	0.94	61	1.88	125	1.82	37	0.47	16	0.21

[1] Includes one death among transport admissions.

[2] Indicates a rate of more than zero but less than 0.005.

casualty, which occurred chiefly in the first 2 years of the war, was obviously not great. Nevertheless, because of the large number of men mobilized, the relatively low admission rates represent sizable numbers of patients, as follows: In 1942, 6,579 heat casualties with 61 deaths; in 1943, 17,404 heat casualties with 125 deaths; in 1944, 6,834 casualties with 37 deaths; and in 1945, 4,470 heat casualties with 16 deaths (tables 41, 42, 43, and 45). The study made by the Army Institute of Pathology, Washington, D.C., of the necropsy material from 125 of the 190 fatal cases of heatstroke which occurred in troops in the United States during the summer months of the 4-year period 1941 to 1944, inclusive,[5] is believed to be the largest series of fatal heatstroke analyzed.

[5] Malamud, N., Haymaker, W., and Custer, R. P.: Heat Stroke. A Clinico-Pathologic Study of 125 Fatal Cases. Mil. Surgeon 99: 397–449, November 1946.

Hospital admission rates are inadequate indexes of the extent of the problem, for they indicate only the outright heat casualties. In all hot regions, there were many men who were not sufficiently incapacitated to report to sick call and who were confined to quarters or "stuck it out," working inefficiently or not at all. These men were, in truth, heat casualties to the effectiveness of the Army; but most of them were never placed on sick lists and their numbers are unknown.

Moreover, since heat casualty has a seasonal incidence, an analysis which averages the low incidence of the cool months with the high incidence of the hot months does not fully present the problem. Thus, the yearly admission rate for an area may be low, but in the hot months heat casualty may be a serious problem to a particular command. In the same manner, data averaged for large areas do not represent the problem in the component commands within the large area. The urgency and magnitude of heat casualty in individual units, for example, the Desert Training Center in southern California, may be serious and yet be completely masked when averaged with the low incidence in the cooler components of the theater, such as the northern United States. Therefore, the average yearly rates will require revision if the true significance of the ill effects of heat is to be appreciated in the units affected. An analysis of heat casualty by area and month is recorded in tables 41, 42, and 43.

Heat casualties assumed significant proportions in the Army in only three areas: The China-Burma-India theater, the Middle East theater, and the United States. High rates were temporary and largely limited to the period immediately after arrival in the areas. In the China-Burma-India theater, casualties for 1942 reached 10.52 per 1,000 per year, with a peak incidence of 70.80 per 1,000 per year for the month of June (table 41). Although heat casualty threatened to become a serious problem, the comparatively small number of troops in the theater at this time resulted in 92 admissions with 2 deaths. In the next 2 years, the incidence by month, and for the year, was decidedly lower, and heat casualty no longer constituted a significant medical problem in this theater.

In the Middle East theater, owing almost entirely to the high incidence in the Persian Gulf Command [6] (table 46), heat casualty in 1943 reached 20.80 per 1,000 per year with 1,103 admissions for the year (table 42). In the summer months of July and August 1943, when the rates reached 57.45 and 88.59 per 1,000 per year, respectively, heat casualty became a major medical problem. A striking decrease occurred in the following year (table 43), when the yearly incidence fell to 3.41 per 1,000, the peak (June) incidence to 15.76 per 1,000, and total admissions to 158.

In the United States, heat casualty presented a somewhat different problem. The admission rates per 1,000 per year were always relatively low (2.20, 2.79, and 1.08 for 1942, 1943, and 1944, respectively), but be-

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[6] Annual Report, U.S. Army Forces in the Middle East, for 1943.

TABLE 46.—*Incidence of heat casualty in U.S. Army Forces in Middle East, by area or command, from 1 July 1942 to 1 October 1943*

[Incidence expressed as number of heat casualties admitted to hospital or quarters or both]

Area or command	Heat exhaustion	Heatstroke	Sunburn	Miscel-laneous	Total
Eritrea	50		1	49	100
Libya	8		2		10
Delta	6	1	6	5	18
Levant	2		1		3
Headquarters, USAFIME					
Air Force	20		4		24
Persian Gulf	1,070	16	10	92	1,188
West Africa			1		1
Total	1,156	17	25	146	1,344

Source: Annual Report, U.S. Army Forces in the Middle East, for 1943.

cause of the large number of men in training, the total number of patients exceeded that of all other theaters combined (tables 41, 42, 43, 47, and 48). In 1942, there were 5,852 cases with 58 deaths; in 1943, 14,470 cases with 111 deaths; and in 1944, 4,299 cases with 23 deaths.[7] These data are for the whole of the United States, whereas the heat casualties occurred in camps in the Southern States. It is of interest that the largest number of casualties and deaths due to heat occurred in troops in the United States where the climate, even in the southeast and southwest, is not ordinarily considered hot when compared with the climate of India, Burma, or Iran.

Since overall statistics tend to minimize the problems encountered by individual units placed in climatic extremes, it seems appropriate to list some of the more serious experiences with heat casualty sustained by different units in the United States (see table 44).

The illustrations given in table 44 were chosen from units reporting high casualty rates. Other units in the same areas did not mention heat casualty. This may have been an omission or such units may have profited by the example of their predecessors and neighbors and instituted measures which reduced heat casualty to such a minor role that it was not deemed worthy of note. Nevertheless, heat casualties were still frequent in troops in the United States (tables 43 and 45), and a survey from 1 to 31 August 1944 revealed 18 stations reporting 6 or more cases during this period (table 49).

Illustrative examples from oversea theaters are more difficult to obtain. In the Middle East, casualty from heat accounted for 11.7 percent of hospital admissions in the Persian Gulf Command, from 6 June to 9 December 1942, and was exceeded in importance only by enteritis (28 percent) and

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[7] In 1945, there were 2,315 admissions with 10 deaths.

TABLE 47.—*Admissions and deaths for heat casualties among troops in the United States, by month and year, January–December, 1942, 1943, and 1944*

[Rate for admissions expressed as number of admissions per annum per 1,000 average strength]
[Rate for deaths expressed as number of deaths per annum per 100,000 average strength]
[Preliminary data based on sample tabulations of individual medical records]

Month	1942		1943		1944	
	Number	Rate	Number	Rate	Number	Rate
	Admissions [1]					
January	4	0.03	20	0.05	4	0.01
February	2	.01	40	.10	18	.05
March	16	.10	30	.07	23	.06
April	47	.27	180	.41	53	.14
May	248	1.30	805	1.75	370	1.04
June	822	4.13	3,250	7.28	1,200	3.58
July	2,693	12.49	5,165	11.15	1,296	3.82
August	1,352	5.80	4,080	8.92	932	2.84
September	569	2.29	800	1.83	386	1.27
October	70	.25	70	.16	13	.05
November	18	.06	5	.01	4	.01
December	11	.03	25	.06	--------	0
Total	5,852	2.20	14,470	2.79	4,299	1.08
	Deaths [2]					
January	--------	0.0	--------	0.0	--------	0.0
February	--------	0	--------	0	--------	0
March	--------	0	--------	0	--------	0
April	--------	0	--------	0	--------	0
May	1	.52	4	.87	1	.28
June	3	1.51	18	4.03	5	1.49
July	32	14.85	63	13.60	4	1.18
August	15	6.43	26	5.68	8	2.44
September	7	2.82	--------	0	5	1.64
October	--------	0	--------	0	--------	0
November	--------	0	--------	0	--------	0
December	--------	0	--------	0	--------	0
Total	58	2.18	111	2.14	23	0.58

[1] There were 2,315 admissions in 1945.
[2] There were 10 deaths in 1945.

TABLE 48.—*Heat casualties in Fourth Service Command, by station, 1 January–26 August 1942*

Station	Heat casualties		
	Total number	Number hospitalized	Number of deaths
Fort Barrancas, Fla	6	6	
Fort Benning, Ga	15	15	1
Camp Blanding, Fla	8	8	
Fort Bragg, N.C	107	107	5
Camp Croft, S.C	86	86	1
Camp Davis, N.C	12	12	
Camp Forrest, Tenn			
Camp Gordon, Ga	9	4	
Fort Jackson, S.C	31	31	
Key West Barracks, Fla	1	1	
Fort McClellan, Ala	511	(¹)	2
Fort McPherson, Ga			
Fort Moultrie, S.C	1	1	
Fort Oglethorpe, Ga	6	6	
Camp Rucker, Ala	28	28	
Fort Screven, Ga			
Camp Shelby, Miss	5		
Camp Stewart, Ga	11	11	
Camp Sutton, N.C	26	26	
Camp Tyson, Tenn	1	1	
Camp Wheeler, Ga	443	35	4
Total	1,307	378	13

¹ Statistics were not furnished.

venereal disease (12 percent).[8] In the same theater from 1 July 1942 to 1 October 1943, 1,344 heat casualties represented 2.5 percent of all admissions.

The 113th General Hospital arrived at Ahvāz, Iran, on 28 May 1943 and by the end of the year had treated 8 cases of heatstroke, 221 cases of heat exhaustion, and 124 cases of ill-defined effects of heat; a total of 353.[9] Apart from the Persian Gulf Command, heat casualties in other parts of the Middle East in 1942 and 1943 were few, except for Eritrea, where 99 cases occurred during the period from 1 July 1942 to 1 October 1943 (table 46).

Most reports from the Central and South Pacific and the Southwest Pacific do not mention heat casualty, or pass over it in general terms. There are some exceptions. The annual report for 1942 of the Office of the Surgeon,

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[8] History of Medical Section, U.S. Army Forces in the Middle East, September 1941 to September 1945. [Official record.]

[9] Annual Report, 113th General Hospital, for 1943.

TABLE 49.—*Stations in the United States reporting six or more casualties from ill effects of heat between 1 and 31 August 1944*

[Rate expressed as number of admissions per annum per 1,000 average strength]

Service Command	Station	Strength	Heat casualties	
			Number	Rate
First	Fort Devens, Mass	13,500	8	7
Third	Aberdeen Proving Ground, Md	24,782	9	4
Do	Fort Lee, Va	34,653	6	2
Fourth	Fort Benning, Ga	71,447	25	4
Do	Camp Blanding, Fla	56,049	60	13
Do	Camp Croft, S.C	20,195	8	5
Do	Camp Rucker, Ala	30,057	15	6
Do	Camp Van Dorn, Miss	33,170	8	3
Fifth	Camp Breckinridge, Ky	35,249	9	3
Do	Fort Knox, Ky	34,625	6	2
Seventh	Fort Riley, Kans	29,897	13	5
Eighth	Camp Barkeley, Tex	44,516	25	7
Do	Camp Chaffee, Ark	27,665	17	7
Do	Camp Claiborne, La	49,208	11	3
Do	Fort Hood, Tex	60,869	77	15
Do	Camp Joseph T. Robinson, Ark	38,501	35	11
Do	Camp Maxey, Tex	31,796	15	6
Ninth	Camp Roberts, Calif	33,176	26	9

U.S. Army Forces in the South Pacific Area, in referring to the activities on Guadalcanal states: "The major medical problems were battle casualties, malaria, dysentery, tropical ulcers, and heat exhaustion." [10] In a report dated 20 February 1943, the surgeon of the 101st Medical Regiment, attached to the Americal Division, considered heat exhaustion a medical problem which in order of frequency of medical admissions stood 10th, with 141 admissions up to 14 February 1943, as compared to 3,102 admissions for malaria (first in the cause of medical admission) over the same period.[11] The leading medical causes for admission to three field hospitals of the 101st Medical Regiment were as follows:

Cause	Number of cases
Malaria (all types)	3,102
Nervous disorders	483
Enteritis	416
Cellulitis	411
Fever of unknown origin	343
Upper respiratory infection	302
Jaundice	248
Skin disease	234
Otitis media	227
Heat exhaustion	141

[10] Annual Report, U.S. Army Forces in the South Pacific Area, for 1942.

[11] Annual Report, 101st Medical Regiment for 1942, with enclosure 8 thereto, dated 20 Feb. 1943.

In the 25th Infantry Division during operations on Guadalcanal, New Guinea, and Morotai (1943 and 1944), heat exhaustion caused from 5 to 10 percent of all medical casualties and occurred chiefly in troops on the offensive or on forced marches.[12] For the 41st Infantry Division, the following was noted:

Especially in the Hollandia operation and the present Biak landing, heat exhaustion cases have been third in the cause of hospital admission. Experience has also shown diminution of combat efficiency in many more personnel who were not prostrated to the extent of requiring hospitalization.[13]

In the China-Burma-India theater, the hot humid climate led to lethargy and decreased efficiency of work, but frank heat casualty was infrequently encountered after 1942. Even so, in Gaya, India, during June 1945, when the air temperature reached 113° F., eight cases of heat exhaustion were treated at the 99th Station Hospital, with one death.[14] The islands in the Pacific Ocean Area do not, for the most part, have hot climates, and the reports do not list heat as a cause of casualty there. Similarly, reports from the Mediterranean, South Atlantic, and Caribbean Commands either fail to mention heat casualty or routinely state "no ill effects of heat," leading to the conclusion that in these areas climate can be disregarded as a detrimental factor.

In summary, heat casualty constituted a medical problem which, though by no means a major one, could not be ignored. In absolute numbers, many men became casualties because of heat, and in specific areas, at given times, the problem was serious and urgent.

Decrease in Incidence

The incidence of heat casualty in all hot theaters decreased steadily as the war progressed, until in the last year of the war it became a minor medical problem, even in the hottest areas. The experience in the Middle East theater is a striking example of this reduction. Troops moved into this theater in the last half of 1942 and the first half of 1943. The summer of 1943 found a considerable body of troops exposed to the hot desert for the first time in their lives. Heat casualties for 1943 numbered 1,103 cases with an admission rate of 20.80 per 1,000 per year and, in August, a peak monthly incidence of 88.59 per 1,000 per year (table 42). In 1944, however, the number of cases declined to 158, the yearly admission rate to 3.41 per 1,000 per year, and the peak monthly (June) incidence to 15.76 per 1,000 per year (table 43). The experience in the Persian Gulf Command set the pattern for the entire theater. This marked reduction in heat casualty was achieved, with the command breaking all records moving supplies,

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[12] U.S. Army Forces, Far East, Board Report No. 145, Questionnaire of Armored Medical Research Laboratory on Problems of Jungle Warfare.

[13] Annual Report, 41st Infantry Division, for 1944 (2d quarter).

[14] Personal correspondence, medical officer in India, to author.

even though the summer of 1944 was as hot as the summer of 1943. Individual unit figures showed the same improvement.

The experience of the Persian Gulf Command is especially significant since this was the hottest theater in which troops were stationed for long periods. The final opinion of the Command was that, once it had learned and instituted proper living conditions, proper working hours, and proper handling of troops, it could maintain effective work without significant illness from the heat.

In the China-Burma-India theater, the experience was essentially the same. During the first year (1942), the admission rate was 10.52 per 1,000 per year and the peak monthly rate, 70.80 per 1,000 per year. In 1943, these rates fell to 2.32 and 8.91, respectively, and in 1944 they were 3.11 and 13.31 (tables 41, 42, and 43). The fact that the total yearly caseload increased from 92 in 1942 to 525 in 1944 was a reflection of the increased number of troops in the theater, for heat casualty was no longer considered a significant medical problem.

In the United States, heat casualties reached their maximum in 1943 and decreased thereafter. High monthly peak rates were encountered during the summers of the first 2 years, 12.49 per 1,000 per year in July of 1942 and 11.15 per 1,000 per year in July 1943, but only slightly increased yearly rates, 2.20 per 1,000 per year in 1942 and 2.79 per 1,000 per year in 1943 (tables 41 and 42). The total yearly caseload of 5,852 in 1942 increased to 14,470 in 1943, the highest figure of the war and indicative of the large number of men in training. Deaths due to heat numbered 58 in 1942 and 111 in 1943. The following year (1944), the number of cases diminished to 4,299, the admission rate fell to 1.08 per 1,000 per year, and the peakload during the summer months dropped to 3.82 per 1,000 per year (table 43). Deaths for the year numbered 23, and in 1945 with 2,315 cases, there were only 10 fatalities.

The reports from the Central and South Pacific and the Southwest Pacific theaters were instructive. Except in some of the earlier island campaigns, heat casualty was not a serious matter. Although these theaters became increasingly active in 1944 and 1945, they profited by the experiences with heat casualty in the other hot theaters in the earlier years of the war. Thus, in the Southwest Pacific Area, the admission rate remained quite uniform throughout the war, 1.72 per 1,000 per year in 1942, 2.03 per 1,000 per year in 1943, and 1.97 per 1,000 per year in 1944, while the progressively increasing number of cases—122, 386, and 1,061 for the 3 years respectively (tables 41, 42, and 43)—was again a reflection of the increase in the number of troops.

In the last years of the war, most of the reports from China-Burma-India, the Southwest Pacific Area, and even the Middle East either do not mention ill effects of heat or indicate that heat casualty was not a medical

problem of significance. The general opinion was that although the efficiency of personnel was reduced there was little overt illness.

The reduction in heat casualty as the war progressed must be evaluated in terms of the progress of events in the various theaters. In some theaters, the movement of troops out of hot areas may have accounted for the reduction in heat casualty; for example, in the United States where troops were moved from training centers to oversea stations. However, similar reductions occurred in theaters where the number of troops remained unchanged while the demands on them increased; for example, in the Persian Gulf Command. Furthermore, low heat casualty rates persisted in still other theaters, such as the Southwest Pacific, which became progressively more active. These observations indicate that the reduction in heat casualties in the later years of the war was real.

These data lead to the implied conclusion that heat casualty as a major problem is preventable under all circumstances in all hot environments. However, it must be considered that in the ho' .est areas on earth (Persian desert, lowland India, and Burma) military activity was concerned largely with stable operations, such as supply and transportation, rather than with the less well regulated activity of combat. Most of the prolonged, large-scale combat was conducted in hot areas of somewhat lesser heat stress. Under these circumstances, it may be said that (1) relatively stable operations were carried out with diminished heat casualty in the hottest areas on earth and that (2) active large-scale combat was successfully waged in hot areas of somewhat lesser heat stress, where it was also possible to prevent a large amount of heat casualty. Since large-scale combat was not conducted in the hottest areas, it is not known whether the available preventive measures against heat casualty could have been effectively applied under such fluid and less ordered conditions.

CAUSE AND PREVENTION

The experience of the Armed Forces during World War II contains the answer to the problem of living and working in hot climates. Why were adverse effects of heat prevalent in the early years of the war? And why did they decrease toward the end of the war? It is the purpose of the remainder of this review to indicate the measures responsible for reducing heat casualty.

A consideration of the military situation at the time the United States entered the war may serve as a background. The last half of 1941 and the first half of 1942 saw much military activity in hot climates. The battles in the African desert between the British and German Armies and the march of the Japanese through the jungles of Southeast Asia and the islands of the Southwest Pacific focused attention on the advantages to be gained by operations in regions previously considered impossible for com-

bat because of climate. Moreover, the strength of the home fortresses of both Germany and Japan was considered so formidable that counterattack seemed most feasible from the periphery; that is, the recently conquered hot desert and jungle areas. Desert and jungle fighters were needed. However, there were many defects in our knowledge and experience of the peculiar stresses imposed by hot climates, of their deleterious effects, and of the measures required to prevent heat casualty.

The factors which led to heat casualty, and the corrective measures taken to prevent such illness, were apparently much the same in all areas regardless of their location. This suggests that the same basic factors were operating in the different areas, whether jungle or desert, and that the experiences from all areas may be combined.

Acclimatization

For some time, it has been known that man must adapt himself (acclimatize) to a hot environment before he can perform physical work in that environment effectively. The failure to appreciate the need for acclimatization led some commanding officers to require men newly arrived from temperate into hot climates to perform hard work immediately.[15] Inevitably, heat casualties resulted. In some areas, they were serious and numerous; in others, relatively mild to moderate. A majority of the cases of fatal heatstroke occurring in the Army in the United States occurred in men who had been stationed in a hot environment for only a short period (a month or less).[16] Moreover, most of these fatalities occurred in men who originally came from the northern part of the United States. Lack of acclimatization may also be considered an important factor in those heat casualties which occurred during a sudden rise in temperature in more temperate areas.

The need for acclimatization was quickly learned. Whenever possible, troops newly arrived in hot climates were not at first required to perform a full day's work but were handled on programs of progressively increased work until they were fully acclimatized. Heat casualties quickly decreased, and troops were able to work hard in the heat without ill effects. It was generally felt that 1 month was required to attain full acclimatization, although considerable adaptation was attained in 4 or 5 days. The need of acclimatization led to the realization that troops should be trained in climates similar to those in which they were ultimately to work or fight.

Laboratory studies on acclimatization to heat confirmed the observations in the field, clarified the physiological processes involved, and pro-

[15] Report, Armored Medical Research Laboratory, Fort Knox, Ky., 20 Oct. 1942, Project No. 2-8, Report on Results of Desert Field Study.

[16] Schickele, E.: Environment and Fatal Heat Stroke; An Analysis of 157 Cases Occurring in the Army in the U.S. During World War II. Mil. Surgeon 100: 235-256, March 1947.

vided a sound basis for corrective measures.[17] These studies, conducted in hotrooms, revealed several pertinent facts. Hard work on first exposure to hot environments (both dry and humid) is never well tolerated and, if continued, leads to disability, no matter how excellent the general physical fitness. The unacclimatized man working in the heat manifests two major undesirable phenomena which usually incapacitate him. He retains heat, with a marked rise in body temperature, and his circulation becomes deranged and unstable. Acclimatization is the development of physiological adaptation of which the mechanism is not yet completely understood but which maintains the body's thermal balance by increasing heat loss to meet the increased heat loads. This appears to be accomplished largely by the development of increased evaporative cooling through more rapid and more copious sweating.[18] In turn, the deranged, unstable circulation of the unacclimatized state, associated with the heat retention, is avoided. Acclimatization begins with the first exposure to heat and is attained most rapidly and completely by progressively increasing the amount of daily work performed in the heat to the point of comfortable tolerance. The major portion of the adaptation is attained in from 4 to 7 days and then progresses more slowly for 3 or 4 weeks. Physically fit men acclimatize more quickly than the unfit. On returning to a cool environment, acclimatization is retained well for 1 or 2 weeks after which it is lost at variable rates. In some men, it is retained to an appreciable extent for as long as 1 to 2 months. The many factors which are detrimental to the well-being and performance of men in the heat produce greater effects in unacclimatized than in acclimatized men.

Water

In the early days of the war, line officers believed in a water discipline, the two principal tenets of which were that drinking water during work in the heat is harmful and that men could be trained to work in the heat with progressively lower intakes of water. Their ideal was the "desert fighter" who could fight on "a pint of water a day." Such a man is a mythical figure,

[17] (1) Bean, W. B., and Eichna, L. W.: Performance in Relation to Environmental Temperature; Reactions of Normal Young Men to Simulated Desert Environment. Fed. Proc. 2: 144, 1943. (2) Eichna, L. W., Bean, W. B., Ashe, W. F., Jr., and Nelson, N.: Performance in Relation to Environmental Temperature; Reactions of Normal Young Men to Hot Humid (Simulated Jungle) Environment. Bull. Johns Hopkins Hosp. 76: 25–58, January 1945. (3) Taylor, H. L., Henschel, A. F., and Keys, A.: Cardiovascular Adjustments of Man in Rest and Work During Exposure to Dry Heat. Am. J. Physiol. 139: 583–591, August 1943. (4) Henschel, A., Taylor, H. L., and Keys, A.: The Persistence of Heat Acclimatization in Man. Am. J. Physiol. 140: 321–325, December 1943. (5) Robinson, S., Turrell, E. S., Belding, H. S., and Horvath, S. M.: Rapid Acclimatization to Work in Hot Climates. Am. J. Physiol. 140: 168–176, November 1943. (6) Machle, W.: The Physiological Effects of High Temperatures. Mil. Surgeon, 95: 98–105, August 1944. (7) Machle, W., and Hatch, T. F.: Heat: Man's Exchanges and Physiological Responses. Physiol. Rev. 27: 200–227, April 1947. (8) Taylor, C. L.: Physical Exertion in the Heat; Some Notes on Its Physiology and Hygiene. J. Aviation Med. 17: 137–145, April 1946.

[18] Report, Medical Department Field Research Laboratory, Fort Knox, Ky., 30 June 1947, Project No. 2-17-1, Thermal Regulation During Early Acclimatization to Work in a Hot Dry Environment.

but the concept played a major role in producing heat casualties, particularly in the United States, where unacclimatized and relatively unfit men were suddenly required to undergo vigorous physical exertion in hot environments with limited, and inadequate, intakes of water. Insufficient water also led to heat casualty in some of the earlier Pacific island campaigns where men went ashore to perform strenuous activities with limited water supplies which could not be augmented until the combat situation improved. Medical officers in the field considered inadequate water intake and the subsequent dehydration one of the most important factors leading to heat casualty. In numerous reports,[19] they pointed out the need for an adequate intake of water based not on preconceived ideas or hopes but on the actual needs of the men as determined physiologically by their water losses.

Studies in laboratory hotrooms [20] and in the field [21] quickly produced data which substantiated the recommendations of the medical officers in the field and disproved completely the possibility of training men to reduce their water requirements. The huge water losses in sweat, approximately a liter per hour for men working in the desert or jungle environment, continue whether or not water is drunk and are only slightly reduced by dehydration. The sweat loss automatically sets the amount of water that must be replaced. Failure to do so leads to dehydration, with reduced blood volume, and predisposes to disability. It was repeatedly demonstrated that hardened, well-acclimatized men, who performed easily and well in the heat while drinking water as desired, either failed to complete the same amount of work or did so with great difficulty and marked inefficiency when on

[19] (1) Annual Report, 87th Infantry Division, for 1943. (2) Annual Report, 99th Infantry Division, for 1943. (3) Letter, Office of the Division Surgeon, Headquarters, 77th Infantry Division, to Commanding General, 77th Infantry Division, 3 Aug. 1943, subject: Summary of Medical Experiences and Problems on Desert Maneuvers. (4) Sneidman, G. I.: Exhaustion and High Temperatures as Experienced in Desert Operations. [Professional paper.] (5) Annual Report, Persian Gulf Command, for 1944. (6) Annual Report, 113th General Hospital, for 1944. (7) Report, Headquarters, XIV Corps, to Commanding General, South Pacific, 3 June 1943, subject: Informal Report on Combat Operations. (8) Annual Report, 102d Infantry Division, for 1943. (9) Annual Report, 81st Infantry Division, for 1943. (10) Letter, Office of The Surgeon General, to Commanding General, Services of Supply, 28 July 1942, subject: Heat Exhaustion and Fatigue. (11) Wallace, A. W.: Heat Exhaustion. Mil. Surgeon 93: 140–146, August 1943.

[20] (1) See footnote 17 (1), (2), (6), (7), and (8), p. 212. (2) Pitts, G. C., Johnson, R. E., and Consolazio, F. C.: Work in the Heat as Affected by Intake of Water, Salt and Glucose. Am. J. Physiol. 142: 253–259, September 1944.

[21] (1) Adolph, E. F., Rahn, H., Gosselin, R. E., Goddard, D. R., Brown, A. H., Kelly, J. J., and Wolf, A. V.: Water Losses From Man in the Desert. Report No. 1, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 20 Mar. 1943. (2) Rothstein, A., and Brown, A. H.: Water Requirements of Air Force Personnel in the Desert During the Hot Season. Report No. 11, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 15 Oct. 1943. (3) Rothstein, A., and Gosselin, R. E.: Rates of Sweat Loss in the Desert. Report No. 15, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 30 Jan. 1944. (4) Adolph, E. F., Brown, A. H., Siple, P. A., and Heald, W. F.: Survival Time of Men Without Water in the Desert. Report No. 8, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 25 May 1943. (5) Adolph, E. F., and Brown, A. H.: Economy of Drinking Water in the Desert. Report No. 5, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 25 May 1943. (6) Adolph, E. F.: Water Shortage in the Desert. Report No. 12, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 20 Oct. 1943.

restricted water intakes. Furthermore, nothing is gained by failing to replace the water losses as they occur. The total 24-hour water intake was found to be just the same whether men drank as they desired, whenever thirsty, or only at stated periods, such as mealtime. Withholding water until stated drinking hours not only did not reduce the water intake but also led to dehydration, with its discomfort and potentially serious consequences.

"Thirst quenchers" were shown to be of no value.[22] They neither reduced the water requirement nor alleviated discomfort. Only one sound way of reducing the amount of drinking water was found; that is, wetting the clothing with nonpotable water.[23] The cooling effect of evaporation of this water reduces the sweat output and conserves body water.

Quantitative studies based on observations in the field [24] and in the laboratory [25] determined the water requirements for different rates of work in various types of hot climates (table 50). When troops received amounts of water adequate to meet these requirements, the incidence of heat casualty decreased sharply.[26]

A byproduct of the quantitative studies was the prediction of survival times in hot climates for men deprived of water and the formulation of a sound plan of action for troops caught in such a predicament:

If men are isolated and have no hope of reaching water in a few hours they should as far as is feasible minimize their rate of water loss (1) obtaining maximal protection from the sun, (2) remaining as inactive as possible, (3) using what water they may

TABLE 50.—*Water requirements for representative types of work in hot climates, by type of activity*

Activity	Illustrative duty	Water requirement [1] in—	
		Moderate temperatures [2] (desert or jungle)	Severe temperatures [3] (desert or jungle)
		Quart	*Quart*
Light_____	Desk work; guard; kitchen police_____	6	10
Moderate___	Routine march on level; tank operation_____	7	11
Heavy_____	Forced marches; stevedoring; entrenching_____	9	13

[1] Number of quarts calculated per man per day, for drinking purposes only.
[2] For desert, air temperature below 105° F.; for jungle, air temperature below 85° F.
[3] For desert, air temperature above 105° F.; for jungle, air temperature above 85° F.

Source: War Department Technical Bulletin (TB MED) 175, June 1945.

[22] Wills, J. H.: Attempted Relief of Distress in Dehydrated Men by Certain Drugs. Report No. 14, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 24 Dec. 1943.

[23] Lifson, N., and Visscher, M. B.: Effect of Wet Garments on Body Weight Loss at High Environmental Temperatures. J. Indust. Hyg. & Toxicol. 25: 434–439, December 1943.

[24] (1) See footnote 21 (1), (2), and (3), p. 213. (2) Adolph, E. F., and Brown, A. H.: Prediction of Water Requirements of Men in the Desert. Report No. 7, University of Rochester, Contract No. OEM–cmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 25 May 1943.

[25] Report, Armored Medical Research Laboratory, Fort Knox, Ky., 20 May 1943, Project No. 2–6, Determination of Water and Salt Requirements for Desert Operations.

[26] Circular Letter No. 119, Office of The Surgeon General, Army Service Forces, 3 July 1943, subject: Acclimatization, Including Water and Salt Requirements of Troops in Hot Climates.

have in moderation and only after dehydration has proceeded for half a day since water is lost slightly more rapidly in early stages of dehydration than later, (4) confining any necessary exertion (walking toward water) to the cooler hours of the night, (5) seeing that no water they already have is spilled or wasted.[27]

Since men are unable to walk after losing body water to the extent of 10 percent of their body weight, but may survive if rescued when they have lost body water to the extent of 20 percent of their body weight, the following survival times at stated activity have been calculated: (1) At daily mean shade temperature below 70° F., 3 nights of walking can be accomplished (65 miles); (2) at daily mean shade temperatures between 70° and 80° F., 2 nights of walking can be completed (45 miles); and (3) with daily mean shade temperature above 80° F., a man can walk only 1 night (25 miles). Also, if the mean temperature is 95° F., a man reaches the limit of his walking ability in 1 day, and at 120° F., in one-third of a day. The importance of limiting activity to the cooler hours of the night, when the water losses through sweating are somewhat diminished, at once becomes apparent.

The importance of an adequate water intake in the prevention of heat casualty cannot be overstressed. Since it is physiologically impossible to reduce the water losses in a hot environment, such losses *must* be replaced.

Salt

The need for an adequate salt intake to replace the salt lost through sweating seems to have been better understood by line officers than the need for water replacement. At times, this need was overemphasized, and salt replacement was sometimes considered more important than water replacement. In some instances, the serious mistake was made by considering that the administration of added salt automatically took care of the water requirement.

Ill effects attributable solely to salt deficiency (heat cramps) were either absent, or infrequently encountered. Nevertheless, reports from hot theaters stated that inadequate salt intake played a significant part in the production of heat casualty and that casualties were salt deficient. Medical officers advocated the use of salt and noted beneficial effects as a result, not only in the reduction of heat casualty but also in the improved well-being and work efficiency of the men. Since so many reports recommended additional salt, its advantages cannot be discounted. However, one cannot overlook the fact that salt was usually taken with water and that the added water may have really been the more significant addition.

The intake of supplemental salt proved to be quite a problem. Compressed tablets of salt did not dissolve well and at times passed through the gastrointestinal tract only partially absorbed. Nausea and vomiting often resulted from their irritation of the stomach. These effects prejudiced the

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[27] See footnote 21 (4), p. 213.

men against salt. Of greater importance was the risk of further dehydration from loss of fluid in the vomitus and through the curtailment of oral intake of fluids. In order to reduce gastric irritation, tablets with different fillers were tried. Sodium bicarbonate and glucose tended to induce more rapid disintegration and solution of the tablet but did not remove the gastric irritation. Another approach was the use of a plastic filler to retard the rate of solution of the tablet yet permit complete solution of the salt within the insoluble plastic matrix. Perhaps the best method developed was to dissolve the salt in water to make a final concentration of 0.1 percent salt—two 10-grain salt tablets or one-fourth of a teaspoonful of salt to each quart canteen of water.[28] Though brackish, such water is not unpleasant and a taste for it is quickly acquired. By the addition of colloids and flavors, such as are contained in milk and barley water for example, the orally tolerated salt content of liquids can be increased up to 0.2 to 0.4 percent. These concentrations are not often necessary. Finally, most of the salt requirement can be supplied by salting the food more heavily, particularly the bland foods, such as potatoes and rice.

Controlled studies in the laboratory [29] and in the field [30] proved that water replacement is much more important, and critical, than salt replacement and that deterioration in working efficiency and heat casualty will result much more quickly when water is denied than when salt is withheld. Maximum work efficiency in the heat is maintained when water is replaced hour by hour; salt, day by day. Although efficiency and output of work fall when the salt intake is inadequate, too much salt, or salt without water, produces not only distressing subjective symptoms but also requires body water for its excretion and actually leads to a reduced work efficiency.

During acclimatization to heat, the body adapts to conserve salt by secreting a sweat low in salt content. This compensating mechanism of the sweat glands is very effective. When salt intake is reduced sharply, the salt concentration in sweat becomes very low, permitting equilibrium on intakes as low as 3 grams daily even though the daily sweat output is from 6 to 8 liters.[31] The adrenal gland is suggested as the mediator of this mechanism.[32]

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[28] See footnotes 25 and 26, p. 214.

[29] (1) See footnote 20 (2), p. 213. (2) Taylor, H. L., Henschel, A., Mickelsen, O., and Keys, K.: The Effect of Sodium Chloride Intake on the Work Performance of Man During Exposure to Dry Heat and Experimental Heat Exhaustion. Am. J. Physiol. 140: 439–451, December 1943. (3) Johnson, R. E., Belding, H. S., Consolazio, F. C., and Pitts, G. C.: The Requirements of Water and of Sodium Chloride for the Best Performance of Men Working in Hot Climates. Report No. 13, Harvard Fatigue Laboratory, for the Committee on Medical Research, Office of Scientific Research and Development, 25 Sept. 1942.

[30] (1) See footnote 21(3), p. 213. (2) Adolph, E. F., Wolf, A. V., and Kelly, J. J.: Salt in Relation to Water Metabolism in the Desert. Report No. 3, University of Rochester, Contract No. OEM–cmr 206, for the Committee on Medical Research, Office of Scientific Research and Development, March 1943.

[31] (1) Conn, J. W., and Johnston, M. W.: Improvment of Ability of Soldier to Work in Humid Heat. Report No. 8, Contract No. OEM–cmr 232, for the Committee on Medical Research, Office of Scientific Research and Development, 1 Mar. 1944. (2) Conn, J. W., and Johnston, M. W.: Improvement of Ability of Soldier to Work in Humid Heat. Report No. 10, Contract No. OEM–cmr 232, for the Committee on Medical Research, Office of Scientific Research and Development, 1 July 1944.

[32] Conn, J. W., and Johnston, M. W.: Improvement in Ability of Soldier to Work in Humid Heat. Report No. 18, Contract No. OEM–cmr 232, for the Committee on Medical Research, Office of Scientific Research and Development, November 1945.

As stated on page 212, sweat output increases during acclimatization to heat. Because salt conserving mechanisms exist but water conserving mechanisms do not, replacement of the salt is physiologically less urgent than replacement of the water. Determinations of the chlorides in the blood and the urine of troops in the American desert area [33] and in the urine of troops on several of the Pacific islands [34] revealed no salt deficits in the men even after long sojourns in the hot climates.

Activity

Most heat casualties occurred during, or shortly after completion of, strenuous physical activity, such as long or forced marches often with heavy packs, close order drill, obstacle course runs, and various types of field exercises. Resting or lightly active men were rarely affected. Thus, of the 265 heat casualties treated by the Station Hospital, Fort Eustis, Va., from 1 May 1943 through September 1943, none occurred on Sunday.[35]

Physical activity as a causative factor in heat casualty was closely associated with the external temperature. Work which could be performed without difficulty in the cooler parts of the day led to heat casualty when attempted in the midday hours. In all hot areas, medical officers quickly recommended decreased physical activity during the heat of the day. Schedules were revised and, where possible, the midday siesta became a part of the daily routine, even to being enforced in some areas. The early morning hours and the nights were utilized for work, and heat casualty diminished; often, work output increased and morale improved. For example, in the summer of 1944, the Persian Gulf Command instituted daily rest periods from 1300 hours to 1700 hours, during which vehicles were not driven across the desert, except in emergencies. Records for the hauling of supplies were broken in July of that year (p. 208). Even in combat, military observers recommended that H-hour be as early as possible for "during the middle of the day the heat is so intense that troops make little progress." [36]

After correlating the incidence of heat casualty in troops in training with observed environmental temperatures, medical officers recommended that physical activity should be reduced when the environmental wet bulb temperature reached 70° F. and that it should be halted for unseasoned

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[33] Rosenbaum, L.: Significance of Salt (NaCl) in Torrid Temperatures. Mil. Surgeon 98: 43–47, January 1946.

[34] (1) Report, Special Survey Team, to The Surgeon General, 22 Aug. 1945, subject: Nutrition Survey in Pacific Theater of Operations. (2) Kark, R. M., Aiton, H. F., Pease, E. D., Bean, W. B., Henderson, C. R., Johnson, R. E., and Richardson, L. M.: Tropical Deterioration and Nutrition. Clinical and Biochemical Observations on Troops. Medicine 26: 1–40, February 1947.

[35] Borden, D. L., Waddill, J. F., Grier, G. S. III: Statistical Study of 265 Cases of Heat Disease. J.A.M.A. 128: 1200–1205, 25 Aug. 1945.

[36] Report, to Commanding General, Army Forces, Army War College, 11 July 1944, subject: Observer Report on the Marianas Operation (FORAGER).

troops when it reached 81° F.[37] When activity in the midday heat could not
be discontinued, men were to be trained by *gradually* increasing their ac-
tivity during the hot hours,[38] and the loads at these hours were to be as light
as possible.

Removing the men from the midday sun also served to prevent in-
capacitating sunburn. The harmful effects of solar actinic rays and the need
for gradually increasing exposure in order to avoid disabling sunburn had
to be emphasized.

The relation between the maximum rate of efficient work possible and
the severity of environmental heat and humidity received considerable
controlled laboratory study during the war.[39] The problem proved to be com-
plex, and its full consideration is beyond the scope of this review. However,
when the severity of the environment increased, the work rate possible
without ill effects always decreased. The simplest index of the severity of
an environment for work proved to be the wet bulb temperature. For fit
men, fully acclimatized to both dry and moist heat, 92° F. was the upper
limit of wet bulb temperature at which they could march, in the nude,
with a 20-pound pack at 3 miles per hour for 4 consecutive hours (work
expenditure, 250 kilocalories per hour) without disability. When clothed in
a single layer of Army fatigues of herringbone twill, the limiting wet bulb
temperature was reduced to 90° F.[40]

The cooling power of the environment, also termed the "thermal ac-
ceptance of the environment" and defined as the amount of heat which a
given environment can remove from the body surface of a workingman,[41]
was also studied. If a man, by his work activity, produced more heat than
the environment could remove from his body surface, obviously his body
temperature would rise and he became a candidate for heat casualty. On
analysis, most of the deaths due to heatstroke (hyperpyrexia) in the Army
stationed in the United States were found to have occurred where the
"cooling power" of the environment was low, less than 500 Cal. per m.[2] per
hr. (calories per square meter of body surface per hour) ; a small number
occurred where it was between 500 and 600 Cal. per m.[2] per hr.; and very

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[37] See footnote 35, p. 217.

[38] See footnote 19 (10), p. 213.

[39] (1) See footnote 3, p. 196; and footnote 17 (8), p. 212. (2) Eichna, L. W., Ashe, W. F., Jr., Bean, W. B.,
and Sheeley, W. B.: The Upper Limits of Environmental Heat and Humidity Tolerated by Acclimatized
Men Working in Hot Environments. J. Indust. Hyg. & Toxicol. 27: 59–84, March 1945. (3) Robinson, S.,
Turrell, E. S., and Gerking, S. D.: Physiologically Equivalent Conditions of Air Temperature and Humidity.
Am. J. Physiol. 143: 21–32, January 1945.

[40] Shelley, W. B., Eichna, L. W., and Horvath, S. M.: The Effect of Clothing on the Ability of Men
to Work in Intense Heat. J. Clin. Invest. 25: 437–446, May 1946.

[41] (1) Report, Climatology and Environmental Protection, Research and Development Branch, Military
Planning Division, Office of the Quartermaster General, 25 Aug. 1944, subject: Conference on the Principles
of Environmental Stress on Soldiers for the Purpose of Developing a Climatic Index Suitable for Mapping
Purposes for the Protection of Troops Operating in All Climates. (2) Report, Climatology and Environ-
mental Protection, Research and Development Branch, Military Planning Division, Office of the Quarter-
master General, 20 Aug. 1945, subject: Thermal Balance of the Human Body and Its Application as an
Index of Climatic Stress. (3) Report, Climatology and Environmental Protection, Research and Develop-
ment Branch, Military Planning Division, Office of the Quartermaster General, 17 Sept. 1945, subject:
Thermal Acceptance Ratio.

few, usually older obese soldiers, where the thermal acceptance of the environment exceeded 600 Cal. per m.[2] per hour.[42]

Physical Fitness

A physically unfit man who is incapable of working in temperate climates at high levels of energy expenditure for as long as a fit man is at a much greater disadvantage in a hot environment. Lack of physical fitness contributed significantly to heat casualty in troops, chiefly in the United States. Mobilization suddenly subjected men to physical conditions requiring effort far beyond that to which they were accustomed. In temperate climates, most recruits were able to tolerate such increased physical activity, although inability to carry on was not infrequent. In hot climates, heat plus the exertion required produced a total load exceeding the physiological capabilities of many men, and casualty resulted. Thus, fatal heat casualties were more frequent in the United States than in any other theater. Furthermore, casualties were more frequent in men who were overweight, who were in the older age groups, and whose service in the Army had been of short (weeks to months) duration. Better physical fitness was believed to be an important factor in the lower incidence of heat casualty in units in hot theaters overseas than while in training in the United States.[43]

Heat casualty rates fell when the physical conditioning programs for recruits were guided by their performance and tolerance and when such programs were, at least initially, less accelerated in hot than in temperate environments. Good physical fitness does not, however, eliminate the need for acclimatization. Controlled observations have amply demonstrated that fit men also suffer disability on attempting hard work on first exposure to hot environments, although they acclimatize more rapidly than unfit men and, when acclimatized, are capable of working more efficiently.[44]

Sleep and Rest

Lack of sleep and rest in areas where high temperatures were sustained day and night predisposed to heat casualty. Men who worked on night shifts and then attempted to sleep during the day in quarters where air temperatures reached 120° to 135° F. (Iran) could not get adequate rest, and more rapidly became heat casualties. A cool place to sleep is the best preventive of heat disease among personnel. Men can tolerate through the day heat loads as great as any occurring naturally if they obtain adequate sleep and

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[42] See footnote 16, p. 211.

[43] Pacific Warfare Board Report No. 60, U.S. Army Forces, Pacific, GHQ, 4 Sept. 1945, subject: Requirements of Tank Design and Operation in Relation to Effectiveness of Armored Personnel.

[44] (1) Adolph E. F.: Physiological Fitness for the Desert. Fed. Proc. 2: 158–164, 1943. (2) Johnson, R. E., and Robinson, S.: Selection of Men for Physical Work in Hot Weather. Report No. 16, Harvard Fatigue Laboratory, Contract No. OEM–cmr 54, for the Committee on Medical Research, Office of Scientific Research and Development.

if they have comfortable quarters in which to relax and rest when not working.

Good housing in which men could sleep and relax, including air-conditioned barracks for night crews, was instrumental in lowering heat casualty rates in the Persian Gulf Command (p. 209). In desert areas, effective air conditioning was obtained by evaporative cooling, using simple "desert coolers," [45] boxes with 6-inch layers of excelsior over which water dripped slowly and, when obtainable, a fan blowing air over the box. Such devices would be of no value in the humid Tropics. But whether in the desert or the Tropics, fans were recommended, since the additional air movement produced a cooling effect.

Nutrition

In some hot areas, malnutrition apparently predisposed to heat casualty, particularly early in the war when much of the food was either packaged (C- and K-rations) or so dehydrated that it was unpalatable. Strict water rations made this food even less edible. Failure to eat led to loss of weight and occasionally to mild avitaminosis. Recommendations were made for better food, for less packaged food (the necessary packaged food in a more palatable and acceptable form), and for additional vitamins. As the rations improved, heat casualties decreased. Since, over the same period, more important corrective measures were also instituted, the role of improved nutrition in the reduced heat casualty rate cannot be evaluated. Medical officers in the field felt that an inadequate diet rendered the men more susceptible to heat casualty only when it produced definite malnutrition.

Controlled studies revealed that no known food factor will prevent the ill effects of heat and that the dietary requirements of men in the heat are essentially similar to those in temperate climates. There is the same need for the maintenance of caloric balance.[46] The specific dynamic action of protein does not adversely affect the thermal equilibrium of men working in the heat.[47] Vitamin losses in the sweat are negligible,[48] even for the water-soluble vitamins (thiamine and ascorbic acid), and the vitamin requirements for work in the heat are not increased. At one time, vitamin C was thought to increase work efficiency in the heat and to prevent heat exhaustion, but this was subsequently disproved.[49] Additional carbohydrates, such as glucose, are not helpful. A nutrition survey, including biochemical

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[45] See footnotes 8 and 9, p. 206; and footnote 19 (5), p. 213.

[46] Johnson, R. E.: Nutritional Standards for Men in Tropical Climates. Gastroenterology 1: 832–840, September 1943.

[47] Pitts, G. C., Consolazio, F. C., and Johnson, R. E.: Dietary Protein and Physical Fitness in Temperate and Hot Environments. J. Nutrition 27: 497–508, June 1944.

[48] (1) Sargent, F., Robinson, P., and Johnson, R. E.: Water Soluble Vitamins in Sweat. J. Biol. Chem. 153: 285–294, April 1944. (2) Taylor, H. L.: Climate and Vitamin Requirements. Lancet 63: 358–359, November 1943.

[49] Henschel, A., Taylor, H. L., Brozek, J., Mickelsen, O., and Keys, A.: Vitamin C and Ability to Work in Hot Environments. Am. J. Trop. Med. 24: 259–265, July 1944.

analyses of blood and urine of combat and garrison troops on several of the
Pacific islands, revealed no deficiency of vitamins, protein, or hematopoietic
factors in the men. Only occasional low values were found.

Overindulgence in alcohol led to heat casualty, but it is not possible to
determine if alcohol alone or the dissipation associated with its use was
the causative factor.

Clothing

Heat casualty directly attributable to clothing was difficult to estab-
lish. Men wearing heavy clothing, relatively impervious to air, tightly fitted
over the body, with the closure of such ventilation ports as the trouser bot-
toms (by leggings), the sleeve openings (by wrist buttons), and the neck
(by flaps and buttons), sustained an additional heat load. Many recommen-
dations were made for light clothing, permeable to air, loosely fitting, and
wherever feasible with neck, trouser bottoms, and sleeves open to permit
greater ventilation of the body. These clothing specifications usually could
not be met in the jungle climates, because of the necessity of covering as
much of the body surface as possible and of closing all ventilation ports in
order to avoid the insect vectors of many of the tropical diseases (malaria,
dengue, filariasis, and scrub typhus). By the war's end, the use of insecti-
cides and insect repellents suggested an avenue of investigation which
might eventually permit the wearing of loose clothing in the Tropics with
reasonable safety.

Clothing is undesirable in hot climates because it interferes with air
movement over the body and thus hinders evaporative and convective cool-
ing, the extent of this interference depending upon the type of cloth and its
fit. Several quantitative studies have determined the heat loads of different
clothing in various environments.[50] Where the solar radiant heat is great
and the evaporative gradient large, as in the desert, clothing is beneficial
since it reduces the radiant heat load more than it interferes with the
evaporation of sweat.[51] Where both the radiant heat and the evaporative
gradient are small, as in the Tropics, the net effect of clothing is harmful
since it seriously hampers an important avenue of heat loss, evaporation of
sweat and produces little benefit by reducing the already small radiant
heat load.

Surgical operations in hot environments present serious difficulties.
Extensive covering with sterile drapes greatly reduces heat elimination by
patients. The administration of the usual preoperative atropine, by cur-

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[50] (1) Report, Armored Medical Research Laboratory, Fort Knox, Ky., 17 July 1945, Project No. T-5,
Test of Flameproofed Clothing, Physiological Effects of Wearing Flameproofed Clothing in Hot Environ-
ments. (2) Report, Armored Medical Research Laboratory, Fort Knox, Ky., 24 Nov. 1943, Project No. 2
(2-3, 18), Test of Adequacy and Ranges of Use of Clothing for Jungle Operations. Effects of Impregnated
and Impervious Clothing Upon Efficiency of Personnel. (3) Robinson, S.: Committee on Medical Research
Interim Report No. 12 (Revised), Indiana University Medical School, 2 Nov. 1944.
[51] See footntoe 21 (3), p. 213.

tailing sweating, greatly aggravated this difficulty. Certainly, anhidrotic drugs are to be avoided in any hot environment since they reduce evaporative cooling as an avenue of heat loss.

Previous and Associated Illnesses

Susceptibility to heat casualty was increased by intercurrent illness, no matter how mild; that is, venereal disease, upper respiratory infections, dysentery, overfatigue, constipation, immunizing inoculations, simple gastrointestinal disturbances, and diarrhea. The predisposing common denominator in these disturbances may have been the associated increased water losses. Return to duty too soon after recovery from any previous illness similarly predisposed to heat casualty, and convalescences had to be prolonged. Previous heat illnesses at times left men particularly prone to subsequent attacks. Medical officers soon realized that greater care, often to relieving men from duty, was required for disturbances which in temperate climates would have been unimportant.

Education

Indoctrination of each individual soldier for life in hot environments is essential to the avoidance of heat casualty. The war threw into the hottest of climates large numbers of men who had neither knowledge nor experience of how to live in the heat and who had to learn all of the acclimatization principles just discussed. These principles were disseminated through Circular Letters No. 119 [52] and No. 136 [53] from the Office of The Surgeon General. These letters did much to remove preconceived and erroneous ideas, particularly concerning water and salt requirements and workloads in the heat, factors which had led to most of the heat casualties. Beneficial results were quickly apparent. For example, a unit previously instructed and prepared, and adhering to these principles, moved from a camp in northern United States into the California desert and trained there without significant heat casualty.[54]

TREATMENT

The war experience contributed no new principles or methods to the treatment of heat casualty but provided a more complete evaluation of previously utilized, or suggested, therapeutic measures. This is important both because of the large number of men treated and because of the un-

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[52] See footnote 26, p. 214.

[53] Circular Letter No. 136, Office of The Surgeon General, Army Service Forces, 28 July 1943, subject: Treatment of Heat Stroke, Heat Exhaustion and Heat Cramps.

[54] Annual Report, 51st Evacuation Hospital, for 1943.

complicated nature of the heat casualties. They occurred in healthy young men, free from the associated, complicating diseases and disabilities so prevalent in civilian heat victims and so likely to confuse the analysis of therapeutic measures.

It is not the purpose of this report to review the various clinical types of heat casualty, but a brief description of the more important, or frequent, types of casualty encountered will be given. Heat cramp, due to loss of body salt, usually through sweating, is characterized by painful contractures of the voluntary muscles, especially of the abdominal wall; the rectal temperature is normal. Ill-defined effects of heat include such manifestations as a sense of overheating, fatigue, headache, giddiness, and skin rashes in an afebrile subject who, though ill and exhausted, can still move under his own power. Heat exhaustion is largely a circulatory fault characterized by a lowered blood volume, resulting from water loss (sweating) without adequate water replenishment. The temperature is normal or moderately elevated (102° F.). There is severe exhaustion, a cool wet skin, anorexia (at times with vomiting), giddiness, syncope (especially when erect), headache, evidence of dehydration, oliguria, and usually tachycardia. Hyperpyrexia (heatstroke) is characterized by a high rectal temperature, over 106° F.; by unconsciousness or delirium, often with convulsions; by circulatory collapse with shock; and by a hot dry skin without sweating. It probably results from a failure of the mechanisms for heat loss. Although each of these categories may be considered a separate clinical entity, not infrequently cases were encountered which did not fit into the accepted classification but showed manifestations of several categories; for example, "borderline hyperpyrexia" which showed symptoms of both heat exhaustion and heatstroke. Furthermore, some patients progressed from one category to another.

Mild cases.—The category of mild cases contains patients with ill-defined symptoms and those with heat exhaustion. The former required little more than rest, in as cool a place as possible, water and possibly salt, by mouth, and observation. Improvement was uniformly rapid, permitting return to quarters within several hours or the next day.

Heat exhaustion was treated much the same way, but the patients were usually hospitalized and treated longer and more intensively. When vomiting interfered with the oral intake, intravenous infusions of isotonic salt solution or of glucose in salt solution (2 to 3 liters) were given until fluids by mouth were retained. Only occasionally were stimulants necessary. Improvement was usually rapid and recovery complete in a day or two. Adequate convalescence was essential before return to full duty.

Both types of mild cases were at times considerably worse when enthusiastic but uninformed aidmen administered salt (usually tablets) with little or no water.[55] Water is decidedly more important than salt for these

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[55] See footnotes 29 (2) and (3) and 30 (2), p. 216.

casualties, and salt alone is interdicted. Salt and water together constitute the optimal treatment.

The most important lesson learned from the mild heat casualties was the realization that all heat casualties are potentially serious and that the mildest of cases may deteriorate quickly and become dangerously ill. Before this was appreciated, men who appeared only slightly ill were frequently sent to their quarters (in some areas tents in which temperatures reached 120° to 137° F.) only to be found several hours later seriously ill and even comatose.[56] Others would suddenly, and unaccountably, become critically ill, even while awaiting attention in busy aid stations or hospital waiting rooms.[57] Again, men who appeared only mildly ill would collapse while being transported in trucks to hospitals at a distance and upon arrival would be in a serious condition.[58] Heat casualty necessitated prompt "on the spot" and continued attention, and men sent to quarters required repeated checking just as well as those in hospitals.

Severe cases.—The category of severe cases contains patients with hyperpyrexia (heatstroke) and those with the more serious of the so-called borderline hyperpyrexias. Only the treatment of hyperpyrexia is discussed here; the treatment of borderline hyperpyrexia became an individualized intermediate regimen based upon the treatment schedules of mild and severe cases.

Treatment facilities.—Hyperpyrexia proved to be a true medical emergency.[59] The high body temperature (107° to 112° F.), the cerebral disturbances of delirium, unconsciousness, and convulsions, and the circulatory shock required prompt, accurate diagnosis and quick, energetic treatment. Proper treatment could be instituted only by organizing in advance the required facilities and the trained personnel. Medical units in hot climates established heat casualty treatment centers consisting of treatment rooms, air conditioned when possible, which were provided with a plentiful supply of the coldest water available and equipped with sprays, fans, and special webbed treatment tables to provide access of air to the greatest possible skin surface. Some centers provided tubs for ice water baths. Well-ventilated, and where possible air-conditioned, wards were set aside for convalescence. In the desert, the air conditioning was easily obtained by desert coolers, already described; in the Tropics, air conditioning was virtually unobtainable. The treatment centers were staffed by trained teams prepared for immediate action. Such preparations played a very important part in the reduction of mortality due to heat casualty.

Reduction of body temperature.—Rapid lowering of the body temperature was the first, and the most important, factor in the treatment of

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[56] See footnote 19 (5), p. 213.

[57] See footnote 19 (4), p. 213.

[58] Nayer, H. R.: Letter to the Editor, Journal, American Medical Association. J.A.M.A. 129: 1123, 15 Dec. 1945.

[59] (1) Annual Report, Station Hospital, Fort Eustis, Va., for 1943. (2) See footnote 35, p. 217.

hyperpyrexia.[60] The goal most frequently set was to lower the rectal temperature to 102° F. within 1 hour. Two approaches were utilized: (1) Evaporative cooling—wetting the patient completely and repeatedly with sprays of water and promoting evaporation of the water by fanning, and (2) conductive cooling—immersing the patient in a tub of cold water, containing ice when possible, and vigorously massaging the body while it was thus immersed.

There has been a long argument between the advocates of these two schools of treatment. Contention has centered about two points: (1) Whether ice or very cold water causes peripheral vasoconstriction which prevents blood from reaching the skin and thus hinders cooling and (2) whether evaporation of water is a more effective method of removing heat than the melting of ice and the subsequent heating of the cold water. From a physiological standpoint, the reasoning on these two points is as follows: Iced water can lower the skin temperature almost to zero, evaporation cannot lower it below the wet bulb temperature of the environment (70° to 80° F.). If there is no interference with the circulation of the blood through the skin, it follows that per unit time ice water will remove more heat from the blood perfusing the skin than will the evaporation of water from the skin. If, however, the cold water causes peripheral vasoconstriction, body cooling will be hindered. Accumulating evidence of successful and rapid lowering of high body temperature by the use of ice water suggests that, at the high body temperatures of heatstroke, undesirable peripheral vasoconstriction may not occur, particularly if the body is massaged. Therefore, rapid reduction in body temperature can be achieved.[61] In regard to the amounts of heat removed by the evaporation of water and by the melting of ice, it is true that evaporation of water removes more heat than the melting of ice per unit mass of each. However, such an argument has force only for equal amounts (masses) of the two agents and does not apply where ample supplies of each are available to keep the body exposed to the lowest temperature each agent can produce. Furthermore, in humid hot environments, evaporation is bound to be slow and, therefore, cooling inefficient.

On the basis of the evidence and reasoning just presented,[62] plus the accumulating experience from the field, the Army adopted, as the therapeutic procedure of choice for hyperpyrexia, the total immersion of the subject in cold, preferably iced, water with continuous massage of the body during the immersion.[63] When ice is not available, the water must be changed

[60] (1) See footnote 9, p. 206; footnote 19 (4) and (5), p. 213; and footnote 35, p. 217. (2) Annual Report, 19th Field Hospital, for 1944. (3) Letter, Maj. John T. Larkin, MC, to The Surgeon General, 20 July 1945, subject: TB Med 175.

[61] Ferris, E. B., Jr., Blankenhorn, M. A., Robinson, H. W., and Cullen, G. E.: Heat Stroke; Clinical and Chemical Observations on 44 Cases. J. Clin. Invest. 17: 249–262, May 1938. ·

[62] Conference on Adverse Effects of Heat, Clinical Investigation Report No. 61, National Research Council, 3 Apr. 1945.

[63] War Department Technical Bulletin (TB MED) 175, June 1945, subject: Prevention and Treatment of Adverse Effects of Heat,

often, or running water used. When water supplies are short, such expenditure may not be possible, and then evaporative cooling must be utilized. Since the effectiveness of evaporation depends on the velocity of airflow over the body, fanning becomes essential. Evaporative cooling was found most effective when the patient was nude, but one medical officer reported that cooling was most rapid from the completely wetted, clothed patient, presumably because of the increased surface area for cooling provided by the clothing.

Care was taken not to lower the rectal temperature too far, usually not below 102° F., although in one report no ill effects attended the lowering of temperature to between 99° and 100° F. Repeated checking of the rectal temperature at 10- to 15-minute intervals was considered necessary to control the period of rapid cooling. Thereafter, temperatures were taken at 30-minute intervals until they had stabilized below 102° F., for 6 to 8 hours. Repeated readings were necessary to detect the not infrequent return of body temperatures to high levels. When hyperthermia recurred, the cooling treatment was repeated.

Central nervous system effects.—Next in importance to lowering the body temperature was the treatment of the associated central nervous system effects. Of these, convulsions, often repeated, required prompt attention. Besides their usual undesirable effects, convulsions produce additional heat. Pentothal sodium (thiopental sodium) administered intravenously proved an effective therapeutic agent. Delirium and restlessness required treatment, usually with other, milder, sedatives, such as barbiturates and paraldehyde. For deep coma, stimulants were used, but usually in association with treatment of circulatory shock.

Parenteral fluids.—The cessation of sweating which occurs in hyperpyrexia usually prevents excessive fluid loss and dehydration, unless the latter is present before the onset of the heatstroke; for example, heat exhaustion progressing into hyperpyrexia. Although most patients with hyperpyrexia are not dehydrated, certainly not markedly so, the administration of fluid by all available routes was recommended. Intravenous infusions of isotonic salt solution, glucose, and particularly glucose in isotonic salt solutions were commonly used. The amount of fluid administered was governed by its need, overadministration being avoided. As treatment produced favorable results, fluids by mouth replaced the parenteral route.

Circulatory shock.—In the most severe hyperpyrexias, peripheral circulatory collapse with shock was commonly present. These patients were particularly prone to develop pulmonary edema (perhaps aided by too vigorous parenteral fluid therapy), of which death was the likely outcome. The treatment of the shock was the same as for any other circulatory shock of medical origin—and usually as unsuccessful. Plasma was given intravenously, 500 ml. at first and repeated after 30 to 45 minutes if there was no improvement. Various circulatory stimulants, such as Coramine

(nikethamide), caffeine, sodium benzoate, ephedrine, and Metrazol (leptazol), were tried, usually without benefit. When pulmonary edema developed, inhalations of 100 percent oxygen and even venesection were employed, but atropine was specifically interdicted. The presence, or the development, of shock was of poor prognostic import.

Antibiotic medication.—In some instances, penicillin and the sulfonamides were administered on the possibility that some infection sensitive to these drugs was present in a masked form and contributing to the hyperpyrexia. This must always be considered in patients with hyperpyrexia for even a mild disease may be an important contributing factor. In other instances, heat casualties turned out to be severe cases of some other disease and required appropriate specific therapy. Proper diagnosis was especially important in those areas where severe and relatively unfamiliar diseases produced clinical pictures similar to heatstroke; for example, malaria. In some areas, an immediate malarial smear became a routine diagnostic procedure for all heatstrokes with the result that "on quite a few occasions the positive malarial smear cleared the picture * * *." [64]

Convalescence.—Following recovery from hyperpyrexia, long convalescences were the rule, at first in air-conditioned surroundings if possible. A too rapid return to duty frequently led only to a repetition of heat casualty. Since a number of these patients become sensitive to heat, the ability of convalescents to work in the heat should be tested under medical supervision before they are returned to full duty.

DETERIORATION DUE TO HEAT

The acute, casualty-producing effects of heat thus far discussed constituted but one phase of the heat casualty problem in hot climates. After men had learned to live in the heat so as to avoid acute casualty, there still remained the problem of the deleterious effects of prolonged stay in hot climates, generally believed to be a physical, physiological, and mental deterioration. Such deterioration is particularly likely where high temperatures are maintained during both the night and the day and throughout the year (Tropics) and less likely where there are seasonal variations in temperature with, in season, exceedingly hot days but usually cool nights (most deserts).

Deterioration did not occur in troops stationed in the hot areas of the United States since they never remained there long enough. In desert areas overseas, troops in the Persian Gulf Command definitely "slowed down" in the hot months, with a drop in morale and efficiency, but were not considered deteriorated since they still performed well under stress. The lassitude during the hot summer cleared quickly with the onset of cooler weather. Although some officers felt that both mental and physical deterioration due

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[64] See footnote 19 (6), p. 213.

to heat had appeared in some troops, the general opinion was that no real deterioration had occurred, even in troops who had been in this hot desert for 2 or 3 years.[65]

For the Tropics, the available data do not afford a definite answer. One survey specifically designed to study tropical deterioration indicated that, even after almost 4 years in the Southwest Pacific Area, troops remained physically fit and capable of performing hard work effectively.[66] Nevertheless, there was a widespread feeling that the enervating effects of the hot climate "slowed the men down" and that "some reduction in efficiency in the absence of any disease seems unavoidable over a long period of time." The terms "loss of efficiency" and "deterioration" were used to cover a variety of manifestations noted in troops long in the Tropics; for example, lessened interest, lessened physical ability to perform at levels of ordinary capacity, increased irritability, lethargy, and lowered reserve stamina. Although these manifestations are not usually considered casualty producing, nevertheless they lowered the full efficiency of the commands and, in that sense, produce the same result as overt casualties. These "deteriorative" changes were usually noted after 8 to 12 months in the Tropics, while the first 2 to 4 months, after attaining acclimatization, were considered the period of maximum efficiency.

It is difficult to evaluate properly the "slowing down" and "loss of vigor" of troops long in the Tropics. The changes were not overt or marked and, on demand, work was still performed effectively. It was not possible to determine whether these changes were the result of true physical and physiological deterioration induced by the hot climate or the result of mental deterioration and lack of motivation of men too long in any undesirable surroundings regardless of climate. Controlled observations on troops in the Southwest Pacific Area suggested that there was no tropical deterioration as a specific entity differing from the deterioration in troops stationed elsewhere under similar circumstances, except for climate. Certainly, the monotony of the hot, humid climate and of the work, the lack of recreation, and the absence of long-accustomed amenities of life removed much, if not all, of the stimulus to exertion. The prevalence of skin disorders and tropical diseases constituted an added physical and mental drain. Thus, it is not possible to state whether true climatic deterioration, physiological or mental, or both, was present in these troops. Some loss of efficiency, whatever its origin, was present, but mild in degree and not limiting. Performance on demand, as in combat, was always high; when the demand relaxed, as in garrison duty, performance deteriorated. More careful observation and quantitative studies on troops in the Tropics are necessary to clarify the problem of climatic deterioration. Until this is accomplished, service of troops in the Tropics might well be limited to periods of 1 to 2 years, as suggested by commanding officers in these areas.

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[65] See footnote 60 (2), p. 225.

[66] See footnote 34, p. 217.

HYPOHIDROSIS SYNDROME

Out of the war experience came the description of the hypohidrosis syndrome, a new clinical syndrome to be added to the ill effects of heat. Described in 8 soldiers in the American desert,[67] in 18 soldiers in Assam,[68] and in a similar though milder form in British troops in southern Iraq,[69] the manifestations of thermogenic anhidrosis or the hypohidrosis syndrome do not permit its inclusion in the standard classification of heat casualty. Isolated cases were also encountered in troops in Louisiana [70] and in sailors in the Southwest Pacific.[71]

The essential features of this syndrome are (1) absence of sweating over most of the skin surface; (2) retention of sweating in profuse amounts in various limited areas (usually the face and then, in descending order, the axilla, the presternal area, and the interscapular area); (3) relatively mild and indefinite symptoms of overheating, weakness, dizziness, and head-ache; (4) diuresis; and (5) nondescript cutaneous changes from prickly heat and transient papules in some cases to a dry skin with fine branny desquamation in most instances. These changes were either sudden or gradual in onset. The syndrome occurred in men who had been in a hot area for some time and usually toward the close of a hot season. Most of the men had always sweated profusely and some noted episodes of particularly profuse sweating shortly before its cessation. All were aware that sweating had stopped and that the urine output had increased. Mild, indefinite sub-jective discomfort for several days preceded the seeking of medical care. Usually, the patients were not very ill and none had hyperpyrexia. Labora-tory determinations have been few, but no abnormalities in blood chloride, calcium, phosphorus, blood count, or glucose tolerance were found in limited studies. The few skin biopsies examined did not show significant pathological changes in the sweat glands.[72] On conservative treatment of rest in a cool place, recovery from subjective symptoms was usually rapid, and sweating returned spontaneously over periods varying from several weeks to several

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[67] Wolkin, J., Goodman, J. I., and Kelley, W. E.: Failure of the Sweat Mechanism in the Desert; Thermogenic Anhidrosis. J.A.M.A. 124: 478–482, 19 Feb. 1944.

[68] Essential Technical Medical Data, U.S. Army Forces, China-Burma-India, for April 1945, dated 10 May 1945, with enclosure No. 1, subject: Hypohidrosis Syndrome—Report of Cases Seen at the 20th General Hospital, 18 Mar. 1945.

[69] Ladell, W. S. S., Waterlow, J. C., and Hudson, M. F.: Desert Climate. Physiological and Clinical Observations. Lancet 2: 491, 14 Oct. 1944, and 527, 21 Oct. 1944.

[70] Blank, H.: Letter to the Editor, Journal, American Medical Association. J.A.M.A. 124: 1153, 15 Apr. 1944.

[71] Novy, F. G., Jr., and Ramsey, J. H.: Letter to the Editor, Journal, American Medical Association. J.A.M.A. 125: 738, 8 July 1944.

[72] (1) See footnote 68, above. (2) Postwar observations have established that the hypohidrosis syndrome results from the closure of sweat pores, usually by keratin plugs in the ostia of the sweat ducts. The surrounding areas are hyperkeratotic, but the walls of the sweat ducts remain intact. Sweat continues to be formed by the gland but is reabsorbed from the occluded duct and overt sweating does not occur. This sequence of changes accounts for the frequent cutaneous manifestations associated with the syndrome, the patchy nature of the anhidrotic areas, and the return of sweating with conservative therapy.

months.[73] In a few instances, large anhidrotic areas persisted for as long as 4 months. Followup studies, particularly on reexposure to external thermal stress, are not available.

The reason for the cessation of sweating is as yet unknown. The present belief inclines toward a functional rather than a pathological etiology, to a "fatigue" or "exhaustion" of the sweat mechanism without defining whether such fatigue is central (neurogenic) or peripheral (sweat gland) in origin.

In connection with this syndrome, it is of interest that approximately 15 percent of the racehorses imported from England and Ireland and raced in Trinidad, British West Indies, develop anhidrosis.[74] Their performance suffers and the horses are removed from racing. In contrast to the laboratory findings in the hypohidrosis syndrome in man, these horses have a lowered blood chloride. When they are retired and turned out to pasture, there is a spontaneous recovery of their sweating mechanism associated with a return of the blood chloride to normal values. Anhidrosis has not been encountered in native horses or crossbreeds.

CONCLUSION

The experience of the Armed Forces in hot climates during World War II (and the almost identical experience of British troops)[75] contains the solution of the problem of living and working efficiently and effectively in hot climates. The answer was learned at the expense of a goodly number of casualties and a fair number of deaths. The underlying principles should not be forgotten but should form a basis for the proper handling of troops in hot climates in future years. That man possesses physiological mechanisms which permit him to adapt to heat and that adherence to sound physiological principles will permit him to work hard, efficiently, and effectively in any naturally occurring hot environment can be concluded from this war experience. In closed spaces and in vehicles where the environment approaches or exceeds the physiologically tolerable upper limits of heat, cooling methods must be provided. The essential features of this review have been incorporated in War Department Technical Bulletin (TB MED) 175, June 1945,[76] which is available for the lines of command as a basis of procedure in hot climates.

[73] Hyman, A. B.: Some Histopathologic Aspects of Disturbances of Sweating. A.M.A. Arch. Dermat. 66: 145–151, August 1952.

[74] Special report, R. T. Gaylor, subject: Chronic Anhidrosis With Lowered Blood Chlorides in Race Horses at Trinidad, B.W.I.

[75] (1) MacLean, K. A.: Observations on Sunstroke and Heat Exhaustion in Tropics. J. Roy. Nav. M. Serv. 29: 31–36, January 1943. (2) Morton, T. C.: Heat Effects in British Service Personnel in Iraq. Tr. Roy. Soc. Trop. Med. & Hyg. 37: 347–372, May 1944. (3) Palmer, H. A.: Case Report of Psychosis Following Heat Stroke. J. Roy. Army M. Corps 82: 186–189, April 1944. (4) Croom, J. H.: Effects of Heat; Account of Group of Cases Admitted to a General Hospital on Arrival in the Middle East. J. Roy. Army M. Corps 83: 288–292, December 1944. (5) Sheperd, H. M. D.: Effects of Heat in Iraq. J. Roy. Army M. Corps 84: 1–8, January 1945. (6) Critchley, M.: Problems of Naval Warfare Under Climatic Extremes. Brit. M.J. 2: 145, 4 Aug. 1945; 173, 11 Aug. 1945; and 208, 18 Aug 1945. (Croonian Lectures.) (7) Stenning, J. C.: Salt Deficiency States in Tropical Climate. J. Roy. Nav. M. Serv. 31: 129–146, July 1945.

[76] Superseded by TB MED 175, 7 Aug. 1957.

CHAPTER X

Nutritional Disorders

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PERSPECTIVES AND PRELIMINARIES

It is often said that the U.S. Army and the people of the United States are the best fed in the world. A tremendous amount of the time and effort of highly trained competent people was applied, with good results, to the ration issue and to the menu planning for the Armed Forces during World War II.

Nevertheless, wars are unpredictable, and not infrequently the best laid plans fail of accomplishment. The fulfillment of normal nutritional requirements in a land of plenty with a highly efficient transportation system presents relatively minor problems. In a war-torn land with a complete breakdown of the normal channels of commerce, transportation difficulties at times become unsurmountable and famine or starvation or less severe nutritional deprivations appear.

All degrees of malnutrition are present in the various parts of the world at all times. These deficiency syndromes are rather characteristic for the regions where they exist; for example, beriberi among the rice-eating peoples, pellagra among the corn eaters, scurvy in the wheat eaters, protein deficiency in those who eat the ground tubers, and caloric and protein deficiency in the areas of crop failure. In time of war, nutritional inadequacies in civilian populations are likely to be accentuated, and soldiers of a well-fed army may acquire similar disorders during captivity or under other circumstances exposing them to local conditions.

Before World War II, the U.S. Army had never had to meet the nutritional problems incident to worldwide dissemination of troops in large units far from their sources of supply. Nevertheless, deficiency diseases did occur occasionally,[1] as follows:

1. In 1921, 11 cases of berberi with 1 death occurred among native troops in the Philippine Islands, and 3 cases occurred among native troops in Puerto Rico. In addition, there were 11 discharges among 20 Puerto Rican soldiers with polyneuritis. All these cases were found to be related to the consumption of overmilled rice.

2. In 1931, one case of berberi was reported in Philippine troops; in 1932, two cases; and in 1934, two cases. In 1934, also, three cases of

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[1] Annual Reports of The Surgeon General, U.S. Army, 1921–39.

pellagra occurred among troops in the continental United States—one in a Negro soldier at Fort Benning, Ga., and the other two in white soldiers, one in New Jersey and the other in Texas. These soldiers, each of whom had 15 years of service, were all returned to duty.

3. A Filipino, admitted to hospital on sick report on 29 April 1936, died on 12 September 1936 from beriberi.

4. In 1938, there was a case of pellagra at the General Dispensary in Boston. The patient, a warrant officer, was admitted to Fort Banks, Mass., where he died.

5. In 1939, a case of pellagra was reported in troops in continental United States.

These scattered cases of severe deficiency disease in the Army occurred either in native troops subsisting on native foods or in personnel receiving money allowances for rations, particularly warrant officers and noncommissioned officers of the higher grades. The British, long accustomed to handling native troops and their own men in the Near East, Middle East, and Far East, had more experience than Americans in such matters.

During the First World War, the British observed many cases of scurvy among their troops in Mesopotamia. In June of 1918, a special investigation was made of scurvy in the South African native labor corps contingent serving in France under British jurisdiction, as 121 cases occurred among 6,795 men. It was concluded that the chief cause was probably destruction of the antiscorbutic principle in the food by overcooking. In German prisoners of war on the island of Rousay off Scotland, the diagnosis of scurvy was firmly established on 6 July 1917. In April of that year, a somewhat restricted ration scale had been introduced, omitting potatoes; also, purchase of food by the prisoners was forbidden on account of food shortages throughout the country. Previously, the prisoners had used money earned by their work to supplement their rations from local sources, buying bacon, which they ate raw, and other articles of food. Symptoms of scurvy appeared after about 7 weeks. Most of the men affected were those doing heavy work in the mines.

The Medical Department of the U.S. Army had been given statutory responsibility for the feeding of the soldier as it affects his health and effectiveness as early as 1863, in an act revised in 1877.[2] The statute reads in part as follows:

The officers of the Medical Department of the Army shall unite with the officers of the line (under such rules and regulations as shall be prescribed by the Secretary of War) in superintending the cooking done by the enlisted men; and the Surgeon General shall promulgate to the officers of said Corps such regulations and instructions as may tend to insure the proper preparation of the ration of the soldier.

It was not, however, until July 1918 that The Surgeon General established the position of "nutrition officer" within the Medical Department. The duties of the nutrition officer, as outlined in General Orders No. 67, War Department, 15 July 1918, were concerned with the quality, quantity, and proper storage of food, and with prevention of waste, with preparation of menus, and with miscellaneous matters relating to nutrition. Dur-

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[2] Act of 3 March 1863 (12 Stat. 744).

ing World War I, the emphasis in the Surgeon General's Office was entirely on the technical side of the food and menu problems. There was no clinician assigned to this particular aspect of the work.

The nutritional problems of the First World War were still fresh in the minds of only a few at the beginning of the Second World War, and those few were for the most part not heeded. Nevertheless, between the two conflicts, attention had gradually focused upon the shortcomings of the Army rations, and some efforts had been made to correct them.[3]

In his 11 December 1926 letter to The Adjutant General, the Quartermaster General, Maj. Gen. B. F. Cheatham, pointed out the wide variations, as of 30 June of that year, in the ration allowances for the armed services and, among these, the unfavorable position of the Army. Masters and first officers of the Army Transport Service were allowed $1 a day and the Navy, 55 cents a day; the current Army garrison ration allowance was 36 cents a day and the Philippine ration, 22 cents a day. He noted further: "The garrison ration is the same today as it was in 1908, although * * * the standard of living of the American people is much higher than that of eighteen years ago." On 3 January 1927, The Surgeon General, in his endorsement to the Assistant Chief of Staff, G-4 (logistics), stated that the current ration did not permit a serving of a well-balanced diet in the Army comparable with that of civilians in similar walks of life, under the existing living conditions in the United States, and that the ration allowance was not sufficient to permit the purchase of an adequate supply of foods rich in the essential protective substances, vitamins, without utilizing other funds.

In October 1923, Maj. Gen. M. W. Ireland, then The Surgeon General, U.S. Army, described nutrition in the Army in the following terms:

The Army ration as now provided does supply sufficient and suitable nourishment for the troops from the standpoint of balance and caloric content. That is, the ration contains a sufficient number of calories to supply the needed energy and is balanced so as to prevent the occurrence of deficiency diseases. * * * Physiological and psychological reactions must be taken into account, and in order to obtain, in terms of body energy, the full value of the ration it must be of such a nature that it will appeal to the troops and be eaten in sufficient quantities.

On 11 January 1927, Paul E. Howe, Ph. D., Bureau of Animal Industry, U.S. Department of Agriculture, then a lieutenant colonel in the Sanitary Corps Reserve, submitted, to the Office of The Surgeon General, an excellent critique on the ration of that time.

In 1929, a mess management course was instituted in the troop schools.

Just before the United States entered into World War II, Colonel Howe, having served a period of active duty from 26 July to 4 August 1940, reported that the garrison ration at its field value was adequate as to calories, proteins, phosphorus, iron, vitamin A, vitamin B_1, and riboflavin and that it was fairly satisfactory with respect to calcium and vitamin C, but he had several very keen and pertinent remarks to make about the ration-savings plan which was then in effect.

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[3] Letter, Maj. Gen. B. F. Cheatham, The Quartermaster General, to The Adjutant General, 11 Dec. 1926, subject: Increase in the Ration Allowance—Regular Army and Philippine Scouts, with 1st endorsement thereto.

By 26 September 1940, there is evidence of The Surgeon General's awareness of the imminence of conflict and of his interest in setting up new rations for the troops. He had already obtained authority for the formation of the Food and Nutrition Subdivision in the Professional Service Division of his office. Col. Paul E. Howe, SnC, became the first chief of the subdivision, serving from 25 September 1940 to 12 April 1944.

Beginning with January 1941, a course for food and nutrition officers of the Medical Department was given at the Army Medical School, Washington, D.C. Even as late as 7 February 1941, however, in a memorandum to the Assistant Chief of Staff, G-4, on the proposed War Department circular on rations, the Office of The Surgeon General makes no mention of clinical examination of the troops who were going to consume the new ration. Unfortunately, too, little had been done to check the influence of the newer techniques of preservation on the nutrient content of foods. Early in the war, however, The Surgeon General, in recognition of the part played by good nutrition in the maintenance of the health of troops, appointed clinicians to the Nutrition Branch within his office.

This move presented something of an administrative problem. Maj. (later Col.) Herbert Pollack was the first Medical Corps officer assigned. There was no slot available for this assignment, and therefore Major Pollack was ostensibly on temporary duty in the replacement depot, but actually he worked on a temporary-duty basis in the Nutrition Branch. Subsequently, Col. John B. Youmans, MC, was made chief, serving from 12 April 1944 through the World War II period. Colonel Youmans brought into the work a whole group of men primarily interested in the clinical aspects of nutrition.

THE RATION TESTS

Plans and organization.—In 1941, with the imminent onset of open warfare, plans were made to start ration trials as rapidly as possible. The Surgeon General, being directly concerned with the nutritional status of the troops, worked closely with the Quartermaster General in designing rations to satisfy the field forces, who must, of course, be capable of fighting the war on the ground in any part of the wide world. A battle may be fought in the mountains, in the deserts, in the rolling plains, or in the trackless, frigid wastes of arctic regions—each locale posing different problems for the maintenance of optimum nutrition of the soldier. A limiting factor at all times is the logistic one. Munitions usually have priority over other supplies. This means that rations must be suitable in terms of stability and storage, under arctic or tropic conditions. Consideration must be given in packaging, field utility, weight, cubic content, and nutrient content at the time of consumption; that is, there must be no more than an acceptable rate of deterioration during the pipeline or

the shelf storage. Acceptability and palatability must also be taken into account. Faced with these, at times, apparently conflicting interests, the joint efforts of all concerned nevertheless succeeded in solving many of the more important problems. After World War II, personnel of both offices, The Surgeon General's and the Quartermaster General's, continued to cooperate in the work on the ration problems discovered during World War II. On 6 November 1944, The Surgeon General opened the Medical Nutrition Laboratory in Chicago, Ill. The laboratory, which has since moved to Denver, Colo., has grown and is now one of the most important agencies dealing with the nutritional requirements of troops in combat.

The purpose of the ration tests conducted by the American and Canadian Armies from 1941 to 1946 was to determine accurately the nutritional adequacy of the various types of rations under the conditions under which the troops would use them. The Canadians were somewhat the more aggressive in these studies and early in the autumn of 1942 had already begun their nutrition surveys. In all, 16 important ration tests were carried out in places varying from the desert training area in California up through the Canadian Army Operation MUSK OX in the Arctic. In addition, there were at least 15 separate surveys of the troops during this period, these varying from a simple determination of nutrient intake to clinical observation. This is the first time that direct clinical observations were made on the troops in the field and under experimental conditions just to determine their health status under various conditions of feeding. An excellent summary of this work was published in 1947.[4]

The underlying principles.—The basic premise of the trials was that rations had to be evaluated in two aspects: (1) Suitability in terms of supplies and logistics, and (2) suitability in terms of effect on the soldier, on his physical fitness and military efficiency, with particular emphasis upon the maintenance of the biochemical balances. Before the war, and during the early days of World War II, much of the clinical thinking with respect to nutrition was distorted by overemphasis on vitamins. The sum of wartime experience was to show that, except under conditions of capture and imprisonment, florid avitaminosis was, in fact, extremely rare in U.S. forces, whereas caloric deficiency with loss of weight was a cause of deterioration among soldiers. In the ration tests, it soon became apparent that the primary problems of the combat soldier's nutrition in order of importance actually were (1) maintenance of water and salt balance, (2) adequacy of caloric intake, (3) adequacy of protein metabolism, and (4) maintenance of vitamin intake.

Water-salt balance.—Maintenance of salt and water balance is so obvious that it is overlooked in many studies on nutrition. In the days

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[4] Johnson, R. E., and Kark, R. M.: Feeding Problems in Man as Related to Environment. An Analysis of United States and Canadian Army Ration Trials and Surveys, 1941–1946. Quartermaster Food and Container Institute for the Armed Forces, Research and Development Branch, Office of the Quartermaster General, Chicago, Ill., April 1947.

before World War II, many officers in the desert training centers attempted to condition the troops to withstand dehydration. As experience accumulated, this "water discipline" was abandoned by a directive,[5] based upon the work of independent observers who agreed that in any climate inefficiency and then exhaustion may come on in a few hours from lack of water.[6]

The clinical syndrome of dehydration exhaustion was seen by a great many officers, although many did not recognize its significance. A man may start a day's work in good condition. If water is not available or if the man does not consume it, thirst becomes noticeable as a dry throat, then as a general subjective sensation of thirstiness. As the negative fluid balance mounts, from any one of a number of causes— sweating from heat in the Tropics, sweating from nervousness in battle, sweating from excessive clothing insulation in the Arctic, and so forth—the face begins to flush, muscular coordination begins to fail and, on a march, the individual begins to lag behind. When the thirst mounts, so that the soldier is actually tormented, discipline and training may be lost and the soldier then discards equipment, piece by piece. At this point, he will be found on physical examination to have a tachycardia and a hyperthermia. The blood pressure drops and orthostatic hypotension sets in. Hallucinations begin, and the soldier may then collapse. His life now is in danger if he is not given treatment consisting of water, salt, and rest in the shade if possible. This type of exhaustion will inevitably occur in the best trained man if his water supply is cut off.

Caloric deficiency.—Clinical descriptions of caloric deficiency in soldiers were well recognized and documented during the ration tests. A composite picture of the effects of caloric deficiency in active young men shows physical and mental disturbances beginning with irritability and annoyance and progressing to a real physical deterioration.[7] When marked caloric deficits exist with high work-output and when the environment is difficult, the signs and symptoms develop in the matter of a few days, but when there is only a minimum of caloric deficiency weeks or months may go by before gross inefficiency appears. This was seen in the B-ration test conducted at Camp Lee, Va., 1943, where the author was the medical officer in charge of the physical welfare of the troops.

In the middle of the test period, we increased the workload from 3,400 to 4,000 calories per day, on the average, without increase in food. * * * A radical change gradually occurred * * *. The men developed a submalar shrunken appearance; the eyes became dull; bodily movements became slower and desire to participate in sports sharply declined, although there was no flagrant attempt at avoiding prescribed formation duties. Touch football and softball were conspicuous by their absence in the early evenings and on

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[5] Circular Letter No. 119, Office of The Surgeon General, U.S. Army, 3 July 1943.

[6] (1) Adolph, E. F.: Water Shortage in the Desert. Report No. 12, University of Rochester, Contract No. OEMcmr 206, for Committee on Medical Research, Office of Scientific Research and Development, 20 Oct. 1943. (2) Pitts, G. C., Johnson, R. E., and Consolazio, F. C.: Work in the Heat as Affected by Intake of Water, Salt, and Glucose. Am. J. Physiol. 142: 253–259, September 1944.

[7] (1) Pollack, H., Berryman, G., French, C., and Henderson, C.: Quartermaster Board Project S-44. The Expeditionary B Ration (Temperate) Test, Parts I and II, Quartermaster Board, Camp Lee, Va., 7 Sept. 1943. (2) Kark, R., McCreary, J. F., Johnson, R. E., Melson, R. R., and Richardson, L. M.: Cold Weather Operational Trials of Rations Conducted at Prince Albert, Saskatchewan, Canada, January 2d to March 3d, 1944. A Report to The Standing Committee on Nutrition, Department of National Defence, Canada. (3) Report, Armored Medical Research Laboratory, Fort Knox, Ky., 10 Apr. 1944, Project No. 1–7, 1–15, 2–5, 2–14, Cold Weather Operations.

Saturdays * * *. The Medical Consultant Board agreed unanimously that practically all the men exhibited some degree of physical deterioration during the test period. The specific manifestations observed by the officer in charge of physical welfare were poor muscular coordination, inability to carry out work of high intensity, falling out in the marches, nervousness, irritability, muscle aches and pains, insomnia, and other significant symptoms.

Unless officers were aware that gross loss of military efficiency and operational fitness could occur as a result of eating too little food, the results, in varying degree, of caloric deficiency were usually ascribed to other deficiencies in the soldier, often of reprehensible nature.

As caloric deficiency increased in the test troops, the physical signs of disturbed function became more obvious. Fatigue, sluggishness, lack of energy and drive, loss of muscular strength, the desire for rest, increasing sleeplessness, sensitivity to the cold, and tremors of the hands were noted; quarrelsomeness was evident. Loss of weight, of course, is manifested very early. Dizziness, nausea, vomiting, exhaustion, and collapse are the late stages. Loss of weight at this point becomes very obvious. The shrunken eyeballs, the dry mouth, the parched lips, the occasional acetone odor to the breath, changes in tendon reflexes, and impairment in physical fitness tests are observed fairly often. Recovery from early effects of caloric deficiency are usually very prompt and dramatic, and the return of morale in the men can occur within the matter of a few hours.

During the Camp Lee tests, there was much discussion about the nature and cause of the physical deterioration observed, and it was decided to give half the troops massive doses of synthetic vitamins. No convincing evidence was found that therapy with vitamins had any significant effect on the health and efficiency of the test troops under conditions of caloric insufficiency.

As will be seen later, caloric deficiency was the most important nutritional problem both in American prisoners of war recovered from the enemy and in the "enemy armed elements" in prison camps of the United States.

Nitrogen balance and surgery.—Concerning this aspect of nutrition, the surgical history of the Fifth Service Command by Col. Claude S. Beck, MC,[8] is relevant. At the Wakeman General Hospital, Camp Atterbury, Ind., a nutrition laboratory was established basically for the use of the surgical services. The nutritional status of the patient was regarded as a factor in surgery, much like hemoglobin and the blood picture in general, to a large extent conditioning the healing of wounds and results of operation. The laboratory group was concerned particularly with the paralyzed patient. In this type of injury, decubitus ulcers, secondary infections, and other complications are probably related to the nutritional status.

It may be recalled that just before our entry into World War II, a committee of the National Research Council reported on the effect of nutrition and nutritional status on recovery from wounds and illness. The committee pointed out the importance of nitrogen balance and similar metabolic studies in both the acute and chronic phases of disease and in trauma, since substantial loss in nitrogen occurs in many patients. This, of course,

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[8] Beck, C. S.: Surgical History, Fifth Service Command. [Official record.]

is enhanced by the large losses of protein and exudates and other secretions from the body. It was pointed out particularly that the general metabolism of an individual who has sustained severe injury or illness is quite different from that of a healthy man and that his nutritional requirements must be based upon the depletions that occurred during the acute episode. For instance, a marked increase in urinary nitrogen was observed reaching a peak during the 3d and 10th day following compound fractures of the leg. When there is decreased food intake through anorexia or other causes, the negative nitrogen balance can run as high as 30 grams of nitrogen a day and over a period of time mounts up rapidly. The results were seen in extensive loss of weight and wasting of tissues with debilitation and prolongation of the convalescent period. After a time, definite changes could be seen in the amount of protein in the circulating blood, particularly in the albumin fraction of the plasma. At first, this circulating protein had a priority over all other forms and was maintained at the expense of tissue stores. As the tissue stores became depleted, plasma volume decreased with attendant hemoconcentration. After all compensatory mechanisms had been exhausted, then the actual decrease in the circulating protein was noted.

The optimum daily intake for the average surgical patient was set at 150 grams of protein with 3,600 calories or more. The physicians had to employ heroic measures to achieve this objective. Acute deficiencies of circulating protein were corrected by the administration of plasma and subsequently human albumin, which contributed a large quantity of circulating protein and enhanced the blood plasma. Beverages fortified with protein were developed and used to supplement the hospital diets. Subsequently, to the close of the war, this type of work has been carried on and extended even further.[9]

SPECIAL PROBLEMS IN THE FIELD

Nutritional difficulties were encountered by all Allied troops at one time or another. In the early stages of the war against Japan, diseases of all kinds were prevalent and severe in the Asiatic areas. During the Owen Stanley-Buna campaign in New Guinea, Australian troops were supplied at first under a schedule of priorities that placed ammunition first, blood second, and food third. Casualties from wounds and diseases, especially malaria, were very heavy, and nutritional diseases including florid beriberi appeared. Owing to difficult conditions of supply, the diet had consisted mostly of tinned beef and biscuits for periods varying from 6 to 12 weeks.[10] By the middle of the campaign, priority in supply was given first to blood, because of its small bulk; second, to food; and third, to ammunition. Many soldiers of Wingate's Force in Burma had for 5 months lived on K-rations, supplemented by tea, sugar, jam, bully beef, and bread which were occasionally dropped to them. A medical officer reported that, of 209 men examined at the end of this time, 182 had lost up to 30 pounds and 27 had lost from 30 to 70 pounds. Deficiency diseases

⁹ Pollack, H., and Halpern, S.: Therapeutic Nutrition. Bull. 234 Nat. Acad. Sc. 1952.
¹⁰ Director-General, Medical Services, Army, Technical Instructions No. 74, 26 Aug. 1943.

such as pellagra and beriberi were recognized. One of Wingate's units in the Dehra Dun area was visited some months after they had last eaten K-rations. At the sight of a box of K-rations, carried by the visitors, two of Wingate's men vomited.

Europe and North Africa

Field trials for special rations were conducted in the several theaters of operations, particularly in ETOUSA (European Theater of Operations, U.S. Army) where facilities were available to study the problems that arose. An extensive report [11] from the European theater, dated July 1943, showed findings similar to the ration trials in the United States. The authors of the report noted that none of the packaged rations were recommended for continued use by active troops for periods in excess of 10 days unless supplemented with additional food. The need for supplements was greatest in the C-ration. Much credit for the work on rations done in the European theater goes to Lt. Col. Wendell H. Griffith, SnC, Lt. Col. Charles G. Herman, QMC, and Maj. William H. Chambers, SnC.

The North African theater saw the first really extensive use of troops in the field and the first really severe test of the newly developed B-, C- and K-rations. The difficulties under which they were tested here were even greater than had been anticipated in designing the rations and were compounded by misunderstanding of the ration systems and the use of rations. Medical officers in general were not thoroughly conversant with the signs and symptoms of nutritional inadequacies. They had been exposed to overemphasis on vitamin requirements and were, for the most part, not proficient in differentiating the numerous complaints that resemble nutritional inadequacies but that are basically due to other causes. In reviewing the report of Col. Perrin H. Long, MC,[12] medical consultant in the North African theater, it becomes apparent that training of personnel in nutrition before their assignment in the field would have saved much time and many mistakes.

In Essential Technical Medical Data and unit commander reports and in surveys done by the headquarters personnel, there was evidence of a tendency in the frontlines to blame a disproportionate amount of their troubles on the rations. Loss of weight regardless of other cause, whether anxiety, supply difficulties, or climatic conditions causing anorexia, was almost invariably blamed on an inadequacy of the ration per se. This generalization is no better than most however; some of the problems were real.

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[11] Field Trial, Special Rations. European Theater of Operations, U.S. Army, July 1943.

[12] Report, Col. Perrin H. Long, MC, Medical Consultants Division, to Chief, Preventive Medicine Service, Office of The Surgeon General, attn: Chief, Nutrition Branch, subject: The History of Nutrition in the North African Theater of Operations, 3 January 1943 to 1 August 1944.

For instance, the chief of the medical service of the 9th Evacuation Hospital states that disturbances noted in two patients with stomatitis were thought to be nutritional in origin and were, in fact, cured with large amounts of vitamin supplements. The 77th Evacuation Hospital had one typical case of pellagra developing in an officer who was eating cold C-rations; the diagnosis was verified by the consultant in medicine, North African theater. In addition, six cases of polyneuritis due to thiamine deficiency, several instances of ariboflavinosis, and several cases of spongy bleeding gums ascribed to ascorbic acid deficiencies, had been seen in that hospital. In the 128th Evacuation Hospital, the chief of the medical service reported two instances of vitamin A deficiency as manifested by cutaneous changes and night blindness. A survey[13] was made of troops in the forward areas and evacuation hospitals of the Fifth U.S. Army on 26 November and 4 December 1943. Almost all soldiers questioned in infantry, engineer, and other units said they had lost weight since the beginning of the Italian campaign. Surgeons commented upon the decrease from the normal in body fat in their patients, and some noted wasting and paleness of muscle substance. Loss of hemoglobin was reported in a survey of the mucous membranes of the mouth and conjunctiva of troops in the forward areas, together with the clinical impression of exceptional pallor for men of the age group examined.

Increasing numbers of soldiers suffering from physical exhaustion were seen in the forward area. These patients required copious feeding in addition to rest, thus confirming the view in the minds of the medical personnel that a state of undernutrition favors development of physical exhaustion. It was noted, however, that frank vitamin deficiencies such as scurvy, pellagra, beriberi, and night blindness had been observed infrequently during the previous year in the American troops in the North African theater.

Perhaps the one attempt at controlled observations on nutritional deficiencies in North Africa was that made by a flight surgeon of the American Air Forces and a medical officer in the Royal Air Force. Using standard dark-adaptation equipment and a slit lamp for determination of capillary loops for riboflavin deficiency, they made the following observations:

The Americans were well within normal limits, having a factor for dark adaptation around 5 and a riboflavin factor of 1. The French had a dark-adaptation factor of 14 and a riboflavin factor of 2. The English had a dark-adaptation factor of 17 and a riboflavin factor of 3 plus and, in approximately 10 percent of them, 4 plus. These medical officers note also that, on a diet ration, the concentration of ascorbic acid in the plasma is usually 1 mg. per 100 cc. of blood or slightly higher. "This must not fall below 0.2 mg. percent before wound healing is adversely effected." In a control group of 17 soldiers admitted from local units, the range was from 0.2 to 1.1 milligrams. None showed a depletion that would be significant in the healing of wounds. Of 60 unselected battle casualties, 28 percent showed ascorbic acid levels below 0.2 milligram. Of the 17 control patients, 11 were under 0.1 mg. percent and 5 were at 0; only 3 of the

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[13] Essential Technical Medical Data, North African Theater of Operations, U.S. Army, for December 1943, dated 27 Jan. 1944, appendix V.

60 patients showed vitamin C levels of 1 mg. per 100 cc. of blood or over. It should be noted that one causative factor in the deficiency was lack of facilities for feeding the troops during evacuation.

Isolated instances of vitamin C deficiency continued to be noted in the European theater.[14] In the 495th AAA Gun Battalion, an officer and several enlisted men showed signs of vitamin C deficiency. These cases were ascribed to failure by the men to eat breakfast, the meal that chiefly supplied this vitamin, and the patients were, in fact, cured with tablets of ascorbic acid. In the Western District, United Kingdom Base, 15.2 percent of 16,868 men inspected had bleeding gums. This was similarly ascribed to failure of soldiers to drink the fortified juices provided at breakfast. Nutritional disturbances could usually be accounted for not so much by the quality as by the distribution or consumption of the rations. On the whole, there were surprisingly few nutritional problems per se among troops in this theater.

Atlantic Bases

Nutritional problems in the isolated areas of the Arctic and North Atlantic were not so great as one might anticipate. No unusual problems were reported. Occasional cases of malnutrition were seen at the station hospitals following the forced landings of planes in the wilds. The survivors, frequently without food for 5 or more days, would attempt to reach civilization. When they were rescued, their type of acute starvation was well known and was handled promptly and properly by the medical personnel. Of more general interest is the report from the 188th Station Hospital, dated 15 March 1944, on a survey of anemia in soldiers with over 12 months of service in Greenland. Red cell counts and hemoglobin determinations were made on 103 soldiers who had dwelt in Greenland for an average of 15 months. There were, of course, numerous subjective complaints. Changes in weight were insignificant: 14 men had lost an average of 13 pounds; 13 men had gained an average of 13 pounds. The average red cell count was found to be 4.56 million. The average hemoglobin was 13.6 gm. per 100 cc. of blood. Of these men, 5 percent had erythrocyte counts below 4 million, 10 percent between 4.0 and 4.2 million, 17 percent between 4.2 and 4.4 million, 22 percent between 4.4 and 4.6 million, 19 percent between 4.6 and 4.8 million, and 12 percent between 4.8 and 5.0 million; 16 percent had counts of over 5 million. Free hydrochloric acid was found in gastric secretions of all men with counts below 4 million. The controls, 16 men who had just arrived from the United States and had served only 4 weeks in Greenland, had an average erythrocyte count

[14] (1) Annual Report, 495th AAA Gun Battalion, 1945. (2) Survey, District Nutrition Officer, Western District, United Kingdom Base, to Surgeon, United Kingdom Base, Communications Zone, ETOUSA, 10 Jan. 1945.

of 4.98 million, and their average hemoglobin was 15 gm. per 100 cc. of blood. It was concluded that a mild chromic anemia existed among approximately 75 percent of the men who had served over a year in Greenland and that the anemia was probably nutritional in origin. Those subject to the anemia had symptoms that could be explained as largely psychic in origin. It was recommended that the vitamin content of the diet be increased as much as possible and that multivitamin pills be made available to all men on this post and, what was most important, that if and when possible men with 1 year's service in Greenland should be reassigned to duty in the United States. It is difficult to differentiate between the emotional problems of the men who were confined to the area and those problems that were truly due to nutritional disturbances.

From the U.S. Army Forces in the South Atlantic, based principally on the Ascension Islands, only occasional cases of true deficiency diseases were reported, and these were due mainly to failure to eat the rations. One patient, with very mild symptoms of pellagra, worked at night and during the day preferred sleeping to eating; he recovered completely with a change in duty assignment plus adequate diet. In the Panama Canal-Trinidad sector in the South Atlantic, the battalion surgeon made this comment: "The general nutritional status of the troops is adequate. Symptoms of vitamin deficiencies have been frequently noted but at present are mild in character." More than the average number of cases of gingivitis were seen by dental officers in men reporting from jungle outposts, where the standard ration was, not in its composition but in its consumption, inadequate to nutritional requirements. In these reports from individual surgeons, it is again noted that the reporting of nutritional deficiencies in troops very largely depends upon the observer and his interpretation of symptoms and their causes.

Nutritional problems in the Far East will be discussed later, since these for the most part concern prisoners of war and recovered prisoners, and that story properly begins in the European theater.

RECOVERED ALLIED MILITARY PERSONNEL,

EUROPEAN THEATER

Before D-day, soldiers of American and Allied origin, in small numbers but more or less continuously, filtered through belligerent and Allied countries in the attempt to rejoin their parent organizations. Most were air force personnel who had been shot down while flying missions over enemy territory. Administratively, they fell into two categories: Escapees, those who had been imprisoned; and evaders, those who had avoided imprisonment in enemy hands. It is not the purpose of this medical report to discuss the methods by which these people outwitted the enemy.

It is sufficient to say that much was made possible by the members of the underground of the occupied countries. The theater Provost Marshal had a small hotel in London located at 63 Brooke Street where those Americans fortunate enough to elude the Nazis and reach England were processed. In March 1945, an installation was set up at the Hotel Francia in Paris which provided the means for the care and processing of these escapees and evaders.

With the liberation of France in September 1944, the possibility of recovering Allied prisoners of war in overrun German camps became real, and administrative plans were made to take care of them. The Provost Marshal instituted a RAMP (Recovered Allied Military Personnel) Division on 18 December 1944. Unfortunately, planning did not include the Nutrition Branch of the Professional Services Division, Office of the Chief Surgeon, ETOUSA. The SHAEF (Supreme Headquarters, Allied Expeditionary Force) policy with respect to RAMP's as outlined in paragraph 555(b) of the "Handbook for Military Government in Germany Prior to Defeat or Surrender," dated December 1944, was somewhat unrealistic in its approach to this problem. Allied prisoners of war, according to the Handbook, were to be "freed from confinement and placed under military control or restriction, as may be appropriate pending further disposition." In the early days of the war, under the conditions disclosed by escapees and evaders, this procedure might well have worked. However, Americans who were captured in the Ardennes bulge late in 1944 related that they had been continuously on the march with hardly any rest and with pitifully inadequate nourishment. Obviously, these men, and others on the march, had suffered great hardships from which the Geneva Convention had not, as expected, protected these prisoners of war. Hence, it was virtually impossible to leave them where they were when the camps were overrun.

On 7 May 1945, the Supreme Commander, SHAEF, made the decision that all American and British ex-prisoners-of-war should be evacuated from the Army areas in the shortest possible time, regardless of any limiting circumstances. CATOR (Combined Air Transport Operations Room), the agency that controlled air transportation, was given as its first concern the movement of the prisoners of war to installations in the Communications Zone. Before this decision, the movement of supplies had priority with CATOR, and the prisoners of war were evacuated wherever camps were located close enough to the delivery points for supplies. This change in policy greatly accelerated evacuation of liberated prisoners of war through administrative channels, and from a daily rate of approximately 1,500 the number jumped to 30,000 on 9 May. Recognized medical cases were evacuated separately. By 22 April 1945, reception camps for the handling of American and British RAMP's were established at Namur, Belgium, and at Reims and Épinal in France.

Camps for Care of Recovered Prisoners

The Lucky Strike Camp, situated near St. Valéry on the north coast of France, had already been designated as a transit camp. Camp Wings, close by the Lucky Strike area, served as the air terminus for the men evacuated by air and also as a base camp for the British RAMP's. Eventually, an airstrip was built at Lucky Strike to relieve the load at Camp Wings. Evacuation from the temporary camps became a sizable problem, and the rail and air facilities were loaded to capacity. The Chief Surgeon made 29 hospital trains available to the Provost Marshal to help the administrative evacuation. Camp Lucky Strike was selected as the installation that would have the greatest part of the work involved in the processing and evacuation of the RAMP's because of its proximity to Le Havre and because it had a capacity expandable to 70,000.

Approximately 60,000 Americans were listed as prisoners of war in the hands of the Germans, but actually over 94,000 recovered prisoners were evacuated through medical and administrative channels. These discrepant figures are accounted for by the many thousands previously listed as missing in action.

Arrival of First Liberated Prisoners

Sorting.—Camp Lucky Strike, then in the Northern District of Normandy Section, was set up as the reception area for the RAMP's being sent through command, as distinguished from medical, channels. Lucky Strike had been intended as a staging area for incoming ground force personnel during hostilities, and much had to be done to adapt it for the present purpose. The Camp proper was divided into four blocks, with a total capacity of about 40,000 soldiers. Block D was set aside originally as the RAMP camp and, in a short time, was made an independent command responsible directly to the Northern District. Block C was set up as a possible 306th General Hospital to take care of convalescent RAMP's. RAMP's were flown from the forward areas to the airport at Le Havre where a 2,000-bed tent setup was made available. All RAMP's were screened medically at the airport by the physicians of the 98th Medical Battalion and by the dispensary officers from the Le Havre units under the direction of the Northern District surgeon. Those few who came in by rail transport were sorted several hours out of Le Havre, and complete triage was effected before the train arrived at the station. Of approximately 7,000 RAMP's evacuated to Le Havre for the Lucky Strike area in the early days, 824 were hospitalized.

Of the total number arriving, there were about 2,400 British personnel, who were kept in Camp Wings for several hours and then transshipped to England, except those who, being too ill, were put into Ameri-

can hospital channels. Of the entire number hospitalized, immediate triage at the landing field accounted for 390. Of these, the sickest were taken directly to the 28th Station Hospital, Yvetot, France, about 30 miles from the airstrip; the rest were sent to the 179th General Hospital at Rouen.

The first batches of returning men were met as they alighted from the plane by the American Red Cross, who gave them hot coffee, doughnuts, peanuts, and a blanket. Transportation thence to the camp was by the usual Army 6 x 6 truck, from 16 to 18 men in a truckload. Here, they were again screened by the dispensary physician of the post aided by the medical officers of the general hospitals staging in the areas. Up to Friday evening 13 April 1945, 4,400 men actually reached Lucky Strike Camp. Of these, 425 were hospitalized by the screening physicians on admission and at morning sick call at the dispensaries. They were admitted to the 77th Field Hospital set up on the campsite. On Saturday morning, 14 April 1945, the 77th Field Hospital had a census of 441 patients. (See also page 249.)

It may be recalled that all these men had been previously screened in forward areas, where RAMP's were divided into those to be evacuated by medical or by command channels. Those sent to the Lucky Strike area had been considered physically fit and ready to be sent home. Forward triage was of course difficult at best, and subsequently many things happened. The trip by air, sometimes through great turbulence, was often enough to upset these men, whose balance was precarious at best. Then came the warm, but nutritionally unsound, welcome by the Red Cross, which was, in fact, secondarily responsible for many cases.

Clinical problems.—The dispensary setup at Camp Lucky Strike was very adequate. There were three such medical installations, each serving 10 packets or companies of 200 men each. There were from two to four physicians in each dispensary. On Saturday morning, 14 April 1945, the sick call reached over 500 RAMP's, despite the fact that the population of the camp that morning had fallen to 2,800 men, owing to the evacuation of 1,500 men for the Zone of Interior during the night. About 80 percent of the men reporting on sick call had for their presenting complaint gastrointestinal disturbances; the rest, predominantly acute infections of the upper respiratory tract, pyodermias, and other skin conditions. Numerous men had complaints referrable to polyneuritis, hyperesthesia, paresthesia, muscle atrophies, edema, and cheilosis. These were seen as complications of the presenting gastrointestinal symptoms. The histories reveal that the acute respiratory infections started in transit. Acute gastrointestinal symptoms also started in transit and at the RAMP camp. It was known that the initial delousing was not always completed before arrival at Camp Lucky Strike. It is to be noted parenthetically that many RAMP's were found to have originated from Stalag XII–A (p. 252) where 22 cases of typhus fever in the Russian prisoners had been reported.

Among the 441 patients in the 77th Field Hospital on the morning of 14 April 1945, the commonest diagnoses were gastroenteritis complicating malnutrition, acute infections of the upper respiratory tract with malnutrition, and pyodermias with malnutrition. Three percent of the RAMP's admitted required intravenous plasma therapy as an immediate supportive measure. As anticipated, the patients tolerated intravenous fluids very, very poorly. Two units of plasma were the most given in one day. No whole blood was available. Vitamin supplies were very poor at that time and were not used as extensively as might have been desired, but supplies arrived very shortly afterward. There was a rather acute shortage also of paregoric, bismuth, and belladonna. In the first group of patients admitted, X-rays of the chest were taken; the diagnosis of pneumonia was made in 7 out of 55, and 1 case of active tuberculosis was found.

The 28th Station Hospital located nearby had admitted 57 RAMP's. One death had occurred shortly after arrival. The autopsy protocol revealed a bronchial pneumonia complicating malnutrition. The serum proteins had been estimated before this soldier's death as 2.5 gm. per 100 cubic centimeters.

Recommendations for therapy.—The medical consultant at the Normandy Base Section, Lt. Col. (later Col.) Theodore L. Badger, MC, invited the nutrition consultant from the Office of the Chief Surgeon to give orientation talks to the chiefs of the medical services of the hospitals in the Northern District of Normandy Base. As a result of these conferences, certain recommendations were made, based in large part upon observations made on recovered prisoners in forward areas (p. 251). Briefly, the first proposal was that a system of two messes be set up in this RAMP reception area, with one to serve a bland diet ration to all newcomers for at least 48 hours, and optionally after that. At the Lucky Strike Camp, this was feasible and acceptable to the administration and to the district surgeon. It was felt that much hospitalization could be prevented and convalescence speeded by early general diet therapy for reeducation of the gastrointestinal tract. The second recommendation was to give the RAMP's short orientation talks on proper eating as far forward as possible. A poster system for the messhalls was devised as a visual aid to this educational campaign. One of the most important recommendations was that every effort be made to stop the American Red Cross and the Army Exchange System from flooding these men with doughnuts, candy, apples, and peanuts. One soldier ate 17 doughnuts on his trip back from the forward areas with results that can be imagined. It was recognized that the acute vitamin deficiency syndromes were precipitated only after full feeding had started and so could not be anticipated, but preventive therapy should have been started earlier.

Medical officers had in general to be oriented with respect to therapy of severe chronic malnutrition. Directives were issued by the Office of the Chief Surgeon on advice from the medical consultant to the Nutrition

Branch. These were basically concerned with avoidance of intravenous therapy, the use of bland soft diets, and the avoidance of such medications as iron. Many physicians, when they found the deficiency anemias, immediately prescribed iron by mouth, but this therapy was not considered rational in the presence of such great protein deficiencies. Also, qualities of the iron compounds irritating to the gastrointestinal tract precipitated secondary problems. Medical officers were further warned about details of treatment of complicating infections. Extra vitamins would be required in the febrile period. The early use of penicillin in adequate dosage should be encouraged. The use of the sulfonamides was to be considered on a very cautious basis because (1) they upset the gastrointestinal tract, and (2) the hemoconcentration, dehydration, and scanty urines called for much smaller doses on account of the minimal excretion and the possibility of precipitation in the genitourinary tract.

A further recommendation was that the evacuation policy from the Communications Zone to the Zone of Interior be modified. It was found that the recovered prisoners, from 3 to 5 days after arriving from forward areas, were put on transports with no provision for special feeding. It was felt that the rough voyage would start nausea and vomiting in a large percentage of these debilitated people, resulting in unnecessary hazards to quick convalescence and possibly endangering life itself. Furthermore, some of them being less than 15 days from known typhus areas might possibly be carrying the disease during the incubating phase. The diphtheria rate also was high among them, and their rapid evacuation to the States risked carrying virulent diphtheria home quickly.

Transport commanders were accordingly informed by *Medical Bulletin No. 1*, dated 15 May 1945,[15] that various degrees of malnutrition had been found in the recovered Allied military personnel. Although marked improvement had been accomplished under a rigidly controlled dietary program, complete rehabilitation would necessitate several more weeks of nutritional management. Accordingly, this program should be continued both aboard ship and in the Zone of Interior. Foodstuffs to be restricted included particularly doughnuts, peanuts, citrus fruits, cauliflower, cabbage, the concentrated components of C- and K-rations, and high fat-containing foods. The general mess should be on a soft or bland diet both before and during the voyage home. The *Bulletin* outlined in detail the various precautions that had been taken to protect the RAMP's from gastrointestinal disturbances, which in so many cases were cause for hospitalization.

Incorporating the essential recommendations just discussed, Circular Letter No. 36, Office of the Chief Surgeon, ETOUSA, was published on 19 April 1945. On 28 April 1945, with the cooperation of the Chief Surgeon

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[15] Medical Bulletin No. 1, Office of the Surgeon, Northern District, Normandy Base Section, 15 May 1945.

and the Chief Quartermaster, the special bland diet menu was issued, and copies of the menu were distributed by the Adjutant General, ETOUSA, with instructions that the special menu was to be used as a basis for feeding recovered malnourished U.S. and British Army personnel until the normal field ration A menu could be tolerated.

Statistics gathered from medical units at the various RAMP camps reiterated the need for taking such action and showed prompt results. In one camp, where the operational 10-in-1 ration was fed on an emergency basis to 1,000 recovered prisoners, 150 were hospitalized after the first meal for acute diarrhea, and a number of others reported on sick call for various gastric complaints. At another camp, there was an average daily sick call of over 20 percent on ordinary Army rations, with 80 percent of the presenting complaints characteristic of enteritis. One week after the introduction of the bland diet, the sick call rate dropped to 4.0 percent with only 15 percent of the complaints related to enteritis and with no instances of nausea and vomiting.

RAMP Camp in Action

By 10 May 1945, the Lucky Strike area had become very well organized. Reception into RAMP camp was in a designated area with a capacity of about 2,000 beds. The men were kept here for about 1 day after which they were transferred to the processing areas for a minimum of from 1½ to 2 days. The capacity of this latter was 4,000 beds. After processing, they proceeded to the "pending shipment" area for a minimum of 1 day, in actual experience from 3½ to 10 days. Each of these designated areas had a different mess. The special bland ration was used by all three except that Mess No. 1, in the reception area, eliminated dried fruits. In addition, there was a supplementary issue of one multivitamin capsule for each man at each meal. Between meals, a nutritional bar was available for all personnel.

On 7 May, this bar served 460 gallons of eggnog, 320 gallons of cocoa, 452 gallons of malted milk, and 128 gallons of tomato juice. The average serving was approximately 12 ounces. In addition, the RAMP's arriving at the camp after the evening meal were served 160 gallons of dehydrated pea soup and 1,400 cheese sandwiches made with white bread. Although no control was maintained at the nutrition bar for second helpings, the length of the line was a deterring factor. In the mess, effective control was exercised by characteristically colored and marked cards issued by the tent commander to the men in formation before each meal and surrendered as they passed through the gate to the mess. It was estimated that the average consumption was well over 5,000 calories per man per day.

Inquiries made among the RAMP's and administrative personnel revealed excellent acceptance of the bland menu by the soldiers. Plate waste, as one would expect, was negligible. The messes were now in excellent condition; concrete flooring for serving and mess tents were completed; ranges and utensils were supplied by the Quartermaster General without further delay and in adequate quantities. The problem of lack of communications remained, however, and the post was frequently not ready for new shipments as they arrived.

After the RAMP's went through the first two areas, they were sent, as stated previously, to the holding or "pending shipment" area. Here, the modified type-A ration was served. This holding area was no longer under the control of the RAMP camp, having been returned to the control of the Lucky Strike Post.

By the middle of May, the general health of the RAMP's was much improved. The sick call rate had dropped to an average of 60 to 75 patients daily in an area whose population varied from 1,500 to 2,800, as contrasted with the earlier rate of 200 for a population of 2,000. The chief complaints at this time were boils, skin infections, cellulitis, and diarrhea; gastro-intestinal symptoms now accounted for only 1.8 percent of the total. Nausea and vomiting were no longer presenting complaints. Infections of the upper respiratory tract were only a minor problem. Triage was still done at Camp Wings located about 43 miles from the RAMP camp. Hospital admissions were made directly from the triage area, and by mid-May the rate was only about 10 percent of the incoming RAMP's. Earlier hospitalizations were over 20 percent, before the initial problems with the American Red Cross had been solved. The common causes for hospital admission at this time were acute respiratory infections (about 50 percent), diarrhea, cellulitis, and edema; 36 cases of hepatitis were picked up in 1 week. The 77th Field Hospital continued to be busy through the middle of May and on the morning of 9 May had a census of over 300. Causes for admission were essentially the same as before, except that in the routine X-ray films six patients with active tuberculosis had been detected. The nutritional deficiency syndromes remained essentially as noted earlier. Problems of hospital care were greatly eased by the decrease to the vanishing point, from over 80 percent 1 month previously, in the number of patients with nausea and vomiting.

Clinical History: Statistics

Information gathered from 214 RAMP's by questionnaire from 28 May through 6 June 1945 may be summarized statistically. In all, they had had an average captivity of 143 days. Their average weight before capture was 163 pounds, and their average present weight was 149 pounds. It was reported by 26 that they had lost only from 5 to 15 pounds; 84 said they had lost from 15 to 25 pounds; and 90 reported losses of over 25 pounds. It was noted that 187 of these people had diarrhea during their incarceration; of these, 31 reported having had diarrhea most of the time, 29 frequently, 69 occasionally, and 53 rarely. As for symptoms, 90 reported they had had swelling of the legs while they were in captivity and 20 of them still showed evidence at the time of the questionnaire; 165 reported nocturia during their imprisonment. These figures are indicative to some extent of the degree of malnutrition that was present among the RAMP's questioned.

In all, 82,320 RAMP's were evacuated through nonmedical channels. Spot-check surveys showed an average of 143 days in German camps and an average weight loss of 14 pounds. Of the RAMP's, 55.6 percent showed evidence of malnutrition, 42.5 percent had nutritional edema while in the German camps, and 25.8 percent complained of night blindness. Secondary hospitalization was 27.8 percent in mid-April but down to 2.5 percent by the middle of May.

Approximately 12,000 RAMP's were evacuated through medical channels. The 15th Hospital Center in the United Kingdom Base admitted 2,516 RAMP's. Severe malnutrition was diagnosed in 412; the rest had malnutrition as a secondary diagnosis. The 179th General Hospital at Rouen admitted 837 RAMP's. Severe malnutrition was present in 188. Of these, 42 had to be tube fed. It was found that the average weight loss of the prisoners from Stalag IX–B was 39.1 pounds per man and from Stalag IX–A, 28 pounds per man. The 217th General Hospital, Paris, France, had 1,098 RAMP admissions. Of these, 275 were severely malnourished; others had malnutrition as a secondary diagnosis. There were eight autopsies done on the RAMP's who died in the Communications Zone.

The total deaths of recovered Allied military personnel in the European theater may be detailed as follows:

In the week ending on 13 April 1945, there were 40 deaths reported. Two of these were from malnutrition, and one was from malnutrition complicated by bronchopneumonia. In the week ending on 20 April, there were 36 deaths. One was caused by diphtheria with malnutrition, one by uremia with malnutrition, two by pneumonia with malnutrition, and one by primary malnutrition. For the week ending on 27 April, there were 42 deaths, of which 3 were directly ascribed to malnutrition. For the week ending on 4 May, there were 27 deaths, of which one was due to malnutrition.

STORY OF IMPRISONMENT

The beginning of the RAMP story had been a series of confusions and misinformation. The Nutrition Branch, Office of the Chief Surgeon, had not been alerted to the possibility of the large-scale starvation that was soon to be encountered. In the *Stars and Stripes*, Paris edition, of 26 March 1945, articles began to appear about the "living hell" and the starvation within the German prisons, but only as referring to the civilian and political prisoners. At first, there was no mention of the American, British, French, Russian, and other Allied soldiers who were incarcerated in these camps. On 30 March 1945, in the Paris edition of the *Stars and Stripes*, a small article appeared, describing how 1,000 American and British prisoners of war for 6 hours made a desperate attempt to ward off attacking U.S. dive bombers. They took off their shirts and, with their naked bodies, spelled out POW in giant letters. The Paris edition of the *Stars and Stripes*, on

5 April 1945, presented to the public the first concrete evidence that the American and British soldiers in the hands of the Germans had been subjected to less than the requirements of the Geneva Convention.

This article began: "150 mile death march comes to end as the Sixth Armored Division liberates 800 Yanks." The writer compared it with the infamous death march of the American and Philippine soldiers captured by the Japanese on Corregidor. These 800 soldiers, taken as prisoners during the Ardennes breakthrough, had been on the road for more than 3 months, stopping only when Nazi transportation officials pirated their ranks, forcing the Americans to fill bomb craters and to haul trestle lumber. The prisoners of war were fed one-sixth of a loaf of black bread and one can of potato soup daily. They suffered from dysentery and had lost up to 80 pounds in weight. The breakthrough had caught them in subzero weather. They had had no medical attention. Lt. Col. Albert N. Ward, whose armored infantry battalion liberated the prisoners of war north of Friedberg, Germany, said: "As we entered the town the doughs looked like walking skeletons staggering out to meet us. They were thin and emaciated and they wept." One soldier reported his poor treatment and said: "After they had deposited their excreta on a manure pile, the Germans had dumped potato peelings on the same heap. The men were so hungry they removed the potato peelings, strung them on a wire, cooked and ate the spud skins." A soldier who lost 80 pounds during the 3 months' labor trek said: "They did everything possible to make life unbearable, threatening us with bayonets and firing small arms over our heads whenever we fell out of the columns during the marches." (See pages 253–255.)

First observations.—Shortly after crossing the Rhine, a survey team, consisting of Lt. Col. Wendell H. Griffith, SnC, Chief, Nutrition Branch, Office of the Chief Surgeon, ETOUSA, Lt. Col. Herbert Pollack, MC, and Capt. Leonard Horn, MC, on verbal orders from the Chief Surgeon, were in the forward areas to make observations on the nutritional status of the German civilian population and to see what the problems with the recovered Allied prisoners of war were to be. Their observations, based on a survey conducted from 4 to 11 April 1945, are summarized as follows:[16]

Trier, 4 April 1945.—The Allied Prisoner-of-War Camp No. 1 contained about 1,500 RAMP's, mostly Russians. Food, supplied by the U.S. Army, consisted of one C-ration supplemented by 4.8 ounces of bread and milk and sugar for coffee. Of these liberated soldiers, 150 were sampled; 15 were examined in detail. The general picture was that of severe emaciation and of weight loss. Many had nutritional edema and other signs of extensive deficiency. The Russian physician stated nevertheless that the men had improved considerably since their liberation and that most of their

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[16] Essential Technical Medical Data, European Theater of Operations, U.S. Army, for April 1945, dated 14 June 1945. Inclosure 30, Report of Nutritional Survey in Occupied Germany.

edema had disappeared. Tuberculosis was noted as one of the important problems.

Diez, 5 April 1945.—Stalag XII–A contained over 4,000 RAMP's, approximately half of whom were Russians. Several hundred American and British prisoners had been recovered at this camp, and the seriously ill had already been evacuated. Superficial examination of the remaining Americans revealed a picture of general malnutrition and nutritional edema. In practically all of them, there were acute changes in the tongue, with the burning and soreness characteristic of glossitis, and changes in the skin referable to vitamin A deficiency. In the Russian section of this camp, the conditions were even worse—22 cases of typhus fever had been reported; tuberculosis was rampant and had been the cause of many deaths; emaciation was extreme; living conditions were filthy; and sanitary facilities were entirely lacking.

Niedergrenzebach, near Ziegenhain, 7 April 1945.—Stalag IX–A contained 1,200 American soldiers and many British, French, Russians and other nationals. The hospital had a capacity of 45 beds which were filled with American and British soldiers who were examined carefully. All showed marked loss of weight, changes in the skin, and tenderness in the calf of the leg; 10 had active cheilosis; and 16 showed acute glossitis. Hepatitis with jaundice was seen in several of these soldiers. Reflexes were hypoactive and unequal or irregular. The physician in charge of the dispensary, an American medical officer, said that many soldiers with peripheral palsy had been evacuated that morning through medical channels. Beriberi had been common, according to this officer, but no evidence of scurvy had been observed. American Red Cross parcels had been plentiful at this camp up to a month before its capture. The German ration issue was very deficient. Breakfast consisted of a cup of ersatz coffee which the soldiers frequently used in lieu of hot water for shaving. Luncheon consisted of a ladle of vegetable soup and a small portion of bread. The soup stock was made from bone from which all meat had been removed. Pine needle infusions were added at times. The daily bread allowance was one 2-pound loaf for from five to seven men. The evening meal consisted of bread and soup; two to four potatoes per man were supplied several times each week. An extremely small piece of meat was issued about once a week. Eating grass was said to be customary. It was here that the practice of bartering Red Cross cigarettes for food was first encountered.

Heppenheim, 10 April 1945.—This was the location of the infamous APW (Allied Prisoner-of-War) Hospital where the official ration for the American patients was said to be about 400 calories a day. Twenty Italians were examined, and all gave a history of edema. An Italian medical officer in the group stated that almost everyone had nyctalopia, nocturnal muscle pains and cramps, paresthesia, and a shuffling gait. Examinations revealed a few tongue changes and in many cases healing ulcers of the buccal mucous

membranes. Butterfly distribution of facial seborrhea was seen as well as cheilosis and marked emaciation. The South Africans, in spite of the extensive marching that they had been forced to do, showed little beyond loss of weight. They, however, had had liberal supplies of Red Cross packages up to a recent date. One of their sergeants reported that the death rate on the marches had been very high. Edema had been very common; no scurvy was seen.

Conclusions.—The recovered Allied military personnel were extremely malnourished and presented a feeding problem demanding emergency measures. These troops had not received humane treatment, and no attempt had been made by the German authorities to maintain even the semblance of observance of the Geneva Convention.

Board of inquiry.—On the basis of the survey findings and the reports forwarded to SHAEF, the Supreme Commander appointed a board of inquiry to go forward with the advancing armies and to investigate the treatment by the German Government of the American and British prisoners of war at the time they were recovered. Testimony and sworn statements were taken in the prison camps on the day of liberation. The board was composed of British, Canadian, and American personnel, among them the medical officer assigned to the Nutrition Branch, Office of the Chief Surgeon. Its observations are the subject of a letter and report dated 7 June 1945, Supreme Headquarters, Allied Expeditionary Force, and are summarized as follows:

Before the crossing of the Rhine, the location of the German prison camps for Allied prisoners was fairly well known in some headquarters, and forecasts were available on the expected population of these camps, but there was little information about the conditions within them. The reports from the International Red Cross and the protecting powers were meager and sketchy and, as time has proved, inaccurate. Paragraph 4 of the letter report states:

In connection with any future consideration of the responsibilities to be placed on a protecting power, it is to be noted that the findings of the Board indicate indirectly, failure on the part of the Protecting Power to discharge its obligations. Quite conceivably, it may have been beyond the capabilities of the Protecting Power to remedy the existing situations, but certainly it must have been within its capabilities to advise the British and U.S. Governments that these conditions existed.

The overwhelming evidence, as reported by the board, indicated failure by the Germans to comply with the Geneva Convention of 1929. In some instances, there was some improvement in the treatment of prisoners as the Allied armies approached. But generally throughout the war, there were violations involving, "at one time or place or another every material condition and circumstance affecting the life and well-being of a prisoner of war." In part, these were "due to the deliberate policy of the responsible German authorities," and in part "to the negligence and/or brutality of the German personnel having charge of the prisoners of war." There were

instances where the German commandant and others "have probably done the best they could for prisoners in their charge with the material and supplies available, [but] the inadequacy of such material supplies has made compliance with the terms of the Convention impossible. In other cases, the German personnel have gone out of their way to increase the hardship and suffering of prisoners in their charge."

The ordinary rations issued by the Germans to the U.S. and British prisoners of war were at all times gravely inadequate both in quantity and in quality to maintain health or even, many times, to sustain life. They were in every instance grossly below the scale of rations issued to the German Army or the civilian population. The food was very inadequate in respect to the specific nutrients, proteins, vitamins, and minerals, as well as calories, and was commonly prepared under unsanitary conditions. In no known instance was provision made for kitchens, messhalls, or mess equipment for 200 men, or any large unit, in any way comparable to that provided for German field or base troops.

In one instance, a daily record was kept of the food issued to prisoners of war on a march lasting 82 days. The average caloric content of the German ration as issued was 850 calories per diem, equivalent to 650 calories per diem as consumed, the difference being due to condemned or other inedible food, which had to be discarded. Labor "Kommandos" were sometimes able to supplement their rations by food begged or stolen from farms on which they worked, or obtained from civilians by barter for cigarettes supplied by the Red Cross. At times also, if employed in heavy labor, they got an inadequate supplementary ration from the Germans, although this with some difficulty and generally through the insistence of the prisoner-of-war representative. Many prisoners were kept alive, and even in reasonably good health, by Red Cross parcels, which may have supplied as much as 70 percent of their average daily nourishment. From time to time, however, there were inexplicably wide variations in the number of Red Cross parcels issued as well as in the quantity of rations issued. Although these irregularities were usually laid to transportation difficulties, particularly in 1945, such difficulties did not have any corresponding effect on the nutrition of German troops.

The results of these conditions were seen when considerable numbers of prisoners of war taken at random in several camps were examined by two members of the board, the British and the American medical officers. They found in many cases present or past malnutrition evidenced by loss of weight, muscle atrophy, edema, pellagra, stomatitis, cheilosis, keratosis, night blindness (mostly in the British), muscle tenderness, and nocturnal polynuria (in almost all). The men who showed fewer signs of malnutrition for the most part were either prisoners from camps where Red Cross parcels had been received regularly or labor "Kommandos" who had been employed in agricultural work. The board also examined German sick and

wounded in two German hospitals and found no single case of primary malnutrition among them. In a large group of German prisoners of war (pp. 265–269) captured by the Allied armies, no cases of malnutrition were discovered comparable to those found among the British and American prisoners of war.

Concerning medical care, the board's report states (1) that hospital rations were insufficient both in quality and in quantity and never comparable to those the board saw the Germans issuing to their own sick and wounded, both military and civilian, and (2) that in many camps there was no difference between the rations issued to the sick and to other prisoners of war. In some camps, supplementary rations for the sick could be recommended by a prisoner-of-war medical officer and then authorized by a German officer, but they were insufficient and unsuitable for a large number of the patients to whom they had been given. On the whole, the German medical service apparently tried to be cooperative, but in many instances it was ineffective in obtaining correction of the deficiencies in accommodations, supplies, and food.

The report goes on to say that during movements of prisoners of war by march and by train all over Poland, Germany, and Austria, the sick and the wounded who were unfit to be moved were in some instances left behind with no medical personnel to look after them; in other instances, in spite of protests of prisoner-of-war medical officers, the unfit were made to march, and some died on the road. In general, the prisoners were compelled to work for excessively long hours.

The cold, strong, formal statement of facts in this report indicates the true picture, but descriptive statements are necessary to recreate the actual conditions. Typical living quarters in these camps were characterized by a stench impossible to describe. Cleansing utensils, water, soap, and disinfectants were completely lacking at times. Many of the hutments contained latrines at one end, and the others were limited to the bucket type of latrine. After the evening meal, the men were locked in their hutments.

About 25 April 1945, word was received that the German High Command of the Armed Forces had agreed to stop the mass evacuation of military prisoners from prison camps threatened by the advancing Allies. This agreement alleviated much of the suffering the prisoners had to endure by forced marches away from the liberating armies. The bulk of Allied military prisoners was recovered shortly thereafter.

Immediate problems.—The problems demanding immediate attention in the overrun camps were sanitation, delousing, provision of adequate living quarters, nursing care, and medical supplies. The prison hospitals were usually found loaded to capacity with from 50 to 400 patients, and there were many hundreds more who required hospitalization if facilities had been available. "Hospitalization" in many of the prison camps, however, was merely a word, with little relation to medical care as practiced in the

American Army. The insatiable desire of the RAMP's for food had also to be satisfied, and the ready generosity of the advancing Allies was one more hazard for these men. The writer, accompanying the advanced parties going into the camps as they were captured, saw how the incoming soldiers hastened to share their K- and C-rations with the RAMP's. Any prisoner who was luckless enough to consume a K-ration immediately would usually be seized with violent gastrointestinal cramps, nausea, vomiting, and diarrhea. Nutritional rehabilitation was in fact required by almost all the prisoners, both the ambulant and the hospitalized.

An urgent problem was the care of RAMP's not sick enough to be hospitalized, who were to be evacuated through command channels by the Provost Marshal's personnel. Accordingly, as has been related, the representatives of the Chief Surgeon's Office did in fact direct the greater part of their time and attention to preventing secondary hospitalization of these liberated prisoners. The experience with the first 4,400 RAMP's to arrive at the Lucky Strike deployment area confirmed the first impression that had been gained by direct inspection of the recently overrun camps at Limburg, Niedergrenzebach, and Heppenheim concerning the extreme sensitivity of the gastrointestinal tract of these men to most foods. As narrated in the earlier section (pp. 245–246), the planned dietary regimen had been instituted and was in practice before the bulk of the prisoners arrived. The need for it was amply proved by the resulting reduction in the number of those who had to be hospitalized, from approximately 25 percent in mid-April 1945 to approximately 0.03 percent 1 month later.

The first inspection of the prisoners of war had revealed malnutrition in all its forms. An immediate necessity was to define categories and set up criteria for hospitalization and treatment (pp. 261–263). The patients were divided into three groups as having (1) simple malnutrition (mild, not hospitalized; moderate, not hospitalized; severe, usually hospitalized); (2) the emaciation syndrome due to prolonged starvation; and (3) acute starvation. The deficiencies noted were listed in order of frequency and severity as follows: Total calories, protein, vitamin C, thiamine, nicotinic acid, and riboflavin. The majority of the recovered personnel were only moderately undernourished and did not require hospitalization on that count alone. Their nutritional rehabilitation could be satisfactorily accomplished in reception camps, although many men, as has been seen, had to be hospitalized because of severe gastrointestinal distress due to improper feeding. (Parenthetically, it may be said here that the field and evacuation hospitals performed their unexpected tasks well.) The sickest prisoners had been the first to be left behind by the retreating Germans, and in these the Army Medical Corps was finally confronted with the end results of malnutrition.

The 1st General Medical Laboratory, Paris, France, was alerted to save all tissues from fatal cases in order to gather as much teaching material as possible for the study of starvation. For Americans, in World War

II, had now indeed every opportunity to study malnutrition, from its early manifestations in trainees to its ultimate outcome in prisoners of war, while in the captured camps they could observe at firsthand its penultimate phenomena, chronic emaciation and acute starvation.

PRINCIPAL SYNDROMES—DESCRIPTION AND MANAGEMENT [17]

From war to war, the repetitive nature of many of the nutritional disturbances observed is well documented, particularly the so-called famine edema, which has been described by many writers in many languages. In the early morning of literature, Hesiod, in his "Works and Days," speaks of the starvation a hard winter brings, and advises prudent thrift "lest the helplessness of evil winter overtake thee, and with wasted hand thou press thy swollen foot." Scaliger attributes to Aristotle the remark that in famished persons the upper parts of the body desiccated and the lower tumefied. Hicker, in his account of the destruction of the French Army before Naples in 1528, referred to soldiers with pallid visages, swollen legs, and bloated bellies, scarcely able to crawl. Sydenham refers to the condition when he makes use of the quotation "Ubi desinit scorbutus, ibi insipit hydrops." He qualifies his quotation by calling it a saying of the vulgar, meaning to imply that, when a dropsy has shown itself by clear signs, the preconceived notion of scurvy falls to the ground. Still, the connection between scurvy and dropsy in a popular saying suggests that the conditions under which the disease arose were closely allied in the minds of the 17th century public.

Lind, quoting van der Myle's description of the diseases observed during the siege of Breda in 1625 says: "Of those who were afflicted with the flux, few escaped. They afterward became bloated, relaxed and dropsical. Watery swellings of the testicles were frequent. Some died early in the disease. Those who had seldom any evacuation of the blood by the nose or stool and seemed from the beginning indolent, dispirited and blown up, as it were, with the wind, their stools were greasy, fetid, and of various colors, but not frequent."

A clear distinction between famine dropsy and scurvy and between beriberi and the various final edemas of inanition or diarrhea was made by Cornish. He described the condition with great precision in 1864 as occurring among prisoners on certain dietaries in the Madras jails. "Under this system of diet the men became unhealthy, and within three months six of the 100 had died of diseases of a scorbutic type such as diarrhea and dropsy." Speaking of the post mortem appearances, he says: "General

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[17] The author has given a very vivid description of the progressive stages of starvation as reflected in the unfortunate inmates of POW and concentration camps during World War II. In so doing, he has also revealed the hazards of improper diet and portrayed the pathognomonic symptoms of nutritional deficiency diseases to present-day clinicians called upon to advise their patients in matters of dieting.— A. L. A.

dropsy and the tendency to serous effusions into the cavities of the pericardium, thorax and abdomen are the only evidence, as indeed are the symptoms just noticed."

Of the various forms of starvation seen during World War II, the total emaciation of the inhabitants of the concentration camps and prison camps received considerable publicity—less well known forms of starvation were also seen. The nutritional degradation of some of the sick and wounded was a clinical problem encountered in all theaters.

Diagnosis.—The differential diagnosis of the end results of malnutrition—of emaciation from starvation—can be made on clinical grounds by a physician well grounded in physiology. Acute starvation phenomena (p. 261) are due to complete deprivation of food. People so starved do not survive very long if the fluid intake is limited also. The malnutrition that leads eventually to the emaciation syndrome is different. Here, there is sufficient caloric and food intake to insure survival for a time but not enough to maintain a normal metabolic level. The outstanding deficiency is of course in calories, but this is not the most important one. The specific nutrient deficiencies, especially in protein, are responsible for much of the clinical symptomatology. Wasting phenomena, particularly of the musculature, will be the end result of a negative caloric and nitrogen balance. The emaciation syndrome, when present, is the predominating one, and calls for the most careful therapy.

Chronic emaciation.—The history elicited from these patients and their physical findings are very characteristic. Usually, there has been a food intake averaging as low as 600 calories daily during long periods of forced labor or forced marching. In surviving individuals, this eventually leads to the total emaciation syndrome. Weight losses up to 60 percent of the original body weight have been recorded. The patient as seen in the late stages presents a very characteristic picture. One observes a completely apathetic, very thin individual, usually lying immobile, legs flexed across the abdomen, arms folded across the abdomen or chest. The position is maintained even if the patient is rolled over. There is no true ankylosis of the joints, as the patient can with much effort and persuasion extend his lower extremities to their full length. This is obviously a painful process and is not done willingly. The skin is dry, coarse, rough, and cold to the touch. Pigmentation is a prominent feature. Pressure points over the sacrum, ischial tuberosities, and head of the femur are the common sites of bilateral, symmetrical, rough, pigmented, and scaling areas. Light pigmentation of infraorbital and frontal areas is frequently seen. In the latter site, it resembles the chloasma pigmentation of the pregnant female. Muscular atrophy is severe and extensive, the temporal atrophy appearing early. This, coupled with the loss of orbital and malar fat pads, gives the peculiar death's head appearance common to all of those affected. The legs and arms appear merely as contours of the long bones covered with a tight

skin. The buttocks are concave and follow the contours of the ilium and ischium. The paravertebral sulci are deep. Even such a muscle as the pectoralis major almost completely disappears, and the second and third ribs as well as the others are visible on the surface.

The stigmata of endocrine changes are universally present; in the female, the breasts and vulva are atrophic. There is always a marked hirsuties of the face and extremities; the voice though weak is coarse. The history reveals a complete amenorrhea usually from the second month of incarceration. The males may have a smooth face with sparse hair growth; the voice is quivering and high pitched. The penis is flaccid and usually shrunken. The tongue is smooth, beefy red, and thin, in the late stages of atrophy. The circulatory system undergoes some very radical changes. Resting pulse rates show a marked bradycardia of approximately 35 to 50 beats per minute. Resting blood pressures are as low as from 60 to 80 mm. Hg systolic and from 30 to 40 mm. Hg diastolic. The slightest activity or excitement precipitates a dyspnea and tachycardia, indicating an extremely limited cardiac reserve, which must be recognized in instituting therapeutic procedures. Histological examination of the heart confirms this clinical impression.

The eyeballs are soft, and the conjunctiva are wrinkled. There is usually a marked enophthalmus and a dry eye. The sclera have a porcelain, bluish-white appearance which is quite characteristic. They are markedly avascular. One frequently sees a malar flush which is cyanotic in hue. The lips will vary in color depending upon the relative amounts of anemia. While there is an absolute depression in the amount of hemoglobin, the hemoconcentration may give an apparently normal value. Deep tendon reflexes will vary from marked hyperactivity to complete absence. Because of the painfulness of the joints, it is difficult to evaluate them properly. Anal incontinence is very common and is manifested by fecal encrustation in the gluteal folds. These people are in a physiologically hibernating stage. Their body weights vary from 50 to 75 pounds, the greater part of their weight representing a skeletal structure which is comparatively inactive metabolically; their daily caloric requirements are as low as 500 calories at this point. Where one is able to get a lucid description of their downhill progress, it is evident that these patients have passed through the stages of nutritional edema with the specific nutritional deficiency syndromes of beriberi and pellagra. Many die during this degradation process. Those who manage to accommodate themselves to the reduced nutrient intake by the compensatory decrease in metabolic levels survive to this condition of emaciation.

At this stage, the adjustment of the circulation and other physiological processes is a very narrow one. The maintenance of life is dependent upon not upsetting this balance too abruptly. Therapy begun too aggressively

in an enthusiastic effort to restore these people to normal may result in a breakdown of the compensatory mechanisms, and death frequently ensues.

It should be borne in mind that those who dehydrate are the ones who survive. It is rare to see nutritional or famine edema in this stage of total emaciation. Nor do these people present the signs and symptoms of the B-complex deficiencies. These vitamins constitute functionally the prosthetic components of the enzyme systems in carbohydrate and protein metabolism. With metabolic levels at a minimum, the demand for these vitamins is very low. When, however, one burdens the body with a sudden plethora of foodstuffs, then the vitamin requirements immediately increase proportionately, and unless this new need is met acute deficiencies result. In addition, the cardiac reserve is so extremely limited that a sudden change in the circulating blood volume throws a burden on the atrophic, flaccid, degenerated cardiac musculature with which it cannot cope.

Therapy, then, must be started very slowly and cautiously, with due regard for all these limiting factors. It should be directed toward supplying, first, calories, then the B group of vitamins, then proteins, and eventually a definitive therapy complete as to calories and nutrients. Experience has shown that oral administration where tolerated is the route of choice. Gavage should be resorted to only when necessity dictates, and intravenous therapy, only in the presence of nausea, vomiting, or intractable diarrhea. Milk and egg mixtures, fresh or powdered, are well tolerated by the majority of these people. No attempt should be made for the first 24 to 48 hours of therapy to do more than reeducate the gastrointestinal tract to the acceptance of these foods. No more than 1,500 cc. of the fluid mixture should be given by mouth in each of the first 24-hour periods. The salt content of the fluid mixture must be carefully controlled; otherwise, edema will result. If nausea or vomiting is precipitated by the oral administration, then intravenous therapy may be instituted. Here, more than ever, extreme caution must be used, or reactions will develop in a high percentage of these extremely sensitive patients. No more than 500 cc. of normal human blood plasma or blood should be given in the first 24 hours at a rate no faster than 2 cc. per minute, preferably slower. Thiamine and niacin should be given regularly in appropriate doses. Such foods as cooked cereals, custards, white bread and dairy butter, mashed potatoes, and thin soups are added slowly, as tolerated. In other words, only low-residue foods, mechanically nonirritating and bland, should be given for several weeks in order to avoid precipitating acute gastroenteritis which, in the debilitated state of these people, would be a serious complication. Autopsy material, as will be shown, lends support to these clinical observations (p. 288). Once recuperation has started and the patient has demonstrated his ability to tolerate food, then more active treatment can be instituted. Iron therapy for the anemia is of no value until a positive nitrogen balance has been well established; in addition, iron salts by mouth notoriously produce gastro-

intestinal upsets. Vitamin therapy is a necessary adjuvant but only as supplementary to the high-protein, high-caloric intake.

Acute starvation.—In contrast to the picture of chronic emaciation that has been described is the clinical syndrome of acute starvation. By this is meant the condition of one who has been deprived of food and fluid for several days. In this condition, there is usually ketosis and acidosis with signs of acute dehydration. These patients require intensive therapy as quickly as it can be given. Intravenous fluids with emphasis on the glucose-saline mixtures is indicated. No special dietetic therapy is necessary except what is required by secondary conditions. Recovery is usually prompt and complete. By contrast, the syndrome of malnutrition is evident, in varying degree, in those people with intakes adequate in calories but inadequate in specific nutrients. This was more commonly observed in the Pacific area than in the European area. With an inadequate intake of specific nutrients the metabolic levels remain high. The requirements for vitamins remain normal. Since the diet does not contain the required amount of vitamins, deficiency syndromes become manifest. The first oral feeding will frequently determine the speed of convalescence. Should the food produce an enteritis or gastroenteritis, convalescence will be greatly prolonged and therapy made more difficult.

Edema was not an infrequent finding in recovered prisoners seen during the intermediary stages leading to total emaciation. This varied from swelling of the dependent lower extremities to generalized anasarca. It was usually due to a low serum protein value with an adequate salt intake. Values as low as 1.8 gm. per 100 cc. of blood have been observed. Mild edema disappeared within a few days after beginning a high-protein intake. Severe anasarca persisted somewhat longer, but a polyuria was manifest by the second day. Over 33 percent of the patients with total emaciation treated in U.S. Army hospitals developed edema in the course of the first week of therapy until attention was directed to the salt content of the nutritive foods given for rehabilitation.

In the literature, famine edema has usually not been associated with albuminuria, cardiac dilatation, or neuritis. It has been observed more particularly in men called upon to perform hard physical work on rations supplying from 800 to 1,200 calories contained, as a rule, in a largely fluid diet comprising 15 percent or more of indigestible celluloses with very little fat and not more than 50 gm. of protein daily.

Treatment in hospital.—Causes for hospitalization of recovered prisoners and details of treatment were outlined in Circular Letter No. 36, for three groups of patients. Group I comprised patients showing a moderate loss of weight, weakness, gastrointestinal distress but no definite signs of protein or specific vitamin deficiencies. Approximately 80 percent of those hospitalized because of malnourishment were in this group. The hospitalization was considered necessary to combat weakness and gastrointestinal dis-

tress by appropriate dietary and medical measures, with complete nutritional rehabilitation contemplated in the reception camps. Certain points emphasized in the dietary treatment of Group I patients were as follows:

The tolerance of the gastrointestinal tract to the first foods eaten will [frequently] determine the immediate dietary procedures to be followed. Soft diets are indicated and full use should be made of milk, eggs, and cooked cereals. Feeding should be frequent and in small portions. Overfeeding must be avoided. The restoration of nitrogen balance and the gain in weight are the primary goals. The diet should supply at least 150 gm. of protein as soon as normal eating is possible. Initial gain in weight will occur on an intake of 2,500 to 3,000 calories, if the protein intake was adequate. Over 4,000 calories will be required for a more rapid restoration of body weight.

Multivitamin supplementation is necessary only during the period when gastrointestinal distress prevents normal eating. No more than four multivitamin tablets daily should be administered.

Group II comprised patients showing marked loss of weight, weakness, and evidence of specific deficiencies such as edema, anemia, and glossitis. Approximately 20 percent of liberated personnel hospitalized because of malnourishment were found in this group. The initial feeding for Group II patients was to be similar to that prescribed for patients in Group I, if food could be tolerated by mouth. Other points of dietary management were as follows:

Patients with edema who cannot tolerate food by mouth will require intravenous therapy. Plasma and whole blood are indicated. Transfusions should be given at a rate of not more than 2 cc. per minute. Dyspnea, precordial discomfort, and apprehension are danger symptoms that should lead to immediate discontinuance of the transfusion. [Unfortunately, human salt-free albumin was not available. The use of salt-poor food was further emphasized periodically as experience was gained with the development of edema in these patients.] The treatment of the macrocytic anemias is dependent on the restoration of the protein deficits. Oral administration of iron is not recommended until nitrogen balance has been reestablished. Multivitamin supplementation is necessary in most of the severely malnourished patients during the first 15 days of treatment.

Group III comprised patients showing extreme weakness, marked dyspnea, nausea and vomiting, and delirium or coma. These were seen in hospitals relatively rarely, because they usually were not able to survive transportation. Such patients required immediate therapy in the form of transfusions of plasma or whole blood given very slowly and with extreme caution. Thiamine hydrochloride, 30 mg., was given parenterally at 24-hour intervals.

As presented in Circular Letter No. 36, diluted milk and soup preparations were suggested for the initial feeding of malnourished soldiers in the forward areas, as follows:

One can of evaporated milk plus 3 cans of water; one-fourth canteen cup of sugar and one-fourth teaspoon of salt.

One canteen cup of whole milk powder plus 5 canteen cups of water; three-fourths cup of sugar and three-fourths teaspoon of salt.

One quarter of a canteen cup of the diluted milk should be given warm every half hour, as tolerated. Water may be taken in sips between feedings to the extent of 2 can-

teen cups daily. Powdered egg or prepared cereal * * * may be added to the diluted milk after the first day if gastrointestinal distress is absent.

Soup may be prepared from canned meat and vegetable stew or from canned meat and noodles if milk is not available. [These were made in dilute form.] Soup may be thickened with flour or cereal.

The medical officer assigned to the Nutrition Branch visited the chiefs of all the major hospitals concerned in the treatment of recovered prisoners. Clinical observations and statistics derived from these visits are described in the section "RAMP's in Hospital" (pp. 284–288).

NUTRITION IN CIVILIAN POPULATIONS, EUROPEAN THEATER, AND IN CONCENTRATION CAMPS

In liberated countries.—While the Office of the Chief Surgeon had direction of the nutrition of troops and of prisoners of war, the relationship of its work to civilian populations was not definitely clarified. Teams [18] were dispatched from the Zone of Interior to conduct nutritional surveys under the general direction of the Chief Nutrition Consultant, Public Health Branch, G–5 Division (civil affairs/military government), SHAEF, and their services were made available to the various missions and to the Army groups. Two types of survey were done. The first was the so-called rapid survey, or observation of a representative sample of the community by means of a simple medical examination to establish the presence or absence of florid manifestations of deficiency disease. Subsequently, the dietary history was obtained in a careful interview in order to estimate as closely as possible the food intake. A study of patients in asylums, hospitals, and orphanages gave information on the basic food supplies. Some laboratory tests were done on a small percentage of those who were examined clinically. It was found, too, at this time that extensive weighings on street corners of random samples of the population yielded significant evidence of caloric intake and work output. This comparatively simple technique can be adapted to any population and can be used as a means of following the progress of any large group under observation.

The civilian population included not only the normal populations of the occupied and liberated countries but also large numbers of displaced persons. On the whole, the state of nutrition in European countries was much better than had been expected except that there was serious malnutrition in Holland, particularly where a complete embargo had been imposed by the Germans. Complete reports [19] of the various areas were submitted by the consultants in nutrition and the survey teams who covered most of the Continent during their course of duty.

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[18] Annual Report, Nutrition Division, Preventive Medicine Service, Office of The Surgeon General, for fiscal year 1945.

[19] Surveys and Reports on Nutrition, Headquarters, U.S. Forces, European Theater, Office of Military Government (U.S. Zone), May through December 1945.

In France itself, when it was liberated, rather detailed reports were given by the French physicians on the situation that had obtained during the time of the German occupation. Edema had been a very common thing among the poor people of Paris. Osteoporosis, or Milkman's disease, with fractures of the vertebrae was very frequent, occurring usually in older women. The X-ray evidence for this story was remarkably good. Amenorrhea, as would be expected, was common in the females. No scurvy was seen in the Parisian groups, but pellagra was present in a relatively small but definite group. Anemia was found rather frequently, particularly the hyperchromic and hypochromic types.

In Holland, in the so-called B area, the situation was remarkably different. Famine, edema, and extreme emaciation were the principal nutritional problems. There was an increase in general mortality. The height and weight of school children showed some decrease from the previous figures in 1939. It was estimated that death occurred in approximately 10 percent of the cases hospitalized for starvation. The preliminary estimate showed that there were approximately 200,000 cases of malnutrition sufficiently severe to be referred for special handling.

In Rotterdam, the average loss of weight was 25 pounds in the 19- to 59-year age group, and 40 pounds in people over 60. In Amsterdam, 41 percent of those sampled were judged normal and 41 percent thin. Of the latter, 16 percent were very thin and 1.9 percent emaciated. In that city, it was estimated there were 56,000 cases of famine edema. In Utrecht, there was mild edema in 2.8 percent of all the people examined. In Delft, where the average loss of weight was 21 pounds in the age group 19 to 59 and 39 pounds in those over 60, edema was found in 10.5 percent of those from 19 to 59 years old and in 25 percent of those over 60 in the poorer economic class. There was less than half this amount of edema in middle-class people, and it was practically unknown among the well-to-do. Dutch physicians studying this starvation edema reported two types: (1) The edema with diuresis that accompanied slight emaciation and disappeared as chronic emaciation set in, and (2) the edema that occurred with extreme emaciation. They found a lowered basal metabolic rate, decreased body temperature, spasms of the voluntary muscles, particularly in eliciting deep tendon reflexes, and extensive brownish pigmentation of the skin. Under therapy of bed rest and high-protein diet, the edema disappeared rapidly.

In Germany and Austria.—Other civilian areas were seen by various people during the postwar period, in particular the German and Austrian concentration camps. The author of this study visited many of these personally. Early in May of 1945, he inspected the concentration camps at Mauthausen and at Güsen. The camps had a population of approximately 18,000 when taken over on 6 May 1945. There were hundreds of unburied bodies lying around at that time. The death rate continued at a very high level. The writer did many autopsies in these camps. Pulmonary tubercu-

losis was, of course, a common cause of death, but malnutrition was probably the greatest. Clinically, the patients presented the usual manifestations of extreme emaciation, some edema, diarrhea, and marked gastrointestinal symptoms. There were questionable cases of beriberi, some riboflavin deficiency, and an occasional case of pellagra. Autopsy findings corroborated the clinical report, and details of these autopsies are presented on pages 288–291.

NUTRITION OF THE GERMAN PRISONERS OF WAR

It was many months after the crossing of the English Channel in June 1944 before the German prisoners of war became much of a problem. In the passage across France, they were at first captured in small groups but never in wholesale lots until the fall of Brest. By the week ending on 9 February 1945, the prisoner-of-war strength climbed suddenly to 241,545. The morning sick reports did not yield any major evidence of nutritional disturbances although approximately 486 were on report for diarrheal diseases and only 8 for Vincent's stomatitis. The bulk of the men reported for common respiratory diseases, trenchfoot, and frostbite. By the week ending on 16 February 1945, there were 246,281 prisoners of war, and, by the week ending on 23 February 1945, there were 249,272. These massive numbers required medical care and subsistence. The Office of the Chief Surgeon became concerned with the nutritional status of these prisoners of war and the adequacy of their rations.

In accordance with the verbal orders of the Chief Surgeon, ETOUSA, and with the concurrence of the Theater Provost Marshal, a survey was made on the nutritional status of the German prisoners of war in representative enclosures, labor camps, and hospitals on the Continent. The survey was conducted under the general supervision of Colonel Griffith and was directed by Colonel Pollack, who had one Medical Corps officer and three Sanitary Corps officers to help him. This team examined 800 prisoners during February and March 1945 at 21 different installations, including 5 continental enclosures, 7 work camps, 2 prisoner-of-war hospitals, and 5 general hospitals. The number of prisoners examined was considered statistically significant, and the findings were believed to be representative of the total prisoner population on the Continent. The prisoners were classified as new or old according to whether they had subsisted on the U.S. Army POW ration for fewer or more than 50 days. The new group included 312 prisoners and the old group, 488 prisoners. The survey was of a clinical type and is reported in detail in the report [20] dated 15 May 1945. The findings in general were as follows:

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[20] Essential Technical Medical Data, European Theater of Operations, U.S. Army, for May 1945, dated 26 July 1945. Inclosure 16, 15 May 1945, subject: Report of Nutritional Survey of German Prisoners of War Under Control of the United States Army on the European Continent.

The body weights of the prisoners as estimated by gross appearance and by the condition of the skin and subcutaneous tissue were approximately the same in new and old groups. Many had lost weight before capture, but over 93 percent appeared normal in this respect. There was definitely no indication of loss of weight in the group who had been fed the U.S. Army POW ration for a period longer than 50 days.

There was no evidence of protein or mineral deficiencies attributable to the diet in the old prisoners. The general health of the old prisoners was better than that of the new prisoners as indicated by daily sick call.

The energy content of the ration fed to the nonworking and intermittently working prisoners averaged 2,800 calories. This was from 10 to 20 percent greater than required for the maintenance of these groups.

The energy content of the ration fed to the working prisoners averaged 3,050 calories. A ration supplying from 2,800 to 3,000 calories was believed to be adequate for this group unless more strenuous labor was performed than was observed during the survey.

Riboflavin deficiency as evidenced by angular lip lesions and magenta-colored tongue and by nasolabial seborrhea was surprisingly common in the new group. The regressing or healed lesions were found in the old group which demonstrated that the U.S. Army POW ration not only prevented a deficiency in this instance but also permitted rehabilitation of tissue damaged by previous dietary insufficiency.

Thiamine deficiency was noted in both groups and was recognized by tenderness of the calf, abnormal reflexes, and diminution of vibratory sense perception. The incidence of this deficiency was definitely lower in the old groups.

It was concluded that subsistence on the U.S. Army POW rations for from 50 to 200 days resulted in marked improvement of the overall status of nutrition in the German prisoners. It was further concluded that the nutritional value of the U.S. Army POW ration was superior to the German Army ration and was adequate for the maintenance of the health of the working prisoners.

With the end of the war and after V–E Day, however, the surrender of hundreds of thousands of men simultaneously had precipitated feeding problems with consequent periods of very restricted food intakes. This resulted in extensive malnutrition among the disarmed enemy elements. Accordingly, surveys to determine their nutritional requirements were made periodically in the prisoner-of-war enclosures and the hospitals treating these people. A report of one such survey,[21] dated 31 August 1945, shows the general problems of the time. It was found that the body weights for the nonworker group studied were below standard in all prisoners except

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[21] Essential Technical Medical Data, European Theater of Operations, U.S. Army, for August 1945, dated 22 Sept. 1945. Inclosure 8, 31 Aug. 1945, subject: Report of Nutritional Survey of German Prisoners of War and Disarmed Enemy Elements Under Control of the United States Army on the European Continent.

those who had recently been evacuated from Italy. The body weights of the workers receiving approximately 2,900 calories were consistently higher than those of the nonworkers and within normal accepted standards for their age groups. Workers receiving less than 2,000 calories daily were definitely undernourished. In some of the nonworking groups receiving less than 2,000 calories a day, there was suggestive evidence of early muscle atrophy indicative of depleted protein reserves.

Deficiency syndromes relating to the B complex vitamins were evident in the nonworkers subsisting on American POW rations. Although there was evidence of these deficiency syndromes in those prisoners subsisting on locally procured German food, it was not so marked as in the groups subsisting on the American POW ration. It was believed that this difference was due to the use of some highly milled unenriched flour which furnished a large part of the energy value of the American POW ration. The German ration included a 95-percent extract flour which supplied many of the B vitamins.

As a matter of practical policy based upon experience, it was decided that rural populations and agricultural workers were to be considered as self-sustaining. The confined prisoner and the urban dweller, on the other hand, had to be assured the minimum food requirements to maintain health and resistance to disease. Persons behind barbed wire could not supplement their rations so easily as civilians could from accumulated stores, garden produce, and such other sources as "the country cousin" and the black market. The difference was found reflected in the respective nutritive condition of civilians and prisoners living on the same official ration scale. The main attention, then, in setting up ration scales had to be directed toward meeting the requirements of those unable to produce or supplement their own.

It was determined that a period of nutritive rehabilitation should be authorized for all prisoners of war and disarmed enemy elements who presented evidence of malnutrition. Such persons should be authorized, upon the personal investigation and recommendations of the responsible U.S. Army Medical Department officer, a full worker's ration for a 20-day period together with relief from work details. This was not to be in lieu of hospitalization for the severe or moderately severe cases of malnutrition.

There was evidence of very extensive malnutrition among the prisoners of war and disarmed enemy elements in the large enclosures maintained by the Third and Seventh U.S. Armies and by the Communications Zone. There was a complete lack of uniformity in the ration scales among the various areas in Germany. The Seventh U.S. Army area, for example, sustained the prisoners of war on U.S. Army food, while in the Third U.S. Army area the disarmed enemy was subsisting on food locally procured. The caloric scales varied with the location from 1,265 to 2,157 calories for

nonworkers, and from 1,450 to 2,296 calories for workers during the month of July.

There was consistent evidence of an insufficient amount of riboflavin and nicotinic acid in the diet for the conditions under which these men were living. These signs were particularly numerous in the younger age group, those under twenty. Among the several factors responsible was the fact, as shown in the report of 15 May 1945 (p. 265), that the standard German Army ration had been deficient in riboflavin and nicotinic acid for some time. Superimposed upon this deficiency intake of fairly long standing was the variable period of severe deprivation of all nutrients during the final weeks of the active campaign and of unavoidably inadequate rations in the forward POW enclosures. At best, the POW ration could only be expected to maintain an existing state; it was never designed as a therapeutic diet.

In the various enclosures, the interpretation of the designation "worker" was quite different. In one, prisoners were made to build roads in the compound area. Men carrying crushed rock in sacks to the point of work, 4 pounds on each trip, were not designated workers because the project was an intracompound improvement. In another compound, men who worked only 4 hours a day were given the full ration for heavy labor because they worked outside. At other camps, clerks and camp administrative personnel were given a full heavy worker's ration even though their work was sedentary. In some compounds, the prisoners subsisting on the nonworker's ration, were put through several hours daily of calisthenics and drill. A survey in the Delta Base Section disclosed that general labor service units, given 2,900 calories daily, had a consistently lower sick call rate than the enclosure population receiving from 1,700 to 2,000 calories daily. The latter were drilled for several hours. The sick call rate for 22 June 1945, for instance, was 233.7 per 1,000 for the confined group, and only 98.3 per 1,000 for the labor service unit. This difference was maintained throughout a considerable period of time.[22]

It was evident that the term "worker" had to be redefined and extra food allotted for extra effort, whatever form it might take. Prisoners of war doing light work were to be authorized the standard worker's ration less 10 percent, or approximately 2,600 calories. Light work included the clerical and sedentary types, kitchen and mess duty, landscaping and policing grounds, general housekeeping in the American installations, and similar activities. Heavy work was defined as manual labor for more than 4 hours daily. The nonworker's ration was to be issued only to inactive prisoners, limited to a routine of self-care in the cage.

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[22] In the Korean War, camp administrative personnel on Kojedo Island were subjecting the North Korean prisoners of war to calisthenics and to exercise such as running several times a day around the compound, a distance of almost half a mile, although the North Koreans were theoretically nonworkers and were subsisting on the nonworker's ration.—H. P.

One of the most important recommendations made in the 31 August 1945 report was that the full worker's ration of 2,900 calories be authorized for issue to prisoners of war under 21 years of age. During the last months of the war, the German Army had recruited boys from 14 to 20 years of age in whom, as is well known, metabolic requirements are higher than in adults.

The German-operated hospitals for disarmed enemy elements fared very well with respect to rations. Most of the hospitals were established institutions with well-planned gardens and large stores of processed foods which had been built up in the past. Furthermore, they were allowed to draw full civilian rations from the local areas for the patients plus the numerous supplements for the special diets involved. Many instances of grossly inaccurate diagnosis by the German medical staff were found. In one hospital, several patients admitted with a diagnosis of nutritional edema were examined. In none of these cases was the diagnosis substantiated, but a multiplicity of causes was found for the edema, principally old frostbite and nephritis.

In view of the evidence of extensive malnutrition found, further surveys were carried out in Austria, and on 26 September 1945 a report [23] was submitted on the nutritional survey of the disarmed enemy forces in that country. At this time, conditions had improved considerably. There were still isolated spots where immediate intensive therapy in the form of high-calorie bland foods was required, but there was direct evidence of gains in weight among the prisoners.

Trench nephritis.—During the survey on the nutritional status of German prisoner-of-war patients, the various surgeons in charge were asked about cases of edema, nephritis, or cardiac failure observed by them. The problem of the co-called trench or, as the Germans called it, "feld" nephritis was discussed with the German medical men in the POW enclosures. A brief summary follows.

There were many cases in the German Army, but the exact number is not known. The syndrome was most prevalent on the Russian front, and its incidence was highest during the autumn and winter months. In Finland, where special rations of high nutritive value were issued to German troops with, in addition, vitamin supplements, the incidence of trench nephritis was much lower than on the adjacent Russian front.

The patient usually presented himself with a history of having been in previously good health and on full duty status before the onset of the illness. There was generally no history of immediately antecedent infection such as tonsillitis, pharyngitis, or other acute respiratory disease. The age group in which this condition occurred was from 35 to 50 years. The disease was first manifest with a swelling of the face and the lower extremities.

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[23] Essential Technical Medical Data, European Theater of Operations, U.S. Army, 26 Oct. 1945. Inclosure 9, 26 Sept. 1945, subject: Report of Nutritional Survey of Disarmed Enemy Forces in Austria.

This might go on to generalized edema in the severe cases. Headache, back-ache, and aching in the neck were generally noted in the prodromal stage. Dyspnea on rest or exertion might occur, and occasionally convulsions were reported early in the illness. Urine was scanty and dark at the onset.

The physical examination showed the edema as the presenting manifestation. The temperature was not always elevated at first. Cardiac rhythm was normal, usually with a sinus bradycardia. Pulse rates were observed to drop as low as 50. Hypertension occurred in some cases and initially was a frequent finding. No organic murmurs were heard in the heart areas. The lungs were essentially clear, although occasionally there were signs of a pleural effusion. Enlargement and tenderness of the liver were common, and in many patients signs of ascites could be elicited. The eye grounds rarely showed evidence of hemorrhage or exudate. The urine had a high specific gravity although albuminuria was absent in the mild cases but was as much as 3 plus in the severe cases. On microscopic examination, the urine was usually found to contain numerous red blood cells and some casts. Blood urea nitrogen or nonprotein nitrogen was normal or moderately increased. Total proteins were usually normal. X-ray examinations of the chest showed pulmonary congestion, small pleural effusions either unilateral or bilateral, and occasionally cardiac enlargement.

Electrocardiographic studies usually showed low voltage; small T wave changes, either low positive deflection or isoelectric or inverted; and of course the sinus bradycardia. The clinical course of the condition was usually uniform. Most patients recovered completely on bed rest regardless of therapy. Some few progressed to the chronic phase with hypertension, eye-ground changes, nitrogen retention, and persistent abnormal urinary findings. Autopsy findings were not available, but reliable reports of two autopsies indicated a lack of significant glomerular pathology.

In conclusion, it was noted that this syndrome, which was said to be prevalent in the German Army and was seen in the German prisoners of war in the U.S. prisoner-of-war compounds, was not reported in the U.S. Army troops. The two Armies were, of course, exposed to the same terrain and climatic conditions, and there had been sufficient contact between them to permit transmission of a communicable agent. There was, however, a very marked difference in the rations of the two Armies. Although no positive statements can be made, the evidence strongly suggests that there was a nutritional factor in the precipitation of this syndrome.

MALNUTRITION IN THE FAR EAST

Repatriated American Soldiers

After the war ended in the Pacific, the results of the imprisonment of the captured American soldiers became and remained the subject of some

discussion. The length of their imprisonment averaged about 39 months. Harris and Stevens [24] state that official studies conducted at the time of liberation or shortly thereafter indicated that almost all had suffered from severe malnutrition in multiple forms, and from many other diseases, during imprisonment. This is confirmed in the report of the U.S.S. *Haven,* published January 1946.[25] In this study, 66 percent of the men who survived gave a history of beriberi; 58 percent, dysentery; 43 percent, malaria; 20 percent, skin disorders; 19 percent, pneumonia; 14 percent, pellagra; 6 percent, tuberculosis; and 9 percent, malnutrition otherwise unclassified— 45 percent of the men experienced edematous swellings. Over 75 percent of the prisoners at Cabanatuan had burning feet. Hibbs,[26] in a study of beriberi in Japanese prison camps, said that 2 percent of the prisoners developed motor paralysis. Recovery in many of these men was rapid. A survey by Brill [27] of neuropsychiatric examinations made from 1 to 8 weeks after liberation of 1,617 men who had been prisoners of war for 39 months, or longer, revealed only 5 of them with psychoses, only 0.7 percent with psychoneuroses, and 12.7 percent with some psychologic disturbances, generally of the overanxiety type. There were 13.1 percent with peripheral nerve disorders, but most of these were not severe. There were 64 cases of optic atrophy in this group. It was stated that the overall mortality during imprisonment of the Pacific prisoners of war was 37.2 percent. The expected mortality in this age group would be less than 1 percent.

These cold figures, however, do not present a real picture. It would be best, perhaps, to present the experiences of an officer who was imprisoned by the Japanese, as described by Goldblith and Harris.[28] The prisoner, Goldblith, kept an accurate daily record, averaging on a monthly basis, of the various nutrients obtained by American officers from the food supplied by the Japanese and by Red Cross parcels during their imprisonment from 1942 to 1945. Goldblith analyzes the specific nutrient intake as follows: During certain months, the dietary fat fell as low as 15 percent of the desired amount. This may have a bearing on the fact that all officers were suffering from dry scaly skin at all times. He suggests the possibility that there was a deficient intake of the essential fatty acids such as aracidonic and linoleic acids. Marked hypoproteinemia began to show in October and November of 1944. The average weights of the officers did not go down but in fact increased, owing to the development of edema. Toward the end, Goldblith noted that the addition of only 16 grams of animal protein per

[24] Harris, B. R., and Stevens, M. A.: Experiences at Nagasaki, Japan. Connecticut M.J. 9: 913–917, December 1945.

[25] Monthly Progress Report, Army Service Forces, War Department, 31 Jan. 1946, Section 7: Health, pp. 14–16.

[26] Hibbs, R. E.: Beriberi in Japanese Prison Camp. Ann. Int. Med. 25: 270–282, August 1946.

[27] Brill, N. Q.: Neuropsychiatric Examination of Military Personnel Recovered From Japanese Prison Camps. Bull. U.S. Army M. Dept. 5: 429–438, April 1946.

[28] Goldblith, S. A., and Harris, R. S.: Final Report on an Analysis of Data on the Nutrition of American Officer Prisoners of War at the Zentsuji Prisoner-of-War Camp at Shikoku, Japan. Project No. NR-123-298, Massachusetts Institute of Technology, Contract No. NRonr-297, for Office of Naval Research.

officer per day was followed by a cure of the edema and a gain in weight in November 1944. He points out that the diet consisted almost entirely of vegetable foods with rice, barley, and to a lesser extent soybean as the staple foods. There was a large amount of green vegetables in the diet and, consequently, no lack of vitamin A, ascorbic acid, or iron. There was sufficient thiamine in the diet of the officers until the last 12 months of the period studied; then, suspected cases of beriberi were discovered during this period of low thiamine intake. The riboflavin intake was never adequate during the entire period, and clinical manifestations of deficiency were apparent. Pellagra was observed intermittently during the 31 months of incarceration between December 1942 and June 1945.

The worst part of the imprisonment was in the Philippine Islands from March to October 1942 where the prisoners were kept in Camps O'Donnell and Cabanatuan. At the close of the Battle of Bataan, American and Filipino prisoners of war were maintained by the Japanese on diets far below the accepted standards in the United States. Of a total of from 14,000 to 16,000 American prisoners and 60,000 Filipino prisoners, over 1,500 Americans and 2,700 Filipinos died during the 60 days they were at Camp O'Donnell, and over 2,100 Americans died in Cabanatuan in as short a period. This can be ascribed to the exertions of the "death march" as well as to malaria, dysentery, and poor sanitation or to malnutrition and actual starvation, although these were perhaps the most important causes.

At Camp O'Donnell, the daily diet consisted of approximately 12 ounces of dry rice of poor quality, from 2 to 4 ounces of native sweet potato, and 3 ounces of sweet potato tops, all boiled together in soup. Once a week, a quarter ounce of meat was issued to each prisoner. This was a never-varying diet for the captives at this camp. At Cabanatuan, the daily rations were somewhat better. Here, about 16 ounces of rice and 4 ounces of vegetable, sweet potato or corn, were included in the daily ration. Once each week, 1 ounce of carabao meat was issued, and, in season, one thin slice of cucumber was given to each man each day. At 2-week intervals, 2 ounces of coconut or banana were issued, cooked with cornstarch and sugar in the form of a pudding. One-quarter of a pound of hydrogenated coconut oil for the soup was issued per man per week.

It must be recalled that when the troops were on Bataan they went on quarter rations early in January 1942. Beriberi was observed by March 1942 and increased to a marked degree by September 1942. Many men were observed to die from the beriberi heart. Pellagra became marked toward the end of September 1942. Scurvy, until October 1942, was very questionable. Ariboflavinosis demonstrated by cheilosis began to be observed by September of 1942. By October 1942, the majority of the prisoners of war were suffering from malnutrition in some form or other. Severe and sharp shooting pains in the feet and legs were complaints during the winter months of 1942–43 (fig. 38). This developed into gangrene in many cases.
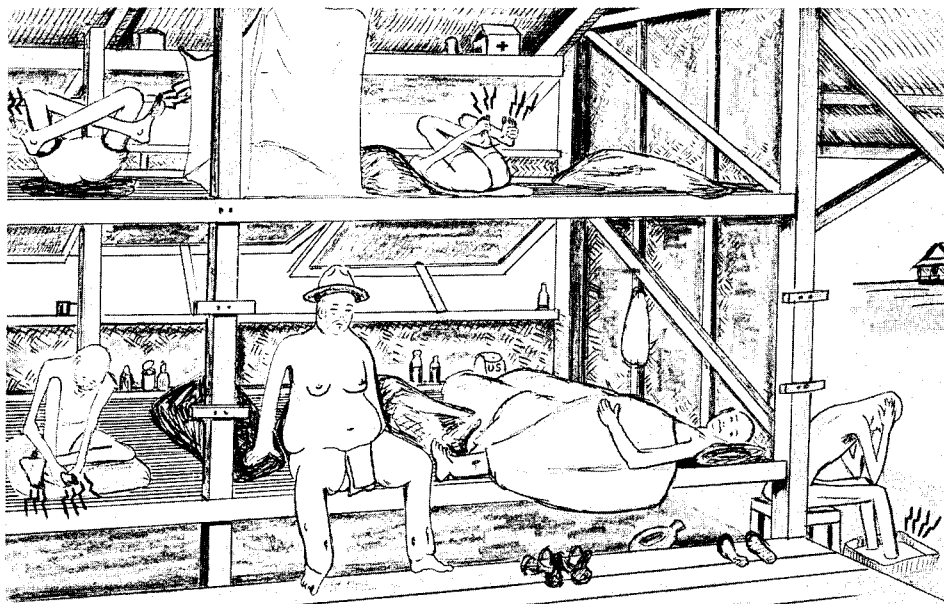
FIGURE 38.—Sketch, attitudes of beriberi, wet and dry, November 1942.

In test cases, this deficiency disease was definitely cured by massive doses of thiamine administered intraspinally and intramuscularly.

It is interesting to note in the conclusions of the report by Goldblith and Harris that beriberi was the first nutritional disease observed, occurring about 3 months after capture. Pellagra and ariboflavinosis were observed after 9 months. Scurvy after 9 months was still questionable, but began to appear definitely after 10 months. Xerophthalmia and nyctalopia, although difficult to diagnose clinically, were unquestionably present in 10 months and rather severe thereafter. These conditions increased in intensity until in many cases complete blindness developed, which was cured by massive doses of vitamin A.

On 30 August 1945, The Surgeon General established the "Board to Survey and Evaluate the Medical Problems of Repatriated American Prisoners of War Returning From the Far East." It is unfortunate that the men were not brought into this survey until, having been released for varying periods of time, they had received therapy for their nutritional disturbances. Nevertheless, much can be gained by a review of the board's report.

For example, certain prominent signs and symptoms of nutritional deficiency as obtained from the history were listed according to their

incidence. Pellagra as evidenced by cheilosis, glossitis, stomatitis, dermatitis, and diarrhea was present in from 50 to 70 percent of the patients. The incidence of pellagra was much greater in the Philippines. Only a rare case, in fact, developed in Japan where the prisoners were sporadically given soybeans to eat. Typical pellagrous photosensitivity dermatitis of the exposed parts was relatively infrequent. This in spite of the fact that the men were constantly exposed to considerable sunlight.

The occurrence of a scaly, sometimes erythematous weeping dermatitis of the scrotum accompanied by extreme tenderness and, in some cases, edema was reported as being relatively common. Occasionally, scrotal tenderness without dermatitis occurred. About 55 percent of the patients with a history of glossitis and stomatitis gave a history of scrotal dermatitis. Cheilosis occurred in five cases in the absence of glossitis and stomatitis. In three cases, glossitis and stomatitis occurred in the absence of cheilosis.

Beriberi was exceedingly prevalent in the group and occurred both in Japan and in the Philippines. A history of "wet beriberi" (with massive edema) was obtained in 77 percent and a history of "dry beriberi" (without conspicuous edema) in about 50 percent. Many individuals had had both types. Often when wet beriberi disappeared, symptoms of dry beriberi developed. Usually, however, the latter preceded the former. Diarrhea was seldom present or severe during the phase of wet beriberi. Massive spontaneous diuresis often took place.

The clinical symptomatology of the dry beriberi was striking. Burning, hyperesthesias, and paresthesias were exceedingly severe, and in some camps hundreds of men would walk the floor during the night because of severe pain. Feet were often soaked in ice water, cooled in the snow, or exposed during the cold nights in attempts to alleviate the pain. The feet were so tender that even the slightest touch provoked severe pain. In one case, a handkerchief was accidentally dropped on the foot of a sleeping soldier. He immediately awoke crying out in agony. Often, just the vibration caused by some one passing within several feet of a soldier with dry beriberi was sufficient to aggravate the pain.

In the interesting summary of the board's report, it is noted that in many individuals, after the intake of a high-caloric diet when they were first liberated, glossitis, stomatitis, and edema reappeared or become more pronounced. Anemia was observed in 52 percent of the first 1,500 RAMP's studied and diminished appreciably in incidence as successive groups were examined until it was found in only 35 percent, 6 weeks after the study was begun. The anemia was macrocytic in 73 percent, normocytic in 23 percent, and microcytic in 4 percent.

The losses of weight ranged from 20 to 110 pounds. There was noted a remarkable ability to regain weight without corresponding improvement in the fundamental nutritional state. Many patients had protuberant abdomens commonly called rice bellies, while their shoulder girdles and extremi-

ties showed very marked wasting. The immediate results of a normal diet of American food in these people paralleled the widespread development of a similar edema under similar circumstances in the European theater. The reason was not clear to these observers who suggested, among other factors, that the diet contained more salt and fluid than that to which the prisoners had been accustomed. Although they associated the scrotal dermatitis with the stomatitis and cheilosis, they were not at all sure that it was part and parcel of the riboflavin deficiency syndrome. This relationship has been subsequently proved.

Almost without exception, the patients had suffered from attacks of diarrhea at some time during their imprisonment. It is necessary to distinguish between the diarrhea that most individuals have from time to time in normal life and the true dysentery consisting of prolonged periods of watery or bloody stools. Of the prisoners, 1,359 had one or more attacks of true dysentery.

Japanese Prisoners of War

When the tide of battle had turned, with defeat after defeat for the Japanese in the Philippine Islands in the spring of 1945, these enemy troops, as evacuation from the islands presented difficulties, retreated into the hills back of Luzon, breaking up into small groups and living off the land. Owing to the hostility of the natives and the scarcity of eatable food in the mountains, these men suffered severe deprivation, particularly starvation phenomena. Coupled with this were the dysenteries, malaria, and other diseases indigenous to this part of the world—maladies that ordinarily deplete metabolic reserves of human beings.

After V–J Day, 2 September 1945, these isolated Japanese troop units surrendered by the thousands to the U.S. Army. By early October, approximately 80,000 had been confined in New Bilibid Prison, Manila. Nearby was the 174th Station Hospital, a 250-bed installation. This hospital was burdened suddenly with the care of approximately 5,700 of these returned Japanese, many of whom were too ill even to move from their cots. It is reported that many died en route on the troop trains that brought the prisoners in. It was decided, as recommended by the Chief Surgeon, AFWESPAC (U.S. Army Forces, Western Pacific), and by others, that a special study [29] should be made of the clinical aspects of this severe malnutrition.

Considering the limitations of personnel and facilities and the administrative pressures to evacuate these prisoners as rapidly as possible, a remarkable amount of clinical observations with chemical determinations were made in these cases of starvation. A special ward was set up to handle a selected group of 24 of the most severely starved patients. This group was

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[29] Schnitker, M. A.: A Study of Malnutrition in Japanese Prisoners of War. [Official record.]

then subdivided into two groups, one of which contained 12 patients with massive edema, the so-called wet beriberi, and the other with 12 patients without edema, the so-called dry beriberi. All the patients were males between the ages of 25 and 35 years of age.

A large proportion of the patients being studied had begun to live on their starvation diets during March, April, and May 1945 and began to experience their difficulties in July, August, and September, approximately 3 months for the onset of severe symptoms. From the history, it was calculated that their diet was about 800 to 1,000 calories a day, at best. At least three-fourths of these patients gave a history of having had malaria, and two-thirds had a history of diarrhea before capture. It was estimated that loss of weight was approximately 40 to 50 pounds per person during the period of escape to the hills. Severe weakness was a complaint common to all. Those patients with edema complained of dyspnea, whereas only one-third of those without edema had dyspnea on exertion.

The physical findings were somewhat varied. In the edema group, the patients had moderate to very marked edema, which was greatest in the abdomen and the lower extremities. Three of this group escaped having pleural effusion, but all had evidence of pulmonary congestion. In contrast was the lack of edema in the "skin and bones" group. Although the history showed that practically all the patients, including these, had had edema in variable degree at some time before hospitalization, only three of the second group had any edema at the time of selection for study and on initial examination, and this was very mild, limited to the feet.

The skin was dry, loose, and atrophic, and most of the patients showed hyperkeratosis, particularly over the anterior aspects of the thigh. No definite cutaneous manifestations of pellagra were found, and no cheilosis. There was evidence of pigmentation over pressure points and other areas. Only four of the patients had severe atrophy and color changes of the tongue that would be indicative of the vitamin deficiency syndromes. Further examination revealed no grossly enlarged hearts; roentgenographic measurements were well within the danger ratio. Auscultation found the heart sounds for the most part impure and distant with an accentuation of P_2, particularly in the edematous group. The pulse was labile and tended to be rapid and considerably increased by even the slightest exertion. The blood pressure was normal to low, in the cases of "dry beriberi" ranging from 80 to 105 mm. Hg systolic and from 50 to 85 mm. Hg diastolic; in those with "wet beriberi," ranging from 100/60 to 130/90 mm. Hg. Control groups observed simultaneously also had low blood pressure with systolic readings of from 80 to 100 mm. Hg and diastolic readings varying from 45 to 80. Neurological examination revealed no definite pattern. Disturbances and abnormal sensations were found principally in the lower extremities in seven of the whole group. The vibratory sensation was intact in all the patients. No frank paralysis was observed, although weakness,

particularly of the quadriceps, was evident. All patients showed generalized muscular wasting. It was difficult or impossible to elicit the deep tendon reflexes, particularly in the lower extremities. Of particular interest was the high incidence of malaria which was, of course, to be expected, and yet none of the 24 patients during the entire period of observation had a palpable spleen. Laboratory findings were variable too. The greatest percentage of positive findings was observed in the hematological studies. There was a considerable amount of anemia in the entire group, ranging from moderate to severe and responding only slightly to iron therapy. Five of the patients showed erythrocyte counts under 2.5 million cells. The anemia was determined to be microcytic and hypochromic. The smears showed stippling and some toxic granulations of the white cells. Although four-fifths of these patients had intestinal parasites, only one-quarter had an eosinophilia above 4 percent. The hematocrit was distinctly lowered in both groups. In the edematous group, the readings ranged from 21 to 44. In the group without edema, the range was from 16 to 41. The sedimentation rate (Wintrobe) was uniformly elevated.

Bacteriologic cultures from rectal swabs were repeated three times. All cultures were negative for the typhoid, paratyphoid, and dysentery groups with the exception of three patients who showed, respectively, *Shigella paradysenteriae,* Boyd P 274; *Salmonella enteritidis;* and *Sh. paradysenteriae,* Boyd P 275. The diarrhea eventually ceased spontaneously in the first few days of treatment with rest and diet. New antidiarrheal drugs were used.

The serum proteins, albumin and globulin and the ratio of albumin to globulin, were determined on each patient at weekly intervals. In the initial studies, all values were low. In the cases of "wet beriberi," the total serum protein averaged 4.48 gm. per 100 cc. of blood with a range of from 3.4 to 5.3 gm., as compared to an average in the cases of "dry beriberi" of 4.75 gm. with a range of from 4.0 to 6.1 grams. The albumin fraction in the edematous group averaged 1.96 gm. per 100 cc. of blood as compared to 1.87 gm. in the nonedematous group. The globulin fraction was slightly higher in the latter group, the average being 2.77 gm. per 100 cc. as against 2.51 gm. in the former. The albumin-globulin ratio in the group with edema averaged 0.810 and in those without edema, averaged 0.675. Oral glucose tolerance tests were done on all patients except two. This was the standard test of 100 gm. of glucose. After determining the fasting blood-sugar level, blood samples were collected at 30, 60, 120, and 180 minutes. Six patients altogether had flat curves; that is, the peak did not rise above 120 mg. per 100 cc. of blood. In each instance, the fasting blood-sugar was on the low side; all were under 90 milligrams. Circulation times were determined by the arm to tongue technique using calcium gluconate. The results were all normal, that is, 12 to 18 seconds, except for one patient with dry beriberi, who had a circulation time of 10 seconds. Studies of

venous pressure, using a spinal manometer showed marked variations. The readings varied for the most part between 50 and 150 mm. of water. Six patients with wet and five patients with dry beriberi had readings of over 100 millimeters. Cardiac failure had not played a part in the edematous group, since there was little difference in the venous pressure readings of the two groups.

Electrocardiographic tracings, made in all these cases, showed consistently low voltage and minor T wave changes. Liver function tests failed to reveal any remarkable changes, but the majority retained Bromsulphalein (sulfobromophthalein) longer than usual. A gastric analysis was done on each patient to determine the presence of free hydrochloric acid in the gastric juice. Only three of the patients, two edematous and one not, had free acid on the first test.

Five autopsies performed on the patients who died of malnutrition alone, of whom there were seven studied, showed a marked atrophy of all the viscera. The fat deposits were gone; the skeletal muscles showed wasting; the hearts weighed from 150 to 200 gm.; the livers weighed from 525 to 1,000 gm.; and the kidneys, from 75 to 100 grams.

All these patients had fever at one time or another. This varied from isolated spikes to continuous fever with temperatures as high as 100° to 101° F. Thick and thin smears for malaria were made on all patients at least four or more times, and 15 were found to be positive.

The observers noted further that in cases of both wet and dry beriberi, edema was a clinical finding which varied moderately from time to time during the period of observation and treatment. They thought that this might have been influenced by the intake of the salty soybean sauce which all these patients insisted upon eating. This observation may be correlated with the findings in the European theater where there was practically no edema during treatment in patients on diets in which salt was a rare component. (See pages 274–275.)

Troops and Civilians in the Pacific

An intensive study of the nutrition of 111 full-duty troops in the Manila area in July and August 1945 is described in a report dated 20 October 1945.[30] Chemical determinations showed considerable variations in the nutritional status of soldiers living in this environment on the basic Army allowance. Although the ration was appraised as apparently adequate for nutrition, it was found that—

1. Twenty-five percent of the subjects were in a state of partial depletion with respect to sodium chloride.

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[30] Letter, Capt. Eliot F. Beach, SnC, Nutrition Officer, 26th Hospital Center, and 1st Lt. Oscar N. Miller, SnC, 248th General Hospital, to Commanding Officer, 26th Hospital Center, APO 75, 20 Oct. 1945, subject: Chemical Determination of Nutritional State of Full Duty Troops, Manila Area, July and August 1945.

2. Plasma protein concentrations were normal and no serious deficiency of hemoglobin existed, although 16 percent were slightly below the accepted normals.

3. Twenty-five percent had concentrations of vitamin C below 0.4 mg. per 100 cc. of blood, but no prescorbutic states were observed.

4. Nine percent appeared to be rather seriously depleted of thiamine, and 6 percent were classified as seriously depleted of riboflavin.

From the results, it was concluded that, in low-score subjects partially desaturated with respect to the vitamin B complex, there is a higher incidence of the nonspecific signs of lowered health, resistance, and sense of well-being. The experiment in itself was not conclusive, but it showed an enthusiasm on the part of the personnel for a better understanding of the problems involved.

A more extensive survey [31] of nutrition in the Armed Forces in the Middle Pacific was carried out during April-June 1945 by a special team appointed by The Surgeon General. The team reported that physical examination revealed no cases of classical nutritional deficiency diseases such as scurvy, beriberi, ariboflavinosis, and pellagra.

A significant percentage of men in each place surveyed showed one or more physical findings that some medical nutritionists have considered to be associated with specific nutritional disturbances. On Guadalcanal, vitamin C intake was low, as was the urinary excretion of ascorbic acid. Here, a significant amount of acute inflammation of gingival margins and swelling of interdental papillae were observed. Biochemical tests showed a deficient riboflavin excretion in 8 percent of the subjects on Guam, in 9 percent of the subjects on Iwo Jima, and in 6 percent among the casualties from Okinawa. Occasional single cases of deficient excretion of thiamine were observed. It was concluded that the basic nutritional status of the troops in the areas surveyed was essentially good. The survey in the Pacific Ocean Area was conducted on garrison troops in Hawaii, Guadalcanal, Guam, and Iwo Jima. Some casualties from Okinawa were studied on Guam and Saipan.

Again evidencing the interest of the medical personnel in nutritional disturbances is a report, "Preliminary Vitamin C Survey," from the 19th Medical Service Detachment (General Laboratory), dated 26 February 1945. The levels of vitamin C in the blood plasma and the urinary excretion of vitamin C for 24 hours were determined on a group of men from two bases in New Guinea. No evidence of scurvy was found among the subjects, even those with low concentrations of vitamin C in the blood. Of 34 subjects whose blood was analyzed, only 3 showed levels in the plasma of 0.2 mg. ascorbic acid or less.

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[31] Letter, Maj. William B. Bean, MC, Capt. Charles R. Henderson, SnC, Robert E. Johnson, M.D., and Capt. Lyle M. Richardson, QMC, to The Surgeon General, Washington 25, D.C., 22 Aug. 1945, subject: Nutrition Survey in Pacific Theater of Operations.

In a very interesting report [32] from the 369th Station Hospital on the nutritional status of civilians, it is noted that about 3 months after the invasion of Saipan there was a marked change in the type of civilian patients admitted to the hospital. During the battle and for some time thereafter, the vast majority of patients were new and old battle casualties. In September 1944, the medical admissions began to exceed the surgical. These patients were admitted for peripheral edema, with and without ascites and hydrothorax. Many of them had muscular weakness, particularly difficulty in raising from a squatting position, and other complaints.

The clinicians at the 369th Station Hospital were skeptical of the diagnosis of beriberi. On therapeutic trial with vitamin B_1 in massive oral and parenteral doses, there was no dramatic improvement. Patients did improve after continued hospitalization on an adequate diet. A dietary review indicated that they had been subsisting on rice, a few greens, onions, and about an ounce of fish a day. It was felt that the edema might be due to hypoproteinemia. A number of autopsies were performed and in no case could the diagnosis of beriberi be confirmed by the gross findings. A series of total serum protein determinations were carried out with the Van Slyke copper sulfate technique. Of 89 civilian patients with edema studied with respect to their serum proteins, 77.5 percent had values below the critical level for edema and only 5.5 percent were within normal limits. A series of children without edema revealed values only 4.8 percent below the critical level for edema. From the study, it was concluded that the cause of edema in the civilian population in Saipan was hypoproteinemia since, although the existence of beriberi could not be excluded, the criteria for a beriberi diagnosis were not satisfied.

In the Philippine Base Section, the clinicians of the 168th Evacuation Hospital conducted an interesting project in nutritional research [33] when it became apparent that civilian personnel in the hospital locale (Puerto Princesa, Palawan, Philippines) presented a health problem, basically because of nutritional deficiencies, malaria, tuberculosis, and, of course, the intestinal parasites.

The population of the province is essentially rural, and had been in part nomadic, migrating from one region to another according to the crop seasons. During normal times, the diet consisted chiefly of rice, fish, corn, tuberous plants, and lesser amounts of pork, poultry, and eggs. With the occupation by the Japanese, the supply of cultivated products was almost entirely cut off from civilians, the great majority of whom isolated themselves in the barrios scattered throughout the hills. These people when they returned to their liberated community presented a most distressing evidence of nutritional deficiencies, comparable to the Japanese troops who

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[32] Essential Technical Medical Data, U.S. Army Forces, Pacific, for October 1945. Appendix I, Hypoproteinemia in Saipan Civilians.

[33] Quarterly Report, 168th Evacuation Hospital, for period January–March 1945, dated 1 Apr. 1945.

had escaped to the hills. Numerous cases of frank beriberi of the wet type were seen. There were several deaths of individuals with marked edema. The nutritional repair or rehabilitation of the Filipino civilians required special attention because of their racial predilections. The regular Army food was unpalatable to them, and the majority developed such acute gastrointestinal disturbances that the nausea or vomiting seemingly interfered with their progress. This, of course, was common experience in other occupied lands.

Troops in India

The establishment of a theater of operations by the U.S. Army in India and Burma presented subsistence problems not encountered in other parts of the world. Here, we were not invading a hostile country where food could be requisitioned and where supply lines could be appropriated and spread out. We were considered as guests in a densely populated Allied country in the throes of its own political problems. A large portion of the population was on the brink of a great famine, which was to destroy by starvation a million and a half people in 1943. The troops could not be concentrated in any well-defined area, but by military necessity were scattered in small groups separated by thousands of miles. The lines of communication between these groups when existent were extremely primitive.

The first troops arrived in India from the United States early in 1942. No adequate provision had been made for the continuous supplying of these soldiers with food from the Zone of Interior. A reserve stock of B-rations had been sent to the theater, but these were not to be used except in emergencies. The original plan was to maintain these troops on supplies obtained from local markets and from rations obtained through the British Army. By October 1942, the theater policy was adopted, prescribing a ration to consist of the field service ration of British troops obtained through the Royal Indian Service Corps and supplemented by local purchase of fresh supplies and by the issues of excess stocks of the reserve B-rations. Experience showed that the British ration was not suitable for U.S. troops because it included such items as pork, soya, links, corned beef, and mutton, and it was largely not eaten. The British Army's milk allowance was only 2 ounces of tinned milk per man per day, which was not considered adequate for U.S. troops. No fresh milk was available because of the unsanitary conditions under which it was produced. Owing to the local prohibition against the slaughter of bullocks in good health, the supply of meat was very poor.

Medical officers began to report a reduction in the efficiency of the command which they attributed to malnutrition. A large proportion of the troops reporting for sick call complained of weakness, insomnia, lassitude, and gastric complaints suggestive of a deficiency state. An increase in the occurrence of gingivitis was observed.

Early in the experience of the Americans in this theater, an interesting outbreak of a nutritional deficiency disease occurred in the form of beriberi among the Chinese troops at the Chinese Training Center at Rāmgarh, India. Between 8 August and 25 September 1943, 199 patients were admitted to the 48th Evacuation Hospital with beriberi as the primary cause of hospitalization. Many others were treated as outpatients. They had other symptoms of deficiency diseases such as night blindness, cheilosis, glossitis, and osteomalacia. A change in the ration was made, and undermilled rice was substituted for the polished rice. With this change, the nutritional disturbances disappeared.

Maj. Frank B. Cutts, MC, reported on 125 cases of beriberi admitted to the 48th Evacuation Hospital during an 11-week period, from late July to October 1943.[34] All the patients were Chinese soldiers. It is interesting to note from Major Cutts' report that in the first patients observed the diagnostic evidence was considered obscure, and many of them were admitted as having rheumatic fever, rheumatic heart disease, phlebitis, and nephritis. A summary of the clinical observations made by Major Cutts follows.

History.—Most of the patients had three major complaints: (1) Shortness of breath on slight exertion; (2) swelling of the legs—less often of the genitalia—hands, and face; and (3) numbness of the legs and muscle pain on walking. Less frequent complaints were palpitations, precordial pain, upper abdominal distention, and numbness of the arms. Most of the patients had been sick at least 1 to 3 weeks before presenting themselves to the hospital. In many instances, it was noted that acute bronchitis, diarrhea, or vaccine injections apparently precipitated the acute manifestations.

Physical examinations.—These patients were big, husky men with no evidence of caloric malnutrition. They showed little or no fever. Examinations of the tongue and mouth revealed some instances of cracking and scaling at the corners of the mouth which were ascribed to riboflavin deficiency. There was definite engorgement of the veins in the neck. The heart was almost always enlarged. With the patient sitting on the edge of the bed, the left quarter of the area of cardiac dullness was consistently 1 to 3 centimeters outside the nipple line. The heart rhythms were usually regular with a rare extra systole. Rates varied from 58 to 120 beats per minute. The first heart sound was loud and booming, and often there was a gallop rhythm at the apex. Systolic murmurs of moderate intensity were heard at the apex and along the left sternal border. There were no diastolic murmurs. Examination of the abdomen revealed an occasional ascites.

Edema of the legs was almost constantly found varying from one to four plus. This edema involved the genitalia and extended up over the

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[34] Cutts, F. B.: Observations on Beriberi. Field Medical Bulletin, Headquarters, Services of Supply, U.S. Army Forces, China-Burma-India, vol. 2, No. 12, December 1943.

back. Muscles of the calf in most instances were normal. Knee jerks and ankle jerks were usually absent. There was a marked hypoesthesia to pinpricks of the lower extremities.

Treatment.—This consisted of bed rest with the regular hospital diet and an autolyzed yeast product rich in vitamin B_1, or vitamin B_1 itself.

Course in hospital.—As a rule, the patients showed prompt improvement. Dyspnea disappeared in 2 or 3 days. The heart rapidly shrank to normal size, the left border receding to 1 to 3 centimeters in the course of the week. Diminution in size was checked by serial chest X-ray plates in a few cases. Heart murmurs and other abnormal sounds were not heard after about a week. Edema of the legs and turgidity of the muscles of the calf were generally gone after from 5 to 7 days of treatment. Numbness, insensitivity to pinprick, and lost reflexes were more persistent and in some instances were but little improved in 6 weeks. In general, the patients were sufficiently well to return to duty in from 2 to 3 weeks. When the autolyzed yeast was withheld, improvement occurred in approximately twice the time required by the patients treated with the yeast, and complete relief of symptoms was usually not obtained until the vitamin B concentrate was given.

One death was reported of a 25-year-old soldier who was admitted complaining of marked shortness of breath for 3 days. The respiratory rate was 35 per minute and the temperature was 99° F. Engorgement of the cervical veins was evident. The heart was enlarged two plus, and auscultation revealed a loud gallop rhythm. The pulse could not be obtained in either wrist. The apical heart rate was 96. The patient remained pulseless and died 12 hours after admission. As the cause of his illness was not recognized at entry, he was not given any parenteral B_1. Autopsy showed generalized congestion and edema of the internal organs. The heart was dilated and distinctly flabby but otherwise normal to gross examination. One ascaris worm was found wandering in the intrahepatic viaduct.

Etiology.—Most of these patients came from one regiment. An investigation revealed that this regiment had been storing rice over and above their daily requirements. In July, with the onset of wet weather, realizing that the rice would spoil, the unit drew no new rice and began to consume its stored surplus. A sample of the rice was obtained and found to be gray, lusterless, and devoid of any of the pericarp. When the old rice was discarded and new rice obtained, the incidence of beriberi in this unit no longer exceeded that in other units in the area.

Early in 1944, Colonel Howe, on a visit to China-Burma-India, attributed the inadequacy of the Army rations to attempts to live off the land, to dependence on British supplies which were often not available or not acceptable, and to the failure or inadequacy of transportation.

CONCLUSION

Throughout the individual reports from all theaters of operations, one finds an overemphasis on the failure of the packaged rations. The principal deficiency seems rather to have been in the briefing of the personnel who were responsible for the nutritional status of the troops in the field in the several theaters. In some quarters, there was failure to comprehend that the most important aspect of rations for the troops was first to supply calories, next protein, and thirdly, the micronutrients or vitamins and minerals, always presupposing, of course, a sufficiency of potable water. Indeed, a review of the prewar debate in the Nutrition Committee of the National Research Council shows a somewhat unrealistic approach to the problem in the light of later experience. In the future, it would seem wise to include either a field officer or a medical or nutrition officer with field experience at any level of discussion concerned with the feeding of troops. A review of ration tests in the United States shows that those who designed them and observed the results had a better appreciation of the problems of nutrition and survival under the various conditions that war may impose.

In the field, there was a tendency for command, endorsed to some extent by the medical personnel, to ascribe to nutritional deficiencies almost any condition that was not otherwise explicable. Medical officers in general showed an uncertain grasp of nutritional problems. The Essential Technical Medical Data reports indicate their lack of training in this respect, and show, as well, their eagerness to learn.

In World War II, and subsequently in the Korean War, there were failures by command to distinguish properly between a resting prisoner and a working prisoner. In both wars, there were instances when extra food was not issued to compensate for calisthenics or work done within prisoner-of-war enclosures although considerable extra effort-output might be involved. Again, there was at first a failure to allow for the nutritional requirements of different age groups, and German prisoners from 14 to 19 years old, conscripted by the Wehrmacht in the last phase of the war, were found faring badly on rations designed for adults in the age group of 21 to 35 years.

Briefing of personnel on nutritional requirements with respect to actual work done and to age, sex, climate, and other relevant factors must be improved before the Army can expect wholehearted and effective cooperation from the field staff.

RAMP'S IN HOSPITAL

The medical officer assigned to the Nutrition Branch visited the chiefs of the medical services of all major hospitals concerned with the treatment of the RAMP's. On 24 May 1945, at the 179th General Hospital, Col. George B. West, Commanding Officer, and Lt. Col.

Oza J. LaBarge, Chief of the Medical Service, Maj. Henry J. Babers, Chief of the Surgical Service, and Capt. Sidney Small, Chief of the X-Ray Service, gave the following information:

More than 800 RAMP's were admitted between the middle of April and the last week in May. About a third were admitted directly to this hospital, and these were for the most part men who had been captured in the Battle of the Bulge and imprisoned in Stalag IX–B at Bad-Orb (mostly enlisted personnel) or in Stalag IX–A at Niedergrenzebach, near Ziegenhain, (mainly noncommissioned officers and men). Those from Stalag IX–B were in the worst condition of all. They said they had seldom received Red Cross packages. As estimated from their histories, their average loss of weight during captivity was 39.1 pounds per man at Bad-Orb, and 28 pounds per man at Niedergrenzebach. One patient had lost 115 pounds.

Of the total number of patients, 198 had hepatitis; pulmonary tuberculosis was suspected in 14 and proved in 11; diphtheria was found in 8. The diagnosis of severe malnutrition was made 188 times. The average erythrocyte count for the entire group was 3,600,000; the average hemoglobin concentration was 60 percent; the average total serum proteins were 6.2 gm., with a range from 2.7 to 7.6 grams. These were determined by the copper sulfate method. Hemoconcentrations and hematocrits were not done. Of stool cultures in 283 cases, 6 were positive—2 for *Shigella paradysenteriae* and 4 for the Flexner types of this species; practically all 283 men had diarrhea. Gastrointestinal studies made on two of these patients were negative. All, including the six with positive cultures, cleared on dietary management without specific hemotherapy. Cardiac study revealed no actual cases of beriberi heart. The majority showed very low blood pressure. Electrocardiographic tracings, made on a number of patients, almost universally showed low voltage Z-R-X complexes and low excursion or very flat T waves. There were 30 cases of nutritional edema, which cleared up on a regimen of bed rest and special diet. Basal metabolic rates were not determined. No manifestations of scurvy were found in these patients.

Of the 283 patients with diarrhea, 42 were fed by the gravity-drip method with the special mixture of powdered milk and powdered eggs suggested by the Nutrition Branch, Office of the Chief Surgeon. Others were given this mixture orally in six feedings daily. Intravenous therapy of any kind was found to present many difficulties, with two types of reactions noted during or after administration: The one, circulatory relapse; the other, chills and fever. The standard treatment for the patients with malnutrition in the 179th General Hospital was tube feeding of the high-caloric liquid protein diet by gravity drip, vitamin therapy, and occasional plasma or blood transfusion or oxygen, when indicated. Four deaths occurred on the Medical Service. An autopsy of one of the patients showed a marked redness and congestion of the entire gastrointestinal tract.

The Surgical Service reported that from 150 to 200 RAMP's were admitted to this service. They were found to be very poor risks, reacting to surgery more like the German prisoners of war than the average American soldier. There was one death on the service. This patient was operated upon for a perforated peptic ulcer, but at operation no ulcer was found and autopsy revealed that the patient had died from congestive heart failure.

In these RAMP's, wound healing and healing of ulcers or infections at first was very poor. Under proper diet and vitamin therapy, the chief of service noticed improvement in healing. The X-Ray Service reported evidence of marked distention of the large bowel in a large percentage of these patients. The pulmonary abnormalities as revealed by X-ray in these early groups were increased bronchial vesicular markings, very prevalent; atypical pneumonias, very frequent; and tuberculosis, not uncommon.

The 77th Field Hospital was visited on 26 May 1945. The diagnoses made from 12 through 18 April were malnutrition 94 times and gastroenteritis 82 times; from 16 to 19 May, they were malnutrition 122 times and gastroenteritis 6 times. Plasma therapy was used on 166 patients. Of these, 19 experienced severe reactions as follows: Five patients

developed pulmonary edema and of these two were in extremely critical condition; two patients developed chills and fever with nausea and vomiting; eleven had chills and fever; and one, a simple urticaria. Again, diarrhea was an acute problem. Therapy was the liquid egg and milk mixture given by mouth; the gravity-drip method was not used at this hospital. Response to therapy was considered excellent. The X-Ray Service, under Capt. Russell D. D. Hoover, reported that of 2,750 RAMP's examined roentgenographically 16 or 0.58 showed tuberculosis; 64 or 2.2 percent, atypical pneumonia; 13 or 0.45 percent, lobar pneumonia; 9 or 0.33 percent, pleural effusions; 4 or 0.14 percent, pulmonary edema; and 43 or 1.56 percent showed foreign bodies, fractured ribs, and so forth.

The 97th General Hospital reported through Maj. Kelse M. Hoffman, assistant chief of the Medical Service. Loss of weight and listlessness were the major presenting symptoms of their patients, a group on the whole not in very bad condition. Only about 20 enlisted men were considered to be seriously ill. The average loss of weight in the whole group was only 15 pounds and was regained in 2 weeks of therapy. Again, the major problem was gastrointestinal disturbances commonly due to dietary indiscretions. Stool examinations on all these patients showed no pathogenic micro-organisms. After publication of Circular Letter No. 36, the chief of the Medical Service noted that the gastrointestinal symptoms diminished markedly. No specific vitamin deficiency syndromes were noted, although several cases manifested tenderness of the calf; a few developed edema after treatment, and the deep reflexes in the lower extremities were diminished or absent.

At the 129th General Hospital in the 804th Hospital Center, Whitchurch, England, Lt. Col. Herbert W. Rathe observed very few seriously ill patients. Specific classical syndromes of vitamin deficiency were not seen, but edema was frequent. The blood protein studies in the Center were not conclusive. The patients who were admitted early all had severe diarrhea, but stool examinations were basically negative. The outstanding problem here was the lack of strength persisting for weeks after the return of a good general appearance. Electrocardiographic tracings showed T wave and voltage changes similar to that reported by other hospitals, with a return to normal in several weeks.

At the 91st General Hospital, 15th Hospital Center, Oxford, England, Lt. Col. Adolph R. Mueller reported that losses of from 15 to 45 pounds were the presenting problem; also, that the Red Cross insisted upon serving chocolate bars on the wards with resultant gastrointestinal problems. Approximately 25 percent of the first admissions presented edema; others developed edema in the course of hospital therapy. The diarrhea, as in other installations, was the biggest problem. The acute gastrointestinal symptomatology generally followed the consumption of rations. In this group, several patients were seen with specific deficiency manifestations, such as cheilosis, tongue changes, and stomatitis.

At the 83d General Hospital, Whitchurch, England, approximately 250 RAMP's were admitted, most of whom were not considered seriously ill. Diarrhea again was the commonest of all findings but became a minimal problem after Circular Letter No. 36 was put into effect. Edema was very evident in many of those admitted. Serum proteins were considered to be definitely low, although the specific figures were not made available. Moderate anemia was the usual finding. Glossitis, cheilosis, and other specific symptoms of the mucous membrane were noted very frequently. Paresthesias were common, particularly of the glove-and-stocking type, with dry, scaling skin. Serial electrocardiographic studies were made.

Among these RAMP's, there were eight severely ill patients who manifested a loss of from 60 to 101 pounds in body weight. These men had been captured at the time of the Battle of the Bulge. Their appetite was good, but diarrhea was precipitated by a full diet. The electrocardiographic tracings showed low T waves, flat or inverted in I and IV low amplitude PQRS. There were no conduction problems. Serial tracings showed a reversal to the normal pattern in the course of the first 2 weeks. Serum proteins in this small group averaged 5.2 grams. Red blood cells ranged from 2.5 to 3.5 million with a marked poly-

chromia. The type of anemia was amacrocytic. Again, in this hospital, chill reactions and febrile reactions frequently followed transfusions of plasma. Multiple neuropathies, hyperactive reflexes, and ataxic gaits were noted in two of these patients. Alopecia was observed, but responded to simple diet therapy. Rapid gain in weight in six of the patients, amounting to from 30 to 40 pounds in five days, was obviously due to the development of an edema. About 10 percent of the patients admitted to the 83d General Hospital were confined to bed.

The 217th General Hospital in Paris cared for a great many RAMP's. Out of 1,098, there were 665 admitted to the Medical Service, of whom 275 were more than moderately undernourished. A survey revealed the following symptoms: There was of course marked loss of weight in all 275; a scaly skin in 186; glossitis described as a clean tongue with a smooth edge, bright red, in 100 patients; diarrhea, with negative stool cultures, was noted in 76 patients; muscle tenderness in 75; a very marked cachexia and asthenia in 67; hypoactive reflexes in 37; cheilosis was observed 30 times; edema and ascites, 24 times; polyneuritis, 12 times; night blindness occurred in 6 patients; scurvy, including gingival hypertrophy with bleeding plus petechiae and increased capillary fragility, was seen three times. Twenty-five of the patients who had diarrhea, nausea, anorexia, or vomiting were selected for X-ray studies of the digestive tract. Six of them showed the so-called small-bowel deficiency pattern manifested by dilatation of the small intestine, especially the jejunum, fluid levels resembling obstructions, clumping and segmentation of barium with hypomotility. The barium meal progressed only as far as the distal end of the jejunum in 6 hours. On reexamination 2 weeks later, considerable improvement was noted. In the fatal cases of malnutrition observed at this hospital, there were no gross or microscopic changes in the esophagus, stomach, or small bowel. Parenthetically, it should be noted that in the brain of a patient examined at autopsy numerous focal necrotic lesions were observed.

In all theaters of operations, the problem of the repatriated prisoners, not only the Americans but also the friendly nationals, was of extreme importance. In the European theater in particular, their condition presented a major medical catastrophe. As an example, a letter dated 3 April 1945 from Lt. Col. Theodore L. Badger, MC, Senior Consultant for Tuberculosis, ETOUSA, to the Chief Medical Consultant, ETOUSA, notes that, on 17 December 1944, 304 tuberculous Russian and Italian recovered prisoners were sent to the 50th General Hospital without advance information. Of these patients, 4 arrived dead, and, as of the date of the letter, an additional 85 had died of advanced tuberculosis.

This group of tuberculous patients was similar to those seen when the 46th General Hospital was visited in the middle of March. There was remarkable improvement in these people in the course of their hospital stay with the gains in weight reaching 45 pounds in the first 3 months. The signs of nutritional deficiency disappeared very rapidly, and the group as a whole began to look in moderately good health. Of the first 50 who died, it was noted that the average stay in the hospital was only 9 days, their average age was approximately 26, their average weight on admission was 110 pounds. The duration of involvement, however, was 8 months, and in 100 percent the involvement was bilateral. This would indicate that the bulk of the destructive effects of the disease occurred before the men were hospitalized in the American installations. The treatment was to increase the food given these people, allowing them 1½ hospital rations per person. Artificial pneumothorax was instituted in at least 30 cases with excellent results. In a letter dated 30 March 1945, to the Office of the Chief Surgeon, Colonel Badger had reported as follows: As of 29 March, 1,676 patients of recovered Allied military personnel were admitted to the 46th General Hospital. Of these, 1,251 were Russian; 102 Yugoslavian; 72 were French; 22, Italian; 6, Polish; 5, Turks; and 15 were Germans. A survey indicated that at least 40 percent had active tuberculosis. Of these, 50 percent were in a far advanced stage, 40 percent moderately advanced, and only 10 percent were minimal. Twenty-seven of the patients were seriously ill, and 20 had already died.

This group of patients had worked in forced labor in the coal mines under German control, reportedly in shifts of 6 hours on and 6 hours off, 24 hours a day, 7 days a week without interruption. The chance of contagion was magnified by the ignorance of the patients and by the complete absence of personal hygiene. Here we see a prime example of the superimposition of tuberculosis on malnutrition and the attendant remarkably high death rates.

AUTOPSY FINDINGS IN PATIENTS DYING OF STARVATION

The writer performed autopsies personally in concentration camps in Austria. A summary of his findings follows.

Tongue

Sections of the epidermis of the tongue examined microscopically show moderate atrophy of the lingual papillae. Bacteria in large, dark-staining clumps are seen in the crypts and on the surface of the organ. In two cases, there are focal collections of dense basophilic round bodies, somewhat larger than cocci, incorporated in the parakeratotic layer, which resemble Monilia. In another section, there is, in addition, focal epithelial invasion by branching septated mycelia. These changes perhaps represent an early sprue.

In three sections, there is a slight to moderate increase in the parakeratotic epithelial layer. All cases display some intracellular edema, and one case demonstrates a superficial acute inflammatory reaction in the parakeratotic layer.

Nerves

Slight demyelinization of the nerve trunks, and an occasional area of basophilic degenration, are seen in all sections. The intraneurolemmal edema is not so apparent as in the sections of the skin. (See also pages 289 and 291.)

Lingual Glands

Of the 11 sections studied, 8 reveal lingual mixed-type glands. In one case, the glandular parenchyma is atrophic, with increase in the intra-acinar connective tissue.

Thyroid Gland

In 9 of the 11 sections studied, there is apparent a slight to moderate decrease in the colloid content of the acini. In one, the colloid is abundant; in the rest, appears normal in amount.

In two cases, the fibrous stroma about the acini is increased, with scattered focal accumulations of lymphocytes prominent in only one case. Epithelium is in all cases of the low cuboidal type and in it is hyperplasia. In one section, there is seen a small rounded true adenoma, benign in character.

Heart

Few changes are present in the 10 heart sections. The most appreciable is the decrease in subepicardial fat, which in many cases has the appearance of fetal adipose tissue. It is pronounced in only five cases. Three cases display moderate fatty degeneration of myo-

cardial fibers, and three cases could be classified as brown atrophy. In one case, there is slight increase in interstitial myocardial fibrosis, with hypertrophy of individual solitary myocardial fibers.

Pancreas

In seven sections, changes in the pancreas are for the most part not prominent. All sections reveal the presence of symogen granules and basophilic substance. One slide shows slight hydropic degeneration of acinar cells, and one displays marked post mortem degenerative changes. There is a significant increase in interlobular and intralobular fibrous tissue in one case, and in three others there is an apparent increase, incident to interstitial edema. In general, little fat is associated with any of the sections.

Islets are in general small, with decrease in the number of both A and B cells, and hyperchromatism of some of the nuclei. A few islets are swollen and edematous, with disruption of islet cells and slight increase in fibrous tissue within the islets and surrounding them.

Skin

Epidermis.—All six sections display marked atrophy of the epidermis, often reduced to a thickness of one to two cells. There is moderate intracellular edema in all cases, particularly in the basal epithelial layer. Pigment distribution is not unusual, and pigmentation is not excessive. Three of the cases demonstrate minimal edema of the dermal papillae, and two display slight inflammatory reaction about the superficial vessels of the derma. In all, the sweat glands are small and inactive in appearance, often with large vacuoles occupying most of the cytoplasm of the cells, as if they were in a stage of metaplasia into sebaceous epithelium. The lumina contain granular debris.

Peripheral nerves.—In five of the six sections, the peripheral nerves located in the derma and subcutaneous tissue display a moderate edema within the neurolemma sheaths. Usually, the nerve fibers appear unaltered, although, in an occasional nerve, there is demyelinization and basophilic degeneration of the reticular supportive connective tissue. There is no inflammatory reaction about the nerves. Dermal arterioles are unchanged.

Subcutaneous fat.—All six sections show atrophy of subcutaneous fat. In all, the lipoid is practically depleted from the adipose tissue cells, so that they closely resemble embryonic fat. The fat is well vascularized.

Hair follicles.—Other dermal appendages are decreased in number. Hair follicles are maldeveloped, and often the hair shaft is degenerate.

Adrenal Glands

In two of the nine sections, ante mortem changes are masked by marked post mortem autolytic changes.

Periadrenal fat.—All nine cases display advanced atrophic changes in the periadrenal fat, giving it the appearance of fetal adipose tissue. There is yellow pigmentation of the remaining supportive stroma.

Cortical changes.—All cases display some degree of edema between cortical cords, and in four cases it is marked. In all, there is an obvious decrease in lipoid deposition of the cortical cells, while in two there is instead a moderate hydropic degeneration. In one case, the cords appear to have acquired a lumen, and resemble tubules, a finding often associated with acute infectious diseases. In two sections, there is a solitary focal adrenalitis involving the cortex, and in another small lymphocytic foci are scattered throughout the medulla.

Medullary changes.—Degenerative changes seen in the medulla are not distinguishable from post mortem changes.

Spleen

In all seven sections, scattered, large, irregular cells with deep acidophilic cytoplasm and hyperchromatic irregular nuclei resemble megakaryocytes. There are no other supporting evidences of extramedullary hematopoiesis. Four of the sections display moderate pigment collections within phagocytic cells. In four sections, granulomatous lesions with central caseation necrosis are encountered, consistent with a disseminated miliary tuberculosis. Follicular lymphoid tissue appears moderately atrophic in only one case.

Testis

Spermatogenesis.—In all 10 sections, there was evidence of spermatogenic arrest at an early stage.[35] Five cases display mitosis in the spermatogonia, although beyond this point there is little progression, so that more mature elements are markedly decreased. One section demonstrates the production of an occasional bizarre spermatid.

Interstitial tissue.—Of the 10 sections, 4 display an increase in fibrous interstitial tissue. In two of these, there is an associated encroachment and fibrosis of the seminiferous tubules. In another, there appears a metaplastic transformation of tubular epithelium into a tall columnar type.

Kidneys

Glomeruli.—All 11 sections reveal hydropic degenerative changes of tuft epithelium; these are extreme in 2 cases. Three cases display mild degrees of capsular fibrosis, and two cases show some increased cellularity of the tufts themselves. In two cases, there is slight hyalin thickening of the afferent arteriole.

Tubules.—Of the 11 sections, 9 display varying degrees of hydropic degeneration of the tubular epithelial cells. In the other two cases, post mortem degenerative changes of tubular epithelium is of sufficient degree to mask this finding if present. Casts, both hyaline and epithelial, are found in small numbers in nine cases, while casts of blood or altered blood pigment (hemoglobinuric nephrosis) are found in two cases. Three cases display small cortical retention cysts.

Interstitium.—Scarring of the cortex is present in 5 of the 11 cases, this varying from an occasional fibrosed glomerulus to wedge-shaped cortical scars. Among these, there are chronic inflammatory infiltrations in three cases. Areas of calcification are found in five cases, usually appearing to occupy the lumen of a former tubule, or also

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[35] Under the histologic examinations of the testicles, evidence of some spermatogenic arrest has been noted. This correlated with the clinical findings to a remarkable degree. This history of these men showed that early in starvation there was a universal loss of libido and an absence of noctural emissions. Months later, the hair on the head and face was soft, fine, and sparse. Even men who before incarceration had had to shave daily, at the end of it found shaving once a week sufficient. Axillary and pubic hair became thin, and there was a tendency in some for the hair to assume feminine distribution. The skin became thin and loose and its oiliness disappeared. Acne vulgaris was very uncommon. A matter of weeks after liberation and feeding, libido, erections, and nocturnal emissions resumed. Several weeks later, the prisoners observed that the hair areas were becoming restored and shaving became a problem.

In Japan, it was noted that from 3 to 12 weeks after the diet became adequate gynecomastia appeared in 6 percent of the prisoners, in age groups varying from 18 to 64. Three percent secreted a colostrum-like substance.

It is to be noted that in the lapse of years since liberation a normal number of pregnancies in the wives of the prisoners of war have occurred, and the children born to these marriages have been apparently healthy.—H. P.

being deposited within the degenerating epithelial cells of tubules. One case displays a significant degree of intestinal edema. In others, the edematous appearance can well be explained on the basis of post mortem degenerative change.

Liver

Periportal areas.—Two of eight sections reveal slight increase in lymphocytes within the periportal areas.

Parenchyma.—All eight sections reveal a mild to moderate fatty metamorphosis of hepatic cells of the parenchyma. In one case this is very marked. The metamorphosis, while present to some degree uniformly throughout the lobules, is most marked at the periphery of the lobules in the moderate to marked cases. Five of the sections examined reveal focal areas of chronic granulomatous reactions with progressing fibrosis (tuberculosis).

Nerves

Edema of the peripheral nerves associated with degeneration of the fibrils and vacuolization are noted in all 10 sections studied, and in all there are hyaline changes in the sheath. Basophilic degeneration of the neurolemma and perineural fibrous tissue is found in nine cases. In three of the sections, proliferation of the nerve sheath is distinct.

Muscle

All cases (nine sections) show edema, hydropic degeneration of the muscle fibers as well as a hyaline-type degeneration. Multiplication of the sheath nuclei indicating proliferation of myofibrils is noted in seven. An interstitial chronic inflammatory reaction is found in three of the sections.

Gastrointestinal Tract

In one section of colon, a small diverticulum is found extending through the circular muscle layer but limited by the longitudinal layer. Edema of the myoneural plexus is present. In another section of colon, there are scattered tiny mucosal ulcerations associated with necrosis and polymorphonuclear leukocytic infiltration. The submucosa is thickened and edematous with vascular dilatation, and infiltrated by numerous round cells, eosinophiles and a few neutrophiles. No amebae are present. Edema of the nerve fibers, atrophy of subserosal fat are noted, but no serosal inflammatory reaction is distinguished. A third section of colon is not remarkable except for moderate edema of the nerve fibers.

Two sections of stomach display moderate neural edema, and two other sections show no unusual findings.

One section of jejunum has a focal chronic inflammatory reaction of the mucosal stroma and lamina propria, and occasional neutrophiles are found. No ulceration is present. Two other sections have only mild edema of the nerve fibers.

Four sections of ileum are not remarkable except for the edema of the nerve fibers noted in the other sections.

CHAPTER XI

Diabetes Mellitus

Alexander Marble, M.D.

Although the incidence of diabetes mellitus in the U.S. Army during World War II was relatively low, those diabetic patients who were encountered presented problems in diagnosis, treatment, and disposition, which in individual cases were often of considerable moment. The small number of diabetics seen in Army hospitals during the war was chiefly due to two factors: (1) By far the greater part of military personnel was drawn from age groups (18 to 37 years) in which the incidence of diabetes is relatively low in the general population, and (2) routine examination of the urine was made at induction stations, with rejection for military service of all found to have diabetes by analyses of urine and blood.

OBSERVATIONS AT INDUCTION STATIONS

General.—Several sources of data [1] relating to the prevalence of diabetes mellitus among registrants examined for military service in World War II are presented in table 51. As may be seen from the table, the reported prevalence rates are quite different. They range from as high as 11.0 (Blotner) to as low as 0.3 (Spellberg and Leff), per 1,000 examinees.

The initial study by Blotner and Hyde [2] was based on registrants examined at an induction station in Boston, Mass. These authors found that of the 45,650 examined selectees and volunteers, aged from 18 to 45 years, 367 examinees (approximately 8 per 1,000) had glycosuria. These examinees were diagnosed as follows: Transient glycosuria, 126 cases; renal glycosuria, 33 cases; and diabetes mellitus, 208 cases. In other words, 4.6 per 1,000 men examined were diagnosed as having diabetes.

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[1] (1) Causes of Rejection and Incidence of Defects: Local Board Examinations of Selective Service Registrants in Peacetime. Medical Statistics Bulletin No. 2, National Headquarters, Selective Service System, Washington, D.C., 1 Aug. 1943, table 7. (2) Physical Examinations of Selective Service Registrants During Wartime. Medical Statistics Bulletin No. 3, National Headquarters, Selective Service System, Washington, D.C., 1 Nov. 1944, app. C, table 6. (3) Blotner, H., and Hyde, R. W.: Studies in Diabetes Mellitus and Transient Glycosuria in Selectees and Volunteers. New England J. Med. 229: 885–892, 9 Dec. 1943. (4) Spellberg, M. A., and Leff, W. A.: The Incidence of Diabetes Mellitus and Glycosuria in Inductees. J.A.M.A. 129: 246–250, 22 Sept. 1945. (5) Blotner, H.: Studies in Glycosuria and Diabetes Mellitus in Selectees. J.A.M.A. 131: 1109–1114, 3 Aug. 1946. (6) Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, Department of the Army.

[2] See footnote 1 (3).

TABLE 51.—*Prevalence of diabetes mellitus among registrants examined for military service, World War II*

[Rate expressed as number per 1,000 examined registrants]

Source and period	Total	White	Negro
Selective Service:			
November 1940 through September 1941 [1]	2.9	3.0	1.9
April 1942 through December 1943 [2]	2.6	2.9	.8
Blotner and Hyde [3]	4.6	--------	-------
Spellberg and Leff [4]	.3	--------	-------
Blotner [5]	11.0	--------	-------
Karpinos:[6]			
Principal disqualifying defect	1.2	1.3	.4
Prevalence of disqualifying defect	1.3	1.4	.5

[1] Causes of Rejection and Incidence of Defects: Local Board Examinations of Selective Service Registrants in Peacetime. Medical Statistics Bulletin No. 2, National Headquarters, Selective Service System, Washington, D.C., 1 Aug. 1943 (table 7).

[2] Physical Examinations of Selective Service Registrants During Wartime. Medical Statistics Bulletin No. 3, National Headquarters, Selective Service System, Washington, D.C., 1 Nov. 1944 (app. C, table 6).

[3] Blotner, H., and Hyde, R. W.: Studies in Diabetes Mellitus and Transient Glycosuria in Selectees and Volunteers. New England J. Med. 229: 885–892, 9 Dec. 1943.

[4] Spellberg, M. A., and Leff, W. A.: The Incidence of Diabetes Mellitus and Glycosuria in Inductees. J.A.M.A. 129: 246–250, 22 Sept. 1945.

[5] Blotner, H.: Studies in Glycosuria and Diabetes Mellitus in Selectees. J.A.M.A. 131: 1109–1114, 3 Aug. 1946.

[6] Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, Department of the Army.

Of the diabetics, 107 were classified as mild, 58 as moderate, and 43 as severe. Only 42 of the diabetics were aware of their disease.

Spellberg and Leff [3] in a later study, based on examinations of some 32,000 registrants at an induction station in New Orleans, La., found a far lower prevalence of glycosuria and diabetes. They found only 37 cases of glycosuria among those examinees, and only 9 of these were diagnosed as having diabetes. The prevalence rates were thus 1.2 for glycosuria and 0.3 for diabetes, per 1,000 examinees.

These wide discrepancies in rates led Blotner [4] to continue his studies which gave him more surprising results than those observed in the first study. Among the 69,088 registrants, aged from 18 to 37 years, examined in this study, Blotner found glycosuria in 1,383 cases; that is, 20 per 1,000 men examined. About 57 percent of these (11 per 1,000 examinees) had diabetes mellitus as judged either by clinical manifestations or, more often, by well-marked glycosuria or by the results of a glucose-tolerance test.

Blotner has explained these discrepancies to be due, in part, to age differentials—the selectees at New Orleans being somewhat younger; in part, to race differentials—one-third of these examinees being Negroes

[3] See footnote 1 (4), p. 293.
[4] See footnote 1 (5), p. 293.

who had lower prevalence rates; and, in part, to differences in the applied diagnostic methods and criteria.

The studies just cited are regional in character. The other studies to be cited were derived from nationwide data.

The first study by the National Headquarters, Selective Service System, deals with the emergency period preceding World War II (November 1940 through September 1941); their second study deals with the period from April 1942 through December 1943. Both were sample studies.[5] The first study comprised some 122,000 medical examination reports; the second was based on an approximate 20 percent sample of over 9 million men examined during this period. Both studies indicate about identical prevalence rates of diabetes mellitus for the total (white and Negro) groups: 2.9 and 2.6 per 1,000 examined registrants, during the first and second periods, respectively. The corresponding rates, by period and race, were: 3.0 and 2.9, per 1,000 white; and 1.9 and 0.8, per 1,000 Negro examinees.

The quoted Selective Service data are from tables showing prevalence rates of all defects, without distinguishing between defects of a disqualifying and of a nondisqualifying nature. Though MR (Mobilization Regulations) 1-9, War Department, 1940, 1942, 1943, and 1944, provide that diabetes mellitus, if so diagnosed is disqualifying, it is possible that these rates include some borderline cases of diabetes which would not have been considered disqualifying.

The study by Karpinos [6] is limited to cases in which diabetes mellitus was either the principal or, at least, the secondary cause of disqualification. (It excludes defects of a nondisqualifying nature.)

This study covers a 14-month period from November 1943 through December 1944. It was a sample study, containing some 384,000 physical examination forms. According to this study, the disqualification rate for diabetes mellitus was 1.2 per 1,000 total (white and Negro); 1.3 per 1,000 white and 0.4 per 1,000 Negro examinees.

The total prevalence of disqualifying diabetes mellitus, which includes both principal and secondary cases of disqualification, was somewhat higher; namely, 1.3—per 1,000 total (white and Negro); 1.4—per 1,000 white, and 0.5—per 1,000 Negro examinees.

Race and age differentials.—The cited studies clearly indicate race and age differences. The disqualification rates for diabetes mellitus were by far lower among Negroes than among whites. The prevalence increases with age (table 52). For example, in the total group (white and Negro), the prevalence increased from 0.8 in the youngest (18-19) age group to 2.7 in the oldest (35-37) age group. The same holds by race.

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[5] See footnote 1 (1) and (2), p. 293.
[6] See footnote 1 (6), p. 293.

TABLE 52.—*Disqualifications of registrants for military service due to diabetes mellitus, by age and race, World War II*

[Rate expressed as number disqualified per 1,000 registrants examined]

Age	Principal disqualifying defect			Prevalence of disqualifying defect		
	Total	White	Negro	Total	White	Negro
18 to 19	0.74	0.81	0.19	0.79	0.87	0.19
20 to 24	.71	.74	.52	.75	.79	.53
25 to 29	1.19	1.34	.35	1.24	1.39	.36
30 to 34	1.61	1.84	.34	1.73	1.95	.48
35 to 37	2.44	2.63	1.30	2.68	2.85	1.70
Total	1.20	1.32	0.45	1.28	1.40	0.53

Source: Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscrip t form). Medical Statistics Division, Office of The Surgeon General, Department of the Army. (This study covers the period from November 1943 through December 1944.)

Number disqualified for diabetes mellitus.—The National Headquarters Selective Service System,[7] estimated that, of the total number of registants (4,828,000) in class IV–F and in classes with "F" designation, 45,300 registrants were so classified because of endocrine diseases. It has been found from the 1943–44 Selective Service experience [8] that some 42.7 percent of the endocrine diseases are cases of diabetes mellitus. Accordingly, some 19,300 registrants were seemingly classified as IV–F, as of 1 August 1945, because of diabetes mellitus. This constitutes a disqualification rate of about 1.2 per 1,000 examinees, as indicated by the rate limited to disqualifying diabetes mellitus (Karpinos, table 51).

The IV–F figures exclude examinees disqualified by the local boards, given in the IV–F table [9] as "Manifestly Disqualifying Defects," without a diagnostic breakdown. It has been estimated that, if the cases disqualified by the local boards for diabetes mellitus were added to the number of registrants classified as IV–F because of this disease as a result of the induction station examinations, the adjusted number would be 23,500.[10]

The overall disqualification for diabetes mellitus in World War II was thus apparently 1.5 per 1,000 examinees.

[7] Physical Examinations of Selective Service Registrants in the Final Months of the War. Medical Statistics Bulletin No. 4, National Headquarters, Selective Service System, Washington, D.C., June 1946, app. B, table 4.

[8] Physical Examination of Selective Service Registrants During Wartime. Medical Statistics Bulletin No. 3, National Headquarters, Selective Service System, Washington, D.C., 1 Nov. 1944, app. C, table 5.

[9] See footnote 7.

[10] The estimate of cases of diabetes mellitus among the "Manifestly Disqualifying Defects" was made by the Medical Statistics Division, Office of The Surgeon General, Department of the Army, from diagnostic data of local board disqualifications.

INCIDENCE, DISPOSITION, AND MORTALITY

World War I

Experience with diabetes mellitus in World War I, in the total Army with an average strength of 1,500,000 for the war period,[11] is summarized in the tabulation which is to follow. During this period, from 1 April 1917 to 31 December 1919, which was before the discovery of insulin, the mortality was 14.5 percent, or one death for each seven admissions.

Summary of data:	Absolute numbers	Rate per 1,000 men [1]
Admissions [2]	718	0.17
Days lost [3]	39,062	.03
Deaths [4]	104	.03
Discharges for disability	330	.08

[1] Number per annum, except that "Days lost" represents the number noneffective daily.
[2] By original cause of admission.
[3] Average days lost per case: 54.
[4] Percent of admissions: 14.5.

In the First World War, General Hospital No. 9, Lakewood, N.J., was designated to receive all diabetic patients from the eastern part of the United States and those evacuated from overseas. Actually, from July 1918 to May 1919, only 37 cases were treated.[12]

World War II

Essential data.—It is not the purpose of the present account to give detailed statistics on the incidence of diabetes in the Second World War, since these are to be found in complete tables elsewhere. However, enough data [13] will be presented to give some idea of the number of soldiers affected. In table 53, the most significant figures are shown.

It will be noted that the annual rates of admission to medical treatment facilities per 1,000 strength were 0.28 in 1941, 0.34 in 1942, 0.28 in 1943, and 0.23 in 1945, with the latter year having an average strength of approximately 7½ million men. The rate for 1944 was only 0.19 for approximately 8 million soldiers. The last figure is close to that of 0.17 for the Army with its strength averaging 1½ million men in World War I. Considering primary and secondary diagnoses, the incidence rate for 1944 was 0.23 per 1,000 and for 1945 it was 0.28 per 1,000, compared to admission rates of 0.19 and 0.23 per 1,000, respectively.

[11] The Medical Department of the United States Army in the World War. Washington: Government Printing Office, 1925, vol. XV, pt. 2.

[12] Allen, F. M., and Mitchell, J. W.: Report of Diabetic Service at U.S. Army General Hospital No. 9, Lakewood, New Jersey. Am. J.M. Sc. 159: 25, January 1920.

[13] All data from World War II (except those on pages 300–302 regarding diabetic coma) were furnished by the Medical Statistics Division, Office of The Surgeon General, Department of the Army.

TABLE 53.—*Summary of data on diabetes* [1] (*primary diagnosis* [2]), *in World War II, 1941–45*

[Preliminary data based on sample tabulations of individual medical records]

Year	Admissions [2]		Military disposition [3]		Deaths [3]	
	Number	Annual rate per 1,000 men	Separated for disability (percent)	Returned to duty (percent)	Number	Percent of admissions
1941	379	0.28			2	0.5
1942	1,110	.34	74.2	24.8	8	.7
1943	1,915	.28	75.0	22.5	21	1.1
1944	1,463	.19	76.4	22.3	15	1.0
1945	1,770	.23	77.7	[4] 10.2	15	.9

[1] Includes diabetic coma and diabetic gangrene.

[2] Includes only cases admitted to medical treatment facilities with a primary diagnosis of diabetes. For a summary of cases admitted with a primary diagnosis other than diabetes, see page 297.

[3] Figures are those of eventual death or disposition, not necessarily in the calendar year of admission.

[4] Approximately 11 percent of the 1945 admissions were separated for nonmedical reasons. This, for the most part, accounts for the difference between the percent of duty dispositions in 1945 and that of preceding years.

As may be seen in table 53, approximately three-fourths of the soldiers with diabetes were separated for disability.[14] Most of the remaining soldiers were retained in the service, presumably because they either had mild diabetes or were key personnel.

Of especial interest is the mortality, as shown in table 53. Of patients admitted with the primary diagnosis of diabetes from 1941 through 1945, death occurred in a minimum of 0.5 percent to a maximum of 1.1 percent, as contrasted with 14.5 percent in World War I (p. 297). Actually, however, there were more deaths due to diabetes in World War II than table 53 would suggest, since some were the underlying cause of death in cases originally admitted with another primary diagnosis. (Conversely, in the deaths summarized in table 53, diabetes mellitus need not necessarily have been the underlying cause of deaths.) Deaths (1942–45) attributable to diabetes according to the calendar year of death without regard to the year of admission, or the original cause of admission to the hospital, were as follows: 1942, 8; in 1943, 20; in 1944, 23; and in 1945, 15. Adding the 2 deaths in 1941 (table 53) brings the total to 68 deaths. Although the number was small, it would appear overly large for the age group concerned.

Race.—In view of the frequently expressed opinion that diabetes is less common in Negroes than in white people, the data in table 54 are of interest. It is evident that diabetes was at least as common among Negro as among white enlisted men, taking into account the much smaller numbers of Negro soldiers.

[14] The percentages, shown in table 53, for those separated for disability are somewhat understated, and conversely the percentages of duty dispositions somewhat overstated, as the result of coding as duty disposition cases which were returned to duty pending separation for disability.

Rank.—The admission rate for officers was consistently higher than that for enlisted personnel (table 55). It should be kept in mind that among commissioned officers there was a higher percentage of older men, in whom diabetes is more common.

Age.—The influence of age upon incidence is shown in table 56. The rate per 1,000 rises from 0.09 at ages under 20 years to 1.60 for ages 45 and over.

TABLE 54.—*Admissions for diabetes mellitus[1] among male enlisted personnel, U.S. Army, by race and year, 1941–45*

[Rate expressed as number of admissions per annum per 1,000 average strength]
[Preliminary data based on sample tabulations of individual medical records]

Year	Total male enlisted		White [2]		Negro	
	Number	Rate	Number	Rate	Number	Rate
1941	337	0.27	321	0.27	16	0.25
1942	997	.33	896	.32	101	.49
1943	1,726	.28	1,504	.26	222	.42
1944	1,188	.17	1,037	.16	151	.23
1945	1,417	.21	1,246	.21	171	.27

[1] Includes diabetic coma and diabetic gangrene.
[2] Includes all non-Negroid personnel.

TABLE 55.—*Admissions for diabetes mellitus,[1] U.S. Army, by rank and year, 1941–45*

[Rate expressed as number of admissions per annum per 1,000 average strength]
[Preliminary data based on sample tabulations of individual medical records]

Year	Total Army		Officers		Enlisted personnel	
	Number	Rate	Number	Rate	Number	Rate
1941	379	0.28	42	0.49	337	0.27
1942	1,110	.34	113	.50	997	.33
1943	1,915	.28	184	.32	1,731	.27
1944	1,463	.19	241	.32	1,222	.17
1945	1,770	.23	343	.40	1,427	.21

[1] Includes diabetic coma and diabetic gangrene.

Sex.—The number of admissions for diabetes among female personnel amounted to only 2 in 1941, none in 1942, 12 in 1943, 44 in 1944, and 30 in 1945. The annual admission rate for women per 1,000 persons in 1943 was 0.15; in 1944, 0.44; and in 1945, 0.21.

Theater.—Throughout the war, the admission rate for diabetes reported from oversea theaters was appreciably less than that reported from the continental United States. Illustrative are the data for 1944

TABLE 56.—*Admissions for diabetes mellitus,*[1] *U.S. Army, by age, 1944*

[Rate expressed as number of admissions per annum per 1,000 average strength]
[Preliminary data based on sample tabulations of individual medical records]

Age	Admissions	
	Number	Rate
Under 20	62	0.09
20–24	386	.13
25–29	364	.17
30–34	241	.21
35–39	246	.41
40–44	57	.56
45 and over	107	1.60
Total	1,463	.19

[1] Includes diabetic coma and diabetic gangrene.

shown in table 57. Undoubtedly, an important factor in the difference was the screening out of those unable to meet medical standards for oversea service. Another factor may have been that personnel overseas usually were more active physically and often had a lower caloric intake. Again, probably fewer of the older men were included among them.

Average duration.—The average length of stay in medical facilities for patients with diabetes was slightly under 2 months. The actual figures were: In 1941, 59 days; in 1942, 58 days; in 1943, 58 days; in 1944, 55 days; and in 1945, 72 days (table 59, p. 305). In evaluating the duration of hospital care in terms of time lost, it must be kept in mind that approximately three-fourths of the diabetics were separated from service. The time in hospital was spent not only in regulation of the diabetic condition with diet and insulin, if indicated, and in instruction to prepare the patients for return to civilian life, but also in effecting the separation itself.

DIABETIC COMA

In December 1945, the files of the Army Institute of Pathology, Washington, D.C., were examined to ascertain the number of deaths from diabetic coma reported since September 1940. Although not all of the autopsy reports for 1945 had been received, study of the available material proved to be instructive.

In all, there were 60 reported deaths from diabetic coma in Army or other personnel treated in Army hospitals. These were distributed as follows: 33 Army personnel, 1 sailor, 1 marine, 3 retired military personnel, 5 beneficiaries of Veterans' Administration, 2 Civilian Conservation Corps

TABLE 57.—*Incidence of diabetes in the U.S. Army, by area and year, 1944*

[Rate expressed as number of cases per annum per 1,000 average strength]

Area	Incidence [1]	
	Number of cases	Rates
Continental United States	1,300	0.33
Overseas:		
North America [2]	19	0.15
Latin America	21	.24
Europe	179	.10
Mediterranean [3]	101	.16
China-Burma-India	16	.09
Central and South Pacific	99	.23
Southwest Pacific	58	.11
Middle East	13	.28
Total overseas [4]	503	0.13
Total Army	1,803	0.23

[1] Includes primary and secondary diagnoses.
[2] Includes Alaska and Iceland.
[3] Includes North Africa.
[4] Includes 6 cases on transports.

enrollees, 10 civilian dependents, and 5 (3 German, 2 Italian) prisoners of war.

In examining the data, it soon became evident that there was a difference in the type of patient in the 33 cases grouped as Army personnel in comparison with the 27 cases otherwise grouped. Since the majority of the latter were chiefly retired military personnel, beneficiaries of the Veterans' Administration, and civilian dependents, they included persons in the older age periods. A high percentage of them had had known diabetes of variable duration, and the terminal diabetic acidosis was often associated with complications serious enough in themselves to cause death. Accordingly, the following is a commentary only on the 33 deaths from diabetic coma of persons on active duty in the Army:

Of these, 32 were men and 1 was a young enlisted woman; 32 were enlisted personnel and 1, an officer. The age at death ranged from 18 to 38 years, inclusive. The length of time in the Army ranged from 2 days to 2 years; only 3 had been in service 12 months or more. Three died in hospitals overseas, one on a troop transport, and twenty-nine in hospitals in the continental United States.

Only three were patients with previously known diabetes. These soldiers entered hospitals in diabetic coma 2 days, 1 month, and 2 months,

respectively, after induction into the Army. Two concealed the fact that they had diabetes; an adequate history is lacking regarding the third.

Of the 33 patients, 21 died in less than 48 hours after admission to the hospital, 14 of them during the first day. The symptoms and signs in most instances were classical, as were also the laboratory findings. Of 16 patients whose mental state on admission was recorded, 8 were unconscious and 4 were drowsy. In 10 of the 33, the blood sugar was 500 mg. per 100 cc. or higher. In only 9 of the 33 cases did necropsy disclose associated conditions of importance; that is, in the great majority death occurred from uncomplicated diabetic coma. It is of note that in seven of the nine patients with complications, acute pancreatitis of varying degree was recorded by the pathologist.

Once the diagnosis was made in the Army hospital, treatment was in general reasonably adequate, although not infrequently much larger doses of insulin were indicated than were given. The chief difficulty lay in the fact that often there was considerable delay in making the diagnosis, owing chiefly to the length of time—in some instances several hours—that elapsed before analyses of urine and blood were carried out and reported. It will be recalled that 29 of the 33 deaths under consideration occurred not overseas but in the continental United States, where ample facilities should have existed, and almost invariably did exist, for prompt diagnosis and early institution of energetic treatment. Furthermore, in the age group concerned, the mortality from diabetic coma should approach zero. Accordingly, although relatively few deaths from diabetic coma occurred in World War II, even fewer might have been expected had diagnoses been more promptly made and followed by vigorous treatment with insulin.

Promptness in diagnosis depends upon the alertness, interest, and industry of the individual ward surgeon. The examination of the urine for sugar and acetone should be carried out immediately on admission. Such tests are simple and, if necessary, can be made easily on the ward by the physician or nurse. Furthermore, a simple and quick nitroprusside test for acetone (using, if desired, commercially prepared powder or tablets) can be carried out directly on the plasma by the physician as an aid in diagnosis. If positive, the degree of ketonemia may be used as a rough guide in determining the initial dose of insulin.

NONDIABETIC GLYCOSURIA

Persistent glycosuria of significant degree (0.5 percent or more in random specimens) was commonly considered disqualifying for military service even though not caused by diabetes. This was generally agreed to be a desirable rule even with benign, symptomless glycosurias. This seeming paradox is explained by what might be termed the "nuisance value" of such conditions. Whenever the soldier with glycosuria came under Medical Department supervision and sugar was found in the urine, the medical officer concerned—most probably unacquainted with the pa-

tient—was likely to decide that the condition warranted admission to the hospital for special studies. This might be repeated over and over, with inconvenience to the soldier and expense to the Government. A simple solution might have been to issue the soldier a statement to carry with him, explaining his condition. However, this would still leave the medical officer in reasonable doubt whether the presenting condition might not be different from that prevailing at the time of last study. Moreover, it is unlikely that soldiers would preserve and carry such papers over a long period of time.

Once the man was in the Army, and persistent, but nondiabetic, glycosuria of significant degree was found, decision as to disposition was, at times, difficult. In actual practice in World War II, the great majority of such men were retained in the service. As shown in table 58, no more than 16.5 percent were separated for disability in any year and usually considerably less. In general, key personnel could be, and were, retained with profit.

TABLE 58.—*Summary of data for nondiabetic glycosuria [1] in World War II, by year, 1941–45*

Year	Admissions [2]		Treatment	Disposition	
	Number	Annual rate per 1,000 average strength	Average duration (days)	Separated for disability (percent)	Returned to duty (percent)
1941	176	0.13	22		
1942	420	.13	18	6.0	94.0
1943	923	.13	25	16.5	82.3
1944	699	.09	20	5.3	94.7
1945	635	.08	19	0	98.4

[1] Includes renal glycosuria and alimentary glycosuria.
[2] Primary diagnosis only.

TREATMENT OF DIABETES IN THE ARMY

Success in the treatment of diabetes in the Army, as in civilian practice, depends upon the interest, training, and experience of the individual doctor perhaps more than in most diseases. The inadequate treatment of diabetic coma in certain cases has been commented on. Since there are varying opinions both in military and civilian practice on details regarding diet, insulin, and other aspects of therapy, it became apparent in World War II that some attempt should be made to standardize methods of diagnosis and treatment. Consequently, War Department Technical Bulletin (TB MED) 168, entitled "Diabetes Mellitus," was prepared by Col. Garfield G. Duncan, MC, and released in June 1945. In this bulletin,

the basic principles of the diagnosis and treatment of diabetes and its complications were outlined for the guidance of medical officers.[15]

Certain features of the care of diabetic patients and of the military physician's responsibility for them deserve special mention at this point. First, medical officers should realize the vital importance of the education of patients. If the greatest success in treatment is to be realized in length of life and freedom from complications, patients must be taught simply, yet thoroughly, known facts regarding diabetes, its home care and the avoidance of complications. Secondly, treatment with a restricted, yet nutritionally adequate, diet and an appropriate dose of insulin must be arranged so that careful and continuous control of the disease is possible. Thirdly, the patient must be urged to seek competent medical advice at frequent and regular intervals following discharge from the service, either from a private physician or from the Veterans' Administration.

THE PLACE OF THE DIABETIC IN THE ARMY

Regulations of the Army and of mobilization boards in effect throughout World War II listed diabetes mellitus as a cause for rejection even for limited service. Altshuler [16] questioned the advisability of this. He recommended that at least some individuals might be accepted to the advantage of the Armed Forces and that those accepted could perform useful duty at fixed installations in continental United States. The opposite point of view was taken by Joslin,[17] who concluded:

The diabetic quota useful for military service is relatively so insignificant, the hazards which both the diabetic and the Government would undergo if they were inducted are so great and the need for their services in civilian occupations, where they would be less exposed to complications, so apparent, that the present rule to omit them from the draft appears proper.

Table 59 shows the days lost in World War II by cases admitted for diabetes during the years 1942–45.

Considered as a loss of more than 1,000 person-years, the figures in table 59 present a cogent argument in favor of maintaining the general policy of rejecting those with diabetes. It has been noted (p. 300) that much of the time spent in hospital was incidental to separation from the service of approximately three-quarters of the diabetics found.

Although the general rule is fully justified, provision should be, and has been, made for exceptions [18] to it, when individuals are needed in assignments in which appropriate treatment (with diet and, if required, insulin) is feasible. Such posts may be available in fixed installations, usually in continental United States. Similarly, both officers and enlisted

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[15] It should be noted that certain new measures in treatment have become generally available since 1945; for example, in October 1950, NPH insulin was admitted to the market, and in 1954, Lente insulin became available.

[16] Altshuler, S. S.: Diabetes in the Armed Services. Proc. Am. Diabetes A. (1944) 4: 111–118, 1945.

[17] Joslin, E. P.: Diabetes and Military Service. J.A.M.A. 121: 198–199, 16 Jan. 1943.

[18] For example, the Defense Department's directive of 12 January 1953 on special registrants under the "Doctors' Draft Law" (24 Dec. 1952) provides that physicians with diabetes may be accepted for service under certain conditions.

personnel in whom diabetes has been discovered while in the service may, with profit, be retained, especially those who are in scarce categories or those who are otherwise hard to replace.

TABLE 59.—*Days lost by cases admitted for diabetes, by year, 1942–45*

Year	Average duration of treatment [1] (days)	Total days lost
1942	58	64,650
1943	58	106,989
1944	55	79,189
1945	72	127,350
Total	61	378,178

[1] Based only on cases with days lost from active duty.

CHAPTER XII

Diseases of the Gastrointestinal Tract

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Napoleon's dictum concerning the relation between military effectiveness and the gastrointestinal tract remains valid. An army still marches on its stomach, despite improvements in mechanized transportation in modern warfare.

Before full mobilization of U.S. military forces, reports came from British [1] and Canadian [2] as well as from German [3] sources, indicating the seriousness of disturbances of the gastrointestinal tract in both garrison and field troops. British reports indicated that the chief cause of illness in their expeditionary force in France was dyspepsia. This term was used to include both organic and functional disturbances of digestion, with an incidence of peptic ulcer of approximately 50 percent. Of all medical cases in large British hospitals, 20 percent were found to have dyspepsia.[4] In England, this high percentage was not reflected in the civilian population, although, during the period of large air raids,[5] there was an increase in the complications of peptic ulcer, such as perforation and bleeding. Although no definite statistics were available concerning the incidence of peptic ulcer among German military forces, several observers concluded that it had increased during 1942 and 1943.[6] In the population of Germany, in contrast to civilian England, there was an apparent increase in gastrointestinal disorders, as attested by the figures of 16.2 percent of all admissions to one large Berlin hospital, compared to 6.5 percent before the war.[7]

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[1] Graham, J. J., and Kerr, J. D. O.: Digestive Disorders in the Forces. Brit. M.J. 1: 473–476, 29 Mar. 1941.

[2] Urquhart, R. W. I., Singleton, A. C., and Feasby, W. R.: The Peptic Ulcer Problem. Canad. M.A.J. 45: 391–395, November 1941.

[3] Geronne, A.: Ueber das Ulcus Pepticum im Kriege mit Bemerkungen zu seiner Pathogeneses und Therapie. Deutsche med. Wchnschr. 69: 121–126, February 1943 [Abstract *in* Bull. War Med. 4: 39, September 1943.]

[4] Tidy, H. L.: Dyspepsia in the Forces. Proc. Roy. Soc. Med. 34: 411–417, May 1941; also J. Roy. Army M. Corps 77: 113–122, September 1941.

[5] Stewart, D. N., and Winser, D. M. de R.: Incidence of Perforated Peptic Ulcer: Effect of Heavy Air-Raids. Lancet 1: 259–261, 28 Feb. 1942.

[6] See footnote 3.

[7] Brühl, W.: Die Behandlung des Ulcus und der Gastritis im Kriege. Klin. Wchnschr. 21: 951–954, 24 Oct. 1942. [Abstract *in* Bull. War Med. 3: 338–339, February 1943.]

ORGANIZATION AND EARLY FINDINGS

In 1917, a committee from the Section of Gastroenterology and Proctology of the American Medical Association suggested to The Surgeon General that a section of gastroenterology should be created in the Division of Internal Medicine.[8] In accordance with this recommendation, experienced gastroenterologists were soon assigned to the various base hospitals in the United States, and a section of gastroenterology was included in the official tables of organization for general hospitals. In 1940, this was amplified to include the authorization of a gastroenterologist in all station hospitals with more than 800 beds. The American Medical Association's Committee on Military Preparedness, as well as the American Gastroenterological Association, prepared lists of qualified men recommended for active duty. However, the number of internists with special training in gastroenterology thus made available was far from adequate to meet the requirements.

Among registrants.—The procedure of the examining physicians on selective service and Army induction boards was governed by MR (Mobilization Regulations) 1–9, issued by the War Department. The mounting incidence in Army hospitals of soldiers with organic digestive diseases, the onset of which antedated their military life, made it evident that during the early period of mobilization registrants with disqualifying digestive disorders were not being adequately screened. In the majority of cases, the histories obtained were grossly inadequate. Some men, motivated by a desire to serve regardless of disqualifying disease, withheld medical data. Others, in spite of a history of organic disease substantiated by hospital records, were told that the Army could make adequate provision for their disability in service.

In Army hospitals.—In the Zone of Interior, station hospitals, serving large groups of men in various phases of training shortly after induction, had approximately 3 to 6 percent of all admissions in the gastroenterologic section. Moreover, these figures did not include all those with gastrointestinal symptoms, since many with functional disorders were admitted to other sections of the hospital, such as the neuropsychiatric or general medical sections. The vast majority of these men had not yet been in combat, but they were sufficiently far removed from civilian life to feel the impact of the mental and physical problems involved in such a separation. Furthermore, a review of many studies from various Army hospitals in the United States soon disclosed that, in approximately 90 percent of patients with peptic ulcer, either an actual diagnosis had been made before induction or the symptoms were so characteristic at the time of induction that the diagnosis should have suggested itself to ex-

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[8] Kantor, J. L.: Digestive Disease and Military Service, With Special Reference to the Medical Department of the United States Army. J.A.M.A. 120: 254–261, 26 Sept. 1942.

amining physicians.[9] Some improvement was brought about by directives making it possible for induction boards to hospitalize, for a period not exceeding 3 days, any registrant who, in the opinion of the examining physician, required special study of the gastrointestinal tract.

In discussing digestive disorders among British soldiers, Hurst [10] suggested three subdivisions for the gastroenterologic section in an army hospital. Division A was to be a diagnostic ward, where patients would be kept until the diagnosis was definitely established; division B was to be reserved for patients suffering from confirmed organic disease; and division C, for those with functional dyspepsia. Such subdivisions were found to be useful in Army hospitals and were generally adopted where adequate facilities were available.[11] This distinction prevented possible alterations in a history of functional disease by a patient in contact with patients with organic disease. It prevented groups who were being separated from the service from emphasizing to others the amount of secondary gain to be derived from the persistence of symptoms.

Evaluation of data.—In evaluating the significance of statistics for organic and functional cases of dyspepsia derived from station and from general hospitals, the differences in the sources of admission to these two types of institution must be borne in mind. Until the facilities of general hospitals in the United States were reserved for treatment of oversea casualties only, these hospitals had served as the final point in the channel of evacuation in the Zone of Interior, and only those individuals offering special problems in treatment or administration were referred to them. Accordingly, patients with functional disorders were seldom seen in general hospitals. This distinction is reflected in a higher relative incidence of organic to functional disorders of the gastrointestinal tract in these hospitals.

In weighing the statistical evidence, variables in clinical interpretation must also be taken into account, particularly in the early reports.

There are many dissimilarities between medical practice in the Army and in civilian life, which alter the usual relationship between patient and physician. These had to be borne in mind in evaluating the patient's history and response to therapy, as well as in deciding his ultimate disposition. The transition to military service proved extremely difficult for many medical officers. Throughout the physician's civilian career, the individual patient had remained the center of his medical attention, and the establishment of

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[9] (1) Berk, J. E., and Frediani, A. W.: The Peptic Ulcer Problem in the Army. Gastroenterology 3: 435–442, December 1944. (2) Chamberlin, D. T.: Military Gastro-Enterology; The First Year. South. M.J. 36: 523–528, July 1943. (3) Flood, C. A.: Peptic Ulcer at Fort George G. Meade, Md. War Med. 3: 160–170, February 1943. (4) Kirk, R. C.: Peptic Ulcer at Fort Sill. Am. J. Digest. Dis. 10: 411–413, November 1943. (5) Loder, H. B., and Kornblum, S. A.: Duodenal Ulcer in a Large Army Camp; Incidence and Statistical Analysis. Mil. Surgeon 96: 492–497, June 1945. (6) Magnes, M.: A Gastro-Intestinal Outpatient Service. Bull. U.S. Army M. Dept. 85: 99–103, February 1945. (7) Schildkrout, H.: Management of Dyspeptic Soldier in a Staging Area. War Med. 6: 151–157, September 1944. (8) Thomas, H. M., Jr.: Peptic Ulcer in the Army. South. M.J. 36: 287–291, April 1943. (9) Zetzel, L.: Experiences With Peptic Ulcer in an Army Station Hospital. Gastroenterology 3: 472–479, December 1944.

[10] Hurst, A.: Digestive Disorders in Soldiers. Am. J. Digest. Dis. 8: 321–323, September 1941.

[11] See footnote 9 (9).

a definitive diagnosis, as an indispensable preliminary step in treatment, was a constant goal. It was often difficult to adjust himself to the change engendered by the emergency, which emphasized the rapidity with which the maximum number of soldiers might be restored to military effectiveness, with necessarily less regard for the immediate effect upon the individual.

The patient in military service was not able to choose his physician but found himself under the care of a stranger whose only mark of proficiency in his eyes was the dubious one of rank. The young and inexperienced medical officer often reacted to this apparent lack of confidence by ordering numerous investigations. In civilian practice, a patient's response to various dietary regimens may be observed diagnostically without radically altering his occupation. But the soldier had to be hospitalized for such studies, at the risk of impairing his eventual military effectiveness. The medical officer soon became aware of the greater responsibility imposed upon him by his authority to make radical changes in the patient's environment, even to the extent of returning him to civilian life. He learned to rely upon an adequate history and physical examination, ordering special studies when these were indicated by the clinical evidence.

To some extent the relative incidence, in the hospital census, of organic to functional disturbances of the gastrointestinal tract, varied with the clinical acumen of the examining physician. As this was sharpened by experience, the variable factor was correspondingly reduced.

PEPTIC ULCER

Incidence

Many of the factors influential in initiating symptoms of peptic ulcer could be found in the various aspects of Army life.[12] In susceptible persons, a combination of factors—physical exhaustion, overt anxiety, and irregular meals of unpalatable food, plus a rebellious attitude caused by forced idleness—produced the aberrations of gastric physiology associated with the clinical picture of peptic ulcer. On the basis of available studies, however, the incidence of peptic ulcer in the Army was in large part a reflection of the incidence of this disorder in the adult population [13] (table 60). It has been noted (p. 308) that, in approximately 90 percent of patients with ulcer first seen in station and general hospitals in the United States, the symptoms antedated the patient's induction into the service. Accordingly, these statistics cannot be interpreted as evidence against the thesis that the emotional problems and physical hardships of Army life, at least for troops in the Zone of Interior, were insufficient to produce symptoms of ulcer in most men, except those so predisposed during their civilian existence (see pp. 313–317).

After many of the patients with ulcer had been eliminated during the various phases of training leading to oversea duty, it was not surprising that in the combat zone the percentage of those with "old" ulcers dropped to 50 percent of the total number with ulcer. Although theo-

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[12] See footnote 9 (9), p. 309.

[13] Wolf, S., and Wolff, H. G.: Evidence on the Genesis of Peptic Ulcer in Man. J.A.M.A. 120: 670–675, 31 Oct. 1942.

TABLE 60.—*Admissions for ulcer of the duodenum and stomach in the U.S. Army, pre-World War II and World War II, by area and year, 1937–41 and 1942–45, respectively*

[Rate expressed as number of admissions per annum per 1,000 average strength]

Area and year	Duodenal ulcer		Stomach ulcer	
	Number of cases	Rate	Number of cases	Rate
1937–41				
Total areas_____	4,606	2.06	907	0.41
1942–45				
Continental United States_____	49,979	3.39	4,709	0.32
Overseas_____	13,774	1.28	1,465	.14
Total Army_____	63,753	2.50	6,174	0.24

retically all of these should have been rejected before embarkation, such a goal could only be approximated, since many either had mild symptoms or had concealed them. According to a survey conducted in MTOUSA (Mediterranean Theater of Operations, U.S. Army), the incidence of peptic ulcer from September 1944 to April 1945 was 2.04 per 1,000 per annum, or only 1 per 1,000 whose symptoms first came on after induction.[14] If one is to evaluate properly the effect of Army life—especially under field and combat conditions overseas—in the production of peptic ulcer, it would be useful to compare this figure of 1 per 1,000 with that for ulcer in a similar age group in civilian life, such as registrants for selective service between the ages of 21 and 36. Among 19,923 registrants, of whom all but 2.1 percent were in this age group, 4.4 per 1,000 were rejected for peptic ulcer.[15] Since this statistical sample of registrants covers a period (November 1940 through May 1941) when many cases escaped detection before induction, this figure (4.4 per 1,000) is probably too low, but it is, nonetheless, conspicuously higher than the incidence (1 per 1,000) of ulcers first manifested during military service. It should be noted also, in making this comparison, that there was a lack of reliable data about the interval of time during which the civilian registrants developed their ulcers.

During World War I, from 1 April 1917 to 31 December 1919, the reported incidence of peptic ulcer among all the troops was only 0.68 per 1,000 per annum.[16] Better diagnostic technique subsequently made

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[14] Report, Head, D. P., Wilen, C. J. W., and Fradkin, N. F., to Surgeon, MTOUSA, subject: Survey of the Peptic Ulcer Problem in MTOUSA, 1943–45.

[15] Analysis of Reports of Physical Examination: Summary of Data From 19,923 Reports of Physical Examination. Medical Statistics Bulletin No. 1, National Headquarters, Selective Service System, Washington, D.C., 10 Nov. 1941.

[16] The Medical Department of the United States Army in the World War. Washington: Government Printing Office, 1925, vol. XV, pt. 2, p. 578.

available probably contributed to the apparent increase in incidence in World War II (table 60).

One of the most intensive surveys was that made in the Mediterranean theater from 1943 to 1945. The diagnosis was peptic ulcer in 0.54 percent of dispositions made on 272,026 patients in 11 general hospitals. This is in contrast to the average incidence of 3.5 percent of the total number of admissions to general hospitals in the Zone of Interior. Of 211,534 dispositions made in 21 station hospitals in the Mediterranean theater, 0.27 percent were for peptic ulcer.

In examining patients with complaints referable to the upper quadrant of the abdomen, many variable factors might be expected in clinical interpretation and roentgenographic confirmation. Nevertheless, the reported percentages of peptic ulcer found were remarkably constant. In large station hospitals in the United States, the average was 10 percent, varying from 7.2 to 12.9 percent. For reasons previously mentioned, the incidence of peptic ulcer in general hospitals in the Zone of Interior was much greater—approximately 30 percent of patients with complaints referable to the upper quadrant of the abdomen. The corresponding figures for station and general hospitals in the Mediterranean theater were 5.9 and 10.2 percent, respectively (p. 322). These figures are strikingly similar to those reported by Eusterman and Balfour [17] who found 13 percent of ulcers among 16,000 civilian patients whose gastrointestinal symptoms warranted roentgenographic examination.

During the North African campaign, hospital staffs were commonly impressed by a higher incidence of peptic ulcer than was subsequently found in the entire theater. This may have been caused by the poor diets prevalent during the early stages of this campaign, but more probably it reflected the poor screening of men for shipment overseas in the early days of the war. In support of this opinion were the findings of Halsted and Weinberg [18] at the Fifth U.S. Army Gastrointestinal Clearing Center (p. 318) in Italy between 1944 and 1945, showing an incidence of peptic ulcer of only 3.4 percent of 183 combat infantrymen with chronic epigastric distress. At this later date, screening before embarkation had been greatly improved, and the men sent into combat represented a better selected group.

Diagnostic Techniques and Criteria

History and roentgenograms.—The diagnosis of peptic ulcer was usually made on the basis of a characteristic history, favorable response to a proper therapeutic regimen, and confirmatory roentgenographic evi-

[17] Eusterman, George B., and Balfour, Donald C.: Stomach and Duodenum. Philadelphia: W. B. Saunders Co., 1935, p. 259.

[18] Halsted, J. A., and Weinberg, H.: Peptic Ulcer Among Soldiers in the Mediterranean Theater of Operations. New England J. Med. 234: 313–320, 7 Mar. 1946.

dence of an actual niche or persistent deformity in the stomach or the duodenum. The typical history of dull, gnawing epigastric pain, occurring from 30 to 90 minutes after meals, frequently waking the patient from his sleep, relieved by food, periodic in type, with remissions of variable length, was obtained in approximately 80 percent of patients.[19] An atypical history was usually obtained in younger soldiers who had had symptoms of relatively short duration. The longer history of ulcer, the more classical were its features. Repeated hospitalization often resulted in the patient's history assuming a more typical form, possibly on the basis of frequent discussion with patients with proved ulcer. Therefore, unless the history was taken very early in the course of the disease, and immediately after admission to the hospital, its significance was dubious unless roentgenographic confirmation was available. For this reason, roentgenographic evidence was considered indispensable in most groups in which diagnosis of peptic ulcer was made.

Laboratory data.—The advisability of doing gastric analyses on all patients with digestive complaints was questioned by many observers.[20] In general, this procedure was not considered worth the effort unless there was roentgenographic evidence of a gastric ulcer; under this circumstance, the repeated absence of free hydrochloric acid after the administration of histamine would constitute strong evidence against the benign nature of the lesion. Otherwise, the degree of the acidity appeared to be of no significance in the diagnosis or the treatment of peptic ulcer. Gastric analysis, however, was defended by others[21] who believed that such an analysis, adequately performed, furnished information on gastric motility and on the presence of parasites in the gastric sediment.

Unless properly interpreted in relation to the clinical picture and the antecedent diet, the routine test for blood in the stools often led to unnecessary and prolonged hospitalization with increased anxiety on the part of the patient, which intensive investigation and subsequent negative findings often failed to allay.

Clinical Response—Psychogenic Factors

All reports, with one exception,[22] on patients with peptic ulcer treated

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[19] (1) See footnote 9, p. 309; footnote 13, p. 310; footnotes 14, 15, and 16, p. 311; footnotes 17 and 18, p. 312. (2) Rush, A.: Gastrointestinal Disturbances in Combat Area; Preliminary Observations on Peptic Ulcer. J.A.M.A. 123: 389–391, 16 Oct. 1943.

[20] See footnote 9 (4) (5) (9), p. 309; footnote 14, p. 311; footnote 18, p. 312; and footnote 19 (2). (2) Alvarez, W. C.: What Value Has Gastric Analysis? Gastroenterology 1: 534–536, May 1943. (3) Rosenak, B. D., and Foltz, L. M.: Digestive Diseases in a Station Hospital Overseas: Observations Over a Two-Year Period. Gastroenterology 4: 213–227, March 1945. (4) Schindler, R.: Gastroenterology in Army; Methods of Examination and Disposition of Cases. War Med. 2: 263–276, March 1942; correction 2: 504, May 1942.

[21] (1) Berk, J. E.: The Case for Gastric Analysis in Military Hospitals. Gastroenterology 1: 1064–1065, November 1943. (2) Chamberlin, D. T.: Gastric Analysis in an Army Hospital. Gastroenterology 1: 533–534, May 1943.

[22] See footnote 9 (3), p. 309.

either in the United States or overseas showed a satisfactory response to treatment.

Two groups of patients, in each of which approximately 10 percent had failed to respond well to the usual regimen, were studied, one by Cheney [23] the other by Gianelli and Bellafiore.[24] Most of the patients became asymptomatic for the first time on a diet to which had been added eggs, butter, peanut butter, lettuce, watercress, parsley, broccoli, romaine, and avocadoes — all foods said to be rich in anti–ulcer factor. This anti-ulcer factor was designated vitamin "U."

In general, the response to treatment was so rapid and so uniform that it served as one of the most important criteria in the differential diagnosis of peptic ulcer from functional dyspepsia. This prompt response is not in itself, however, evidence against the possible influence of psychogenic factors on the activity of an ulcer. When a soldier was admitted to a hospital, although the change in dietary management may have been the only tangible prescription in the physician's order book, there were many other changes from the conditions of his previous environment, including physical rest, relief from strict field discipline, and the knowledge that the most important hurdle to rehabilitation had been taken with the commencement of medical care.[25]

In the various theaters of World War II, there was afforded an opportunity to study the personality of patients with organic and functional dyspepsia and to evaluate the influence of the different aspects of their military life on the initiation or the aggravation of symptoms. The fact that in the Zone of Interior the symptoms of peptic ulcer had originated during civilian life in approximately 90 percent of the patients makes it easy to understand that those individuals differed very little from the usual patients with ulcer seen in civilian life. In contrast, the patient with ulcer who was first seen overseas may well have been an individual with an entirely different personality and physical constitution, since he had previously withstood the rigors of civilian life and life with the Army in the Zone of Interior without developing, or without admitting, symptoms of peptic ulcer.

Comparative studies.—A study of 200 consecutive patients with ulcer was conducted at the 6th General Hospital, Casablanca, in the North African theater, between March 1943 and January 1944, in an effort to determine whether the nervous tension of military life was a factor in the occurrence of the course of the disease.[26] These 200 patients represented one-third of all patients admitted to this hospital with digestive complaints during that period. Such a high rate of ulcers was explicable by the fact that the 6th General Hospital functioned as a final point in

[23] Cheney, G.: Peptic Ulcer and Nutrition. Mil. Surgeon 95: 446–454, December 1944.

[24] Gianelli, V. J., and Bellafiore, V.: Fundamental Importance of Diet in the Treatment of Peptic Ulcer in an Army General Hospital, With Special Reference to Vitamin "U" Therapy. M. Clin. North America 29: 706–713, May 1945.

[25] See footnote 9 (9), p. 309.

[26] See footnote 18, p. 312.

the chain of evacuation of Army personnel from overseas to the Zone of Interior and thus received a large quota of patients with ulcer in the North African theater. Later in 1944, the 6th General Hospital was moved to Rome, Italy, and it then received a different type of evacuee— one who was only a few days removed from the front. At that time (between 1 July and 1 November 1944), only 8 percent of the chronic dyspeptics were found to have ulcers.

The patient with ulcer, in the series of 200 cases, rarely volunteered information regarding the degree of his epigastric pain and seemed unconcerned with other somatic complaints. He was found to be aggressive, independent, and often anxious to return to duty after his original discomfort had been relieved. Only in response to direct questioning was a history obtained and then given in succinct, clear-cut fashion without elaboration. Admittedly, this examination of the patient's personality was superficial from the psychiatric point of view and more extensive investigation might well have disclosed important neurotic features. However, the observations are comparable, and the results in striking contrast, with observations made on functional dyspeptics, which were based on the same criteria. Only 5 percent of the 200 patients in this particular study overseas demonstrated definite psychoneurosis in association with peptic ulcer. This figure corresponds closely to the results (4.2 percent) obtained in the study of patients with peptic ulcer in the Mediterranean theater as a whole between 1943 and 1945.[27]

It should be noted that aside from these observations in which a special effort was made to study the association of the two conditions,[28] it is probable that any statistics gleaned from hospital records or disposition boards did not show the true incidence of this association, since there was a tendency on the part of ward officers to omit mention of functional disorders in the presence of well-established organic disease.

The patient with ulcer seen in the United States presented on the whole a totally different picture with reference to any associated neurosis. Flood's [29] figures of definite overt anxiety and psychoneurosis in at least 50 percent of his patients were fairly representative of findings in station hospitals. Again, in one large staging area in the United States, psychoneurosis was found in 23 percent of patients with ulcer.[30]

The objective data.—Thus, in men in whom peptic ulcer first appeared or became troublesome during military service, there was no striking correlation found between the organic disease and the psychopathic disorders. As to the incidence of ulcer under combat conditions, it has been noted (p. 311) that, in the Mediterranean theater from September 1944 to April 1945, it was only 1 per 1,000 in whom symptoms were first manifested after induction. Again, from 1943 to 1945, peptic ulcer

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[27] See footnote 14, p. 311.
[28] See footnote 18, p. 312.
[29] See footnote 9 (3), p. 309.
[30] See footnote 9 (7), p. 309.

accounted for 0.54 percent of dispositions of patients from 11 general hospitals and 0.27 percent of dispositions from 21 station hospitals in the Mediterranean theater. Moreover, the incidence of complications during military service was remarkably low, as reported from station hospitals, both in the United States and overseas. The average figure of many reports indicated the occurrence of gross hemorrhage or perforation in approximately 4 percent of peptic ulcers.[31] In general hospitals, the incidence of these complications was two to three times as high because of the selective nature of their patients.[32]

No radical departure in treatment of complications was introduced; thus for bleeding, conservative measures — such as gradual increases in a strict Sippy diet or various modifications of a full Meulengracht diet — were employed with excellent results. The mortality for perforated ulcers was very low because, undoubtedly, a select group of patients — in relation to their general physical condition and the ready availability of treatment — was involved.

Evaluation of evidence.—The reason advanced by most patients for the onset or the recurrence of their digestive symptoms was inability to tolerate Army rations. In many instances, however, these symptoms actually began at the port of embarkation or while the men were being transported overseas, at a time, that is, when their food was satisfactory both in quality and in quantity. Many of the men ate field rations without developing complaints under conditions of oversea activity, until they experienced additional strain, such as repeated air raids.

The high incidence of ulcer among base troops, as compared with men recently in combat, in part indicates the effect of frustration and regimentation, with frequent periods of inactivity. In 70 percent of the patients seen by Halsted and Weinberg (p. 312), a definite correlation was established between aggravation or recurrence of symptoms and the increased nervous tension associated with embarking for overseas. The important effect of such a projected journey upon the incidence of peptic ulcer was suggested by the studies made at a large staging area where men were observed in the final steps of their preparation for duty overseas.[33] In this group was recorded the highest percentage in any American series of peptic ulcer—34 percent in patients with digestive complaints.

Summary.—There is, thus, no overwhelmingly conclusive evidence of psychogenic factors in the initiation or exacerbation of peptic ulcer during oversea service. However, the possible influence of such factors is not ruled out. In less selected groups of men, in the Zone of Interior, there was a high incidence of peptic ulcer under conditions of frustration and

[31] (1) See footnote 9 (3) (4), p. 309; footnote 14, p. 311; and footnote 18, p. 312. (2) Annis, J. W., and Eldridge, F. G.: Military Gastroenterology. South. M.J. 36: 791–798, December 1943.

[32] (1) See footnote 9 (1), p. 309. (2) Chamberlin, D. T.: Peptic Ulcer and Irritable Colon in the Army. Am. J. Digest. Dis. 9: 245–248, August 1942. (3) Chamberlin, D. T., and Wallace, W. C.: Perforated Peptic Ulcer in an Army General Hospital. Mil. Surgeon 92: 193–196, February 1943. (4) Harrell, W. B., and Wilson, R. O.: Ruptured Peptic Ulcer Among United States Troops in Panama (Report of 10 Cases). Mil. Surgeon 96: 336–342, April 1945.

[33] See footnote 9 (7), p. 309.

anxiety and a high incidence of recurrence or aggravation under the strain of embarkation. On the other hand, men who had weathered induction, Army life in the United States, and transport, before presenting evidence of ulcer, may well have been, as they seemed to be at clinical examination, of a type more resistant to psychological stress. Nevertheless, as evidence of peptic ulcer did appear in them under the strains of combat, it cannot be assumed that the psychogenic element was completely absent, but probably in such men a more severe strain was required as the precipitating factor. These considerations had to be taken into account in separating such men from service, or in giving them special assignments.

Disposition

With very few exceptions, once the diagnosis of peptic ulcer was established, these patients were considered to be totally and permanently unfit for any further military service and were discharged for physical disability (table 61). An occasional exception was made in the case of highly trained individuals with special skills, if facilities were available to secure them proper diet. Some question had been raised concerning the advisability of such a general rule, since it often resulted in the separation from service of individuals who were extremely able, aggressive, and ambitious, while a greater number of men who had functional complaints without organic basis, and were considerably less effective soldiers, were often retained. Halsted in particular advocated the retention in a limited service capacity of the well-trained soldier who had proper morale and a desire to remain in the Army.

Although some such individuals might properly have been salvaged, patients with ulcer must be regarded as subject to exacerbations of symptoms when some untoward element is introduced into their environment, and the prolonged hospitalization required by such symptoms made further attempts at service applicable to only a very few (table 62). This, at least, was the experience with those patients in whom the diagnosis was established while in the Zone of Interior, representing, as they pre-

TABLE 61.—*Percentage distribution of admissions for peptic ulcer in the U.S. Army, by type of disposition, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]

Type of disposition	Ulcer of duodenum	Ulcer of stomach
Death_____	0.2	1.3
Disability discharge_____	75.1	53.8
Return to duty_____	22.3	43.9
Other_____	2.4	1.0

TABLE 62.—*Average number of days lost per admission for peptic ulcer, 1945*

Duodenal ulcer	Number of days lost	Stomach ulcer	Number of days lost
With obstruction_____	108	With obstruction_____	139
Without obstruction_____	65	Without obstruction_____	74
With perforation_____	92	With perforation_____	96

sumably did, the average patient with ulcer seen in civilian life.[34] Those whose ulcers were first manifested under field conditions overseas may well have been more suitable for modified service.

Head, Wilen, and Fradkin (p. 311), on the basis of their survey in the Mediterranean theater, were so impressed with the superior quality of the average patient with ulcer seen overseas that, influenced by the mildness of the disease and the relatively low incidence of complications, they recommended further trial of duty in exceptional cases during an acute manpower crisis. However, their selections for such duty had to meet the following criteria: (1) Complete relief of symptoms while on a regular diet after a preliminary treatment with a bland diet; (2) absence of complications and other diseases, such as psychoneuroses and anxiety states; (3) absence of roentgenographic evidence of activity after therapy; and (4) assignment to noncombat unit organizations. They were particularly struck with the results obtained during the early part of the Italian campaign when, because of a manpower crisis, 54 patients with ulcer who had met the criteria just listed were returned to duty. During a subsequent period of observation, averaging 9½ months, only eight patients (15 percent) required further hospitalization.

The recommendation had been made that radical surgery be performed on naval personnel whose ability made them particularly valuable to the Navy [35] and whose ulcers developed during service. Such procedures, however, were not generally resorted to among Army personnel; it was felt that, in the absence of complications that would by themselves warrant surgery, it was impractical and of questionable value to treat patients by such an empirical method.

FIFTH U.S. ARMY GASTROINTESTINAL CLEARING CENTER

The gastrointestinal clearing center was organized by order of the surgeon of the Fifth U.S. Army and functioned in Italy from 23 October 1944 to 23 April 1945 under the direction of Maj. (later Lt. Col.) James

[34] See footnote 9 (1) (2) (9), p. 309; and footnote 31 (2), p. 316.

[35] Montgomery, H., Schindler, R., Underdahl, L. O., Butt, H. R., and Walters, W.: Peptic Ulcer, Gastritis and Psychoneurosis Among Naval Personnel Suffering From Dyspepsia. J.A.M.A. 125: 890–894, 29 July 1944.

A. Halsted, MC.[36] It was instituted to counteract the loss of effective manpower resulting from overhospitalization of men with psychosomatic disorders. Patients were sent directly to the clearing center instead of being sent to base hospitals in a stream of evacuation moving farther and farther from the front.

The pivotal men in this organization were an experienced clinician, a gastroscopist, a trained psychiatrist, and a competent roentgenologist. As soon as a diagnosis of organic disease seemed probable, the patient was transferred to a base hospital for further disposition. In the event of overt psychoneurosis, the psychiatrist made the recommendation for disposition. All mild functional cases were returned to duty without any unnecessary delay, but not until they had been given the benefit of a thorough but prompt examination and discussion.

One group of 113 patients with chronic dyspepsia was studied intensively by means of history, physical examination, gastroscopy, gastrointestinal roentgenograms, and neuropsychiatric consultations. Among these, only four (3.5 percent) were found to have peptic ulcers. Of the remaining 109 patients, 41 percent showed slight to moderate abnormalities of the gastric mucosa on gastroscopic examination. In six patients, an ulcer was suspected from the history and the physical examination, but none was found. Although typical symptoms were found by Halsted and Weinberg in only 72 percent of proved cases of peptic ulcer in another series of 200 cases (p. 314), roentgenographic and gastroscopic examinations in this group revealed no ulcer or other gastric lesions in any patient in whom it had not previously been suspected clinically. Thus, it was shown that roentgenographic facilities were not indispensable in making a diagnosis in a forward area.

Of 442 patients studied at the clearing center during 6 months, 74 percent were returned to full duty, 11 percent to limited service, while 15 percent (including hepatitis, and doubtful cases, with no definite evidence of organic disease nor of psychoneurosis) were sent to a base hospital. Over half (286 cases) were designated psychogenic dyspepsia. Of these, 79 percent were returned to full duty and 15 percent to limited service, the average length of hospitalization being 7.8 days.

For comparison, there is the record of the 6th General Hospital, when it was removed from Casablanca to Rome, where 55 percent of similar cases were returned to full duty, after an average hospital stay of 39 days. Halsted could find no significant factor to account for the lower percentage except the longer hospitalization.

Contrasting both records with the earlier experience of the 6th General Hospital in Casablanca, many factors could account for the high incidence of peptic ulcer found there (33 percent) and for the poor re-

[36] (1) See footnote 19, p. 313. (2) Halsted, J. A.: Clearing Company for Gastrointestinal Disease. Bull. U.S. Army M. Dept. 88: 90–95, May 1945. (3) Halsted, J. A.: The Management of Patients With Gastric Complaints in the Army Area. M. Bull. Mediterranean Theat. Op. 3: 178–185, June 1945.

sults of attempted rehabilitation. At that time, this hospital was a funnel of evacuation of such cases to the Zone of Interior; many of the patients were base troops, who had been poorly screened during the early war period; others reached this hospital some weeks after leaving combat units. In Italy, the patients were for the most part combat infantrymen who were received on the day, or within a few days, of leaving their units.

Thus, experience had taught the value and the methods of prompt diagnosis and prompt disposition. As demonstrated by the Fifth U.S. Army Gastrointestinal Clearing Center, this was good therapeutics. Soldiers more willingly returned to duty, and were less liable to relapse of psychogenic symptoms, when they felt that their complaints had been given competent and thorough attention. Evaluation and management of cases were more effective both from the medical and from the military standpoint.

FUNCTIONAL GASTROINTESTINAL DISORDERS

Incidence

Gastrointestinal symptoms without demonstrable lesions were responsible for great loss of effective manpower in World War II. Dyspepsia, along with its psychosomatic counterparts—backache, headache, arthralgia, myalgia, and functional cardiovascular symptoms—constantly challenged the skill and judgment of the Medical Corps. Of the psychosomatic disabilities, functional gastrointestinal disorders [37] composed the largest single group. Aside from the emotional factors, the alterations in diet and regimen of life frequently induced digestive symptoms, particularly in new recruits and subsequently among those on oversea rations.

The problem of dyspepsia or gastroduodenal disorders in World War I was apparently less important, since there is almost no reference to them in the history of "The Medical Department of the United States Army in the World War." During the period between 1 April 1917 and 31 December 1919, the occurrence of "other diseases of the stomach," evidently including dyspepsia, was reported as 31,491, a rate of only 0.26 per 1,000. The significance of these statistics is confused, however, by the lack of uniform diagnostic criteria. That the problem was greater than these figures indicate was suggested by Kantor's report [38] that, after eliminating those patients admitted for harboring intestinal parasites, more than one-third of all cases were found to be suffering from one form or another of gastrointestinal neurosis.

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[37] Includes dyspepsia, gastric neurosis, abdominal neurasthenia, disordered action of the stomach, and soldier's stomach.

[38] Kantor, J. L.: Experience With a Gastrointestinal Service in an Army Hospital. Mil. Surgeon 46: 507–513, 1920.

Seeking dependable statistics on the overall incidence in the Army in the Second World War, one finds that before 1944 dyspepsia as such was included in the miscellaneous group "other diseases of the stomach." However, individual reports indicated the magnitude of the problem at various installations in the Zone of Interior and overseas.

Thus, Annis and Eldridge [39] at the Station Hospital, Camp Blanding, Fla., stated that the vast problem of functional gastrointestinal disease and psychoneurosis had been by far the outstanding cause of admission to that hospital. The incidence of these gastric neuroses had fluctuated in accordance with age groups (rising when older men were inducted, particularly those with dependents) and with the prevailing state of hostilities (declining immediately after the attack on Pearl Harbor).

Pulsifer [40] reported that gastrointestinal disorders were responsible for 45 percent of admissions to the general medical wards of the Station Hospital, Camp Livingston, La. In 43 percent of these patients, definite emotional causation was evident, and no organic lesions were demonstrable. Of 100 consecutive patients who had been discharged from the neuropsychiatric service, gastrointestinal complaints had caused the hospitalization of 48. Immediate discharge from the Army had been recommended for 82 of these 100 patients. The duration of the disabling presenting symptoms was recorded as from childhood in 46 of the 82 patients, and averaged 5 years in the remaining 36. Tidy [41] reported that in 1941 Graham and Kerr found that the history of symptoms in 80 percent of functional disorders antedated military service in the British forces, and he himself reported similar figures for 1942.

An interesting and carefully conducted survey was reported by Skobba [42] from the Lawson General Hospital, Atlanta, Ga. Of all the patients admitted to the gastrointestinal service at this hospital up to 1 August 1942, one-third (137) had no evidence of organic disease. These patients were subjected to roentgenographic examinations of the entire gastrointestinal tract, gallbladder, proctoscopic and gastroscopic examinations, gastric analyses, stool examinations, and neuropsychiatric consultations. Of these 137 patients, 75 showed no evidence of any neuropsychiatric condition. The remaining 62 had gastrointestinal symptoms that were related to psychoneuroses in 18, to a constitutional psychopathic state in 33, and to mental deficiency in 11 patients. Of the enlisted men who were admitted as patients to the neuropsychiatric service, those having pain, vomiting, or diarrhea were studied. Patients with only vague gastrointestinal symptoms were not included. There were functional gastrointestinal complaints in 20 percent of the constitutionally psychopathic patients, in 27

[39] See footnote 31 (2), p. 316.

[40] Pulsifer, L.: Psychiatric Aspects of Gastrointestinal Complaints of the Soldier in Training. Mil. Surgeon 95: 481–485, December 1944.

[41] Tidy, H.: Peptic Ulcer and Dyspepsia in the Army. Brit. M.J. 2: 473–477, 16 Oct. 1943.

[42] Skobba, J. S.: Functional Gastro-Intestinal Conditions. South. M.J. 36: 528–533, July 1943.

percent of the psychoneurotic patients, and in 20 percent of the mentally defective.

The magnitude of the problem of dyspepsia in an oversea theater was vividly portrayed by Head, Wilen, and Fradkin in the report of their experience in the Mediterranean theater (p. 311). In 11 general hospitals in which 14,451 roentgenograms of the upper gastrointestinal tract were taken, positive evidence of ulcer was found in 10.2 percent, or 1,747 patients. In 21 station hospitals, in which 9,813 roentgenographic examinations were made, only 5.9 percent were positive for ulcer. A rough comparison with experiences elsewhere is presented in table 63. It may be inferred that the difference between 100 percent and the percentages in this table denotes roughly the number of patients with dyspepsia.

The true incidence of dyspepsia was not accurately portrayed by the foregoing figures; the actual occurrence was apparently far greater, for numerous personnel with these symptoms were not hospitalized. These reports indicated, however, that the problem was widespread and that, if more stringent diagnostic criteria based on history and physical examination had been employed, many patients would not have been hospitalized and many others would not have burdened the roentgenographic facilities of the Army installations.

TABLE 63.—*Percentage of peptic ulcer in hospital patients with dyspepsia*

Reports	General hospitals	Station hospitals
	Percent	*Percent*
Berk, Tilton General	40	
Chamberlin, Lawson General	31	
British (various reports)	55	
German	33	
Kirk, Fort Sill		12.9
Annis, Camp Blanding		10.0
Zetzel, Camp Berkeley		7.2
Rush, South Pacific	19	
Mediterranean theater	10	
Cumulative, 1943–45		6.0

Clinical Manifestations of Dyspepsia: Differential Diagnosis

Symptoms.—The symptoms of functional gastrointestinal disorders comprised numerous manifestations. Upper abdominal distress, heartburn while eating or immediately thereafter, regurgitation of acid, sensation of fullness, nervousness, fatigability, and anorexia were characteristic. Distress at night was rare. Ingestion of food only occasionally gave relief; indeed, it frequently caused exacerbation of symptoms. Occasional vomiting was a frequent complaint. Characteristically, numerous other symptoms

were described, as follows: Headache, pains in the chest, backache, burning sensation in the eyes, palpitation, weakness, and disturbed sleep. The symptoms in the great majority of men antedated entry into the Army, at times extending back to childhood. Exacerbations of the complaints were often related to periods of emotional stress and strain.

In evaluating such symptoms, a careful history and physical examination, with a psychiatric consultation when indicated, established a reasonably accurate diagnosis in the great majority of cases without recourse to hospitalization for roentgenographic or other studies. For this, a sound psychiatric orientation was required of the medical officer, and usually sufficed. In the few doubtful cases, the opinion of a psychiatrist was invaluable and, by being so restricted, could be the more carefully considered. The psychodynamics of dyspepsia were excellently described by Halsted and also by Pulsifer (p. 321) who concluded that the clinician should be able to distinguish psychogenic disturbances from organic disease with fair accuracy by means of the history and physical examination alone.

Roentgenographic examination.—The vast number of soldiers with gastrointestinal symptoms obviously precluded complete laboratory and roentgenographic examinations and these, indeed, proved to be of limited value. Accurate examination required not only the services of an experienced roentgenologist but also elaborate equipment for spot films and other techniques. Without these facilities, organic lesions would be missed or transient fluoroscopic abnormalities might be taken for pathological lesions. In about 10 percent of the cases, however, reasonably accurate differential diagnosis between psychogenic and organic disease could not be made without gastrointestinal fluoroscopy. Among 113 consecutive patients with dyspepsia who were given roentgenographic examinations at the Fifth U.S. Army gastrointestinal center, as part of an intensive clinical and gastroscopic study, Halsted reported that only 4 patients had an ulcer; these were correctly diagnosed on the basis of the history and the physical examination.[43] From their history, six additional patients were believed to have ulcer, but roentgenographic studies were negative. In no instance, among another group of 190 patients with dyspepsia who had had roentgenographic examination, was an ulcer demonstrated when the clinical diagnosis was psychoneurosis. It thus appears that the diagnostic error in such cases is statistically insignificant, nor is it likely to be serious in itself in view of the low incidence of exacerbations actually occurring during military service.

On the other hand, a thorough physical examination required but little more time than a superficial one, and was of inestimable value. Signs pointing to the diagnosis were frequently found, and if the diagnosis of psychogenic or functional disorder was finally made, the patient had the reassurance that serious disease had not been overlooked by a cursory examination.

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[43] See footnote 36 (3), p. 319.

In a station hospital in the Zone of Interior, Magnes [44] found that 73 percent of the soldiers referred for hospitalization could be successfully diagnosed and treated in the outpatient service on the basis of a careful history and physical examination. The other 27 percent were fluoroscoped as ambulatory patients. Halsted, in his extensive experience, found that a thorough history supported by the results of physical examination in 90 percent of his patients was adequate independently of other studies.

History.—There was no better index of the skill and wisdom of a medical officer than the quality of the history elicited from a patient with gastrointestinal symptoms. Practically all neuroses expressed themselves in part by "body language," and all organic disease imposed psychological problems, in either case requiring sound clinical judgment. A history limited to the presenting complaint usually wasted, rather than saved, time.

Some pitfalls in taking the history have been pointed out by Rosenak and Foltz.[45]

There may be some slight variation from the so-called typical ulcer story which will suggest to the experienced physician that an ulcer is not apt to be present. The frequent occurrence of early morning pain is such a phenomenon. Alvarez had often warned that the ulcer patient does not present this symptom and it has been our experience that the dyspeptic soldier who complains of burning pain in the epigastrium upon arising even though he obtains relief from eating, probably has no ulcer.

Feelings of distress with varied pains and aches, but without pre-eminence of one, were more characteristic of dyspepsia than of ulcer.

The presence or absence of gastrointestinal symptoms first in civilian life, then during the soldier's military service, plus the possible relation to stresses and strains were ascertained. When these symptoms continued with varied intensity but without real remission, they were more likely to be psychogenic than organic. Symptoms of brief duration increased the probability of organic disease.

Halsted [46] has summarized, as follows, the implications of statistics for differential diagnosis:

Because of the low incidence of organic disease and the high incidence of neurosis among soldiers complaining of chronic gastric complaints, it is safe to adopt the following point of view in the diagnostic evaluation of such patients in the Army area: If the symptomatology does not fit in with any organic disease, if the physical examination is negative, and if simple clinical examinations such as measurement of temperature, examination of urine, stool and blood count are all normal one should then disregard symptomatology and make a psychiatric appraisal. The answer will usually be found in this sphere. If one makes an exhaustive search for an organic explanation of symptoms by prolonged medical investigation harm will be done to the 70 percent of patients who have psychogenic dyspepsia. Furthermore many men will be lost for further useful military service. The occasional diagnostic error which may be made is not likely to be serious in the case of chronic stomach complaints among soldiers.

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[44] See footnote 9 (6), p. 309.

[45] See footnote 20 (3), p. 313.

[46] Halsted, J. A.: Gastro-Intestinal Disorders of Psychogenic Origin. Management of Forward Areas. Proc. Conference Army Physicians, Central Mediterranean Forces, 1945, pp. 131–134.

Comparison of the symptomatology of peptic ulcer and psychogenic dyspepsia, as tabulated by Halsted, is shown in table 64.

Response to treatment.—As has been pointed out (p. 314), the favorable response of the patient with peptic ulcer to dietary and antacid treatment was in striking contrast to the characteristically poor response in the functional dyspeptic. This response served as one of the most important, although insufficiently regarded, criteria of differential diagnosis.[47] The symptoms of peptic ulcer nearly always abated in a few days, if the patient had frequent feedings and antacid medication, but the symptoms of a psychogenic gastric disorder usually were not materially influenced by such measures.

TABLE 64.—*Differential diagnosis between peptic ulcer and psychogenic dyspepsia*

Symptomatology	Peptic ulcer	Psychogenic dyspepsia
Pain	Dull ache from 1 to 3 hours after meals.	Burning, immediately after meals.
Night pain	Common	Infrequent.
Relief by food or alkali	Usual	Unusual.
Vomiting	Uncommon	Common.
Appetite	Good	Usually poor.
Remissions	Present	Absent.
Relief by hospital treatment	Usual	Rare.
Other somatic symptoms	Rare	Frequent.
Psychiatric features	Aggressive, independent, minimizes symptoms, no anxiety, socially successful.	Outwardly submissive, dependent, emphasizes symptoms, anxiety close to surface, maladjusted socially.

Disposition

The central problem was concerned with whether or not the individual patient with functional dyspepsia was of sufficient potential value to the Army to warrant the effort and time expended for salvage. Functional gastrointestinal disorders, including particularly the classic complaints of dyspepsia, were frequently witnessed among new recruits. The manifold psychological adjustments as well as the rigid regimen and the change in diet were important factors. Many men with transient problems of adjustment and the resulting vague gastrointestinal complaints were readily rehabilitated into useful soldiers. In contrast, individuals who, in the course of their previous civilian life, had such complaints for many years offered less promise. It was not surprising that the patients with the most intractable forms of dyspepsia had symptoms long antedating their entry into the

[47] See footnote 9 (9), p. 309.

service. They finally were of but little service to the Armed Forces, and many had to be released after varying periods of training.

New recruits who had such symptoms before they were acclimated to Army routine could usually be dealt with satisfactorily in their own units. Symptomatic treatment in the dispensary, reassurance, and other forms of psychotherapy safeguarded these individuals from fixation of their attention on such diagnostic terms as gastritis, duodenitis, or even dyspepsia. Persistence of symptoms, in spite of therapy, suggested the desirability of more intensive study of the emotional factors by a trained psychiatrist outside of the hospital. The possibility that dyspepsia was a manifestation of well-marked psychoneurosis or of constitutional inferiority was kept in mind. In each case, the cardinal question was whether a person was fit for service as a soldier. The answer depended not only on the evaluation of the patient but also on extraneous considerations. Among these were the needs of the Army for manpower, the opportunities of placement for limited service, the soldier's special capabilities, and the need of the Army for his particular qualifications.

Divergent viewpoints were expressed regarding the general advisability of attempting to salvage the confirmed dyspeptic. Thus, Annis and Eldridge [48] stated: "Regarding functional dyspepsia as a whole, the Army provides neither the time, the environment, nor the facilities necessary to attempt what is at best the extremely difficult, and often unsuccessful, task of rehabilitation."

On the other hand, certain carefully planned and well-organized efforts to rehabilitate such patients were inaugurated. Goldbloom and Schildkrout [49] at Camp Kilmer, N.J., organized a regimen for the rehabilitation of the chronically dyspeptic soldier. One hundred patients were studied and comprehensive investigations of the digestive and psychiatric symptoms were completed in the hospital. The soldiers were then discharged for duty in various echelons of the camp but were brought regularly to the hospital for their meals. By followup studies and conferences, it was sought to improve morale and arrive at a better understanding of each man's problems. Of the entire group of 100, 42 patients were classified as having dyspepsia. Of these, only 14 were placed on full duty, 21 were retained on the regimen, 3 were transferred to a general hospital, and 4 were discharged from the Army.

It was evident, from a survey of common experience in the Army, that no broad generalizations regarding disposition of all cases could be made concerning a group that comprised such heterogenous conditions as were included under the term "dyspepsia." The constitutionally inadequate had to be dealt with on the basis of their fundamental and fixed inadequacy rather than on the basis of their superficial symptoms. More thorough

[48] See footnote 31 (2), p. 316.

[49] Goldbloom, A. A., and Schildkrout, H.: Dyspepsia Regimen; Method of Rehabilitation. War Med. 6: 24–26, July 1944.

screening, earlier diagnosis, and swift disposition on the basis of ineptitude or constitutional inadequacy—when indicated—would have prevented much wastage of professional skill and facilities.

Summary

Briefly, then, one may say that, in Army experience with gastrointestinal disorders, the large percentage of patients without organic disease but with poor morale, including those with definite psychoneurosis, was in contrast with the small percentage of patients with peptic ulcer, particularly after those with preexisting lesions had been screened out. Although exacerbations of peptic ulcer were induced in some men under strains of sufficient severity, the incidence was low, and the response to treatment good.

Gastrointestinal symptoms without demonstrable lesion caused great loss of effective manpower in World War II and comprised the largest single group of psychosomatic disabilities.

In such cases, those who responded favorably to symptomatic therapy and firm but understanding discussion of their problems, for the most part were the men who experienced symptoms soon after entering on active duty, during the period of becoming acclimated to Army diet and the new mode of life. Transient problems of adjustment with vague gastrointestinal complaints, occurring at later periods of active service, likewise responded favorably if excessive medical care and elaborate investigation were avoided.

On the other hand, the dyspeptic whose symptoms were the reflection of deeply rooted anxiety had to be regarded as a psychiatric problem, diagnostically and therapeutically, and disposition made accordingly. Patients intermediate between these groups were frequently encountered. Decision in such cases could be difficult and was often postponed for prolonged observation, with or without repeated trials at various duties.

GASTRITIS AND GASTROSCOPY

Such wide divergence of opinion existed regarding the incidence and significance of abnormal gastroscopic findings that the subject seems worth discussing in a separate section. Even the term "gastritis" was surrounded by confusion. Some authors designated abdominal distress as gastritis in the absence of ulcer or other organic disease although gastroscopy had not been performed. Generally, however, the word was used to refer to changes in the gastric mucosa visualized through the gastroscope. Such changes were estimated to occur in about 25 percent of all patients suffering from abdominal distress [50] and were usually classified as (1) superficial, (2) atrophic, or (3) hypertrophic.

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[50] See footnote 20 (4), p. 313.

The clinical significance of the morphologic findings viewed through the gastroscope was not clear. Some observers regarded the mucosal changes as organic disease and ascribed the patient's symptoms to these abnormalities. Hurst (p. 309), for instance, stated that gastritis is an organic disease as definite as ulcer and that it is most undesirable to confuse it with functional gastric disorders, which have no organic basis.

Extensive military experience led to the conclusion that definite clinical syndromes could not be ascribed to the different types of gastritis.[51] Erosive or ulcerative gastritis and possible chronic hypertrophic gastritis at times might produce symptoms, but no clear-cut clinical correlation was generally possible. Morever, the limits of the normal variations of the gastric mucosa had not been sufficiently established to permit accurate appraisal of what was abnormal.

Even the gastroscopic description in pathological terms could be verified histologically in only about 50 percent of the cases.[52] That the gastroscopic findings were a reflection of a functional state was suggested by the observations of Wolf and Wolff.[53] With episodes involving anxiety, hostility, and resentment, the mucosa became red, the acid production was sharply accelerated, and vigorous contraction began. With hypermotility and hypersecretion, the gastric mucosa became engorged and turgid, and the folds became thicker and succulent, presenting the picture of hypertrophic gastritis as seen by gastroscopists.

The foregoing observation, which suggested that hypertrophic and other forms of gastritis could be temporary and functional, was in accord with the experience of others. Fitzgibbon and Long [54] found that 2 of 40 healthy students, or 5 percent, had hypertrophic changes. Berk [55] examined 50 patients with upper abdominal distress diagnosed as psychoneurotic by competent psychiatrists. All had failed to show abnormalities roentgenographically, and some had therefore been given prior to admission, the diagnosis gastritis. On gastroscopic examination, approximately 30 percent showed gastritis; if those who exhibited merely patches of the superficial variety were excluded, only 20 percent showed chronic gastritis worthy of note. Berk concluded that no set of clinical symptoms inevitably indicated the presence of chronic gastritis. These studies were in accord with those of other observers.[56]

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[51] See footnote 4, p. 307.

[52] Berk, J. E.: Trends and Shortcomings in the Approach to Gastro-Intestinal Diseases; Review Based on Experience in an Army General Hospital. Pennsylvania M.J. 47: 897–901, June 1944.

[53] See footnote 13, p. 310.

[54] Fitzgibbon, J. H., and Long, G. B.: Gastroscopic Study of Healthy Individuals; A Preliminary Report. Gastroenterology 1: 67–71, January 1943.

[55] See footnote 52.

[56] (1) Ruffin, J. M., Brown, I. W., Jr., and Clark, E. H.: The Occurrence of Gastritis as Diagnosed by Gastroscopy in Gastric Neuroses. Am. J. Digest. Dis. 7: 414–417, October 1940. (2) Howard, J. T.: Gastroscopy and Use of Gastroscope in the Military Services. War Med. 3: 274–281, March 1943.

A similar experience was reported by Cutler and Walther [57] and from the Central Pacific Area.[58]

In one group 264 soldiers (average age 29) with upper abdominal complaints of variable duration (1 month to 17 years) were gastroscoped. X-ray examinations of stomach and duodenum were negative. The stool examinations were negative. Cholecystography was made in 11 percent of cases and was found to be negative.

1. 106 patients (40 percent) showed chronic gastritis.
2. 138 patients (52 percent) had normal gastric mucosa.
3. 13 patients (5 percent) revealed mucosal hemorrhage.
4. 7 patients (3 percent) had mucosal erosions.

Only a small number of the 40 percent with chronic gastritis revealed the hypertrophic variety. These patients presented a pattern of complaints very similar to those found in peptic ulcer. They were benefited by alkalis and antispasmodics.

The greater majority revealed the superficial and atrophic type of gastritis. It is interesting to note that clinically a conspicuous feature was the lack of uniformity of digestive complaints. The symptoms were of a bizarre nature, implicating several systems. Thus, nervous tremors, poorly localized headaches, dyspnea, precordial pain, giddiness, and arthralgias were among the common complaints. No correlation existed between the degree or extent of gastritis and the avowed incapacity of the soldier to perform duty. The nature of the gastroscopic picture could not serve, therefore, as the only factor in determining the ultimate disposition of the patient as to future usefulness in the service.

Many of these cases of chronic gastritis were seen by the neuropsychiatrist and were reported to have a definite psychoneurosis.

A second group of 33 asymptomatic volunteers (average age 25) were gastroscoped and considered as controls. Only 3 showed a patchy mild atrophic gastritis; all others were normal.

A third group of 36 soldiers (average age 29) with positive findings of duodenal ulcer were studied, 52 percent showed superficial, atrophic or a combined superficial and atrophic gastritis with duodenal ulcer.

From these observations, the following conclusions were drawn:

1. Asymptomatic subjects may show evidence of gastric mucosal changes by gastroscopy.

2. Chronic gastritis is much more prevalent in patients with chronic upper abdominal distress.

3. Apart from the hypertrophic group which clinically simulated peptic ulcer, the largest group of patients with chronic gastritis showed no uniform symptom complex. Because of the frequency of associated complaints unrelated to the gastrointestinal tract it was difficult to believe that the gastritis was the only etiologic factor.

4. A predominance of psychogenic factors was present in this group; the possibility therefore exists that the changes in gastric mucosa points to a more basic disturbance of psychiatric importance.

5. A useful guide to the general fitness of the "gastric soldier" was preferably an accurate evaluation of the severity of the psychogenic factors rather than the appraisal of the gastritis per se.

Of 22 patients, gastroscoped in a naval hospital, who had chronic dyspepsia without ulcer, 11 had a normal gastric mucosa and 11 had some form of gastritis; 5 of these were classified as mild or insignificant.[59] Psychiatric

[57] Cutler, J. G., and Walther, J. E.: The Significance of Chronic Gastritis in an Army General Hospital. Gastroenterology 5: 112–116, August 1945.

[58] History of Internal Medicine in the Central Pacific in World War II. [Official record.]

[59] See footnote 35, p. 318.

evaluation revealed that 11 of the 22 had a marked neurosis and 6 a mild neurosis; 5 were normal, but it was noted that 2 of the latter were high strung and restless.

Annis [60] and Gold [61] each reported that about 35 percent of patients with nonulcerative dyspepsia in Army installations in the Zone of Interior showed definite gastroscopic changes.

Of considerable significance were the results (reported by Halsted) of a survey [62] conducted by two internists, one of whom was a skilled gastroscopist, aided by a psychiatrist, a clinical psychologist, and a radiologist. A total of 109 patients with chronic nonulcerative dyspepsia were examined. Of these, 59 percent had a normal gastric mucosa; 26 percent showed slight abnormalities, consisting of redness and increased highlights; and 15 percent showed more marked changes, with edema and adherent mucus. The changes were regarded as signs of chronic superficial gastritis. In nine patients, spasm of the antrum or midbody was seen without changes in the mucosa. There were no instances of hypertrophic or atrophic gastritis. Psychiatrically, no differences were noted between the group showing gastroscopic changes and the group with a normal mucosa. It was believed that the benign changes noted gastroscopically were circulatory in origin, the result of chronic anxiety.

Thus, in summary, a gastroscopy was not, in Army experience, an indispensable or even a necessary adjunct in the evaluation, clinical management, and disposition of patients with chronic or recurrent dyspepsia. The procedure proved to be helpful, however, under the same circumstances as in civilian life. Occasionally, it enabled the medical officer to reach a decision as to the presence of a neoplasm or of a radiologically doubtful ulcer [63] and, at times, to diagnose the source of an otherwise unexplained gastric hemorrhage.

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[60] Annis, J. W.: Gastritis in Military Service. Gastroenterology 2: 85–92, February 1944.

[61] Gold, R. L.: Gastroscopic Findings in Patients With Dyspepsia at an Army Hospital. Gastroenterology 1: 254–257, March 1943.

[62] See footnote 36 (3), p. 319.

[63] See footnote 9 (2), p. 309.

CHAPTER XIII

Viral Hepatitis

W. Paul Havens, Jr., M.D.

The emergence of viral hepatitis as one of the most important causes of loss of time among U.S. troops during World War II was as unexpected as it was dramatic. Conditioned largely by memories and descriptions of the medical experiences in World War I in which this disease played an almost unnoticed role in our forces both here and abroad, it is no wonder that those charged with the preparation of programs for the control and treatment of infectious diseases turned their attention first to respiratory infections. Records of the bitter ravages of influenza and secondary bacterial pneumonias doubtless prompted the Preventive Medicine Service of the Surgeon General's Office to establish early in 1941 the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army. This board was approved by the Secretary of War in January 1941 and, eventually, became known as the Army Epidemiological Board. The investigation of such diseases as yellow fever, typhus, malaria, dengue, sandfly fever, and venereal infections, among others, was given high priority, but viral hepatitis received little or no consideration as a potential troublemaker.

In retrospect, the grim record of 71,691 cases of jaundice (of which many were doubtless infectious hepatitis) among white Union troops in our Civil War,[1] as well as the oft repeated story of the military importance of this disease among foreign troops in Germany,[2] in the Mediterranean littoral,[3] in the Dardanelles,[4] and in Rumania [5] during the 18th and 19th centuries, and in World War I, had little impact on our thinking. This is readily understandable in view of the remoteness of these experiences both temporally and spatially. In addition, it is curious but true that our concept of the nature of viral hepatitis was generally somewhat more naive than that of certain of our European medical colleagues despite the fact

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[1] Medical and Surgical History of the War of the Rebellion. Medical History. Washington: Government Printing Office, 1888, pt. III, vol. I, pp. 874–879.

[2] Monro, Donald: An Account of the Diseases Which Were Most Frequent in British Military Hospitals in Germany, From January 1761 to the Return of the Troops to England in March 1763. London: Millar, Wilson, and Durham, 1764.

[3] Larrey, D. J.: Relation Historique et Chirurgical de l'Expédition de l'Armée d'Orient en Egypte et en Syrie. Paris: Demonville et Soeurs, 1803.

[4] Sarrailhé, A., and Clunet, J.: La "Jaunisse des camps" et l'épidémie de paratyphoïde des Dardanelles. Bull. et mén. Soc. méd. d. hôp. de Paris, 3 sér., 40: 563–567, 1916.

[5] Cantacuzène, J.: Sur une épidémie d'ictère observée en Roumanie pendant la campagne de 1917. Presse méd. 26: 541–543, 24 Oct. 1918.

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that occasional pioneers in this country, including Blumer [6] and Rich,[7] had pointed the way to a better understanding of the disease.

It is particularly ironic that the concern about another acute infection producing necrosis of the liver—yellow fever—and the aggressive efforts made to expedite the production of enormous supplies of vaccine against it did not potentiate our awareness of the importance of viral hepatitis. Our introduction, in 1942, was a rude one and was marked by the great epidemic of homologous serum hepatitis transmitted by the injection of yellow fever vaccine stabilized with human serum containing a strain of hepatitis virus. Unfortunately, this catastrophe was not to be the last. Subsequently, in 1942–45, as our troops appeared in the Middle East, in North Africa, in the Far East, in Europe, and in the Pacific Ocean Areas, they were riddled by the naturally occurring epidemic disease, infectious hepatitis. It is pertinent to point out here that recognition of the differences between the transmitted disease and the naturally occurring one was not immediate, and, indeed, it was not until 1944–45 that two separate entities, serum hepatitis and infectious hepatitis, were generally recognized. However, it is a tribute to the vigor and sagacity of a number of military medical officers and their civilian consultants that many of the problems associated with this unexpected and unwelcome situation were quickly recognized and that many of the etiologic, clinical, and epidemiologic unknowns were solved.

Viral hepatitis, with close to 200,000 cases, erupted in the period between 1942 and 1945 as a matter of prime importance to our Armed Forces. It is the purpose of this account to set down the experiences of the Army with serum hepatitis and infectious hepatitis during the period of World War II (table 65).

TABLE 65.—*Admissions for infectious and serum hepatitis in the U.S. Army, by broad geographic area and by year, 1942–45*

[Rate expressed as number of admissions per annum per 1,000 average strength]

Area	1942–45		1942		1943		1944		1945	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Continental United States	46,750	3.17	33,569	12.63	3,906	0.75	3,175	0.80	6,100	2.08
Overseas	135,633	12.63	15,664	26.74	24,966	14.79	24,608	6.44	70,395	15.16
Total Army	182,383	7.16	49,233	15.18	28,872	4.20	27,783	3.57	76,495	10.10

[6] Blumer, G.: Infectious Jaundice in the United States. J.A.M.A. 81: 353–358, 4 Aug. 1923.

[7] Rich, A. R.: The Pathogenesis of the Forms of Jaundice. Bull. Johns Hopkins Hosp. 47: 338–377, December 1930.

SERUM HEPATITIS

Historical Background

Doubtless, the earliest record of serum hepatitis is a report by Lürman[8] of an outbreak of jaundice occurring in shipworkers several weeks after vaccination with human glycerinized lymph. Stokes and his coworkers,[9] in the United States, and Ruge,[10] in Germany, subsequently reported the occurrence of jaundice in patients undergoing antisyphilitic therapy, although they apparently considered its cause to be infectious jaundice occurring in patients made more susceptible either by their syphilitic infection or by the treatment given for it. It was reserved for Flaum and his associates,[11] in 1926, to point out that, in a clinic caring for persons with diabetes, those patients who acquired hepatitis were doubtless infected by contaminated needles or syringes; further, they suggested that the long incubation period of this disease distinguished it from the shorter incubation period of infectious hepatitis and raised the question whether two viruses might not exist. The prescience of these workers merits special mention, particularly in view of the considerable period of time that elapsed before their speculations were proved to be true.

In the late 1930's, Findlay and his associates[12] described the occurrence of jaundice in Africa in persons who had been immunized against yellow fever with a vaccine containing human serum and suggested the viral nature of the icterogenic agent. During the same period, Soper and Smith[13] and Fox and his associates[14] described outbreaks of jaundice in Brazil, following the use of yellow fever vaccine stabilized with human serum.

In addition, in England in 1938, both Propert[15] and McNalty[16] also incriminated human serum as the probable medium of transmission

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[8] Lürman, A.: Eine Icterusepidemie. Berl. klin. Wchnschr. 22: 20–23, 1885.

[9] Stokes, J. H., Ruedemann, R., Jr., and Lemon, W. S.: Epidemic Infectious Jaundice and Its Relation to the Therapy of Syphilis. Arch. Int. Med. 26: 521–543, November 1920.

[10] Ruge, H.: Zehn Jahre Gelbsucht in der Marine (1919–1929), Beobachtungen an 2500 Fällen. Ergebn. d. inn. Med. u. Kinderh. 41: 1–112, 1931.

[11] Flaum, A., Malmros, H., and Persson, E.: Eine nosocomiale Ikterus-epidemie. Acta med. Scandinav. Suppl. 16: 544–553, 1926.

[12] (1) Findlay, G. M., and MacCallum, F. O.: Note on Acute Hepatitis and Yellow Fever Immunization. Tr. Roy. Soc. Trop. Med. & Hyg. 31: 297–308, November 1937. (2) Findlay, G. M., and MacCallum, F. O.: Hepatitis and Jaundice Associated With Immunization Against Certain Virus Diseases. Proc. Roy. Soc. Med. 31: 799–806, May 1938. (3) Findlay, G. M., MacCallum, F. O., and Murgatroyd, F.: Observations Bearing on the Aetiology of Infectious Hepatitis (So-Called Epidemic Catarrhal Jaundice). Tr. Roy. Soc. Trop. Med. & Hyg. 32: 575–586, February 1939.

[13] Soper, F. L., and Smith, H. H.: Yellow Fever Vaccination With Cultivated Virus and Immune and Hyperimmune Serum. Am. J. Trop. Med. 18: 111–134, March 1938.

[14] Fox, J. P., Manso, C., Penna, H. A., and Para, M.: Observations on Occurrence of Icterus in Brazil Following Vaccination Against Yellow Fever. Am. J. Hyg. 36: 68–116, July 1942.

[15] Propert, S. A.: Hepatitis After Prophylactic Serum. Brit. M.J. 2: 677–678, 24 Sept. 1938.

[16] McNalty, A. S.: Acute Infectious Jaundice and Administration of Measles Serum. In Great Britain, Ministry of Health. On the State of the Public Health. Annual Report of the Chief Medical Officer of the Ministry of Health for the Year 1937. Publication No. 42. London: His Majesty's Stationery Office, 1938.

of hepatitis. They described the occurrence of the disease in children, following the injection of pooled measles immune serum.

Thus, it would appear that by 1940 serum hepatitis was either suspected or regarded in some parts of the world as a disease potentially transmissible by human serum containing an icterogenic agent. Despite this recognition in certain circles, the subject received little attention in the United States, and although an account of it had already been published here in 1939,[17] the concept of the true nature of serum hepatitis, and indeed of infectious hepatitis, had not yet reached a level of widespread general awareness in our medical profession. This, combined with the facts that (1) serum hepatitis had never been recognized as a military disease and (2) the human serum used in the vaccine had been heated to 56°C., for at least 30 minutes, apparently lulled any suspicion that might have arisen. It is easy to see, then, how the pressure created by the decision to immunize large numbers of troops that might be going into areas where yellow fever was highly endemic or epidemic made defensible the acceptance of the calculated risk of producing and inoculating millions of doses of yellow fever vaccine stabilized with human serum. That this would end in a catastrophe that evoked unjustly critical editorials [18] in certain segments of our press and outraged demands for congressional investigation by a member of the House of Representatives [19] was not anticipated.

The Epidemic and Its Characteristics

Although the exact number of cases of serum hepatitis that occurred in 1942 is not known, it is presumed that most of the 49,233 admissions to hospitals for hepatitis reported for the total U.S. Army were caused by the injection of yellow fever vaccine stabilized by human serum containing an icterogenic virus. Of these total Army figures, 33,569 cases were reported from the continental United States and 15,664 from theaters outside the continental United States.

Late in the autumn of 1941, the immunization of U.S. troops against yellow fever was initiated on a large scale. This program had been recommended by the Subcommittee on Tropical Diseases of the National Research Council in 1940 primarily because of the epidemic of yellow fever that year in the Nuba Mountains of the Anglo-Egyptian Sudan and the possibility that U.S. troops might eventually operate in Africa, India, and

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[17] See footnote 13, p. 333.

[18] Editorial: J.A.M.A. 120: 1110, 1 Aug. 1942.

[19] Representative J. Parnell Thomas (R–N.J.), ranking minority member of the House Military Affairs Committee, on 30 July 1942, urged congressional investigation of the cause of the 28,585 cases of yellow jaundice in the Army, apparently from the use of yellow fever vaccine. "The disclosures on the number of cases of jaundice are a national disgrace and the country is entitled to know what happened." Thomas continued: "I am sure that the parents of the stricken youths whose life expectation may have been reduced by the attack are not satisfied with the report that the Army hopes the situation has been cleaned up. The Nation is entitled to know what happened and who is to blame."

the East. The decision to immunize large numbers of men created a huge demand for yellow fever vaccine, and the burden for its production was undertaken, late in 1940, by the International Health Division of the Rockefeller Foundation, New York, N.Y. It is not the purpose of this paper to discuss the various aspects of this immunization program or the decisions that led to its adoption, but this whole subject has been carefully reviewed and documented by Long [20] and by Paul and Gardner. [21]

The first cases of hepatitis that were subsequently to be identified as serum hepatitis caused by yellow fever vaccine appeared in February 1942, and by the end of the first week in March of that year, it became clear from reports emanating from widely separated areas that an epidemic disease associated with jaundice had appeared in the Army. Although early suspicions were directed toward the possibility that yellow fever itself or epidemic catarrhal jaundice might be involved, it was rather quickly recognized that the occurence of jaundice in men throughout this country and in far-flung places abroad was associated with the previous injection of yellow fever vaccine and, indeed, with certain specific lots of it.

The possibility was early considered that the administration of the vaccine might have activated a virus latent in the host, causing hepatitis; however, the true nature of the situation was soon appreciated, and the human serum used to stabilize the vaccine was indicated as carrying an icterogenic agent that produced hepatitis. A speedy solution of this aspect of the problem was made possible by the work of a number of different groups and individuals working together and independently. The history of this indictment and the fascinating tale of the incrimination of certain lots of human serum that came from the Johns Hopkins University School of Medicine, Baltimore, Md., were well recorded by Sawyer and his associates. [22] Suffice it to say that Dr. Kenneth F. Maxcy, of the Army Epidemiological Board, and Dr. Karl F. Meyer, of the George Williams Hooper Foundation, were among those who furnished the penetrating and incisive epidemiologic evidence that made the solution possible. As a result, The Surgeon General, Maj. Gen. James C. Magee, on 14 April 1942, approved the recommendation to suspend the use of the yellow fever vaccine made by the International Health Division of the Rockefeller Foundation for 2 months, and to use the U.S. Public Health Service vaccine produced in its Rocky Mountain Laboratory, Hamilton, Mont. Subsequently,

[20] Long, Arthur P.: The Army Immunization Program. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume III. Personal Health Measures and Immunization. Washington: U.S. Government Printing Office, 1944, pp. 271–341.

[21] I am deeply indebted to Dr. John R. Paul with whom I worked closely from 1943 to 1946 in Egypt and in New Haven, Conn. Many of the points of view expressed in this history were derived from this association and from subsequent ones over the years. His concepts concerning hepatitis and its military importance were eventually set down in the following document: Paul, John R., and Gardner, Horace T.: Viral Hepatitis. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume V. Communicable Diseases. Washington: U.S. Government Printing Office, 1960, pp. 411–462.—W. P. H., Jr.

[22] Sawyer, W. A., Meyer, K. F., Eaton, M. D., Bauer, J. H., Putnam, P., and Schwentker, F. F.: Jaundice in Army Personnel in the Western Region of the United States and Its Relation to Vaccination Against Yellow Fever. Am. J. Hyg. 40: 35–107, July 1944.

human serum was omitted from the vaccine entirely. Justification of this action was borne out by the fact that, after it, cases of serum hepatitis following immunization with yellow fever vaccine failed to occur.

From its point of recognition in the week ending on 7 March 1942, the epidemic in the United States progressed rapidly and reached its peak of incidence in the week ending on 20 June, after which there was a steady, progressive decline (chart 2). A similar situation was recognized in widely

CHART 2.—*Weekly admissions for jaundice (essentially serum hepatitis) in the U.S. Army in continental United States, January–December 1942*
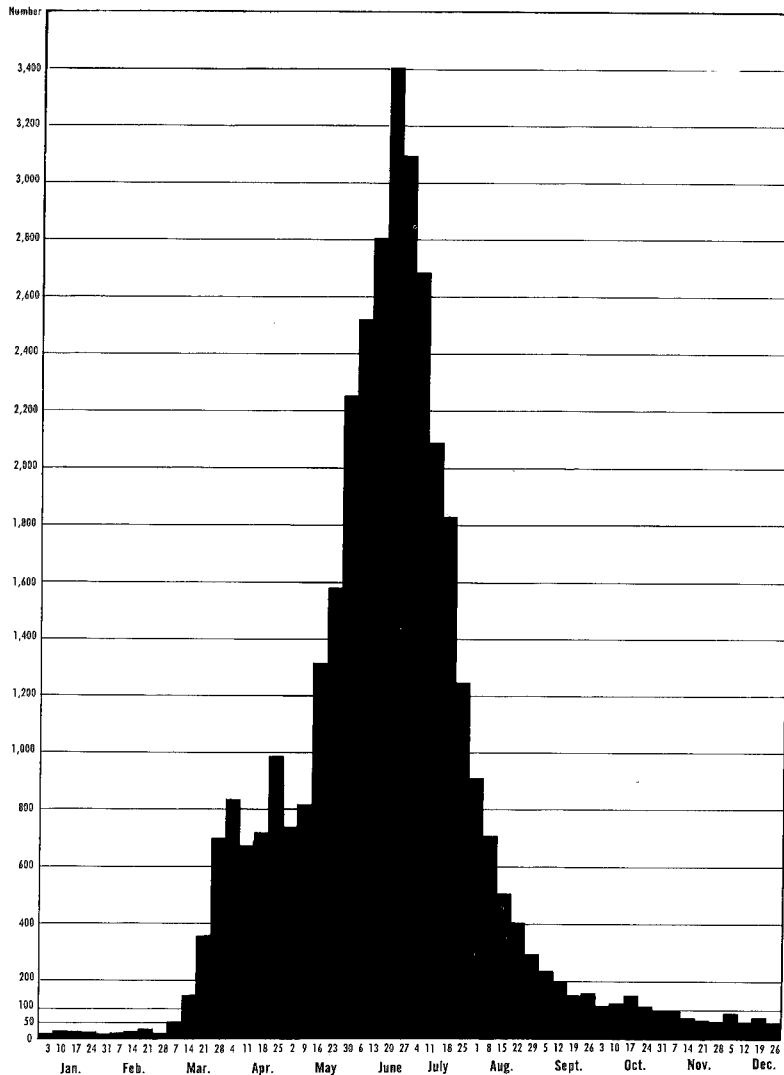
CHART 3.—*Weekly admissions for jaundice (essentially serum hepatitis) in the U.S. Army overseas, January–December 1942*

Number

1,200

1,000

800

600

400

200
100
50
0

3 10 17 24 31 7 14 21 28 7 14 21 28 4 11 18 25 2 9 16 23 30 6 13 20 27 4 11 18 25 1 8 15 22 29 5 12 19 26 3 10 17 24 31 7 14 21 28 5 12 19 26

Jan. Feb. Mar. Apr. May June July Aug. Sept. Oct. Nov. Dec.
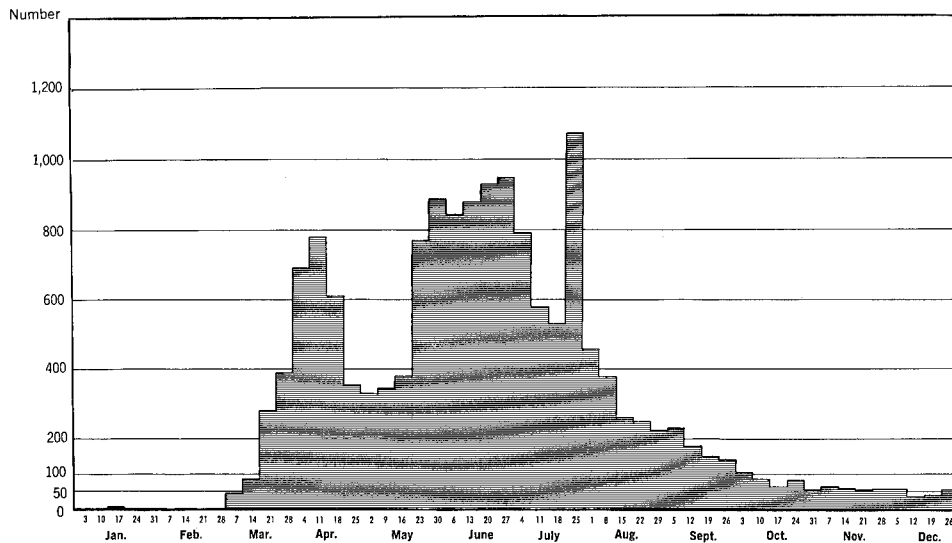
separated localities abroad during the first 2 weeks in March, but the peak of incidence of the disease appeared to occur 1 or 2 weeks later than in the continental United States. The decline of incidence abroad was also similar to that in this country (chart 3).

The first information about jaundice on board American troop ships came by way of a telephone message from Dr. Andrew Davidson, Chief Medical Officer of Health for Scotland, on Wednesday, 13 May 1942, advising that there were 26 cases among approximately 20,000 troops. These men continued to their destination in Northern Ireland, and during the ensuing weeks, the number of cases increased. Almost all these patients were sent to the 5th General Hospital, near Belfast. By 20 May 1942, 83 patients had been admitted to the wards, and by the end of the next week, 231 patients had been admitted. A number of clinical and laboratory investigations were initiated, and the relationship of the epidemic with the previous injection of yellow fever vaccine stabilized with human serum was established. A total of 1,915 cases occurred, of which 1,591 were in Northern Ireland and 324 in Great Britain.

In the course of the inquiry made in Northern Ireland during the period of 20–27 May 1942, repeated reference was made to "Honolulu disease" by a number of the medical officers who had accompanied the affected troops from the United States, and the statement was made that the jaundice prevalent in U.S. troops in Ireland was identical with that condition. Honolulu disease appeared to have originated at Fort Sam

Houston, Tex., in January 1942, where it was studied by staff members of the Rockefeller Foundation who were said to have come to the conclusion that the jaundice there was due to the ingestion of infected pork and that the infectious agent was a filtrable virus. It was regarded as communicable, and the incubation period was fixed at about 10 to 14 days. Subsequently, troops from this post moved to Fort Ord, Calif., for embarkation to the Hawaiian Islands. Two convoys, members of the 27th Infantry Division, were moved to the Islands. One, including 5,252 men, left San Francisco, Calif., on 10 March and arrived in Honolulu on 14 March 1942. The second convoy left on 30 March and arrived on 3 April, carrying about 5,800 men. During the passage to Hawaii, 1 case of jaundice developed in the first convoy and 11 in the second convoy. On arrival in Honolulu, additional cases began to appear at about 2-week intervals, tending to occur in crops. By 3 April 1942, there were 500 patients in hospitals in Honolulu with jaundice. Although it was the belief of some of the physicians in Hawaii that the condition was unrelated to the administration of yellow fever vaccine, it indeed seemed to represent the same situation as occurred in the Zone of Interior, in Northern Ireland and Great Britain, and in other parts of the world. Its appearance, in January 1942, suggested that lots of vaccine inoculated as early as October 1941 were probably involved. [23]

An epidemic of serum hepatitis with approximately 1,520 cases occurred in Iceland in 1942, beginning with troops arriving there during March and April. Most of these men had been vaccinated against yellow fever with lot No. 368. In Canada, U.S. troops had the first case of serum hepatitis in the middle of May 1942, with an increasing number of new cases until a peak was reached around the first or second week of July. A few new cases appeared after this in August, but none thereafter. In the Central Pacific Area, serum hepatitis made its advent in troops arriving at Oahu between 10 and 16 March 1942, and in the Southwest Pacific Area, an outbreak occurred in 1942 among U.S. troops in Australia. In the entire Pacific Ocean Area, several hundred patients were hospitalized.

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[23] At the time of the Pearl Harbor raid and subsequent thereto, Fort Armstrong was the post guarding the entrance to Honolulu Harbor. As one of his duties, the Port Surgeon was required to board and inspect all troop convoys before they docked. The occurrence of one case of jaundice of undetermined origin in the first convoy of troops cited above did not appear to warrant restriction of the whole convoy, and the Hawaiian Department surgeon, Col. Edgar King, MC, transmitted instructions to permit the convoy to dock, which was done. Soon after debarking, other cases of jaundice developed, and it was then thought that they represented mild cases of yellow fever contracted from the yellow fever inoculations. This introduced an immediate problem since the mosquito vector of yellow fever, Aedes aegypti, was present in Hawaii. Emergency measures were set in motion by quickly erecting a tent camp next to the Honolulu docks and surrounding it by a fence for quarantine purposes. The debarked troops were returned to dockside, placed in this quarantine, and mosquito control measures instituted. Daily inspections of the troops were carried out and all new cases of fever or jaundice hospitalized. When word was received concerning cases of jaundice aboard the second convoy, the quarantine camp was immediately expanded and these troops debarked directly into it when they arrived. Of course, many more cases developed subsequently, and the affected personnel were hospitalized. Finally, the number of cases subsided, the true nature of the jaundice was revealed, and the quarantine was lifted.—A. L. A.

Seven different lots of yellow fever vaccine (Nos. 331, 334, 335, 338, 367, 368, and 369) were identified as those that produced the outbreak of serum hepatitis. Six of these lots were highly icterogenic, and to three of them (Nos. 367, 368, and 369) were traced the greatest number of cases. Personnel of the entire Air Corps and those of the Ground Forces troops who were scheduled for duty overseas were immunized with yellow fever vaccine in the latter part of 1941. Among the lots used were three highly icterogenic ones. The second phase of immunization occurred between 20 January and 15 April 1942 when all the personnel in the Army were vaccinated. The remaining icterogenic lots of vaccine were used during this time. The first peak of the epidemic, occurring in March–May 1942, represented cases occurring in men immunized in the previous autumn; the second peak, occurring from late May through July ,was made up of cases occurring in men immunized during the second period of vaccination.

It was early appreciated that the incubation period of this disease was unusually long and, in addition, highly variable, ranging from 60 to 150 days. This variability was emphasized by Parr,[24] who studied a large outbreak at Camp Polk, La., where 5,000 men were inoculated with lot No. 369, on 27 February 1942; 1,004 cases of hepatitis with jaundice occurred among these men. The differences in incubation period were interpreted as the result of variations in the state of health of the hosts.

A striking characteristic of the outbreaks that occurred both in the continental United States and abroad was the apparent failure of the disease to spread to persons who had not been similarly immunized. Occasional incidents were reported, however, in which the wives of men with postvaccinal hepatitis acquired hepatitis. This lack of communicability by personal contact except possibly under most intimate terms was a matter of great interest, particularly to those charged with the responsibility of attempting to determine the relationship between serum hepatitis and the naturally occurring epidemic disease.

There were those, however, who felt that actually a considerably greater communicability existed, and postulated the concept that the immunization with the yellow fever vaccine had not been directly responsible for the occurrence of hepatitis but rather that it rendered the men more susceptible to the naturally occurring disease. Freeman [25] described outbreaks at Fort Belvoir, Va., Fort Sill, Okla., and Fort Lewis, Wash., in which an increase in incidence of hepatitis among unvaccinated troops occurred during outbreaks in men who had been immunized with icterogenic lots. It seems fair to say that this concept was probably not valid in view of the vast amount of evidence incriminating certain lots of serum

[24] Parr, L. W.: Host Variation in the Manifestation of Disease, With Particular Reference to Homologous Serum Jaundice in the Army of the United States. M. Ann. District of Columbia 14: 443–449, October 1945.

[25] Freeman, G.: Epidemiology and Incubation Period of Jaundice Following Yellow Fever Vaccination. Am. J. Trop. Med. 26: 15–32, January 1946.

as icterogenic. However, complete unanimity of opinion on this subject was not attained.

Among the curious strokes of fate was the statistical improbability that allowed the absence of postvaccinal hepatitis in the Navy. They had received only two lots of icterogenic vaccine (Nos. 334 and 369) and had used them sparingly. Thus, at the meeting, on 14 April 1942, at which the recommendation to discontinue yellow fever vaccine produced by the International Health Division of the Rockefeller Foundation was approved by Surgeon General Magee, Capt. (later Rear Adm.) Charles S. Stephenson, MC, of the Navy, was able to state that there had been no jaundice among Navy personnel following immunization with this vaccine. About half a million men had been immunized before the end of December 1941, and its use had been continued since that time.

Clinical Aspects

Numerous opportunities occurred for large clinical studies, and a number of good ones were made. It was early recognized that, after onset of the disease, the clinical course was indistinguishable from that of epidemic hepatitis or so-called catarrhal jaundice. For this reason, the major discussion of the clinical aspects will be reserved for inclusion in the section dealing with infectious hepatitis.

Certain special features were observed, however, that served to differentiate serum hepatitis from the epidemic disease. Important among these was the type of onset that was described as insidious in contrast to the more abrupt beginning of infectious hepatitis. Fever of any significance was unusual in patients with serum hepatitis in contrast to the common occurrence of fever, often of considerable degree, in patients at the onset of the epidemic disease. In addition, arthralgia, urticaria, and itching were common enough in patients at the onset of serum hepatitis to mark these symptoms as clinical differences between the two conditions.

Among the best clinical accounts was that of Turner and his colleagues [26] who described an outbreak at Camp Polk among men who had been immunized with yellow fever vaccine lot No. 369. The epidemic was heralded by a sharp increase in admissions of patients with jaundice to the hospital during the first week in May, progressing to its peak during the week of 20 June, and declining thereafter with a low level attained in the first week in September. The incubation periods ranged from 8 to 23 weeks. During the period of 1 May–12 September 1942, 4,083 patients were observed and, of these, 14 died. It was of interest that those who died had their first symptoms in the early part of the outbreak, from 15 May to 10 June, and the disease appeared to be milder in those patients who were

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[26] Turner, R. H., Snavely, J. R., Grossman, E. B., Buchanan, R. N., and Foster, S. O.: Some Clinical Studies of Acute Hepatitis Occurring in Soldiers After Inoculation With Yellow Fever Vaccine, With Especial Consideration of Severe Attacks. Ann. Int. Med. 20: 193–218, February 1944.

admitted after the incidence was declining. Since these men were inoculated at the same time, the question may be raised whether prolongation of the incubation period might have been another manifestation of the mildness of the disease.

Because every effort was made to get patients into the hospital promptly, it was possible to study a goodly percentage of these men early in the course of disease. Fifty-two percent were admitted during their first week of illness and 41 percent during their second or third week of illness. The remaining 7 percent straggled in thereafter. The onset of disease was usually vague and insidious, with mild afternoon fatigue and malaise, followed subsequently by the appearance of anorexia, weakness, nausea, abdominal pain and distress, and vomiting. Other symptoms of note, although less common, were arthralgia, pain in the back, urticaria, burning of the eyes, lassitude, and headache. Despite the frequency of these symptoms, attention was called to the fact that a fair number of patients with jaundice were completely asymptomatic. Fever was not common and, if it occurred, lasted only 2 or 3 days. Diurnal variations of anorexia, abdominal distress, and even enlargement of the liver were described, with an increase in signs and symptoms at the end of the day. In a certain number of patients, sudden attacks of severe weakness and sweating occurred, suggesting hypoglycemia, and relief was afforded by the ingestion of a meal of carbohydrates. A small percentage of patients had actual pain in the right upper quadrant of the abdomen or the lower part of the right side of the chest, radiating up to the neck and the right shoulder. This was often made worse by walking or deep breathing. Although suggestive of diaphragmatic irritation, no report was made of hearing a friction rub. On occasion, pain in the right lower quadrant of the abdomen simulated acute appendicitis, and it was sometimes not possible to make a differential diagnosis without laparotomy.

Aside from jaundice, enlargement and tenderness of the liver were the two most striking findings, occurring in 40 percent (hepatomegaly) and 20 percent (hepatic tenderness) of patients. Petechial hemorrhages in the skin and mucous membranes were frequently observed in the seriously sick patients but also, on occasion, in the mildly sick. They extended over the lateral aspects of the chest and arms and were often widespread. Occasional patients had spider nevi that disappeared during convalescence.

Classification of cases in relation to degree of severity was made on the basis of three different criteria—the intensity and the duration of jaundice and the maximum loss of weight. Under these terms, 81 percent were regarded as mildly sick, 17 percent moderately severely sick, and 2 percent severely sick. Included in those regarded as mildly sick was a group of patients with so-called "trivial illness." The diagnosis of hepatitis in these patients was made not infrequently on the basis of symptoms and the presence of bilirubinuria without clinical jaundice. It is indeed of

interest that the diagnosis of hepatitis without jaundice, subsequently to become a controversial subject in some quarters, should have been made so early in this clinical experience. However, it is obvious that the epidemiologic pattern of disease in men who had been inoculated with a highly icterogenic lot of yellow fever vaccine (No. 369) supported the validity of this concept. Of even greater interest, however, was the suggestion that, although there was little unequivocal evidence of a subclinical form of the disease, the medical officers involved in this study felt that there was sufficient to cause them to believe in the existence of this entity also.

It was appreciated that worsening of the course of the disease could occur quite subtly and quickly, and certain guides in prognosis came to be used. Considerable confidence was placed in the capacity of patients to respond vigorously to the parenteral administration of vitamin K as a favorable sign. Frequent measurements of the degree of bilirubinuria, the gain or loss of weight, and the amount of food consumed were made, and continued anorexia and loss of weight with deepening jaundice were regarded as ominous.

Among the fatal cases, death occurred from 24 to 101 days after onset of the disease. In a goodly percentage of them, death came later rather than earlier in the course of the disease, and attention was called to the fact that, in patients who lived for a longer period, alterations in type of hepatic involvement occurred as well as changes in other organs. Thus, it was believed that, during the more prolonged course of the disease that eventually terminated fatally, the continuing necrosis and regeneration brought about structural changes in the liver, resulting in (1) certain manifestations of intrahepatic obstructive jaundice and (2) changes in vascular patterns, with increase of portal pressure. Portal hypertension with congestive splenomegaly did occur and, on occasion, with excessive hemolysis and rupture of esophageal varices.

Lucké [27] described in detail the findings at necropsy of a larger group of fatal cases, and they will be dealt with more fully in the section on "Infectious Hepatitis." At this point, they may be summarized as ranging from massive acute hepatic necrosis in those dying early to varying degrees of hepatic necrosis and regeneration with alterations of the lobular architecture in those succumbing later in the course of the disease. Edema and hemorrhagic changes in the gastrointestinal tract were common.

Complications

Complications fundamentally related to the underlying disease included neurologic disturbances, gastrointestinal hemorrhage, ascites,

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[27] Lucké, B.: Pathology of Fatal Epidemic Hepatitis. II. Structure of Liver After Recovery From Epidemic Hepatitis. Am. J. Path. 20: 471–593, 595–619, May 1944.

macrocytic anemia, gingivitis, renal dysfunction, hemorrhages into the skin and mucous membrane, and morbilliform rashes. Most of them were evidence of increased severity of the disease, although on occasion milder cases did have numerous petechial hemorrhages in the skin and mucous membranes. Neurologic disturbances were often bizarre. Severe emotional and mental disarray were followed often by tremor and coma. Gastrointestinal hemorrhage occurred not only from rupture of esophageal varices but also from direct bleeding into the gastrointestinal tract from multiple small points. In fatal cases, hemorrhage into the mesentery was observed, and in at least one patient, this was associated with considerable abdominal pain and tenderness before death. Gingivitis was thought to be due to multiple minute hemorrhages in the gums. Renal dysfunction was manifested largely by albuminuria, although in seriously sick patients or fatal cases azotemia occurred. Of particular interest was the description of the so-called tremor syndrome. It was observed during convalescence or even after apparent recovery and consisted of a slow, coarse tremor of the extremities at rest, made worse by movement. This, at times, appeared to be associated with weakness, and one patient was described as having his knees "buckle under him" so that he fell down. There was no apparent association of this with hypoglycemia, and the ingestion of food gave no relief.

Delayed recovery occurred in a small percentage of patients, whose complaints were primarily concerned with easy fatigue and disorders of the gastrointestinal tract. Anorexia, intolerance for fatty foods, pain in the right upper quadrant of the abdomen after exercise, anxiety, and tremor were common symptoms. They appeared to reflect, in most instances, what was subsequently termed the "posthepatitis" syndrome.[28] In a survey of 200 soldiers who had been sent back to the United States from overseas after several months of hospitalization because of such delayed recovery, Col. Julien E. Benjamin, MC, and Maj. Ralph C. Hoyt, MC,[29] found that most of the soldiers were without objective evidence of hepatic disease and required only an adequate diet, physical reconditioning, and indoctrination to restore them to health. In many instances, the cause of disability was a neurosis that had been latent but reactivated by the advent of hepatitis. Of 127 of these soldiers whose capacity to excrete intravenously administered Bromsulphalein (sulfobromophthalein) was measured, only 11 (8.7 percent) had abnormal tests and most of these eventually returned to normal.

Treatment

Treatment was concerned with rest and frequent feedings of carbohydrates. The prescribed diet was high in carbohydrate and protein and

[28] Caravati, C. M.: Posthepatitis Syndrome. South. M.J. 37: 251–257, May 1944.

[29] Benjamin, J. E., and Hoyt, R. C.: Disability Following Postvaccinal (Yellow Fever) Hepatitis; Study of 200 Patients Manifesting Delayed Convalescence. J.A.M.A. 128: 319–324, 2 June 1945.

low in fat. Clinical trials of the administration of various vitamin supplements, methionine and choline, apparently did not expedite recovery. In seriously sick patients, it was believed that the course of their disease was not favorably altered by administration of vitamins, transfusions of blood or plasma, or intravenous infusions of dextrose in saline. However, it is hard to believe that the provision of adequate amounts of fluid and electrolytes with dextrose might not have played a role in the recovery of certain patients.

Other Sources of Serum Hepatitis

Despite the fact that the major outbreak of homologous serum hepatitis was terminated by the omission of human serum from yellow fever vaccine, this was not to end our experience or that of others with this disease. The tremendous need for transfusions of blood and plasma and the lack of effective methods of ridding these materials of viable hepatitis viruses made serum hepatitis a continuing problem.[30] Maj. Paul B. Beeson, MC,[31] in England, predicted early in 1943 the hazards attending the use of such transfusions, and on 1 June 1945, in a survey of 1,762 cases of hepatitis under treatment in general hospitals in the United States, Sartwell [32] justified this prophecy. Of these patients, 500 gave a history of receiving transfusions of blood or its products before the onset of hepatitis, and of the 500, a large proportion appeared to have been infected by this means. There is every reason to believe that the early awareness of this hazard in the minds of British and United States medical officers in England was important in the education of our medical officers in the Zone of Interior in the recognition of this disease.

The pooling of plasma from large numbers of persons augmented the risk of infection, and the course of the disease was often much more severe in patients debilitated by trauma and exhaustion. Because of these problems, efforts were made in 1944–45 to determine whether the prophylactic effect of normal human gamma globulin that had been recently demonstrated in infectious hepatitis might also be true for serum hepatitis. Grossman and his associates [33] were successful in demonstrating protection when two intramuscular injections of 10 ml. each were given 1 month

[30] (1) Morgan, H. V., and Williamson, D. A. J.: Jaundice Following Administration of Human Blood Products. Brit. M.J. 1: 750–753, 19 June 1943. (2) Homologous Serum Jaundice. (Memorandum prepared by medical officers of the Ministry of Health.) Lancet 1: 83, 1943. (3) Editorial: Hepatitis After Transfusion. Brit. M.J. 2: 279, 1944.

[31] Beeson, P. B.: Jaundice Occurring One to Four Months After Transfusion of Blood or Plasma. Report of Seven Cases. J.A.M.A. 121: 1332–1334, 24 Apr. 1943.

[32] Sartwell, P. E.: Infectious Hepatitis in Relation to Blood Transfusion. Bull. U.S. Army M. Dept. 7: 90–100, January 1947.

[33] Grossman, E. B., Stewart, S. G., and Stokes, J., Jr.: Posttransfusion Hepatitis in Battle Casualties and a Study of Its Prophylaxis by Means of Human Immune Serum Globulin. J.A.M.A. 129: 991–994, 8 Dec. 1945.

apart following transfusion, while Duncan and his associates [34] failed to find any protective effect when a single injection was given.[35]

The painfully won awareness of other methods of artificial transmission of hepatitis also emerged during these years of World War II. Inadequately sterilized syringes and needles were indicated in its transmission in procedures involving withdrawal of blood for laboratory determinations or injection of medications.[36] Clinics for the care of patients with syphilis, diabetes, and arthritis achieved recognition as areas of high risk for the accidental transmission of hepatitis, and ample proof of the role of the needle and the syringe was afforded by a sharp reduction in the incidence of the disease following the institution of adequate sterilization of these instruments. It can truly be said that the widespread recognition of these various hazards constituted a major advance in medical knowledge, initiated largely by military experience but penetrating deeply into civilian practice.

INFECTIOUS HEPATITIS

Historical Background

The importance of infectious hepatitis in medical military history has long been recognized. Troops concentrated during war appear to have been particularly vulnerable, and in this country and abroad the military history of the last two centuries is replete with accounts of epidemics of jaundice, many of which doubtless represented this disease. During World War I, British[37] and French troops[38] in the Mediterranean area and in the Dardanelles suffered serious outbreaks, and during World War II, it was a major cause of loss of time in both Allied and Axis forces.[39]

Attention has been called to the fact that the concept of the nature of infectious hepatitis generally held in this country was somewhat naive at the beginning of World War II. The term "catarrhal jaundice" was widely used to define sporadically appearing cases or outbreaks of jaundice.

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[34] Duncan, G. G., Christian, H. A., Stokes, J., Jr., Rexer, W. F., Nicholson, J. T., and Edgar, A.: Evaluation of Immune Serum Globulin as Prophylactic Agent Against Homologous Serum Hepatitis. Am. J.M. Sc. 213: 53–57, January 1947.

[35] The discrepancy in these results became a matter of discussion intermittently during the ensuing years and, eventually, prompted the studies of Mirick and his coworkers who, in 1962, reported that the intramuscular administration of 10 ml. of gamma globulin on two occasions, 1 month apart, to recipients of transfusions of whole blood significantly reduced the incidence of hepatitis with jaundice, although the attack rate of anicteric hepatitis was similar to that in transfused patients who had not received gamma globulin. *See* Mirick, G. S., Ward, R., and McCollum, R. W.: Gamma Globulin in the Control of Hepatitis Following Blood Transfusion. Vox Sang. 7: 125–126, 1962.

[36] (1) Role of Syringes in Transmission of Jaundice. (Memorandum prepared by medical officers of the Ministry of Health.) Lancet 2: 116, 1945. (2) Mendelssohn, K., and Witts, L. J.: Transmission of Infection During Withdrawal of Blood. Brit. M.J. 1: 625–626, 5 May 1945.

[37] Martin, C. J.: Concerning the Pathology and Etiology of the Infectious Jaundice Common at the Dardanelles, 1915. Brit. M.J. 1: 445–447, 7 Apr. 1917.

[38] See footnote 4, p. 331.

[39] See footnote 21, p. 335.

Despite the fact that Eppinger [40] and Rich [41] had long since described diffuse hepatocellular necrosis in patients with this disease at necropsy, the early concept of Virchow [42] that catarrhal jaundice resulted from the obstruction caused by a plug of mucus in the ampulla of Vater was widely accepted, resisting even the reports of later investigators, including Roholm and Iversen,[43] who described inflammatory and degenerative changes in the hepatic parenchymal cells in specimens of the liver obtained by biopsy from patients with infectious hepatitis. It was actually not until we were well along in World War II that the true nature of this infection was generally appreciated by our civilian physicians and medical officers in this country and abroad.

Knowledge of the causative organism of this disease was slow to develop, and recognition of its viral etiology, although suspected somewhat earlier, was largely a product of studies carried on during World War II. Prior investigations were concerned with the possible role of *Leptospira icterohemorrhagiae,* and during World War I, the recovery of certain strains of salmonellae from the blood or feces of patients with jaundice, as well as the development of antibodies in their blood to certain strains of salmonellae, suggested that these organisms might be etiologically involved.[44] In view of information made available during World War II, it is likely that these latter observations reflected the simultaneous occurrence of two diseases whose manner of spread (the intestinal-oral route) was the same.[45]

It would appear that infectious hepatitis enjoyed little prominence in the U.S. Army during the decade before World War II. Up until 1939, it was reportable not as an entity but under such entries as "spirochetal hemorrhagic jaundice," "other protozoal diseases," or "other disease of the gallbladder and biliary passages"; after that, and until 1943 when the term "hepatitis" was used, it was variously reported or coded as "spirochetal jaundice," "cholangitis," or "other disease of the gallbladder and biliary ducts." During the period from 1938 to 1941, the incidence ranged from 1.2 to 1.93 per annum per 1,000 average strength. This was not unlike the incidence recorded from 1931 through 1937 when a few cases of disease specifically involving the gallbladder or ducts were also included with cholangitis. Similar figures characterized the situation in the British Army in England; however, in contrast to both was the experience of the British garrison in Malta in which there was a steady increase in the

[40] Eppinger, H.: Die Pathogenese des Ikterus. Verhandl. d. deutsch. Gesellsch. f. inn. Med. 34: 15–39, 1922.

[41] See footnote 7, p. 332.

[42] Virchow, R.: Ueber das Vorkommen und den Machweis des Hepatogenen, Insbesondere des Katarrhalischen Icterus. Virchows Arch. f. path. Anat. 32: 117–125, 1865.

[43] Roholm, K., and Iversen, P.: Changes in Liver in Acute Epidemic Hepatits (Catarrhal Jaundice) Based on 38 Aspiration Biopsies. Acta path. et microbiol. Scandinav. 16: 427–442, 1939.

[44] See footnote 4, p. 331.

[45] Havens, W. P., Jr., and Wenner, H. A.: Infectious Hepatitis Complicated by Secondary Invasion With Salmonella. J. Clin. Investigation 25: 45–52, January 1946.

incidence of hepatitis from 1932 to 1939 when it reached 13.9 per 1,000.[46] In retrospect, it should not have been surprising that our immunologically naive troops sustained tremendous casualties from this disease after they entered the Mediterranean area that was to serve as the scene of a great outbreak as well as the seeding place of the disease in troops who were eventually to go to the European theater and act as a reservoir for its spread there. In the vast Pacific area as well, infectious hepatitis was to loom as one of the most important causes of morbidity (table 66).

TABLE 66.—*Admission rates for infectious hepatitis and serum hepatitis among U.S. Army personnel at all medical treatment facilities in selected areas, 1942-45*

[Preliminary data based on tabulations of individual medical records and summaries of statistical health reports]
[date expressed as number of cases per 1,000 average strength per annum]

Year	Total Army	Continental United States	Southwest Pacific	Europe
1942-45	7.16	3.17	27.50	6.89
1942	15.18	12.63	26.51	23.49
1943	4.20	.75	3.40	7.81
1944	3.57	.80	9.21	2.58
1945	10.10	2.08	45.97	9.46

Although a number of interesting observations were made, particularly from the epidemiologic standpoint in the latter two areas, the major studies that eventually reached publication were carried on in the Mediterranean area, and it is with these activities that this section is largely concerned.

Mediterranean Area and Middle East Theater

Relatively small numbers of U.S. troops went into Egypt in the early autumn before the subsequent major landings in North Africa in November 1942. It became known very shortly that French, British Commonwealth, and Axis troops had had a bitter experience with epidemic hepatitis at various times during the period from 1939 to 1942 in the North African desert. The French stationed large bodies of troops in southern Tunisia during the spring and summer of 1939 to handle any threat the Italians might make from Libya. Hepatitis appeared among them in September 1939, reaching its peak in December, and declining in January 1940.[47] Jaundice first developed among the German troops near Sirte and Benghazi during the fall of 1940, rapidly became a serious problem among

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[46] Dixon, H. B. F.: Notes on Infective Hepatitis in Malta, 1938-1942. J. Roy. Army M. Corps 82: 44-48, January 1944.

[47] Essential Technical Medical Data, North African Theater of Operations, U.S. Army, for September 1944, dated 1 Oct. 1944.

them, and later spread to the Italian ground troops and air force. Thousands of cases occurred but the Germans appeared more vulnerable than the Italians, with a ratio of three to one cases. In May 1943, the closing of the Tunisian campaign revealed that large numbers of German and Italian prisoners were jaundiced.[48] Australian troops were involved late in 1941 while attempting to hold Tobruk, and in the following year they, the New Zealanders, and the British Eighth Army were caught up in a great epidemic during and after the campaign for El Alamein.

In 1942, the epidemic was well on its way in August and reached a peak in November. In U.S. troops in Egypt during that autumn and winter, the disease first occurred in the fliers and ground troops of the Ninth Air Force, as these men operated between Alexandria, Benghazi, and Tobruk. Despite the fact the U.S. troops in Egypt had an appreciable amount of hepatitis among the small numbers of men there, the incidence among U.S. forces in North Africa (Algeria and Tunisia) was low during the autumn and winter of 1942–43 and remained so into the summer of 1943.

This security was not to last for long, however, and in the late summer of 1943 began the volcanic experience that was to erupt into the most expensive and devastating problem that we were to encounter in relation to infectious hepatitis. It came to be, during 1943–45, the most important cause of man-days lost due to illness among U.S. forces in the Mediterranean-North African theater. As a cause of death due to medical disease it ranked high, although the case fatality was low (about 1.8 per 1,000). That this should have occurred coincident with the invasion of Sicily and should involve British Commonwealth and American troops in Egypt, in North Africa, and subsequently in Sicily and Italy was a hindrance of inestimable magnitude to military activity and strained the medical facilities almost beyond their capabilities. It is no exaggeration to say that the hospitals from Cairo to Palermo were filled with patients with hepatitis, with beds occupying the corridors and every other available space. The task of caring for all these patients in addition to the mounting numbers of battle casualties was indeed a formidable one.

Thus, for the second time within a short period, U.S. forces and their medical officers and civilian consultants were confronted with a great epidemic of hepatitis, this time, however, the naturally occurring disease. Our first major experience with hepatitis in the North African theater started when the disease appeared in a seasoned combat division in the late summer of 1943. These men had been in prolonged combat at Hill 609 and later in bivouac and guarding Axis prisoners. A severe outbreak of diarrhea occurred among them in May, June, and the first half of July, and hepatitis began to appear at the end of July. The incidence increased

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[48] Report, Col. Marion H. Barker, MC, to Surgeon, Mediterranean Theater of Operations, APO 512, 23 July 1945, subject: Final Report on Infectious Hepatitis in MTOUSA.

sharply in this division and the disease spread rapidly to others.[49] This was to harass us during the next 18 months in the long and bitter campaign in Italy where the incidence rose astronomically in the autumn and winter of 1943–44 and again, although in lesser magnitude, in 1944–45 (table 67).

TABLE 67.—*Incidence of hepatitis among U.S. troops in the Mediterranean and Africa-Middle East theaters, 1942–45*

[Preliminary data based on summaries of statistical health reports]

[Rate expressed as number of cases per annum per 1,000 average strength]

Year	Mediterranean theater			Africa-Middle East theater		
	Mean strength	Number of cases	Rate	Mean strength	Number of cases	Rate
1942	21,328	33	1.5	5,764	81	14.1
1943	423,114	15,865	36.8	52,349	257	4.8
1944	659,661	14,980	22.7	47,376	294	6.2
1945	331,325	7,584	22.9	40,884	351	8.6

It was quite natural that those interested in and charged with the responsibility of solving the many problems associated with this situation should be influenced by their recent experiences with the outbreak of the artificially transmitted disease, serum hepatitis. However, it was impossible to apply some of the information previously gained without confusing the present circumstances. As might be expected, attempts were made early to think in terms of the long incubation period of homologous serum hepatitis in considering certain epidemiologic problems confronting us in North Africa. That this was untenable was soon appreciated, and our awareness of this was expedited by consultation with British medical officers who marked the incubation period of the epidemic disease as between 30 and 40 days. That this or possibly an even shorter period was indeed true was borne out by experiences encountered later in fresh U.S. troops who contracted hepatitis 1 month after arrival in Italy and only 6 weeks after leaving the Zone of Interior.

Outstanding among the problems associated with this vast epidemic was the lack of knowledge of how the disease was transmitted. In the desert campaigns in 1940–42, British, German, and Italian forces had been ravaged by infectious hepatitis. In early October 1942, just as the British launched their counteroffensive at El Alamein, the disease again became a problem, and as the battle progressed, the acquisition of hepatitis by troops became clearly associated with their exposure to unsanitary conditions that were almost unbelievable. The British were impressed with the

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[49] Report, Col. Marion H. Barker, MC, Maj. Richard B. Capps, MC, and Maj. Frank W. Allen, SnC, to Surgeon, MTOUSA, APO 512, U.S. Army, subject: Clinical Monograph on Infectious Hepatitis.

likely role of feces in the spread of the disease. Along the "Black Area" of the Alamein Line, the ground was covered by human excrement and incompletely buried corpses of German and Italian troops. Myriads of flies were present, and Lt. Col. Raymond Kirk,[50] of the New Zealand General Hospital, reported the occurrence of 1,060 cases among 7,000 troops in the area. He suggested that the disease might well be flyborne on the basis of the rapid spread of disease among troops living and fighting under these unsanitary conditions in contrast to the failure to spread in hospitals and prisoner-of-war camps where hygiene was good and fly abatement was successful. Others hypothesized that the method of spread of disease was by (1) droplet infection among contacts; (2) vectors, such as rodents, insects, or pigs; and (3) man, as a manifestation of bacterial warfare. The possibility that it was due to or made worse by malnutrition and inadequate diets was also mentioned.

An early proponent of the importance of feces in the spread of epidemic hepatitis was Maj. C. E. van Rooyen, RAMC, who was stationed at the 15th Scottish General Hospital in Cairo. Major van Rooyen who was interested in testing this hypothesis in volunteers expressed this view on more than one occasion to certain members of the Commission on Neurotropic Virus Diseases, Army Epidemiological Board.[51] This group had been in Cairo since early 1943, sent by the Preventive Medicine Service of the Office of The Surgeon General to work on certain diseases of military importance in the Middle East, and sandfly fever and poliomyelitis had engaged their efforts during the first part of their stay.

Early in September 1943, Brig. Gen. James S. Simmons, MC, Chief, Preventive Medicine Service, representing the Army Epidemiological Board, came to Cairo after visits to Sicily and North Africa. At his request, certain members of the Commission on Neurotropic Virus Diseases directed their attention to the epidemiologic and etiologic aspects of infectious hepatitis and, among other things, made a field trip to Algiers, Sicily, and Tunis, in November 1943. As a result of the observations made on this trip and on others, certain concepts were elaborated concerning the length of the incubation period of epidemic hepatitis, its age distribution, and its relationship to serum hepatitis. The incubation period appeared to range from 18 to 25 days; the paucity of cases among adult natives suggested it was a disease of childhood, with immunity acquired early; and U.S. soldiers recovered from serum hepatitis were not immune to epidemic hepatitis when exposed in the Mediterranean theater. The vulnerability of air forces personnel was particularly noticeable, and it was not unusual for complete units to be grounded because of the high incidence (25 to 30 percent) of disease among them. The coexistence of dysentery and hepatitis in many military units stimulated interest in their relationship; how-

[50] Kirk, R.: Spread of Infective Hepatitis. Lancet 1: 80–81, 20 Jan. 1945.

[51] Members included Dr. John R. Paul, Director; Maj. (later Lt. Col.) Albert B. Sabin, MC; Maj. (later Lt. Col.) Cornelius B. Philip, SnC; and Capt. (later Maj.) W. Paul Havens, Jr., MC.

ever, there was usually rather wide separation in time between the peak of dysentery and the peak of hepatitis.

In February 1944, Dr. John R. Paul and Maj. W. Paul Havens, Jr., MC, of the Commission on Neurotropic Virus Diseases, returned to the United States and established under the auspices of the Army Epidemiological Board a laboratory for the study of acute hepatitis in the Section of Preventive Medicine of the Yale University School of Medicine, at New Haven, Conn. The experiments conducted there employing human volunteers will be discussed in a later section.

The whole epidemiologic pattern of hepatitis in the Mediterranean theater was described by Gauld.[52] He depicted the drawn-out progress of an infectious disease among large numbers of susceptible young adults thrust into an area where it was widely endemic and where the conditions for spread were highly favorable. In general, the highest morbidity occurred in the immunologically more naive troops from the United States and Europe in contrast to a lower incidence among troops from civilizations of less well established sanitary practices, although there were exceptions to this. Gauld was particularly interested in the respiratory route as a possible way of spread of hepatitis, and the sharp increase in incidence among American troops in 1943 and 1944, both in August and in November and December, respectively, suggested to him that this might be important, although he took cognizance of the evidence that the disease could be spread by filth through the medium of personal contact. Explosive outbreaks were rare, and of the two observed only one was well enough documented to warrant mention. This occurred in the 86th Mountain Infantry Regiment and appeared to have resulted from the drinking of contaminated well water.

In some groups of U.S. troops, the incidence of the disease was significantly greater among officers than among enlisted men. The incidence decreased as the age of the individual soldiers advanced, and a certain degree of immunity to hepatitis was manifested in the seasoned troops. The attack rate among seasoned U.S. troops in 1944-45 was 42 per 1,000 compared with a morbidity of 109 per 1,000 among fresh reinforcements. Men who had been vaccinated against yellow fever in 1941-42 and who had acquired serum hepatitis at that time were not protected from acquiring infectious hepatitis later. Indeed, the attack rate among such men was significantly higher than among others.[53]

European Theater of Operations

Infectious hepatitis was unimportant in the European theater until the winter and spring of 1944-45. True, there had been a brief flurry of

[52] Gauld, R. L.: Epidemiological Field Studies of Infectious Hepatitis in the Mediterranean Theater of Operations. Am. J. Hyg. 43: 248-313, May 1946.

[53] Gauld, R. L.: Field Studies Relating to Immunity in Infectious Hepatitis and Homologous Serum Jaundice. Am. J. Pub. Health 37: 400-406, April 1947.

the disease in the United Kingdom in the winter of 1943–44 among troops arrived from the epidemic area in Italy in November 1943; however, this appeared to be self-limited. The First U.S. Army, of which these troops became a part, was not involved in any widespread epidemic until the winter and spring of 1945 when the incidence rose to 12 per 1,000 per annum.[54]

During the winter of 1944–45, the incidence of the disease in the European theater rose sharply to 17 per 1,000 per annum, potentiated largely by the entry of troops who had served in Italy and Africa. The Seventh U.S. Army invaded southern France, on 15 August 1944, from Italy and was initially made up of three infantry divisions from the Fifth U.S. Army. It was apparently thoroughly seeded with infectious hepatitis, and as it advanced northward, it contacted troops from the Normandy beachhead and received directly into its ranks units that had just come from the United States. The story of the role of the Seventh U.S. Army in the introduction and spread of hepatitis among its own new nonimmune troops and among its contacts, the First and Third U.S. Armies, was well recorded by Gauld[55] and Gowen.[56] It was their impression that localized outbreaks again were rare and that the disease had a widespread distribution, with its manner of spread by some form of person-to-person contact.

Pacific Area

In the vast Pacific area, infectious hepatitis also assumed a tremendous importance, and actually its morbidity in the Southwest Pacific increased from 1943 to 1945 when it and the number of troops involved exceeded that of any other theater; 39,277 cases were treated in 1945, causing an incalculable loss of time. Likewise in the Western Pacific Area, hepatitis proved to be a leading cause of disability.

The epidemiology of the disease, as it made its appearance in various far-flung islands, presented different problems from those involved in the Mediterranean and European theaters. Occasional outbreaks were investigated, including one on Biak Island by Maj. James L. Borland, MC, [57] and another on Hollandia by Maj. Ray E. Trussell, MC,[58] in October 1944. The former was concerned about the possibility of spread by a vector such as a night-biting *Phlebotomus* or common fly, while the latter attributed the spread of disease to mechanical transfer from infected feces by flies or

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[54] Whether the early seeding in 1943–44 of the First U.S. Army by men from Italy with hepatitis contributed to the spread of the disease subsequently when these troops were in combat in Europe was questioned later by Paul and Gardner (see footnote 21, p. 335).

[55] Gauld, R. L.: Epidemiology of Hepatitis—Military Experience. [Unpublished manuscript.]

[56] Gowen, G. H.: Observations on Infectious Hepatitis in Seventh Army, 1944–45. Bull. U.S. Army M. Dept. 6: 456–461, October 1946.

[57] Essential Technical Medical Data, U.S. Army Forces in the Far East (Southwest Pacific Area), for December 1944, dated 15 Feb. 1945, Appendix H thereto.

[58] Trussell, R. E.: Epidemiologic Aspects of an Outbreak of Infectious Hepatitis. Am. J. Hyg. 45: 33–42, January 1947.

by infected foodhandlers and contaminated food and utensils. Much of the clinical and epidemiologic experience in this area was recorded by Col. Henry M. Thomas, Jr., MC.[59]

China-Burma-India and Latin American Theaters

The incidence of infectious hepatitis in the China-Burma-India theater was moderately high, but in Latin America, it was low. This is of interest since the rates of enteric infections were high in both of these areas and yet there was no correlation between them and the attack rates for infectious hepatitis.

Clinical Pattern

Clinical descriptions of the course of the disease in two large groups of U.S. troops were made by Havens [60] in 1944 from the 38th General Hospital in Egypt and by Barker, Capps, and Allen,[61] in 1945, from the 12th General Hospital in Naples. The former outlined the initial experience of U.S. troops in the Middle East with infectious hepatitis in the autumn and winter of 1942–43 and again in 1943–44.

The latter in association with the 15th Medical General Laboratory set up a center for the care and study of patients with infectious hepatitis in the Mediterranean theater. This came about as the result of a suggestion made, in December 1943, to the Surgeon, Peninsular Base Section, by Col. Perrin H. Long, MC, Consultant in Medicine, Mediterranean theater. Colonel Long had suggested that, when the 12th General Hospital arrived from North Africa, Lt. Col. (later Col.) Marion H. Barker, MC, be assigned the problem of finding out what he could about infectious hepatitis. The suggestion was carried out in January 1944, and in March 1944, Maj. (later Lt. Col.) Richard B. Capps, MC, of the 12th General Hospital, was assigned to assist Colonel Barker.

With the 12th General Hospital, the 15th Medical General Laboratory joined forces, and its commanding officer, Col. Virgil H. Cornell, MC, and members of his staff, including Lt. Col. Tracy B. Mallory, MC, Maj. (later Lt. Col.) Ross L. Gauld, MC, Maj. Frank W. Allen, SnC, Capt. (later Maj.) Frederick C. Robbins, MC, and Capt. Hugh B. Wilson, MC, contributed their technical advice and skill toward the solution of the numerous problems. A number of clinical studies were described, and the correlation of histologic alterations of the liver obtained by biopsy with clinical status

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[59] Technical Memorandum No. 16, Office of the Chief Surgeon, U.S. Army Forces in the Far East, 1 Oct. 1944.

[60] Havens, W. P., Jr.: Infectious Hepatitis in Middle East; Clinical Review of 200 Cases Seen in a Military Hospital. J.A.M.A. 126: 17–23, 2 Sept. 1944.

[61] Barker, M. H., Capps, R. B., and Allen, F. W.: Acute Infectious Hepatitis in the Mediterranean Theater, Including Acute Hepatitis Without Jaundice. J.A.M.A. 128: 997–1003, 4 Aug. 1945.

was made. Attention was drawn to the danger of relapse or the development of chronic disease, and the need for adequate rest was emphasized.[62]

Nonicteric hepatitis

Although hepatitis without jaundice was a recognized entity among our Allied military medical colleagues and despite the fact that attention had been called to its existence in the clinical descriptions of serum hepatitis following the reception of yellow fever vaccine by our troops, there were many of our medical officers who at first were reluctant to accept its recognition as a part of the broad clinical spectrum of infectious hepatitis. However, it was not long before educational progress was made along this line, and its existence was generally admitted. Nonicteric hepatitis was regarded as a milder form of the disease, with a shorter duration. How often it occurred could not be determined owing to the lack of specific serologic diagnostic tests; however, that it occurred far more frequently than suspected is doubtless true. Gowen [63] suggested that its ratio to hepatitis with jaundice was as much as 8 : 1 in Tunisia, on the basis of epidemiologic and clinical evidence. The occurrence of malaise, anorexia, easy fatigue, nausea, and vomiting, with evidence of hepatic dysfunction, in soldiers who, although not jaundiced, were stationed in epidemic areas was enough to suggest the diagnosis of nonicteric hepatitis. In many of these patients, the liver was palpable and tender. Although recovery was usually prompt, relapse with jaundice on occasion occurred.

Icteric hepatitis

When jaundice was present, the disease could usually be divided into two phases—preicteric and icteric. Among the troops studied in Egypt and Italy, approximately 83 percent had a well-defined preicteric phase and about 17 percent presented themselves with jaundice as the first evidence of the disease (fig. 39).

The preicteric phase ranged in length from 1 day to 3 weeks, averaging 5 days. In some patients, this was biphasic, with a short remission of signs and symptoms from 4 to 5 days after onset followed by their recurrence and eventually jaundice. All grades of severity of constitutional reaction occurred; however, it was not possible to predict the degree of severity of the total course of disease from the character of its beginning. Anorexia, beginning insidiously, was the most common initial symptom and, indeed, often directed the group medical officer's attention to the diagnosis. That this was a more sensitive indicator of hepatitis in the field, where rations were less than appealing to a capricious appetite, is understandable. Easy

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[62] (1) Circular Letter No. 19, Office of the Surgeon, Headquarters, North African Theater of Operations, U.S. Army, 28 Mar. 1944. (2) Circular Letter No. 37, Office of the Surgeon, Headquarters, North African Theater of Operations, U.S. Army, 8 July 1944. (3) Circular Letter No. 21, Office of the Surgeon, Headquarters, Mediterranean Theater of Operations, U.S. Army, 20 June 1945.

[63] See footnote 56, p. 352.
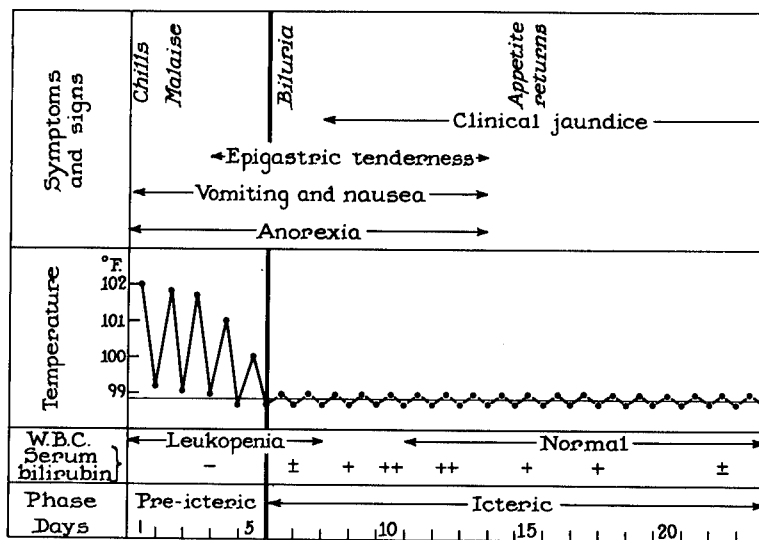
FIGURE 39.—Schematic diagram illustrating the clinical course of an average case of infectious hepatitis in an adult. (Paul, J. R., and Havens, W. P., Jr. Tr. A. Am. Physicians 59: 133–141, 1946.)

fatigability and disinterest in occupation, with nausea after meals, soon occurred, and toward the end of the preicteric phase, vomiting was not uncommon. Actual abdominal pain was unusual, although on occasion it did occur in the right upper or lower quadrant, and acute cholecystitis or acute appendicitis was at times suspected and unwarranted operations performed. Under such circumstances, the gallbladder or appendix was normal, and enlarged mesenteric lymph nodes were found. Discomfort in the upper quadrant of the abdomen occurred early in a goodly percentage of patients and was described as distress or fullness in the epigastrium and right upper quadrant, made worse by eating and activity. Riding in a jeep was particularly aggravating and not infrequently was the event that precipitated sufficient discomfort to cause a soldier to go to sick call. Constipation, flatulence, and diarrhea were present in a small percentage of patients, as were symptoms of infection of the upper respiratory tract.

Among the patients having a definite preicteric phase, the onset was abrupt in 53 percent of those described by Havens [64] and in 80 percent of those described by Barker and his associates.[65] It was ushered in with fever, chilliness (rarely frank chills), malaise, headache, and generalized muscular aches. Prostration was not uncommon, and aching eyes with pain of the eyeballs were associated complaints. Fever was usually remittent, with a daily maximum temperature of 102°–103° F., declining to

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[64] See footnote 60, p. 353.
[65] See footnote 61, p. 353.

normal during the ensuing 5 to 7 days. Some patients had a frank chill daily, followed by fever with a temperature of 104° F., for the first few days. Symptoms directing attention to the gastrointestinal tract, including anorexia, nausea, vomiting, and upper abdominal distress, developed in these patients as they did in those without fever. Within 48 hours after the temperature reached normal, clinical jaundice was evident.

Palpation of the abdomen often elicited tenderness particularly in the right upper quadrant and epigastrium where pressure evoked a sense of nausea. The liver and spleen were uncommonly palpable in this early phase of the disease; however, percussion with the first over the right lower ribs frequently caused discomfort or pain in the area of the liver. Barker and his associates called attention to the rather constant early appearance of cervical adenopathy occurring as "a soft, slightly tender, lima bean sized gland * * * found along the posterior border of the sternocleidomastoid muscle low in the neck." It was often easy to demonstrate this visually by having the patient bend his neck away from the involved side. Also of particular importance was the occurrence of bilirubinuria that usually appeared later in the preicteric phase but from 48 to 72 hours before clinical jaundice. More than one soldier made his own diagnosis of infectious hepatitis by noting a change in the color of his urine.

Icteric phase

The duration of the icteric phase ranged from as short a time as 4 days to as long a period as 4 months, with an average of 2 to 4 weeks, in different groups of patients. Fever was uncommon; when present, it lasted a short time. Jaundice reached its maximum within 3 to 10 days in most patients. As it increased, the malaise and gastrointestinal symptoms worsened, and during this period, nausea and vomiting were at times severe enough to require the administration of fluid parenterally. It was not unusual for patients to have reasonable appetites in the morning but to complain of a sense of fullness after lunch that progressed to the point of such discomfort after the evening meal that vomiting, either spontaneous or self-induced, occurred. In the mildly sick patients, these symptoms were slight and of short duration, but in those who were seriously sick, they persisted as long as 3 to 4 weeks. In such seriously sick patients, lassitude, emotional instability, and depression occurred. Increasing jaundice was accompanied by diminishing amounts of pigment in the feces, and among the sicker patients, acholic stools were found. Disorder of bowel function was common in this group, with constipation or, on occasion, diarrhea. Itching occurred in only a small percentage of patients.

The liver was enlarged and tender in a large percentage of patients by the time jaundice was evident, and although their presence did not always coincide, both were found in 43 percent of one group of patients. Splenomegaly was found in 10 to 15 percent of patients, and posterior cervical

lymphadenopathy persisted into the icteric phase in a small percentage. Bradycardia was unusual and occurred during the first 2 weeks of icterus.

Jaundice usually reached its maximum in 10 days, and at this point, a remarkable clinical change occurred, with sharp regression of symptoms and return of sense of well-being. Appetite improved and was frequently voracious. Hepatic tenderness subsided, and the liver diminished in size so that it was usually no longer palpable 2 weeks after the appearance of jaundice. Loss of weight in amounts of 5 to 10 or even 20 pounds in the more seriously sick patients was usual, but strength was regained fairly promptly in the mildly or moderately sick patients. Even in this group, however, activity was often followed by upper abdominal fullness and discomfort for several days after the disappearance of all other symptoms.

The duration of hospitalization became a matter of considerable importance and discussion. The first documented experience of U.S. soldiers with infectious hepatitis in World War II was in the Middle East in 1942–43. In this group, described by Havens,[66] the duration of hospitalization ranged from 7 to 87 days, with an average of 29.8 days. Somewhat later, in 1944, Barker and his associates [67] described the course of the disease in another large group of soldiers in Italy and pointed out that the average duration of hospitalization ranged between 6 and 8 weeks. It is likely that the exhaustion and physical disability caused by battle conditions that the latter group had sustained before acquiring hepatitis prolonged the course of their disease. The period in hospital included 3 to 5 weeks of rest in bed, followed by 7 to 10 days as an ambulant, followed by 7 to 10 days of exercise before returning to duty. It was emphasized that patients who had apparently clinically recovered and who were without jaundice while at rest in bed not infrequently developed signs and symptoms of the disease, with or without jaundice, following increased activity. Because of this, an exercise tolerance test was devised to select those patients who required further hospitalization. Using these criteria, about 10 percent of patients with icteric hepatitis had not made complete recovery after 3 months of hospitalization.

Infectious hepatitis, in spite of its high morbidity and frequently prolonged course, was, in general, a benign and self-limited disease. The case fatality was low—less than 4 per 1,000. Complications were rare and included pneumonia, myelitis, and aseptic meningitis. Seborrheic dermatitis and labial herpes occurred in a small percentage of patients.

Relapse

Although the vast majority of patients made an uneventful recovery, there were those who suffered an interruption of convalescence, with a return of symptoms and signs of the disease. Relapse was often mild,

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[66] See footnote 60, p. 353.
[67] See footnote 61, p. 353.

although at times it was more severe than the initial attack. Its incidence was variable, ranging from 1½ to 10 percent, and the factors that caused it were not completely defined. Indulgence in alcoholic beverages and excessive activity before recovery were incriminated in some cases; however, a certain number of patients relapsed in spite of what appeared to be ideal treatment. Patients who did sustain relapse made eventual complete recovery in almost all cases, but Barker and his associates [68] felt strongly that this could only be defined by the capacity of the patient to perform graded exercise tolerance tests without having a return of symptoms, signs, or laboratory evidence of hepatitis.

Chronic Hepatitis

A small percentage of patients with acute hepatitis had evidence of hepatic disease long after the expected time of recovery. Barker and his associates [69] found 18 percent in one group of 431 soldiers in this category, 4 months after the onset of disease, and emphasized the prolonged treatment required to effect recovery. These patients had a characteristic history of hepatitis, with or without jaundice, followed by partial recovery and subsequent return of weakness, anorexia, and epigastric discomfort. The liver was often enlarged and tender, and while jaundice was not always present, the results of the Bromsulphalein excretion test and thymol turbidity test were abnormal. Unfortunately, adequate followup of these patients was not possible in all instances; however, it was the impression that recovery was complete in most cases. That evidence of continuing hepatic disease could exist for many months, culminating in complete recovery, was well established by these observations. It was postulated that the development of cirrhosis was rare, although serial biopsies of the livers of civilian patients in various stages of hepatitis had previously suggested that it did occur.[70]

Two other groups of patients were distinguished from those just described with persistent activity of the disease: (1) those with subjective complaints but without any objective evidence of hepatic disease, and (2) those with vague mild complaints and slight stable abnormality of serum bilirubin and Bromsulphalein excretion, with or without enlargement of the liver. The former group fell in the same category as those patients described previously in the section on serum hepatitis as having "posthepatitis syndrome." [71] The latter when tested by exercise tolerance manifested no clinical worsening and were regarded as having an inactive disease with mild residual hepatic dysfunction.

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[68] See footnote 61, p. 353.

[69] Barker, M. H., Capps, R. B., and Allen, F. W.: Chronic Hepatitis in the Mediterranean Theater of Operations; A New Clinical Syndrome. J.A.M.A. 129: 653–659, 3 Nov. 1945.

[70] Krarup, N. B., and Roholm, K.: Development of Cirrhosis of Liver After Acute Hepatitis, Elucidated by Aspiration Biopsy. Acta. med. Scandinav. 108: 306–331, 1941.

[71] See footnote 28, p. 343.

Pathology

In the Hepatitis Study Center, composed of the 12th General Hospital and the 15th Medical General Laboratory, in Naples, biopsies of the liver were performed on patients in various phases of nonfatal infectious hepatitis.[72] During the acute icteric period, the following were found: Periportal cellular infiltration, predominantly mononuclear; swelling of the reticuloendothelial cells and intralobular infiltration; focal necrosis with acidophilic degeneration of hepatic cells; lobular disarray; numerous mitotic figures and multinucleate cells; and biliary thrombi in dilated canaliculi. The pattern of the lobular reticular framework was usually intact, although on occasion it was distorted with areas of condensation apparent. Similar changes were found in the preicteric phase or in nonicteric hepatitis except that biliary stasis was rarely seen. Of particular interest was the demonstration of the wide variation in time of recovery, as manifested by the histologic appearance of the liver. Although complete regeneration was found after 1 or 2 months in some patients, in others evidence of activity persisted for several months. No evidence of cirrhosis was found in 89 nonfatal cases.

The possibility that the severe progressive chronic hepatic disease described earlier among civilians [73] might eventuate in some soldiers prompted biopsy of the livers of men whose recovery had been long delayed. [74] Of 40 such patients examined from 100 to 500 days after onset, the specimens of liver studied were normal in 15; doubtful in 10; and in 15 there were periportal and lobular inflammation and focal hyaline necrosis. Unfortunately, these patients were lost to followup examinations so that nothing could be said about their eventual outcome. Thus, it was suggested that, although the incidence of continuing disease was indeed low, the possibility of its rare occurrence demanded recognition. Opinion in this regard was not unanimous, and Lucké [75] was impressed with the concept that nonfatal viral hepatitis was followed by complete recovery and restitution of normal hepatic structure. At all events, the preponderance of evidence indicated that the occurrence of cirrhosis in soldiers following nonfatal epidemic hepatitis was rare.[76]

In fatal cases, the pathologic changes were described in two groups by Lucké [77] and by Lucké and Mallory:[78] (1) the fulminant form in which death occurred within 10 days after onset, and (2) the subacute form in which death occurred from 3 to 8 weeks after onset. The liver was smaller

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[72] Mallory, T. B.: The Pathology of Epidemic Hepatitis. J.A.M.A. 134: 655–662, 21 July 1947.

[73] See footnote 70, p. 358.

[74] See footnote 72.

[75] See footnote 27, p. 342.

[76] It is pertinent to point out that at present (1963) some investigators feel that cirrhosis *never* follows epidemic hepatitis. However, the evidence adduced for this concept is far from complete.—W. P. H., Jr.

[77] See footnote 27, p. 342.

[78] Lucké, B., and Mallory, T.: Fulminant Form of Epidemic Hepatitis. Am. J. Path. 22: 867–945, September 1946.

than normal, soft and smooth, and massive central necrosis completely destroyed the parenchyma in the fulminant form. There was no evidence of regenerative hyperplasia, and mononuclear cellular infiltration was found at the periphery of the lobule. In the subacute form, the liver was also often reduced in size but not infrequently the surface was irregular, with red depressed areas surrounded by yellow-green nodules. Parenchymal destruction was irregular and associated with areas of regeneration. Destruction of lobular architecture had occurred. Inflammatory reaction, again of a mononuclear type, was present but less intense in the portal areas and interlobular boundaries. The central and efferent veins were often involved in endophlebitis.

In both forms of the disease, lymphoid hyperplasia and splenomegaly were frequently present. Ascites was common, and hemorrhage, edema, and inflammation of the gastrointestinal tract were often found. The kidneys were enlarged with fat storage in the fulminant cases, and bile nephrosis in those of longer duration. Alterations in the central nervous system included swelling of ganglion cells, distortion of nuclei, meningeal lymphocytic infiltration, and perivascular lymphocytic cuffing in the basal ganglions.

The pathologic changes which have been briefly described here are well illustrated by the authors; selected plates, from the published literature, are reproduced here as plates I through VI, through the courtesy of the *American Journal of Pathology*.

Clinical Laboratory Studies

The laboratory tests that could be performed were often quite limited by the exigencies of the situation; however, in some areas, a considerable amount of data was accumulated. The number of erythrocytes and the amount of hemoglobin were normal except in certain patients who had prolonged debilitating disease. Of particular interest, however, was the pattern of leukocytic response that occurred, characterized by the appearance of leukopenia with both neutropenia and lymphopenia early in the acute febrile phase of the disease. Relative lymphocytosis subsequently occurred, and numerous atypical lymphocytes identical with those commonly associated with infectious mononucleosis made their appearance. In general, the hematologic pattern had returned to normal by the end of the second week of the disease.[79] Determinations of the coagulation and bleeding time and the fragility of erythrocytes were found to be normal in small groups of patients.[80] Prolongation of the prothrombin time in severe degree was regarded as an ominous sign, particularly if there was no favorable response to the parenteral administration of vitamin K. The

[79] (1) Havens, W. P., Jr., and Marck, R. E.: Leukocytic Response of Patients With Experimentally Induced Infectious Hepatitis. Am. J.M. Sc. 212: 129–138, August 1946. (2) See footnote 61, p. 353.

[80] See footnote 60, p. 353.
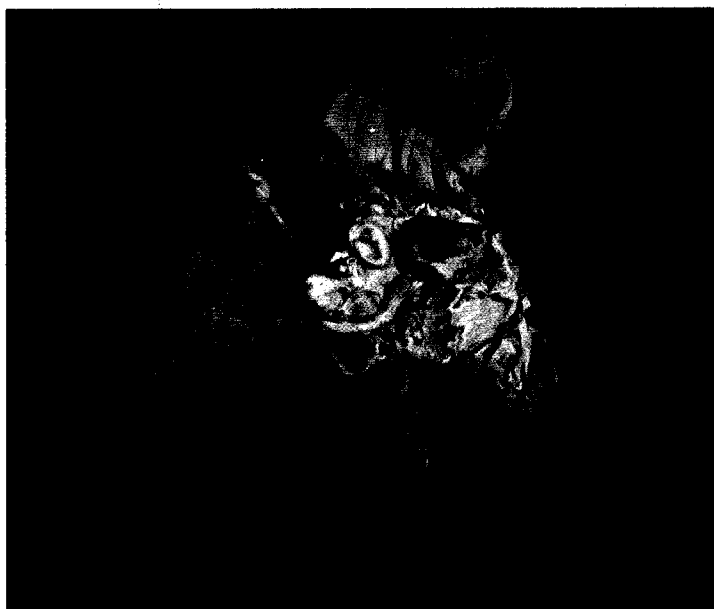
PLATE I.—Duration of hepatitis, 36 days. Undersurface of a liver which weighed 1,320 gm. The liver is shrunken, particularly the left lobe. The surface of the right lobe shows a number of flat or elevated nodular areas, between which the tissue is finely wrinkled. The surface of the left lobe is deeply furrowed. At the hilum is a cluster of enlarged edematous lymph nodes. (Hemorrhages in heart and gut of this case are shown in plate VI.)

sedimentation rate of erythrocytes was usually normal early in the acute phase, increasing after the appearance of jaundice.[81]

Numerous attempts were made to develop specific serologic tests, but none of these was successful. Saline extracts of normal liver and liver from fatal cases of hepatitis were used as antigens in complement fixation [82] and precipitin tests.[83] Although positive tests were found in as many as one-third of the patients, they were of no practical value. A heterophile antibody absorbable on boiled guinea pig kidney and human liver was found in the acute phase serums of some patients,[84] and falsely positive Wassermann and Kahn [85] reactions were also described in as many as 20 percent of some groups of patients.[86]

[81] Unpublished personal observations.—W. P. H., Jr.

[82] Eaton, M. D., Murphy, W. D., and Hanford, V. L.: Heterogenetic Antibodies in Acute Hepatitis. J. Exper. Med. 79: 539–557, May 1944.

[83] Olitzki, L., and Bernkopf, H.: Precipitation in Infective Hepatitis. J. Infect. Dis. 77: 60–67, July–August 1945.

[84] See footnote 82.

[85] Rizzell, W. C., and Puccinelli, V.: False Positive Serology in Infectious Hepatitis. M. Bull. North African Theat. Op. (No. 3) 2: 57–59, September 1944.

[86] Subsequent efforts to detect this heterophile antibody and falsely positive Wassermann and Kahn reactions were unsuccessful, with rare exceptions. See Havens, W. P., Jr., Gambescia, J. M., and Knowlton, M.: Results of Heterophile Antibody Agglutination and Kahn Tests in Patients With Viral Hepatitis. Proc. Soc. Exper. Biol. & Med. 67: 437–440, April 1948.
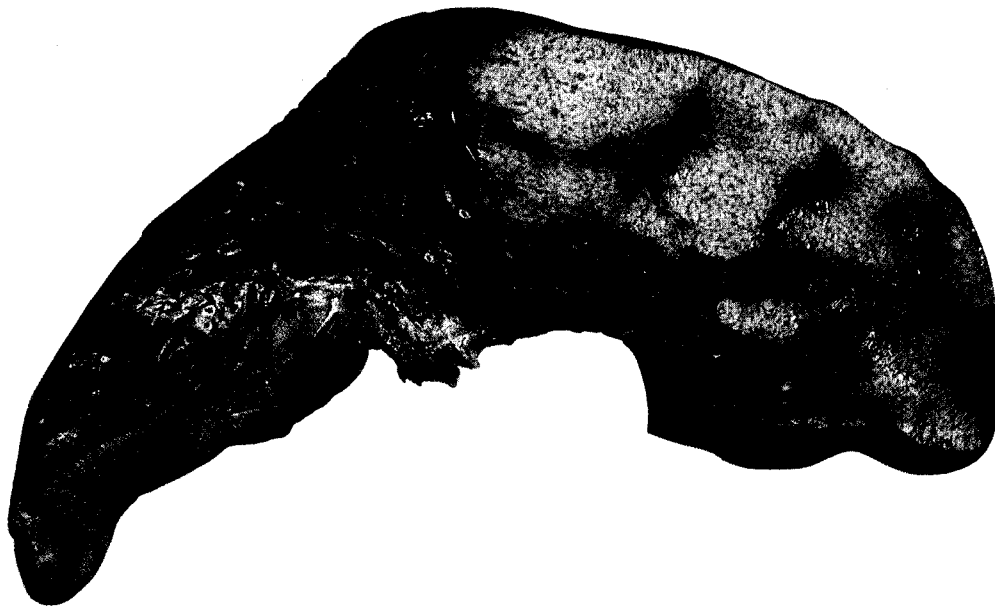
PLATE II.—*See legend on opposite page.*

The desirability of early diagnosis, before jaundice appeared, or in patients with nonicteric hepatitis, as well as the need to determine when recovery had occurred, focused attention on certain laboratory determinations. Doubtless, the most commonly used test in the field was the determination of bilirubin in the urine. Bilirubinuria appeared in the latter part of the preicteric phase and, as mentioned before, often served as a diagnostic aid to the soldier himself. The icterus index was widely used as a measure of the amount of jaundice where facilities were not available for determining the serum bilirubin. After jaundice had disappeared, the Bromsulphalein excretion test was used, when possible, to determine if activity of hepatitis persisted. In small groups of volunteers[87] under controlled conditions, it was shown that the excretion of intravenously administered Bromsulphalein was impaired on the third day of the disease, with bilirubinuria appearing the following day. The cephalin-cholesterol flocculation test was positive by the fifth day, when the 1-minute direct serum bilirubin was increased above normal. By the seventh day, the total serum bilirubin and the urinary urobilinogen were above normal. The thymol turbidity and colloidal gold tests were positive in the early part of the icteric phase. Bilirubinuria disappeared before clinical jaundice, and the serum bilirubin usually was normal in the fifth or sixth week of the disease. Bromsulphalein excretion tests performed shortly thereafter were usually normal. The cephalin-cholesterol flocculation and thymol turbidity tests became negative in 6 to 10 weeks and in 8 to 12 weeks, respectively. The persistence of a strongly positive thymol turbidity test was regarded as indicating persisting activity of the disease.[88]

Among the interesting phenomena encountered were tiny motile spirochetal-like filaments visualized by dark-field microscopy in the serums of patients with hepatitis. [89] More than 1 hour was spent convincing their

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[87] See footnote 81, p. 361.

[88] Serums obtained from volunteers with experimentally induced infectious hepatitis were subsequently subjected to determinations of serum proteins. The characteristic pattern of change was a sharp, early decline in serum albumin with a rise in globulins, largely gamma globulin. The albumin returned to normal levels by the fifth week, but the globulins remained somewhat elevated often for a few weeks thereafter. Persistence of large amounts of serum gamma globulin was associated with activity of the disease. See Havens, W. P., Jr., and Williams, T. L.: Changes in Serum Proteins in Patients With Experimentally Induced Infectious Hepatitis. J. Clin. Invest. 27: 340–345, May 1948.

[89] Kuzell, W. C.: "Artifact Spirochetes" in Infectious Hepatitis. Bull. U.S. Army M. Dept. 89: 112–114, June 1945.

PLATE II.—(Top) Duration of hepatitis, 19 days. Cut surface of a liver which weighed 890 gm. Over one-half of the organ has a fleshy, red appearance; here all liver cells have been destroyed. The yellow nodular patches are relatively ischemic and are composed of large "lobules" of regenerating tissue. (The microscopic appearance of the red part is shown in plate III (top).)

(Bottom) Duration of hepatitis, 43 days. Vertical cut section of a liver which weighed 850 gm. The large red fleshy area consists entirely of vascular stroma and bile ducts; all liver cells have been destroyed. The remainder of the organ is composed of yellowish green nodular areas of regenerating parenchyma.
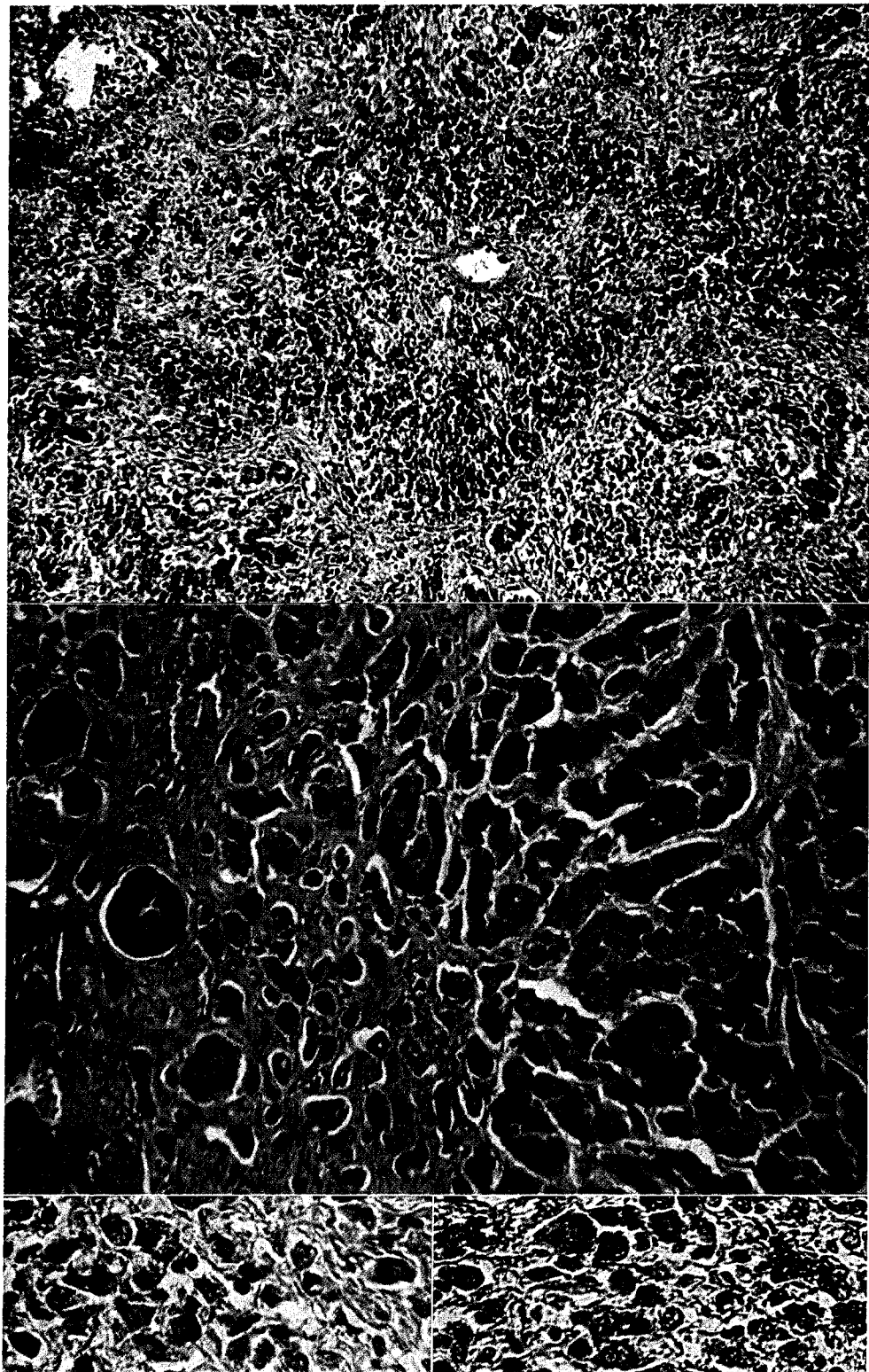
PLATE III.—*See legend on opposite page.*

observers that they were artifacts and not the causative organisms of hepatitis.

Roentgenographic evidence of gastroduodenitis and gastroscopic evidence of acute gastritis were demonstrated in volunteers [90] with experimentally induced hepatitis, corroborating the clinical and pathologic data that emphasized the involvement of the gastrointestinal tract in this disease.

Differential Diagnosis

The elevated temperatures and often severe constitutional symptoms in the preicteric phase made diagnosis difficult, particularly in areas such as Sicily, North Africa, the Middle and Far East, and the Pacific where a number of other acute infections, largely unfamiliar to our medical officers, were present. Thus, it should not be surprising that this disease was an important cause of "fever of undetermined origin" in its preicteric phase. Our British medical colleagues pointed out that in this phase pressure over the epigastrium frequently caused nausea, and this proved to be a valuable sign. Barker and his associate [91] regarded tenderness to percussion over the liver, posterior cervical adenopathy, and splenomegaly as important diagnostic aids. The occurrence of leukopenia and relative lymphocytosis was also of some assistance, but the appearance of bilirubinuria was doubtless the most important evidence pointing to the diagnosis. During the febrile preicteric period, the diseases considered were malaria, sandfly fever, dengue, pharyngitis with fever, acute bacillary dysentery, typhoid and paratyphoid fevers, acute appendicitis, acute cholecystitis, and infectious mononucleosis. After the appearance of jaundice, the diagnostic dilemma was less, although on occasion poisoning due to carbon tetra-

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[90] Havens, W. P., Jr., Kushlan, S. D., and Green, M. R.: Experimentally Induced Infectious Hepatitis: Roentgenographic and Gastroscopic Observations. Arch. Int. Med. 79: 457–464, April 1947.

[91] See footnote 61, p. 353.

PLATE III.—(Top) Duration of hepatitis, 19 days. Microscopic appearance of the red fleshy area of the liver shown in plate II (top). The parenchyma has been destroyed. The lobular outlines are indicated by numerous small biliary ducts. The sinusoids are greatly engorged. Masson's trichrome stain. (X 250)

(Center) Duration of hepatitis, 93 days. Microscopic appearance of pale nodular areas of regenerative hyperplasia. Cords of liver cells form a pseudolobule which is noticeably ischemic. Elsewhere small bile ducts and large tubules composed of hepatic cells are scattered throughout the collapsed stroma; these large tubules are reminiscent of the liver in the early stage of embryonic development. (X 250)

(Bottom, left) Duration of hepatitis, 18 days. Numerous macrophages with yellow-brown granules are scattered throughout the lobular stroma from which the liver cells have been removed. (X 500) (Bottom, right) A section from an area similiar to the one shown on the left, but stained with Sudan III. The pigment granules take the fat stain well. (X 500)

PLATE IV.—*See legend on opposite page.*

chloride, Weil's disease, acute cholangitis, or even yellow fever had to be considered. Jaundice due to excessive hemolysis or extrahepatic obstruction rarely occurred and did not constitute a problem in diagnosis. Epidemiologic evidence, the subsequent course of the disease, the number and type of leukocytes in the blood, the results of tests of hepatic function, and the demonstration of specific causative agents or their antibodies furnished the correct diagnosis in most instances. Confusion with infectious mononucleosis with jaundice was resolved by the heterophile antibody test, which is negative in infectious hepatitis.

Treatment

Treatment was supportive and symptomatic. The administration of methionine, choline, crude liver extract, normal human gamma globulin,[92] and the antibiotic and chemotherapeutic agents then known was of no benefit. Emphasis was placed on rest in bed and diet, although it is fair to say that there was not complete agreement on their exact specifications with some of our Allied medical colleagues or even among our own medical officers. Actually, most of the precepts of therapy that emerged by the end of the war were derived from the principles set down by Barker and his associates [93] whose experience was largely with troops who had been exhausted by physical hardship before acquiring hepatitis. In addition, these patients were frequently hospitalized under conditions in which it was not easy to furnish a diet that would be welcome to men whose appetites at best were capricious. It is doubtless true that their therapeutic regimen could have been modified with impunity for men who started their disease in relatively good physical condition and who were hospitalized under circumstances favorable for obtaining attractive food. That this was the case was substantiated by the experience in Egypt [94] at the 38th General Hospital where the therapeutic regimen was more relaxed without prolonging the course of disease.

Nevertheless, it is important to remember that when Barker and his colleagues set up their study group in Naples, the therapy of patients with hepatitis was without order and was dependent on the ideas of many differ-

[92] Gellis, S. S., Stokes, J., Jr., Forster, H. W., Jr., Brother, G. M., and Hall, W. M.: Use of Human Immune Serum Globulin (Gamma Globulin) in Infectious (Epidemic) Hepatitis in the Mediterranean Theater of Operations; Studies on Treatment in Epidemic of Infectious Hepatitis. J.A.M.A. 128: 1158–1159, 18 Aug. 1945.

[93] See footnote 61, p. 353.

[94] See footnote 60, p. 353.

PLATE IV.—(Top) Duration of hepatitis, 36 days. Heart showing petechiae of epicardium and ecchymosis beneath the endocardium of the interventricular septum, near the bases of the aortic cusps.

(Bottom) Colon with mesocolon and epiploic appendages. An extensive hemorrhage is seen in the mesocolon.
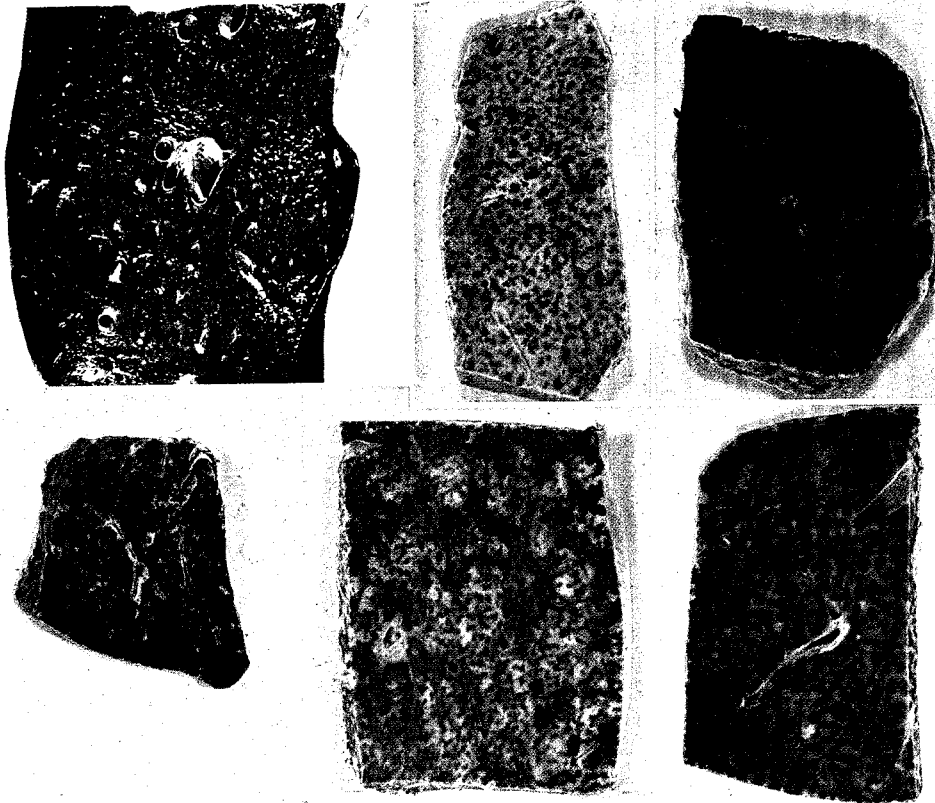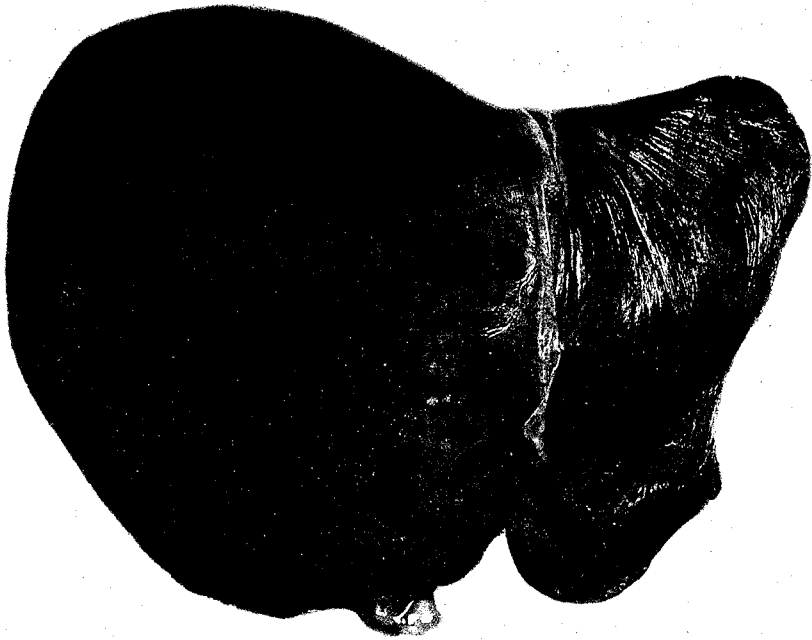
PLATE V.—*See legend on opposite page.*

ent medical officers, most of whom actually had little comprehension of the disease or of its therapeutic requirements. It was indeed the frequency of relapse in patients sent back to duty too soon that prompted the emphasis on prolonged rest in bed (3–5 weeks), followed by a gradual exercise tolerance test (7–10 days) when jaundice disappeared and the excretion of intravenously injected Bromsulphalein measured 10 percent or less. Only after a convalescent was able to pass such a test was he regarded as fit for duty. [95]

The dietary regimen recommended by Barker and his colleagues [96] was high in carbohydrates (350 gm.) and protein (250 gm.) and low in fat (40 gm.). The reason for reduction in fat was far from clear; however, restriction of this foodstuff had long been practiced in the therapy of catarrhal jaundice and doubtless this influenced the recommendation. Actually, it was shown in other patients [97] that the ingestion of a diet rich in protein and carbohydrate without restriction of fats was well tolerated and associated with equally speedy recovery.[98]

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[95] Over the years after World War II, the duration of hospitalization for hepatitis increased until it became as long as 89 days in certain groups during the Korean War. This was doubtless a natural outcome of the failure to discern the reason for the occurrence of relapse or prolonged disease and the belief that more rest would prevent them. The point was finally reached when this concept was questioned, and it was subsequently shown by Chalmers and his associates that men could be sent back to duty quite safely in shorter periods. In addition, they demonstrated that allowing men out of bed around the room or ward except for an hour's rest after each meal did not prolong the course of the disease but actually hastened an earlier return to duty. See Chalmers, T. C., Reynolds, W. E., Eckhardt, R. D., Cigarroa, J. G., Dean, M., Reifenstein, R. W., Smith, C. W., and Davidson, C. S.: Treatment of Acute Infectious Hepatitis in Armed Forces. Advantages of ad lib. Bed Rest and Early Reconditioning. J.A.M.A. 159: 1431–1434, 10 Dec. 1955.

[96] See footnote 61, p. 353.

[97] See footnote 60, p. 353.

[98] The difficulties encountered in the field in particular in providing such a diet were considerable, and it was often not easy to make a solution of powdered milk in water palatable as a source of protein. It was not unusual that dietary excesses should have evolved, and, on occasion, regimens including as much as 350 gm. of protein were advised. This in combination with large amounts of carbohydrate and little fat was far from appealing to jaded appetites. However, as with the duration of rest in bed, a more realistic dietary approach eventually emerged, recommending well-balanced, high-caloric meals similar to those described in the early experience with hepatitis in Egypt (see footnote 60, p. 353). Of importance in this evolution was the demonstration of the advantage of a diet of 2,000 to 3,000 calories, made up of 19 percent protein, 120 to 150 gm. of fat, and the remainder in carbohydrates, by Chalmers and his associates (see footnote 95).

PLATE V.— (Top) Clinical duration of hepatitis, 4 days. Upper surface of the liver, which weighed 1,200 gm. The surface of the right lobe is smooth; there are a number of subcapsular hemorrhages. The surface of the left lobe is finely wrinkled. (Center, left) Cut surface of liver shown at top. The appearance is similar to that of an acutely congested and hyperplastic spleen.

(Center, middle and right, and bottom row) Representative areas of cut surfaces of livers from two of five cases of fulminant hepatitis; all have an exaggerated "nutmeg" mottling. Naked-eye examinations of these livers gave no indication of the extent of the parenchymatous destruction or of the prominence of inflammatory infiltration. The duration of the disease and the weight of the liver in the two cases (center middle and right) were, respectively, 3 days and 4 days; 1,205 gm. and 1,200 gm. For the three cases (bottom row), the duration of the disease and the weight of the liver were, respectively, 5, 8, and 8 days; 1,025 gm., normal size, and shrunken.
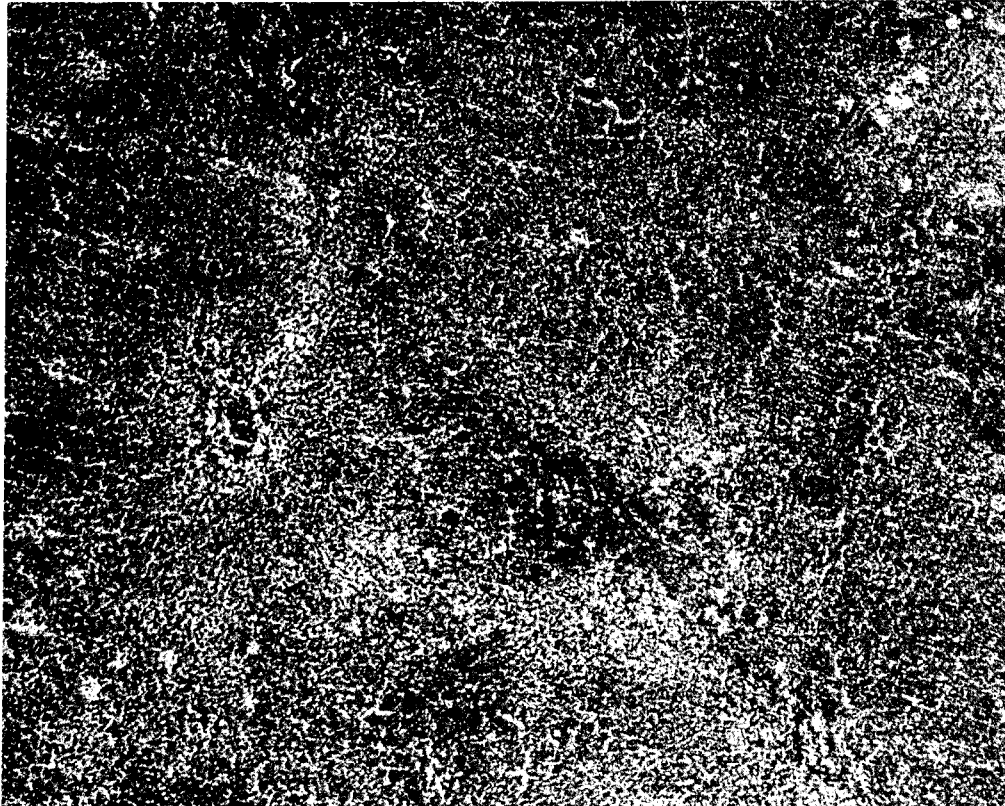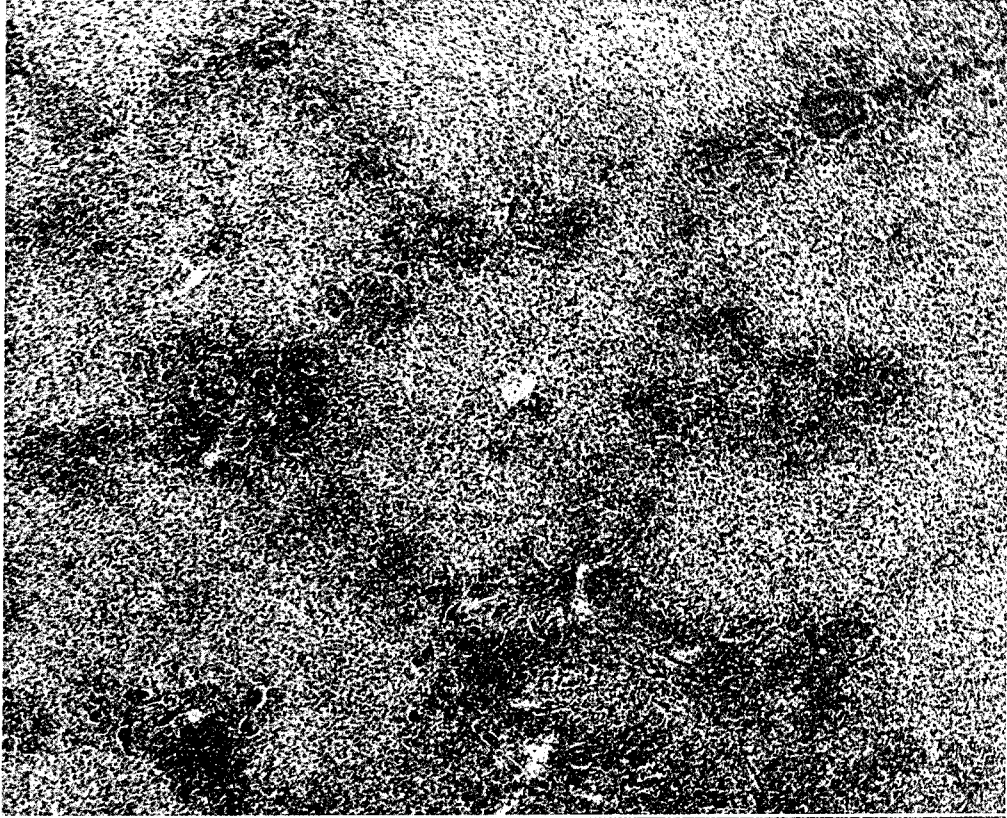
PLATE VI.—*See legend on opposite page.*

Early in the course of the disease when anorexia, nausea, or vomiting were problems, the intravenous administration of 2,000 to 3,000 ml. of 5 percent dextrose in isotonic solution of sodium chloride was of value. When oral feedings could be taken, they were better tolerated in the early phase of the disease in small, frequently administered amounts.

As recovery progressed, the caloric intake was maintained at 3,000–4,000 calories per day. There was no reason to believe that supplemental vitamins were of any value; however, the administration of vitamin K parenterally (Hykinone, 2.4 mg. (1/28 gr.)) daily for several days frequently brought about an increase of plasma prothrombin when it was low. The danger of using opiates and barbiturates was stressed. Alcoholic beverages were interdicted throughout the course of the disease and for 6 months after recovery, although there was no evidence that modest amounts were harmful after recovery and it is likely that the injurious effects of small amounts were stressed without adequate evidence.

Prophylaxis and Control

The association of epidemics with poor sanitation and the subsequent incrimination of the intestinal-oral route as a way of spread of the disease directed measures toward (1) improvement of the general sanitation of camps, (2) fly abatement, (3) sterilization of food receptacles, (4) elimination of possibly infected foodhandlers, and (5) prevention of fecal contamination of food, water, and milk. Under conditions of battle, these measures were obviously impossible to carry out, and reference has been made to the frightful sanitary situation prevailing in certain sectors of the Alamein Line, and early site of the great epidemic in North Africa. An important problem appeared, although late, with the realization that the Lyster bag technique of treatment of water that was ordinarily practical was not effective in destroying the hepatitis virus.[99]

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[99] (1) Neefe, J. R., Stokes, J., Jr., Baty, J. B., and Reinhold, J. G.: Disinfection of Water Containing Causative Agent of Infectious (Epidemic) Hepatitis. J.A.M.A. 128: 1076–1080, 11 Aug. 1945. (2) Subsequently, Neefe and his associates showed that coagulation, settling, and filtration of water before treating it with chlorine made possible the inactivation of hepatitis virus. See Neefe, J. R., Baty, J. B., Reinhold, J. G., and Stokes, J., Jr.: Inactivation of the Virus of Infectious Hepatitis in Drinking Water. Am. J. Pub. Health 37: 365– 372, April 1947.

PLATE VI.—(Top) Duration of epidemic hepatitis, clinically less than 1 day. Microscopic appearance of the liver at low magnification. The hepatic parenchyma has been destroyed. The portal regions and the perilobular boundaries are densely infiltrated with inflammatory cells. (X 25)

(Bottom) Duration of epidemic hepatitis, 3 days. Photomicrograph of the liver at low magnification. The hepatic cells have been destroyed. The lobular remnants are engorged with blood. The peripheries are outlined by bands of inflammatory cells. (X 25)

Specifically, some success was achieved in the prevention of the disease in certain groups of heavily exposed troops in the campaign in Italy by the intramuscular administration of normal human gamma globulin.[100]

EXPERIMENTAL STUDIES WITH HEPATITIS VIRUSES

The enormity of the problem created by the outbreaks of serum hepatitis and infectious hepatitis in both Allied and Axis troops, in addition to the failure to propagate the causative agents by the various laboratory techniques known at that time, urged the use of human volunteers as the means of acquiring necessary information. Experimental studies were carried on in Germany, in the Middle East, in England, and in the United States, and although the natural limitations of this method of investigation were great, an imposing amount of knowledge was accumulated in the period of World War II. In reviewing these data, it is evident that the positive results were of greater value than the negative ones, although it is also apparent that there was sufficient consistency among the negative results reported by various investigators to give them considerable worth. The prolonged course of disease in viral hepatitis made it an undesirable candidate for investigation in volunteers; however, its extremely low mortality made defensible the acceptance of the challenge created by the exigencies of the times. Much is owed to the relatively small number of volunteers who contributed so generously of themselves, and their roles can never be forgotten. To those who shared these experiences, they were frequently harrowing, on one occasion accompanied by tragedy, but never without dignity.

In the United States, Dr. J. W. Oliphant, of the U.S. Public Health Service, was the pioneer in these studies. Faced with the huge outbreak of serum hepatitis following the use of yellow fever vaccine, he produced this disease in volunteers by the parenteral inoculation of icterogenic serum in 1943. After this, studies in volunteers were carried on under the auspices of the Army Epidemiological Board. It is pertinent to point out here that the Medical Department of the U.S. Army and, in particular, the Preventive Medicine Service of the Office of The Surgeon General have reason to be proud of the contributions made with their support to our knowledge of viral hepatitis. Under the aegis of the Army Epidemiological Board, three of its Commisions were primarily concerned with carrying out in this country and abroad various studies: the Commission on Measles and Mumps, the Commission on Neurotropic Virus Diseases, and the Commis-

[100] (1) Gellis, S. S., Stokes, J., Jr., Brother, G. M., Hall, W. M., Gilmore, H. R., Beyer, E., and Morrissey, R. A.: Use of Human Immune Serum Globulin (Gamma Globulin) in Infectious (Epidemic) Hepatitis in the Mediterranean Theater of Operations; Studies on Prophylaxis in 2 Epidemics of Infectious Hepatitis. J.A.M.A. 128: 1062–1063, 11 Aug. 1945. (2) What was then regarded as prevention subsequently was determined to be a modification of the disease by Krugman and his associates. *See* Krugman, S., Ward, R., Giles, J. P., and Jacobs, A. M.: Infectious Hepatitis; Studies on the Effect of Gamma Globulin and on the Incidence of Inapparent Infection. J.A.M.A. 174: 823–830, 15 Oct. 1960.

sion on Influenza. The laboratories of these Commissions were widely sepa-
rated—in Philadelphia, Pa., New Haven, Conn., and Ann Arbor, Mich.—
and to facilitate a ready exchange of ideas without loss of individual inde-
pendence, the Army Epidemiological Board established the "Hepatitis
Study Group" in July 1944. The respective field and laboratory work was
carried out by and under the direction of (1) Dr. Joseph Stokes, Jr., and
Capt. John R. Neefe, MC, at the Children's Hospital of Philadelphia and the
School of Medicine, University of Pennsylvania; (2) Dr. John R. Paul and
Maj. W. Paul Havens, Jr., MC, of the Section of Preventive Medicine of the
Yale University School of Medicine, New Haven; and (3) Dr. Thomas
Francis, Jr., at the School of Public Health, University of Michigan, Ann
Arbor.

The Commission on Measles and Mumps worked with a number of
different units of volunteers, including inmates of the New Jersey State
Prison at Trenton, N.J., and groups of conscientious objectors from a
special organization for this purpose known as the Civilian Public Service
Unit No. 140 of Philadelphia, Pa. The Commission on Neurotropic Virus
Diseases found volunteers in various groups of conscientious objectors
working in State institutions in the vicinity of New Haven, including
Civilian Public Service Unit No. 81 at the Connecticut State Hospital,
Middletown, Conn., Civilian Public Service Unit No. 68 at the Norwich
State Hospital at Norwich, Conn., and subsequently a special Branch of
Civilian Public Service Unit No. 140 of New Haven, Conn., housed in a
fraternity house at Yale University. Volunteers were also found among
prisoners at the Federal Correctional Institution in Danbury, Conn., and
at the State Prison in Wethersfield, Conn. The Commission on Influenza
found volunteers in the State Prison of Southern Michigan, Jackson, Mich.

The results of the various studies carried on by these groups as well
as by certain other investigators abroad are described in the sections on
"Serum Hepatitis" and "Infectious Hepatitis," which follow.

Serum Hepatitis

The pioneer experiments of Oliphant and his colleagues [101] were re-
ported in 1943 and described the transmission of hepatitis to volunteers
by the parenteral inoculation of serum obtained from patients in the acute
phase of homologous serum hepatitis, resulting from the administration of
known icterogenic yellow fever vaccine. Cameron,[102] working in the
Middle East, also reported in the same year the transmission of hepatitis

[101] Oliphant, J. W., Gilliam, A. G., and Larson, C. L.: Jaundice Following Administration of Human
Serum. Pub. Health Rep. 58: 1233–1242, 13 Aug. 1943.
[102] Cameron, J. D. S.: Infectious Hepatitis. Quart. J.M. 12: 139–155, July 1943.

to volunteers by inoculating blood obtained from patients acutely sick with the disease. These results were corroborated and extended by others.[103]

In contrast, attempts to demonstrate virus in the feces of patients in the acute phase of the disease by oral or parenteral inoculation were unsuccessful,[104] as were, with two possible exceptions [105] attempts to transmit the disease experimentally by feeding serum or nasopharyngeal washings. Limited attempts to detect virus in nasopharyngeal washings and urine were unsuccessful, with the possible exception of a single report by Findlay and Martin,[106] who described the occurrence of jaundice in a volunteer 50 days after intranasal inoculation of nasopharyngeal washings from a patient in the acute phase of hepatitis caused by the administration of yellow fever vaccine. Unfortunately, the number of experiments performed were insufficient to offer conclusive evidence whether serum hepatitis virus was in the urine, the nasopharyngeal washings, or the feces, or whether the disease could be produced by the ingestion of infectious material. In regard to the latter, however, Havens and his colleagues [107] and Neefe and his associates [108] were unable to transmit serum hepatitis to volunteers by feeding infectious serum that produced the disease regularly when inoculated parenterally.

The accidental contamination of pools of serum or plasma by the blood of apparently healthy persons carrying virus suggested that a carrier state might exist more often than was hitherto suspected. The importance of this was augmented by the tremendous use of human blood and plasma and stimulated the investigation of the period of infectivity of patients with this disease. Only a limited number of experiments were done; however, virus was found in the blood of volunteers during the

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[103] (1) MacCallum, F. O., and Bauer, D. J.: Homologous Serum Jaundice: Transmission Experiments With Human Volunteers. Lancet 1: 622–627, 13 May 1944. (2) Neefe, J. R., Miller, T. G., and Chornock, F. W.: Homologous Serum Jaundice; Review of Literature and Report of Case. Am. J.M. Sc. 207: 626–638, May 1944. (3) Neefe, J. R., Stokes, J., Jr., Reinhold, J. G., and Lukens, F. D. W.: Hepatitis Due to the Injection of Homologous Blood Products in Human Volunteers. J. Clin. Invest. 23: 836–855, September 1944. (4) MacCallum, F. O.: Transmission of Arsenotherapy Jaundice by Blood; Failure With Faeces and Nasopharyngeal Washings. Lancet 1: 342, 17 Mar. 1945. (5) Paul, J. R., Havens, W. P., Jr., Sabin, A. B., and Philip, C. B.: Transmission Experiments in Serum Jaundice and Infectious Hepatitis. J.A.M.A. 128: 911–915, 28 July 1945. (6) Paul, J. R., and Havens, W. P., Jr.: Recent Advances in the Study of Infectious Hepatitis and Serum Jaundice. Tr. A. Am. Physicians 59: 133–141, 1946. (7) Neefe, J. R., Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis; Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents. Am. J. Med. 1: 3–22, July 1946.

[104] (1) Neefe, J. R., Stokes, J., Jr., and Reinhold, J. G.: Oral Administration to Volunteers of Feces From Patients With Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis. Am. J.M. Sc. 210: 29–32, July 1945. (2) See footnote 103(4). (3) Havens, W. P., Jr.: The Period of Infectivity of Patients With Homologous Serum Jaundice and Routes of Infection in This Disease. J. Exper. Med. 83: 441–447, June 1946.

[105] (1) Findlay, G. M., and Martin, N. H.: Jaundice Following Yellow-Fever Immunization; Transmission by Intranasal Instillation. Lancet 1: 678–680, 29 May 1943. (2) See footnote 103(1).

[106] See footnote 105(1).

[107] (1) Havens, W. P., Jr., Ward, R., Drill, V. A., and Paul, J. R.: Experimental Production of Hepatitis by Feeding Icterogenic Materials. Proc. Soc. Exper. Biol. & Med. 57: 206–208, November 1944. (2) See footnote 104(3).

[108] (1) Neefe, J. R., Stokes, J., Jr., and Gellis, S. S.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis; Experimental Study of Immunity and Cross Immunity in Volunteers; Preliminary Report. Am. J.M. Sc. 210: 561–575, November 1945. (2) See footnote 103(7).

incubation period as well as in the acute phase of the disease by Neefe and his coworkers [109] (87 days before the onset of hepatitis), by Paul and his associates [110] (60 days before the appearance of jaundice), and by Havens [111] (16 days before the appearance of jaundice). During convalescence, at intervals of 1 to 5 months after the onset of disease,[112] similar attempts to recover virus were unsuccessful. It was not determined whether a carrier state might exist after recovery or whether patients with relapse or chronic hepatitis were infectious.

Evidence suggesting that serum hepatitis virus evoked homologous immunity was furnished by Neefe and his group,[113] who reinoculated nine volunteers convalescent 6 to 9 months from experimentally induced homologous serum hepatitis. None of the convalescents became sick, while eight out of nine controls contracted serum hepatitis, with incubation periods ranging from 60 to 110 days. However, there was no apparent cross-immunity between homologous serum hepatitis and infectious hepatitis as far as could be determined from the studies of Havens [114] and of Neefe and his colleagues.[115] Volunteers convalescent from the former disease contracted the latter when reinoculated with a strain of infectious hepatitis virus. The report of Oliphant,[116] who described complete protection in 10 volunteers convalescent from serum hepatitis when they were reinoculated with a strain of virus presumed to be infectious hepatitis, requires consideration in this regard. Although the strain of virus he used to challenge his convalescents was obtained in Italy where infectious hepatitis was epidemic, it is important to note that it produced hepatitis in the controls after a long incubation period of 85 to 106 days, suggestive of the behavior usually associated with serum hepatitis virus. The geographic coexistence of serum hepatitis and infectious hepatitis viruses that produce disease with long and short incubation periods, respectively, was evident from the reports of Paul and Havens [117] and of Cameron [118] in the Middle East, and it would appear that Oliphant's experience reflected a similar situation.

As a result of such studies in volunteers, it was shown that the serum hepatitis virus was (1) filterable through Berkefeld N and Seitz E K filters, (2) resistant to temperatures of 56° to 60° C. for at least 30 minutes, and (3) transmissible to man in serial passage by parenteral inoculation of infectious material. The studies also showed that the virus survived at a

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[109] See footnote 103 (3), p. 374.

[110] See footnote 103 (5), p. 374.

[111] See footnote 103 (3), p. 374.

[112] See footnote 101, p. 373; footnotes 104 (3) and 105 (1), p. 374.

[113] See footnote 103 (7), p. 374.

[114] Havens, W. P., Jr.: Experiment in Cross Immunity Between Infectious Hepatitis and Homologous Serum Jaundice. Proc. Soc. Exper. Biol. & Med. 59: 148–150, June 1945.

[115] See footnote 103 (7), p. 374.

[116] Oliphant, J. W.: Infectious Hepatitis: Experimental Study of Immunity. Pub. Health Rep. 59: 1614–1616, 15 Dec. 1944.

[117] See footnote 103 (6), p. 374.

[118] See footnote 102, p. 373.

temperature of 4° C. for a long period;[119] at a temperature of —10° to —20° C. for 4½ years, but apparently became inactive after 5 years at this temperature;[120] in a desiccated state at room temperature for at least a year;[121] and in serum containing Merthiolate in concentration 1 : 2,000,[122] in a mixture of equal parts of phenol and ether in 0.5 percent concentration,[123] and in an 0.2-percent concentration of tricresol[124] (tables 68, 69, and 70).

Infectious Hepatitis

The first successful transmission of infectious hepatitis to volunteers was described in Germany in 1942 in a short report by Voegt,[125] who fed them duodenal fluid and blood obtained from patients in the acute phase of the disease. In 1944, MacCallum and Bradley,[126] in England, and members of the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board, in the United States,[127] were independently and almost simultaneously successful in producing the disease in volunteers by feeding feces and serum obtained from a patient in the acute phase of infectious hepatitis. The source of this strain of hepatitis virus was a soldier who had sickened on the Anzio beachhead in 1943. Because of pain in the right lower quadrant of the abdomen, an appendectomy was performed. The appendix was normal, but mesenteric adenitis was found. The patient was transferred back to the 38th General Hospital in Egypt where he subsequently became jaundiced and had a typical course of infectious hepatitis. The role of feces and the intestinal-oral route in the transmission of the disease was thus well established.

Also of epidemiologic importance was the subsequent recovery of the hepatitis virus in 1945 by Neefe and Stokes[128] from water drawn from

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[119] See footnote 101, p. 373.

[120] Blanchard, M., Jr., and Stokes, J., Jr.: Personal communication.

[121] See footnote 103 (3), p. 374.

[122] Beeson, P. B., Chesney, G., and McFarlan, A. M.: Hepatitis Following Injection of Mumps Convalescent Plasma. Lancet 1: 814–815, 24 June 1944.

[123] See footnote 30 (2), p. 344.

[124] (1) See footnote 12 (2) and (3), p. 333. (2) Attempts to find a method of sterilizing serum of hepatitis virus appeared to be successful in that exposure to ultraviolet light for 1 hour at 2650 Angstrom units inactivated the virus experimentally. (See Oliphant, J. W., and Hollaender, A.: Homologous Serum Jaundice; Experimental Inactivation of Etiologic Agent in Serum by Ultraviolet Irradiation. Pub. Health Rep. 61: 598–602, 26 Apr. 1946.) Subsequent attempts some years later during the war in Korea to adapt this technique to large-scale sterilization of plasma were, unfortunately, unsuccessful. (See Sborov, V. M., Giges, B., and Mann, J. D.: Incidence of Hepatitis Following Use of Pooled Plasma; Followup Study in 587 Korean Casualties. A.M.A. Arch. Int. Med. 92: 678–683, November 1953.) (3) Heating the virus to 60° C. for 10 hours in human albumin was subsequently shown to inactivate the virus. (See Gellis, S. S., Neefe, J. R., Stokes, J., Jr., Strong, L. E., Janeway, C. A., and Scatchard, G.: Chemical, Clinical, and Immunological Studies on Products of Human Plasma Fractionation; Inactivation of the Virus of Homologous Serum Hepatitis in Solution of Normal Human Serum Albumin by Means of Heat. J. Clin. Invest. 27: 239–244, March 1948.)

[125] Voegt, H.: Zur Aetiologie der Hepatitis Epidemica. München. med. Wchnschr. 89: 76, 23 Jan. 1942.

[126] MacCallum, F. O., and Bradley, W. H.: Transmission of Infective Hepatitis to Human Volunteers. Lancet 2: 228, 12 Aug. 1944.

[127] See footnote 107 (1), p. 374.

[128] Neefe, J. R., and Stokes, J., Jr.: An Epidemic of Infectious Hepatitis Apparently Due to a Water Borne Agent. J.A.M.A. 128: 1063–1075, 11 Aug. 1945.

TABLE 68.—*Results of administration, to volunteers, of materials obtained from patients in the acute phase of serum hepatitis*

[In the "Route" column, O = oral; IG = intragastric; P = parenteral; IN = intranasal]

Inoculum	Author	Year	Route	Volunteers		Incubation period
				Inoculated	Jaundiced	
				Number	*Number*	*Days*
Feces	Neefe *et al* [1]	1945	O&IG	19	0	
	Neefe *et al* [1]	1945	P	5	0	
	MacCallum [2]	1945	O	15	0	
	Havens [3]	1946	O	6	0	
Serum	Cameron [4]	1943	P	6	6	30–30+
	Oliphant *et al* [5]	1943	P	186	33	28–133
	Oliphant *et al* [5]	1943	P	10	4	120–160
	Oliphant *et al* [5]	1943	IN	3	0	
	MacCallum & Bauer [6]	1944	P	16	6	50–127
	MacCallum & Bauer [6]	1944	IN	10	1	80(36)
	Havens *et al* [7]	1944–46	P	13	7	56–71
	Havens *et al* [7]	1944–46	O&IN	13	0	
	MacCallum [2]	1945	P	19	12	42–80
	Neefe *et al* [8]	1946	P	25	14	60–135
	Neefe *et al* [8]	1946	O	10	0	
Nasopharyngeal washings.	Findlay & Martin [9]	1943	IN	4	1	50
	MacCallum [2]	1945	IN	17	0	
	Neefe *et al* [8]	1946	IN&O	4	0	
Urine	Neefe *et al* [8]	1946	O	1	0	

[1] Neefe, J. R., Stokes, J., Jr., and Reinhold, J. G.: Oral Administration to Volunteers of Feces From Patients With Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis. Am. J.M. Sc. 210: 29–32, July 1945.

[2] MacCallum, F. O.: Transmission of Arsenotherapy Jaundice by Blood; Failure With Faeces and Nasopharyngeal Washings. Lancet 1: 342, 17 Mar. 1945.

[3] Havens, W. P., Jr.: The Period of Infectivity of Patients With Homologous Serum Jaundice and Routes of Infection in this Disease. J. Exper. Med. 83: 441–447, June 1946.

[4] Cameron, J. D. S.: Infective Hepatitis. Quart. J.M. 12: 139–155, July 1943.

[5] Oliphant, J. W., Gilliam, A. G., and Larson, C. L.: Jaundice Following Administration of Human Serum. Pub. Health Rep. 58: 1233–1242, 13 Aug. 1943.

[6] MacCallum, F. O., and Bauer, D. J.: Homologous Serum Jaundice; Transmission Experiments With Human Volunteers. Lancet 1: 622–627, 13 May 1944.

[7] (1) Havens, W. P., Jr., Ward, R., Drill, V. A., and Paul, J. R.: Experimental Production of Hepatitis by Feeding Icterogenic Materials. Proc. Soc. Exper. Biol. & Med. 57: 206–208, November 1944. (2) See footnote 3.

[8] Neefe, J. R., Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis; Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents. Am. J. Med. 1: 3–22, July 1946.

[9] Findlay, G. M., and Martin, N. H.: Jaundice Following Yellow-Fever Immunisation; Transmission by Intranasal Instillation. Lancet 1: 678–680, 29 May 1943.

NOTE.—Although the occurrence of nonicteric hepatitis is recognized, only jaundiced cases, in whom the diagnosis could be definite, are recorded here.

a well in a children's camp in Pennsylvania during an epidemic of the disease. The volunteers who ingested this water that was proved to have fecal contamination and the volunteers who ingested feces obtained from children with infectious hepatitis in the camp contracted the disease, giv-

TABLE 69.—*Results of administration, to volunteers, of materials obtained from patients in various stages of the incubation period and convalescence of serum hepatitis*

[The minus sign = before onset of the disease; the plus sign = after appearance of jaundice]

Author	Year	Day material was obtained	Volunteers	
			Inoculated	Jaundiced
			Number	Number
Neefe *et al* [1]_____	1944	−87_____	2	[2] 2
Paul *et al* [3]_____	1945	−60_____	8	3
Havens [4]_____	1946	−16_____	4	1
Havens [4]_____	1946	28 to 32_____	5	0
MacCallum & Bauer [5]_____	1944	66+_____	5	0
MacCallum & Bauer [5]_____	1944	141+_____	5	0
Oliphant *et al* [6]_____	1943	75 postjaundice_____	15	0

[1] Neefe, J. R., Stokes, J., Jr., Reinhold, J. G., and Lukens, F. D. W.: Hepatitis Due to the Injection of Homologous Blood Products in Human Volunteers. J. Clin. Invest. 23: 836–855, September 1944.

[2] No definite statement of jaundice.

[3] Paul, J. R., Havens, W. P., Jr., Sabin, A. B., and Philip, C. B.: Transmission Experiments in Serum Jaundice and Infectious Hepatitis. J.A.M.A. 128: 911–915, 28 July 1945.

[4] Havens, W. P., Jr.: The Period of Infectivity of Patients With Homologous Serum Jaundice and Routes of Infection in This Disease. J. Exper. Med. 83: 441–447, June 1946.

[5] MacCallum, F. O., and Bauer, D. J.: Homologous Serum Jaundice; Transmission Experiments With Human Volunteers. Lancet 1: 622–627, 13 May 1944.

[6] Oliphant, J. W., Gilliam, A. G., and Larson, C. L.: Jaundice Following Administration of Human Serum. Pub. Health Rep. 58: 1233–1242, 13 Aug. 1943.

TABLE 70.—*Results of attempts to demonstrate immunity and cross-immunity in volunteers convalescent from experimentally induced serum*

[In the "Challenge virus" column, IH = infectious hepatitis and SH = serum hepatitis]

Author	Year	Challenge virus	Convalescents			Controls		
			Inoculated	Jaundiced	Incubation period	Inoculated	Jaundiced	Incubation period
			Number	Number	Days	Number	Number	Days
Oliphant [1]_____	1944	IH	10	0	_____	11	4	85–106
Havens [2]_____	1945	IH	3	3	20–25	11	5	23–31
Neefe *et al* [3]_____	1946	IH	5	4	28–37	6	5	28–32
Neefe *et al* [3]_____	1946	SH	9	0	_____	9	8	60–100

[1] Oliphant, J. W.: Infectious Hepatitis: Experimental Study of Immunity. Pub. Health Rep. 59: 1614–1616, 15 Dec. 1944.

[2] Havens, W. P., Jr.: Experiment in Cross Immunity Between Infectious Hepatitis and Homologous Serum Jaundice. Proc. Soc. Exper. Biol. & Med. 59: 148–150, June 1945.

[3] Neefe, J. R., Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis: Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents. Am. J. Med. 1: 3–22, July 1946.

ing unequivocal proof to the concept previously based on epidemiologic evidence, that common source waterborne outbreaks could and did occur.

Attempts were also made to determine the infectivity of urine and nasopharyngeal washings in limited experiments. The results following

the ingestion of urine were contradictory, and although Voegt [129] and Findlay and Willcox [130] reported success, MacCallum and Bradley,[131] Havens,[132] and Neefe and Stokes [133] failed to transmit the disease in this way. With one possible exception,[134] the results of testing naso-pharyngeal washings were also negative.[135] However, the small number of volunteers employed in these latter experiments and the possibility that both urine and nasopharyngeal washings were obtained from the patients at a time when insufficient amounts of virus were present denied the right to draw any conclusions concerning the infectivity of either urine or nasopharyngeal washings.

After the demonstration of the presence of virus in the blood and feces of patients in the acute phase of the disease, attention was directed to determining when the virus appeared in these materials and how long it remained there. This was of particular concern in relation to the possi-bility that patients with relapse or chronic hepatitis might be infectious or that those who had made a complete recovery might remain carriers of the virus. The period of infectivity of patients with infectious hepatitis was therefore investigated in a few experiments. Virus was found in the blood 3 days before the onset of symptoms.[136] However, a single attempt to detect it in the blood halfway through the incubation period of experi-mentally induced infectious hepatitis was unsuccessful, as were attempts to recover the virus from the blood and feces 1 month [137] after onset, and from the feces 3 months [138] after the disappearance of jaundice.[139] The whole question of whether a "carrier state" existed either in the blood or in the feces remained unanswered, although there was epidemiologic evi-dence, particularly from civilian experience, to suggest that it did.

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[129] See footnote 125, p. 376.

[130] (1) Findlay, G. M., and Willcox, R. R.: Transmission of Infective Hepatitis by Faeces and Urine. Lancet 1: 212, 17 Feb. 1945. (2) Findlay later suggested that the apparent infectivity of urine in his experiment was due to the presence of erythrocytes associated with urinary bilharziasis. However, recent experiments by Krugman (personal communication) and his associates indicate that the virus is excreted in the urine in the acute phase of the disease and may be transmitted to volunteers by feeding.

[131] See footnote 126, p. 376.

[132] Havens, W. P., Jr.: Period of Infectivity of Patients With Experimentally Induced Infectious Hepa-titis. J. Exper. Med. 83: 251–258, March 1946.

[133] See footnote 128, p. 376.

[134] See footnote 126, p. 376.

[135] See footnote 128, p. 376, and footnote 132.

[136] Francis, T., Jr., Frisch, A. W., and Quilligan, J. J., Jr.: Demonstration of Infectious Hepatitis Virus in Presymptomatic Period After Transfer by Transfusion. Proc. Soc. Exper. Biol. & Med. 61: 276–280, March 1946.

[137] See footnote 132.

[138] See footnote 104, p. 374.

[139] From patients complaining of symptoms 6 to 9 months after the onset of hepatitis, Neefe and his asso-ciates obtained specimens of liver (by biopsy), blood, and feces, and fed them to volunteers who developed cer-tain vague symptoms and slight alterations of tests of hepatic function. The results, however, were not clearly defined, and no conclusion was made concerning whether such patients harbored the virus or might be infectious. See Neefe, J. R., Stokes, J., Jr., Garber, R. S., and Gellis, S. S.: Studies on the Relationship of the Hepatitis Virus to Persistent Symptoms, Disability, and Hepatic Disturbance ("Chronic Hepatitis Syndrome") Following Acute Infectious Hepatitis. J. Clin. Invest. 26: 329–338, March 1947.

Experimentally, a limited amount of data indicated that immunity develops during recovery from hepatitis. Both Havens[140] and Neefe and his associates[141] showed that volunteers convalescent 6 to 9 months from experimentally induced infectious hepatitis were immune when reinoculated with the homologous strain. In addition, Neefe and his group[142] showed that volunteers recovered from hepatitis experimentally induced by a strain of virus obtained from the stools of children with the disease in Pennsylvania were immune when inoculated with a strain of hepatitis virus obtained from the stool of a soldier who contracted the disease in Sicily.[143]

Evidence thus became available that more than one strain of hepatitis virus might cause hepatitis in man, and at least two strains of virus were described as being immunologically distinct.[144] These strains of virus were termed "infectious hepatitis" and "homologous serum hepatitis," and the similarities and differences between them will be discussed more fully at the end of this section. However, it may be mentioned here that, in a limited number of experiments, volunteers convalescent from hepatitis produced by one strain of virus were not immune when reinoculated with the other strain of virus.[145] In regard to immunity, it was shown by Stokes and Neefe[146] and by Havens and Paul[147] that normal human gamma globulin in amounts of 0.06 to 0.12 ml. per pound of body weight, administered intramuscularly, prevented the epidemic disease.[148]

As a result of these studies and others in volunteers, it was also demonstrated that the etiologic agent of infectious hepatitis was filterable through an L2 Chamberland or Seitz E K filter, that it was resistant to a temperature of 56° C. for at least 30 minutes, and that it was transmissible to man in serial passage by feeding or parenteral inoculation of infectious material.[149] The virus withstood chlorination, namely, one part chlorine residual per million for 30 minutes,[150] and remained active in materials frozen for 1 to 1½ years, but not for 3 years, at —10° to —20° C. Another strain of virus was inactive after storage at Dry Ice temperature for 32 months[151] (tables 71, 72, and 73).

[140] Havens, W. P., Jr., Immunity in Experimentally Induced Infectious Hepatitis. J. Exper. Med. 84: 403–406, November 1946.

[141] See footnote 108(1), p. 374.

[142] See footnote 103(7), p. 374.

[143] See footnote 107(1), p. 374.

[144] See footnote 103(7), p. 374.

[145] See footnote 103(7), p. 374, and footnote 114, p. 375.

[146] Stokes, J., Jr., and Neefe, J. R.: Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin; Preliminary Note. J.A.M.A. 127: 144–145, 20 Jan. 1945.

[147] Havens, W. P., Jr., and Paul, J. R.: Prevention of Infectious Hepatitis With Gamma Globulin. J.A.M.A. 129: 270–272, 22 Sept. 1945.

[148] See footnote 100(2), p. 372.

[149] Havens, W. P., Jr.: Properties of the Etiologic Agent of Infectious Hepatitis. Proc. Soc. Exper. Biol. & Med. 58: 203–204, March 1945.

[150] See footnote 99(1), p. 371, and footnote 128, p. 376.

[151] (1) See footnote 81, p. 361. (2) Stokes, J., Jr.: Unpublished observations.

TABLE 71.—*Results of administration, to volunteers, of materials obtained from patients in the acute phase of infectious hepatitis*

[In the "Route" column, O = oral; NP = nasopharyngeal; P = parenteral]

Inoculum	Author	Year	Route	Volunteers		Incubation period
				Inoculated	Jaundiced	
				Number	*Number*	*Days*
Feces_____	Voegt (duod. fl.)[1]_____	1942	O	4	[2] 1	28
	MacCallum & Bradley [3]__	1944	NP	26	3	27–31
	Havens *et al* [4]_____	1944–46	O	12	9	15–27
	Neefe *et al* [5]_____	1944–46	O	46	25	18–37
	Neefe *et al* [5]_____	1944–46	P	3	0	_____
	Findlay & Willcox [6] _____	1945	O	18	[2] 7	17–28
Serum_____	Voegt (blood)[1]_____	1942	O	(?)	1	(?)
	Voegt (blood)[1]_____	1942	P	(?)	1	19?
	MacCallum & Bradley [3]__	1944	P	6	3	64–92
	Havens [4]_____	1944–46	P	17	8	20–31
	Havens [4]_____	1944–46	O	8	7	21–34
	Oliphant [7]_____	1946	P	21	4	85–106
	Francis *et al* [8]_____	1945	P	8	4	35–43
	Neefe *et al* [5]_____	1945	P	6	1	35
	Neefe *et al* [5]_____	1946	O	3	2	26&33
Nasopharyngeal washings.	MacCallum & Bradley [3]__	1944	NP	16	0	_____
	Neefe *et al* [5]_____	1945	NP	8	0	_____
	Havens [9]_____	1946	NP	3	0	_____
Urine_____	Voegt [1]_____	1942	O	(?)	[2] 1	(?)
	MacCallum & Bradley [3]__	1944	NP & O	19	0	_____
	Findlay & Willcox [2]_____	1945	O	6	[2] 3	(?)
	Neefe & Stokes [10]_____	1945	O	7	0	_____
	Havens [9]_____	1946	O	3	0	_____

[1] Voegt, H.: Zur Aetiologie der Hepatitis Epidemica. München. med. Wchnschr. 89: 76, 23 Jan. 1942.

[2] No definite statement of jaundice.

[3] MacCallum, F. O., and Bradley, W. H.: Transmission of Infective Hepatitis to Human Volunteers. Lancet 2: 228, 12 Aug. 1944.

[4] (1) Havens, W. P., Jr., Ward, R., Drill, V. A., and Paul, J. R.: Experimental Production of Hepatitis by Feeding Icterogenic Materials. Proc. Soc. Exper. Biol. & Med. 57: 206–208, November 1944. (2) Havens, W. P., Jr.: Properties of the Etiologic Agent of Infectious Hepatitis. Proc. Soc. Exper. Biol. & Med. 58: 203–204, March 1945. (3) Havens, W. P., Jr.: Period of Infectivity of Patients With Experimentally Induced Infectious Hepatitis. J. Exper. Med. 83: 251–258, March 1946. (4) Havens, W. P., Jr.: Immunity in Experimentally Induced Infectious Hepatitis. J. Exper. Med. 84: 403–405, November 1946. (5) Havens, W. P., Jr.: Experiment in Cross Immunity Between Infectious Hepatitis and Homologous Serum Jaundice. Proc. Soc. Exper. Biol. & Med. 59: 148–150, June 1945. (6) Havens, W. P., Jr.: Elimination in Human Feces of Infectious Hepatitis Virus Parenterally Introduced. Proc. Soc. Exper. Biol. & Med. 61: 210–212, March 1946.

[5] Neefe, J. R., Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis; Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents. Am. J. Med. 1: 3–22, July 1946.

[6] Findlay, G. M., and Willcox, R. R.: Transmission of Infective Hepatitis by Faeces and Urine. Lancet 1: 212, 17 Feb. 1945.

[7] Oliphant, J. W.: Infectious Hepatitis: Experimental Study of Immunity. Pub. Health Rep. 59: 1614–1616, 15 Dec. 1944.

[8] Francis, T., Jr., Frisch, A. W., and Quilligan, J. J., Jr.: Demonstration of Infectious Hepatitis Virus in Presymptomatic Period After Transfer by Transfusion. Proc. Soc. Exper. Biol. & Med. 61: 276–280, March 1946.

[9] See footnote 4(3).

[10] Neefe, J. R., and Stokes, J., Jr.: An Epidemic of Infectious Hepatitis Apparently Due to a Water Borne Agent. J.A.M.A. 128: 1063–1075, 11 Aug. 1945.

NOTE.—Although the occurrence of nonicteric hepatitis is recognized, only jaundiced cases, in whom the diagnosis could be definite, are recorded here.

TABLE 72.—*Results of administration, to volunteers, of materials obtained from patients in various stages of the incubation period and convalescence of infectious hepatitis*

[F = feces; S = serum; the minus sign = before onset; the plus sign = after onset]

Author	Year	Inoculum	Day material was obtained	Volunteers	
				Inoculated	Jaundiced
				Number	*Number*
Havens [1]	1946	F	−15	3	0
Francis et al [2]	1945	S	−3	8	4
Havens [1]	1946	F&S	25+ to 31+	10	0
Neefe et al [3]	1945	F	21 post jaundice	7	0
Neefe et al [4]	1947	Liver	180+	5	0
Neefe et al [4]	1947	S	106+ to 367+	5	0
Neefe et al [4]	1947	F	92+ to 342+	5	0

[1] Havens, W. P., Jr.: Period of Infectivity of Patients With Experimentally Induced Infectious Hepatitis. J. Exper. Med. 83: 251–258, March 1946.

[2] Francis, T., Jr., Frisch, A. W., and Quilligan, J. J., Jr.: Demonstration of Infectious Hepatitis Virus in Presymptomatic Period After Transfer by Transfusion. Proc. Soc. Exper. Biol. & Med. 1: 276–280, March 1946.

[3] Neefe, J. R., Stokes, J., Jr., and Reinhold, J. G.: Oral Administration to Volunteers of Feces From Patients With Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis. Am. J.M. Sc. 210: 29–32, July 1945.

[4] Neefe, J. R., Stokes, J., Jr., Garber, R. S., and Gellis, S. S.: Studies on the Relationship of the Hepatitis Virus to Persistent Symptoms, Disability, and Hepatic Disturbance ("Chronic Hepatitis Syndrome") Following Acute Infectious Hepatitis. J. Clin. Invest. 26: 329–338, March 1947.

TABLE 73.—*Results of attempts to demonstrate immunity and cross-immunity in volunteers convalescent from experimentally induced infectious hepatitis, in 1946*

[In the "Challenge virus" column, IH = infectious hepatitis, and SH = serum hepatitis]

Author	Challenge virus	Convalescents			Controls		
		Inoculated	Jaundiced	Incubation period	Inoculated	Jaundiced	Incubation period
		Number	*Number*	*Days*	*Number*	*Number*	*Days*
Havens [1]	IH	9	0		12	8	21–30
Neefe et al [2]	IH	17	0		14	6	25–37
Neefe et al [2]	SH	4	2	101, 102	9	8	60–110

[1] Havens, W. P., Jr.: Immunity in Experimentally Induced Infectious Hepatitis. J. Exper. Med. 84: 403–406, November 1946.

[2] Neefe, J. R., Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis; Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents. Am. J. Med. 1: 3–22, July 1946.

Relationship of Serum Hepatitis to Infectious Hepatitis

The exact relationship between infectious hepatitis and homologous serum hepatitis eluded solution, and, indeed, an appellative dilemma was created by the arbitrary definition of the latter form of the disease on the basis of probable route of transmission. Whether homologous serum hepatitis merely represented the artificial transmission of the naturally occur-

ring disease was the subject of frequent discussion. While this may have occurred more frequently then was suspected, there was no evidence to indicate that it explained the relationship between the two.

The results of epidemiologic, clinical, and experimental studies revealed that certain similarities and differences existed between the two conditions and their causative agents. Although these two forms of hepatitis are clinically and pathologically indistinguishable after the onset of disease, attention was early directed to the fact that in infectious hepatitis the onset was more apt to be abrupt, with an elevated temperature of over 100° F. (37.8° C.).[152] In addition, serum hepatitis was described as being at times more severe as it occurred in debilitated patients. The causative agents of both diseases were found to be filtrable, resistant to a temperature of 56° C. for at least 30 minutes, and transmissible to man in serial passage, evoking homologous immunity. They were regarded as viruses; however, they were not successfully transmitted to laboratory animals or embryonated eggs.

In contrast to these similarities were certain differences that were consistently reproducible by two different groups of investigators, members of the Commission on Neurotropic Virus Diseases and of the Commission on Measles and Mumps, working under the auspices of the Army Epidemiological Board. In table 74 is recorded a comparison of the behavior of two apparently different strains of virus, summarized from the results of Paul and Havens and of Stokes and Neefe in experiments with volunteers described earlier in this section.

The incubation period of infectious hepatitis was short, ranging from 20 to 40 days, in contrast to the long period (40 to 160 days) of homologous serum hepatitis. That the prolonged incubation period of the latter disease was determined by the parenteral inoculation of virus partially

TABLE 74.—*Comparison of behavior of viruses of infectious hepatitis and serum hepatitis in experimentally infected volunteers*

Virus	Infectious hepatitis	Serum hepatitis
1. Filtrable	Seitz E. K.	Seitz E K.
2. Resistance to heat	56° C., 30 minutes	56° C., 60 minutes.
3. Susceptible host	Man	Man.
4. Incubation period (days)	15 to 34	56 to 134.
5. Route of infection (experimental)	Parenteral or oral inoculation.	Parenteral inoculation.
6. Virus in stool	Acute phase	Not demonstrated.
7. Virus in serum	do	Incubation period and acute phase.
8. Immunity:		
a. Homologous	Present	Present.
b. Heterologous	None apparent	None apparent.

152 See footnote 26, p. 340.

neutralized by antibody in the serum was considered. However, the short incubation periods following both parenteral and oral inoculation of volunteers with serum containing the same strain of infectious hepatitis virus suggested that such a mechanism was not the complete explanation of difference in time interval.[153] Prolonged incubation periods were indeed reported in experimentally induced infectious hepatitis when the inoculation was by the parenteral route,[154] but the failure to test the same inoculums for infectivity by the oral route denied any comparison of the effect of route of inoculation on length of incubation.

The virus of serum jaundice was found in the circulating blood during the long incubation period as well as in the active stage of the disease. Experimentally, it appeared to be infectious only when inoculated parenterally, with two possible exceptions. The disease thus produced was not as contagious as infectious hepatitis, evidence of contact infection was rare, and the virus was not found in the feces. This fact, in combination with the failure to produce this disease in volunteers by the oral administration of serum known to contain virus, suggested that the intestinal-oral route was not important in its spread, differentiating it in some degree from infectious hepatitis. Of interest in this regard was the comparison of the elimination of two strains of virus in the feces after parenteral inoculation.[155] A strain of infectious hepatitis virus was readily detected in the feces during the acute phase of the disease produced by parenteral inoculation. In contrast, a strain of serum hepatitis virus also inoculated parenterally in other volunteers was not found in the feces during the acute phase. In addition, studies on the immunity of volunteers corroborate the epidemiologic experience that patients who have had either infectious hepatitis or homologous serum hepatitis were susceptible when exposed to the other disease. Lastly, the long period of viremia in patients with serum hepatitis, in contrast to the much shorter period of viremia in infectious hepatitis, was adduced to explain the difference in the prophylactic effect of normal human gamma globulin in the two conditions. In the former, questionably favorable results followed the administration of two doses a month apart, while no protection was demonstrable when only one dose was given. This suggested that the efficacy might have a quantitative relationship with the amount of circulating virus. It was not determined by the end of the war whether the differences in route of inoculation, length of incubation period, onset of disease, distribution of virus, period of infectivity, and lack of cross-immunity represented the activities of actually different viruses or of antigenic differences of various strains of one virus.[156]

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[153] Havens, W. P., Jr.: Elimination in Human Feces of Infectious Hepatitis Virus Parenterally Introduced. Proc. Soc. Exper. Biol. & Med. 61: 210–212, March 1946.

[154] See footnote 116, p. 375, and footnote 126, p. 376.

[155] See footnote 153.

[156] It is pertinent to point out that many of these unknowns still persist at the time of writing this chapter in 1963.—W. P. H., Jr.

CHAPTER XIV

Nephritis

John P. Merrill, M.D.

An evaluation of nephritis occurring in the military during World War II must necessarily be considered in the light of our knowledge of the disease in general, since there appears to be little difference in its various aspects between military and civilian experience. In this discussion, we shall concern ourselves principally with glomerulonephritis.

GLOMERULONEPHRITIS

Etiology.—The present evidence for the etiology of glomerulonephritis implicates an immune response in which the glomeruli are primarily involved by inflammatory change. The disease can be produced experimentally in rats by the injection of rabbit serum from animals who have been previously immunized to a homogenate of rat kidney.[1] Other hyperimmune reactions involving small vessels generally may also affect the glomeruli by inflammatory change. Such changes have been produced by hypersensitivity to the sulfonamides.[2] The disease in man appears to be closely associated with an antecedent infection by so-called nephritogenic strains of the hemolytic streptococcus. The lag period between infection with the streptococcus and the onset of nephritis probably represents development of an immune process, similar to that found in the experimental animal. Interpretation of animal and human data suggests that in some fashion renal tissue and streptococcal protein combine to form an antigen, the immunologic reaction to which produces the inflammatory changes.[3] This protein has been tagged by tracer substances and actually found to be localized in the glomeruli. In this way, an autoantibody is produced and may help to explain the continuing progress of the disease in some clinical situations long after the initial infection has subsided.

Clinical aspects.—In man, glomerulonephritis also appears to be preceded by infection with the Group A hemolytic streptococcus. This correlation, however, is not a perfect one since frequently a history of previous

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[1] Farr, L. E., and Smadel, J. E.: Experimentally Induced Nephritis in Rats, Functional and Clinical Studies. J. Clin. Invest. 15: 449, 1936.

[2] Rich, A. R.: The Role of Hypersensitivity in Periarteritis Nodosa, as Indicated by 7 Cases Developing During Serum Sickness and Sulfonamide Therapy. Bull. Johns Hopkins Hosp. 71: 123–140, March 1942.

[3] Lange, K., Craig, F., Oberman, J., Slobody, L., Ogur, G., and LoCasto, F.: Changes in Serum Complement During the Course and Treatment of Glomerulonephritis. A.M.A. Arch. Int. Med. 88: 433–445, October 1951.

streptococcal infection cannot be obtained; in addition, well-documented cases of nephritis have followed infection with other micro-organisms, such as the pneumococcus. Undoubtedly, however, the hemolytic streptococcus is the prime offender, and the analogy with rheumatic fever and previous streptococcal infection is an interesting one. Probably both represent hyper-immune responses to previous infection with the streptococcus. There are, however, striking differences as shown in table 75.[4] Whereas rheumatic fever rather consistently occurs in about 3 percent of hemolytic strepto-coccal infections, the rate for nephritis is extremely variable (table 76).[5] A survey of the literature indicates that the percentage of nephritis follow-ing scarlet fever varies from 0 to 18 percent. Furthermore, nephritis may occur in pseudoepidemics. These variations in incidence suggest to one author that the streptococcus may vary in its nephritogenic properties. In the United States, type 12, and to a lesser extent type 4 of Group A, strepto-cocci have been usually associated with this complication.

The latent period following streptococcal infection as well as the drop in serum complement during the acute phase again suggest the possibility of hypersensitivity to this organism or to a product thereof. Other forms

TABLE 75.—*Biological differences between glomerulonephritis and rheumatic fever*

Biological feature	Glomerulonephritis	Rheumatic fever
Geographic distribution	Uniform	Most common in northern latitudes.
Age	Any age	Rare in infancy.
Familial factors	Family contacts	Familial tendency.
Sex incidence	Males predominate, 2 to 1	Equal.
Second attacks	Rare	Common.
Average latent period between infection and first attack.	10 days	18 days.
Latent period between infection and second attack.	Shortened as compared to latent period in first attack.	Usually same as latent period in first attack.
Relation of degree of ASL [1] increase to incidence of attacks.	No known relation	Incidence of attacks pro-portional to ASL [1] increase.
Time of ASL [1] increase in rela-tion to onset relapse.	After	Before.
Serum complement	Decreased	Increased.
Type of initiating Group A hemolytic streptococcus.	4, 12, 25 and untyped (12 predominates).	Any type.

[1] Antistreptolysin titer.
    Source: Modified from Earle, D. P., Jr., and Seegal, D.: Natural History of Glomerulonephritis. J. Chron. Dis. 5: 3–13, 1957.

[4] Earle, D. P., Jr., and Seegal, D.: Natural History of Glomerulonephritis. J. Chron. Dis. 5: 3–13, 1957.
    [5] Rammelkamp, C. H., and Weaver, R. S.: Acute Glomerulonephritis; Significance of the Variations in Incidence of Disease. J. Clin. Invest. 32: 345–358, April 1953.

TABLE 76.—*Variations in incidence of nephritis following scarlet fever observed in four hospitals*

Author	Year	Number of cases of scarlet fever	Nephritis (percent)
Granud	1890	668	7.2
	1913	1,338	2.2
	1937	259	3.5
	1938	208	1.4
	1939	1,298	2.6
	1946	338	1.5
Hunter	1904	114	2.6
	1905	135	.7
	1906	179	1.6
	1907	220	5.0
Joe and Williamson	1920	--------	1.4
	1921	--------	2.7
	1922	--------	1.3
	1923	--------	2.1
	1924	--------	4.6
	1925	--------	4.9
Peters and Cullum	1910–14	2,771	1.9
	1915–19	1,329	1.9
	1920–24	2,496	2.5
	1925–29	3,148	.9
	1930–34	2,427	.4
	1935–36	1,350	3.2

Source: Rammelkamp, C. H., and Weaver, R. S.: Acute Glomerulonephritis; Significance of the Variations in Incidence of Disease. J. Clin. Invest. 32: 345–358, April 1953.

of hypersensitivity in man may also cause glomerulonephritis. These include disseminated lupus erythematosus, polyarteritis from unknown causes, and variants of these phenomena due to hypersensitivity to penicillin, to the sulfonamides, and to other drugs.

The clinical course of acute glomerulonephritis (figs. 40 and 41) is also extremely variable. It may be manifested only by hematuria and proteinuria which may go entirely unnoticed. At the other end of the spectrum, the disease may occur suddenly and with severity. Oliguria, marked hematuria, hypertension, edema, and convulsions may all be present. In some cases, the initial attack may be followed by progressive diminution in renal function and by death from uremia or hypertensive cardiovascular disease. In others, the patient may enter a so-called latent phase with minimal proteinuria and hematuria, which may persist without other manifestations. Chronic glomerulonephritis does follow well-documented attacks of acute disease, but many cases of chronic glomerulonephritis give no history of such an acute attack. In these cases, which undoubtedly have been smoldering for months or years before brought to the physician's attention, the
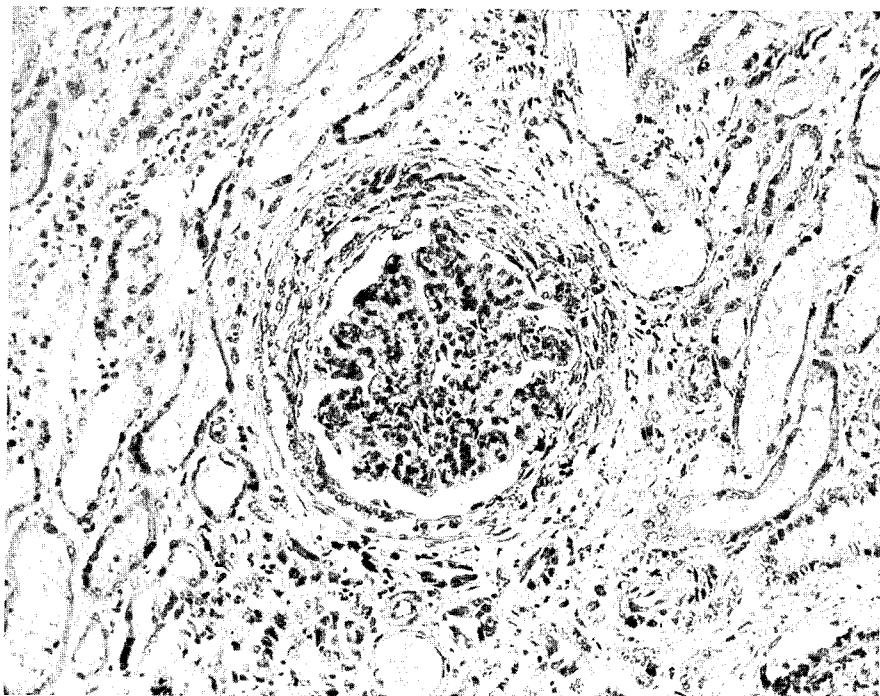
PBBH–A40–24

FIGURE 40.—Photomicrograph, acute glomerulonephritis. Note epithelial crescent, erythrocytes in Bowman's space, and slightly increased cellularity of the tuft. There is protein precipitate in the tubules with some cells and cell debris. There are also interstitial edema and increased cellularity of the interstitial tissue. [Description, courtesy Dr. G. J. Dammin.]

pathology is somewhat different. Indeed, Ellis [6] believes that the history and pathology in these instances are distinct enough to suggest that the disease itself may be different. It is entirely possible, however, that the underlying etiologic factors are the same but that the resultant differences in clinical picture and pathology may reflect failure to note the early inflammatory response and the difference in the degree and rate of change. Glomerulonephritis—latent, subacute, or chronic—may be characterized by exacerbations. These may follow reinfection with the hemolytic streptococcus but may also be related to other infections, to trauma, or to stress.

Pathophysiology of glomerulonephritis.—The variability in the clinical course is paralleled by variability in the pathophysiology of the acute disease. Mild inflammatory change in the glomeruli may be reflected only by proteinuria and slight hematuria. In the more severe cases, the rate of glomerular filtration is decreased out of proportion to diminution in tubular

6 Ellis, A.: Natural History of Bright's Disease: Clinical Histological and Experimental Observations (Croonian Lectures). Lancet 1: 1, January 1942.
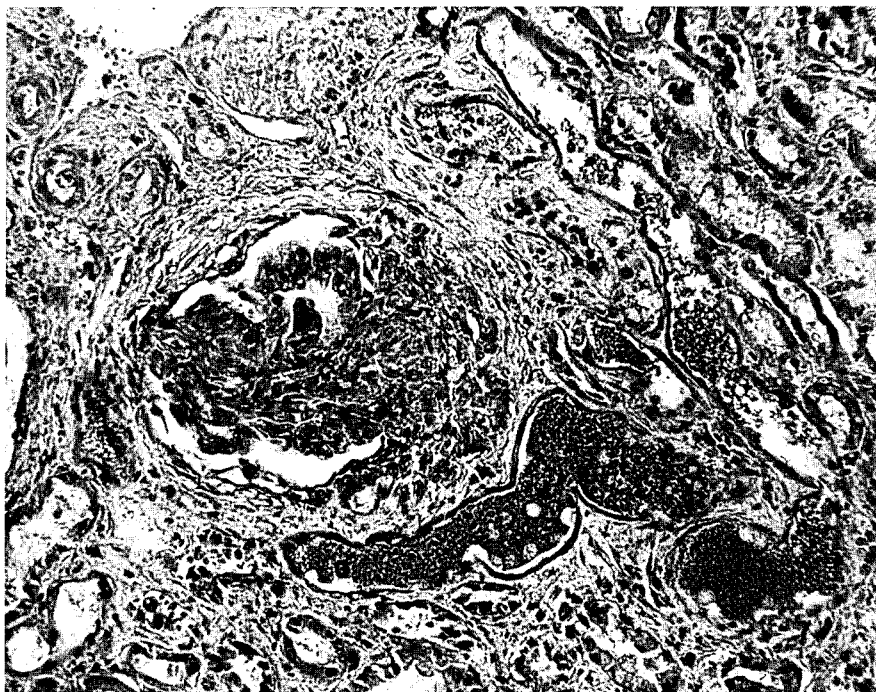
PBBH–A40–24

FIGURE 41.—Photomicrograph, acute glomerulonephritis. Note epithelial proliferation of the glomerular tuft, the interstitial edema, and protein precipitate in the tubules. [Description, courtesy Dr. G. J. Dammin.]

function. The proteinuria is thought to be the result of increased permeability of the glomerular capillaries, but since there may be generalized edema some authors have suggested that the disease may actually represent generalized capillary changes. The evidence for this idea is not good, however, and it is possible to explain the generalized edema by retention of sodium secondary to diminution in rate of filtration with continued ingestion of salt and water. This explanation may also account for the hypertension, the hypervolemia, and the congestive failure that occur in some of these patients. With marked inflammatory change, decrease in rate of filtration leads to oliguria, and although tubular function remains good the urine may be of high specific gravity. Some degree of hypertension occurs in 50 percent of hospitalized patients with acute glomerulonephritis, and this in part may be explained by hypervolemia. In addition, however, in many instances it must represent "true renal hypertension." Patients with severe disease may manifest striking anemia. This has been shown in part [7] to be due to decreased survival of circulating red cells. With the onset of uremia,

[7] Emerson, C. P.: Pathogenesis of Anemia in Acute Glomerulonephritis; Estimations of Blood Production and Blood Destruction in Case Receiving Massive Transfusions. Blood 3: 363–372, April 1948.

it undoubtedly represents both decreased survival of the erythrocytes and depression of the bone marrow.[8] Congestive heart failure is due to both hypervolemia and hypertension. In some instances, Aschoff bodies have been found in the myocardium of patients with acute glomerulonephritis, but it is questionable whether primary myocardial involvement is a significant factor in the heart failure. The nephrotic syndrome may be a striking manifestation of any stage of glomerulonephritis.

Treatment.—Treatment of the acute phase of glomerulonephritis is relatively nonspecific. Although the use of penicillin following streptococcal infections appears to decrease the incidence of subsequent nephritis,[9] there is little evidence that penicillin modifies the course once the full-blown disease has appeared. Bed rest during the acute phase appears to be the treatment of choice, as long as evidence of activity is manifested by fever, marked hematuria, tachycardia, or elevation of the sedimentation rate. In the presence of oliguria and edema, the diet should be low in sodium. If oliguria is severe and prolonged and marked retention of nitrogen occurs, the patient should be treated like any other patient with acute renal failure. Congestive heart failure may be prevented by the drastic limitation of salt and water, but, once this complication has ensued, digitalis may be indicated. The anemia of acute glomerulonephritis does not require treatment unless it becomes severe (hematocrit below 25). Under such circumstances, treatment should be by infusion of small amounts of freshly drawn, packed red blood cells. Rest in bed should be continued until all evidence of activity of the disease has subsided. Once the temperature and sedimentation rate have returned to normal, however, there is little evidence that bed rest per se over a period of more than 6 weeks modifies the course of the disease.

Although the adrenal corticosteroids have achieved striking therapeutic results in the treatment of the nephrotic stage of glomerulonephritis, their use in the treatment of acute nephritis has been disappointing.[10] The treatment of chronic glomerulonephritis is beyond the scope of this chapter. There is little that can be done for the underlying disease except to prevent exacerbations. Treatment of the renal failure accompanying chronic glomerulonephritis is a complex problem and must be carefully individualized.[11]

INCIDENCE

The data on the incidence of nephritis during World War II are difficult to collect. Most of the reports include nephritis under the broad category of

[8] Scheitlin, W., and Merrill, J. P.: Pathogenesis of Anemia in Chronic Rental Failure. [Unpublished data.]

[9] Rammelkamp, C. H., Jr.: Prevention of Acute Nephritis. Ann. Int. Med. 43: 511–517, September 1955.

[10] (1) Thorn, G. W., Merrill, J. P., Smith, S. III, Roche, M., and Frawley, T. J.: Clinical Studies With ACTH and Cortisone in Renal Disease. Arch. Int. Med. 86: 319–354, September 1950. (2) Burnett, C. H., Greer, M. A., Burrows, B. A., Sisson, J. H., Reiman, A. S., Weinstein, L. A., and Colburn, C. G.: The Effect of Cortisone on the Course of Acute Glomerulonephritis. New England J. Med. 243: 1028–1032, 1950.

[11] Merrill, John P.: The Treatment of Renal Failure: Therapeutic Principles in the Management of Acute and Chronic Uremia. New York: Grune & Stratton, Inc., 1955.

cardiovascular renal disease. Of those for which the information is broken
down, few give any information beyond the number of cases admitted.
Preliminary data are available, however, from the Medical Statistics Divi-
sion, Office of The Surgeon General, U.S. Army. These are shown for the
years 1942–45 as the number of admissions per year per 1,000 average
troop strength for the various theaters (table 77).

Approximately 6,100 admissions for nephritis were reported during
the 4 war years. Of 4,800 admissions for nephritis that were specified as
acute or chronic during the 4-year period, 35 percent were labeled acute,
giving a ratio for chronic nephritis to acute nephritis of approximately
2 to 1. Data indicating the extent to which nephritis appeared as a secondary
diagnosis are available for 1944 and 1945 only. For these 2 years combined,
the total incidence (cases admitted for nephritis plus cases admitted for
another cause with nephritis as a secondary diagnosis) in the entire Army
exceeded the admissions for nephritis by about 50 percent.

TABLE 77.—*Admissions for nephritis in the U.S. Army, by area or theater and year, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number of admissions per year per 1,000 average strength]

Area of theater	1942–45	1942	1943	1944	1945
Continental United States_____	0.27	0.26	0.24	0.25	0.35
Overseas:					
Europe_____	0.24	0.16	0.22	0.13	0.34
Mediterranean [1]_____	.23	.22	.22	.25	.20
Middle East_____	.29	.33	.32	.43	0
China-Burma-India_____	.15	.34	.63	.17	.09
Southwest Pacific_____	.15	.37	.17	.11	.15
Central and South Pacific_____	.11	.16	.18	.11	.06
North America [2]_____	.25	.35	.31	.15	.15
Latin America_____	.20	.26	.17	.21	.14
Total overseas [3]_____	0.20	0.24	0.23	0.15	0.23
Total Army_____	0.24	0.26	0.24	0.20	0.28

[1] Includes North Africa.
[2] Includes Alaska and Iceland.
[3] Includes admissions on transports.

The data in table 77 are somewhat difficult to interpret since the ad-
mission rates were for all types of nephritis and not limited to acute
glomerulonephritis. In 1944–45, for example, nearly 45 percent of the
admissions for nephritis were diagnosed as chronic glomerulonephritis and
25 percent as acute glomerulonephritis. Approximately 30 percent were
unclassified. Thus, although it appears that admission rates were con-

sistently lower in the Pacific theaters than in the continental United States and in Europe, a fact which is contrary to the criteria listed in table 75, it is not certain that this comparison is valid for acute glomerulonephritis.[12] It is probable also that diagnostic facilities and medical admissions for urinary abnormalities differed in the continental United States and in the Pacific theaters.

Table 78 compares the incidence of rheumatic fever, scarlet fever, and streptococcal sore throat. The data here are based on sample tabulations of individual medical records. Incidence data (new admissions plus secondary cases) for rheumatic fever and nephritis are not available for 1942–43. However, the extent to which incidence exceeded admissions in the U.S. Army, worldwide, in 1944–45 (for rheumatic fever, incidence exceeded new admissions by about 10 percent; for nephritis, incidence exceeded new admissions by approximately 50 percent), may be used as a rough approximation to incidence. These data suggest, although they do not conclusively prove, that the incidence of both rheumatic fever and nephritis was lower in the Southwest Pacific Area and the China-Burma-India theater than in the continental United States and Europe. The interpretation here is open to the same criticisms raised in the preceding paragraphs. The data in table 78 also suggest that the increase or decrease in the yearly incidence of rheumatic fever and nephritis in the continental United States and Europe varied independently in each disease. The variation, however, appeared to be in the same direction in the China-Burma-India theater. The relationship between the incidence of rheumatic fever and scarlet fever, in terms of variation of yearly rates, appeared to be roughly the same in the continental United States. Variations in incidence in scarlet fever bore no apparent relationship to that of nephritis. Thus, the table gives some hint that incidence of rheumatic fever and scarlet fever in the continental United States may follow roughly the same trend, but there is little correlation in other areas. This discrepancy points up again the observation that there are nephritogenic strains of Group A streptococci and that apparently the epidemic streptococci of World War II were less capable of producing nephritis and rheumatic fever and erythema (scarlet fever). It should be noted, however, that before the end of 1944 scarlet fever was a poor index of the presence of streptococcal disease generally.

The relative rarity of nephritis is borne out by an examination of extracts from the medical service reports of various general hospitals in the

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[12] In contrast are the epidemics of acute glomerulonephritis at the U.S. Naval Training Center, Bainbridge, Md., early in World War II and again during the winter of 1951–52. The data unfortunately are available only for the latter outbreak (Annual Report, Commission on Acute Respiratory Disease, Armed Forces Epidemiological Board, 1952–53). During this time, cases of glomerulonephritis outnumbered those of rheumatic fever by 2 to 1. It was found that nearly half the cases of exudative pharyngitis at Bainbridge were due to Group A, type 12 streptococci, and there was a close association between infections due to this type of streptococcus and the subsequent development of acute nephritis. During a control study involving approximately 400 patients, 15 cases of acute nephritis occurred following type 12 streptococcal infections, but no cases were observed after infections with types 3, 6, or 19.—J. P. M.

TABLE 78.—*Morbidity rates* [1] *of rheumatic fever, nephritis, and certain streptococcal infections among U.S. Army personnel stationed in selected areas, by year, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number per year per 1,000 average strength]

Year and area	Rheumatic fever [2]	Scarlet fever	Streptococcal sore throat	Nephritis [2]
1942				
Continental United States	0.58	1.08	(3)	0.26
Europe	.33	.41	(3)	.16
Southwest Pacific	.46	1.26	(3)	.37
China-Burma-India	.23	1.26	(3)	.34
1943				
Continental United States	1.29	2.43	(3)	.24
Europe	.31	.44	(3)	.22
Southwest Pacific	.26	.17	(3)	.17
China-Burma-India	.48	.40	(3)	.63
1944				
Continental United States	1.12	1.93	.82	.25
Europe	.43	.65	.31	.13
Southwest Pacific	.36	.03	.34	.11
China-Burma-India	.26	.06	.62	.17
1945				
Continental United States	.50	.98	3.58	.35
Europe	.50	.59	1.13	.34
Southwest Pacific	.38	.01	.94	.15
China-Burma-India	.20	.09	1.15	.09

[1] Rates shown for rheumatic fever and nephritis are in terms of new admissions and for which the diagnosis indicated was the primary cause of admission; whereas, for scarlet fever and streptococcal sore throat the rates are incidence rates (include secondary cases as well as new admissions).

[2] Incidence data are available only for 1944 and 1945. During this period, for the Army as a whole, the incidence of rheumatic fever exceeded the new admissions by about 10 percent, and the incidence of nephritis exceeded the new admissions by approximately 50 percent.

[3] Data are not available.

Zone of Interior and from oversea theaters. In general, the diagnosis of glomerulonephritis accounted for 5 percent or less of all admissions. Of those patients in whom a diagnosis of renal disease was made, renal and ureteral calculi were the most frequent cases. Usually, the incidence of chronic glomerulonephritis exceeded that of acute glomerulonephritis. Occasionally, glomerulonephritis was seen following bacterial endocarditis, sensitivity to sulfonamides, and disseminated lupus erythematosus. The pathology and clinical course did not appear to differ significantly from cases seen in civilian installations. The preponderance of diagnoses of chronic glo-

merulonephritis over acute may reflect a disease that was not present upon induction, or more probably the progression of a disease whose only manifestation, proteinuria, was missed on the examination of the urine at induction. This fact points up again the insidious onset of this form of a disease which has led some observers to believe it to be of different etiology.

The incidence of renal disease in Army Air Forces installations was comparable. In one Army Air Forces regional hospital of 500 beds, 117 cases of renal disease in men aged from 18 to 38 were reported over a 12-month period. The majority of these were renal calculi and congenital anomalies of the kidney with and without evidence of infection. Of the remainder, 35 were cases of acute pyelonephritis, of mixed idiopathic albuminuria, and only 2 of acute glomerulonephritis.

Prognosis.—Deaths from nephritis from all theaters and areas per year per 100,000 average troop strength are shown in table 79. Although these overall figures are not broken down with regard to the acute and the chronic forms, extracts of reports from various general hospitals indicate again as in civilian life that deaths from chronic nephritis greatly exceeded those from the acute phase. About one-half of the number of patients admitted for nephritis in World War II received separation for disability. Although data on separations due to nephritis are not yet available, the cited figure may be regarded as a close approximation to the number of cases receiving separation due to disability from nephritis.

TABLE 79.—*Deaths from nephritis in U.S. Army, by area and year, 1942–45*

[Rate expressed as number of deaths per year per 100,000 average strength]

Area	1942–45	1942	1943	1944	1945
Continental United States_____	0.9	1.0	1.2	0.8	0.4
Overseas_____	1.1	1.2	1.1	1.1	1.1
Total Army_____	1.0	1.1	1.1	0.9	0.8

TYPES

Field nephritis.—Two types of nephritis of particular interest to the military deserve special mention. Trench nephritis, also called field or war nephritis, was reported in World War I and was suggested as a special entity. It was said to be characterized by frequent presence of bronchitis and dyspnea, by sudden onset of uremic manifestations, and by an extraordinarily low mortality. It is of interest that this represented about 5 percent of medical diseases admitted and was strikingly more frequent than acute nephritis in a general civilian hospital. The author of one report[13] noted

[13] Fitz, R.: Trench Nephritis at a British General Hospital in France. Mil. Surgeon 45: 80–98, July 1919.

that it occurred most commonly among relatively old soldiers. This author did believe that acute nephritis, of which "trench nephritis" appeared to be a variant, was more common in France than in the United States. In no case, it was said, was there evidence for believing that the disease showed any chronic progressive tendency and recovery was the rule.

In World War II, field or war nephritis again received considerable attention. In several reports,[14] it is represented as of increased incidence in the German Army, and it is mentioned as "quite a problem in the German Army in Italy during the winter of 1944–45." Although German concepts at that time favored a virus etiology, there was no evidence to support this view. Many authors noted massive edema without some of the other features of the nephrotic syndrome, notably proteinuria. This may perhaps have been due to the poor state of nutrition in the troops. Two later reports from Holland [15] stressed the increased incidence of acute glomerulonephritis with a tendency to appear in epidemic form, in which the disease characteristically occurred in older patients and was manifested by massive edema. The similarity of these "epidemics" to "trench nephritis or war nephritis" was noted.

Since at least one epidemic occurred among political prisoners, it is possible that here, too, poor nutrition played a role. A survey of extracts of reports from the various general hospitals in the oversea theaters bore out the impression that acute hemorrhagic nephritis was more frequent among prisoners of war. The fact that substandard nutrition may have had something to do with this is suggested by a report from a general hospital in the Zone of Interior, in which it is noted that asymptomatic subacute and chronic glomerulonephritis was discovered in a considerable number of prisoners returned from both Japanese and German camps.[16] The repeated emphasis on its occurrence in soldiers in whom the elasticity of tissues may have been poorer than in soldiers in the younger age group may again explain the massive edema. German medical officers stressed the fact that a history of recently antecedent nasopharyngitis due to hemolytic streptococcal infection was rare, and these officers considered that sudden chilling or wetting played an important role as a precipitating etiologic factor in field nephritis. Most American medical officers did not consider this disease a separate entity but rather a modification by environment and dietary circumstances of the ordinary type of acute glomerulonephritis. It may be noted that typical field nephritis did not occur in any appreciable

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[14] (1) Essential Technical Medical Data, Mediterranean Theater of Operations, U.S. Army, for May 1945, dated 1 June 1945. (2) Semiannual Report, Chief Consultant in Medicine, Office of the Chief Surgeon, European Theater of Operations, U.S. Army, 1 Jan.–30 June 1945, Exhibit D, Report on Acute Nephritis in Prisoners-of-War; Exhibit E, Report on Survey of Edema of Undetermined Etiology ("Trench Nephritis").

[15] (1) Klein, F.: Acute Glomerulonephritis. Acta med. scandinav. 129: 156–163, 1947. (2) Formijne, P.: On an Epidemic of Acute Glomerulonephritis in Amsterdam. Acta med. scandinav. 129: 509–512, 1948.

[16] Annual Report, Schick General Hospital, 1945.

amount in American troops who were in contact with the Germans in the northern Apennines during the winter of 1944–45.

Nephritis in scrub typhus.—A second type of nephritis of some interest was that seen with scrub typhus. Albuminuria, diminished renal function, and even azotemia were not uncommon in epidemic typhus.[17] The autopsied cases of scrub typhus showed evidence of interstitial nephritis in varying degrees. The kidneys were usually swollen and congested [18] with characteristic focal interstitial lesions and occasionally evidence of severe vascular damage and glomerular injury. The glomeruli were not uniformly affected, however, but some definitely showed increased cellularity and ischemia. Occasionally, clinical manifestations were those of acute glomerulitis with numerous granular casts and erythrocytes. An occasional death in uremia is reported in this disease, but where mentioned it seems to be as much due to dehydration and hypotension with generalized vascular collapse as to renal disease per se.

SUMMARY

In general, experience with glomerulonephritis in the Army did not differ from that in civilian life.

The incidence of acute glomerulonephritis in World War II was rather low and was exceeded by a number of other renal diseases, of which congenital defects and renal calculi predominated.

The diagnosis of chronic glomerulonephritis was somewhat more frequent than the diagnosis of acute glomerulonephritis, emphasizing the insidious nature of the former.

So-called trench or field nephritis, although thought by some to differ in etiology and clinical manifestations, was probably acute glomerulonephritis possibly modified by the poor nutritional status of many of the patients in whom it was seen.

Interstitial nephritis with some of the manifestations of acute glomerulonephritis was seen occasionally in scrub typhus, but was rarely the primary cause of death.

[17] Yeomans, A., and others: Azotemia in Typhus Fever. Ann. Int. Med. 23: 711–753, November 1945.
[18] Settle, E. B., Pinkerton, H., and Corbett, A. J.: Pathologic Study of Tsutsugamushi Disease (Scrub Typhus) With Notes on Clinicopathologic Correlation. J. Lab. & Clin. Med. 30: 639–661, August 1945.

CHAPTER XV

Diseases of the Blood and Blood-Forming Organs

Maurice B. Strauss, M.D.

Disorders of the hematopoietic and lymphatic systems did not constitute a major problem of the Medical Department during World War II. Nevertheless, over 7 percent of all accessions to the Army Institute of Pathology, Washington, D.C., received between 7 December 1941 and 2 September 1945, numbering almost 5,000 specimens, were classified under this heading.[1] For many of the diseases under consideration, the problems of diagnosis, treatment, and ultimate prognosis differed in no significant way from the same problems in civilian life. However, the experience of the members of the Medical Department revealed eight noteworthy observations in this field, as follows:

1. Severe anemia (p. 398) was rarely encountered among soldiers who had had repeated attacks of malaria in contrast to its frequent occurrence in infected civilian populations.

2. Although hookworm infection (p. 398) was common in certain areas where U.S. troops were stationed, severe anemia—the outstanding cause of disability in hookworm disease in civilians—was rare.

3. Eosinophilia (p. 399) as high as from 67 to 83 percent, with total leukocytes numbering between 50,000 and 60,000, were encountered in both hookworm infection and schistosomiasis and sometimes created a diagnostic problem in differentiation from eosinophilic leukemia.

4. In a small number of cases, Atabrine (quinacrine hydrochloride) was implicated as a causative factor in apalstic anemia (pp. 401–404).

5. Infectious mononucleosis (p. 405) was recognized in troops more often than in civilian populations and at times reached minor epidemic proportions. Spontaneous rupture of the spleen was observed at least seven times in infectious mononucleosis.

6. Despite the liberal and widespread use of sulfonamide drugs, agranulocytosis (p. 406) was uncommon and rarely fatal.

7. Nitrogen mustard (p. 406), a chemical warfare agent, was shown to have much promise in the treatment of lymphomatous disease.

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[1] Custer, R. P., and Miller, M. H.: Lymphatic and Hematopoietic Disease in the United States Army During World War II: General Survey and Consideration of Histopathologic Diagnosis. [Professional paper.]

8. Aplastic anemia (p. 412) was produced in a goodly number of individuals exposed to irradiation from atomic bomb explosions at Hiroshima and at Nagasaki, Japan.

SEVERE ANEMIA

Anemia due to the destruction of parasitized erythrocytes was present to some degree in all cases of malaria. A single severe paroxysm of falciparum malaria might reduce the number of erythrocytes by 1 million cells per cubic millimeter. Although such severe hemolysis was uncommon in vivax infections, a significant degree of anemia frequently occurred. It is therefore of interest that anemia from malaria was so rarely encountered among the troops of the United States. In part, this may be explained by the fact that treatment was generally prompt so that repeated paroxysms did not occur in any single attack, although recurrent attacks were general. Of 435 soldiers evacuated from islands in the South Pacific Area and admitted to Harmon General Hospital, Longview, Tex., with recurrent malaria, the average number of attacks before admission was 5.7.[2] Of these 435 soldiers, there were 287 whose records contained adequate data on the hematopoietic status. Only three patients had less than 13.0 gm. and only 26 had less than 14.0 gm. of hemoglobin per 100 cc. of blood. The erythrocytes of seven men numbered less than 4.0 million per cubic millimeter and in 72 men the number was under 4.5 million per cubic millimeter. In connection with this conspicuous absence of anemia, it may be mentioned that the spleen was palpable in only 23 percent of the acute attacks, and then only transiently. This also may be related to the prompt institution of therapy in each attack.

HOOKWORM INFECTION

Hookworm infection[3] was acquired by a goodly number of troops in the combat areas of the Pacific. However, signs or symptoms (other than eosinophilia) which could be attributed to the infection alone were almost never found. Among civilian populations with hookworm infection, hypochromic anemia is the outstanding feature and, in a majority of patients, is the chief cause of disability. Rhoads, Castle, Payne, and Lawson[4] clearly showed (1) that this anemia is due to a deficiency of iron brought about by the chronic loss of blood, by defective diets, and by gastrointestinal changes; (2) that it may be corrected by therapy with iron without removing the

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[2] Gordon, H. H., Lippincott, S. W., Marble, A., Ball, A. L., Ellerbrook, L. D., and Glass, E. W., Jr: Clinical Features of Relapsing Plasmodium Vivax Malaria in Soldiers Evacuated From the South Pacific Area. Arch. Int. Med. 75: 159–167, March 1945.

[3] See also chapter V, pp. 146–153.

[4] Rhoads, C. P., Castle, W. B., Payne, G. C., and Lawson, H. A.: Hookworm Anemia; Etiology and Treatment With Especial Reference to Iron. Am. J. Hyg. 20: 291–306, 1934.

parasites; and (3) that the removal of the hookworms does not cause a prompt remission of the anemia. Although a great many writers indicate a belief that the presence or absence of anemia in hookworm infection depends on the number of worms, Scott [5] points out that it is the host's reserves of iron that determine the onset and degree of the anemia. Two studies are available among troops infected with hookworm—hemoglobin and determination of the number of erythrocytes. In 100 malarial and surgical patients infected with hookworm, not a single case had signs or symptoms which could be attributed to the infection alone, and only 10 patients had fewer than 4.0 million erythrocytes per cubic millimeter. In these, the anemia could be related to other causes. [6] Examinations of the blood of 1,000 soldiers, 93 of whom had hookworm infection and 907 of whom did not, showed that 19 men (20 percent) of the infected patients had fewer than 4.0 million erythrocytes per cubic millimeter and that 34 percent had less than 80 percent hemoglobin. In the nonparasitized group, 15 percent had fewer than 4.0 million erythrocytes per cubic millimeter and 37 percent less than 80 percent hemoglobin. The smallest number of erythrocytes encountered was 3.1 million per cubic millimeter and the lowest hemoglobin was 60 percent. [7] Although it is probable that the infection of troops was not heavy, the general absence of signs and symptoms—and of anemia—can best be ascribed to the excellent nutritional state of the men and the adequacy of their diet.

EOSINOPHILIA

Eosinophilia of moderate degree in both hookworm infection and schistosomiasis has long been recognized. Extreme eosinophilia is mentioned in many textbooks on these disorders. Ashford, Payne, and Payne, in 1933, [8] reported a case of uncinariasis with 87 percent eosinophils and a total count of 41,200 leukocytes per cubic millimeter and another case with a total count of 78,400 leukocytes per cubic millimeter, 68 percent of which were eosinophils.

Among troops, it was noted that both eosinophilia and leukocytosis generally reached a maximum between 3 and 4 months after hookworm infection. [9] The highest percentage of eosinophils was 67 percent of 28,000 leukocytes; the highest number was 47,000 in a patient with 48 percent eosinophils. Eosinophilia may persist for a year or more, although the

[5] Scott, J. A.: Iron-Deficiency Anaemias. Lancet 1: 357, 549, 1938; also Am. J. Hyg. 26: 455–505, 1937.

[6] Most, H., Hayman, J. M., Jr., and Wilson, T. B.: Hookworm Infections in Troops Returning from the Pacific. Am. J.M. Sc. 212: 347–350, September 1946.

[7] Essential Technical Medical Data, U.S. Army Forces, South Pacific Area, dated 1 Feb. 1944.

[8] Ashford, B. D., Payne, G. C., and Payne, F. K.: Acute Uncinariasis From Massive Infestation and Its Implications. J.A.M.A. 101: 843–847, 1933.

[9] (1) Liebow, A. A., and Hannum, C. A.: Eosinophilia, Ancylostomiasis, and Strongyloidosis in the South Pacific Area. Yale J. Biol. & Med. 18: 381–403, May 1946. (2) Whitehouse, F. R.: Massive Eosinophilia in Uncinariasis; Report of Two Cases. Gastroenterology 9: 303–306, September 1947.

leukocytosis generally disappears sooner. It should be pointed out that both leukocytosis and eosinophilia of marked degree may occur before hookworm ova can be demonstrated in the stools, thereby creating a diagnostic problem. Löffler's syndrome, tropical eosinophilia, and eosinophilic lung, which were reported, may well represent instances of hookworm infection or of schistosomiasis. Wright and Gold [10] have reported from Camp Blanding, Fla., nine cases of creeping eruption (caused by *Ancylostoma braziliense*) with transient migratory pulmonary infiltration and eosinophilia. In schistosomiasis, Billings and his coworkers [11] reported 83 percent eosinophils in a patient whose total leukocytes numbered 53,000 per cubic millimeter. Mason and his coworkers [12] noted that 14 percent of their 300 cases of schistosomiasis had over 70 percent eosinophils and that 32 percent had between 50 and 70 percent eosinophils. Of the 300 patients, 8 percent had leukocytes numbering between 30,000 and 60,000 and 25 percent had between 20,000 and 30,000. Thus, it is apparent that both hookworm infection and schistosomiasis may present a picture of the blood suggestive of eosinophilic leukemia.

MALARIA

It was pointed out by Lt. Col. Richard P. Custer, MC, of the Army Institute of Pathology,[13] that, during the first year of the war in the Pacific, bitter experience proved that malaria could neutralize U.S. combat forces more rapidly and more effectively than enemy fire. Guadalcanal, New Guinea, and certain areas of the China-Burma-India theater were among the most highly malarious regions of the world. Control measures for malaria could not be put into effect so long as the military situation remained unstabilized and U.S. soldiers were living and fighting in the jungle. Although mosquito repellents and protective clothing afforded a small measure of protection, it was not until control of malaria by suppressive-drug therapy was introduced in November 1942 in Guadalcanal, and subsequently employed in New Guinea, that the inroads of the disease began to diminish.[14] Within a year after the beginning of suppressive-drug therapy, its value was so thoroughly established that it was intensively used in all malarious regions of the Pacific. This intensive use began in November 1942.

During the next year, medical officers in the Southwest Pacific Area called attention to a characteristic cutaneous lesion which was occurring in

[10] Wright, D. O., and Gold, E. M.: Loeffler's Syndrome Associated With Creeping Eruption (Cutaneous Helminthiasis). J.A.M.A. 128: 1082–1083, 11 Aug. 1945.

[11] Billings, F. T., Winkenwerder, W. L., and Hunninen, A. V.: Studies on Acute Schistosomiasis in Philippine Islands; Clinical Study of 337 Cases With a Preliminary Report on Results of Treatment With Fuadin in 110 Cases. Bull. Johns Hopkins Hosp. 78: 21–56, January 1946.

[12] Mason, P. K., Daniels, W. B., Paddock, F. K., and Gordon, H. H.: Latent Phases of Asiatic Schistosomiasis. Arch. Int. Med. 78: 662–678, December 1946.

[13] Custer, R. P.: Aplastic Anemia in Soldiers Treated With Atabrine (Quinacrine). Am. J.M. Sc. 212: 211–224, August 1946.

[14] Dieuaide, F. R.: Personal communication.

soldiers who had been evacuated from New Guinea and adjacent islands.[15] This lesion, termed "atypical lichen planus," but which also included eczematoid reactions, was associated with Atabrine therapy so frequently that an etiological relation between the drug and the skin lesion seemed probable.

During 1943 and 1944, it was noted that the incidence of aplastic anemia in the Southwest Pacific and the South Pacific Areas and in the China-Burma-India theater was considerably higher than in all the other foreign theaters and also higher than in the continental United States.[16] A study of aplastic anemia made at the Army Institute of Pathology is quite revealing (chart 4). Throughout the entire period from January 1942

CHART 4.—*Incidence of aplastic anemia among U.S. Army troops, 1942–45*
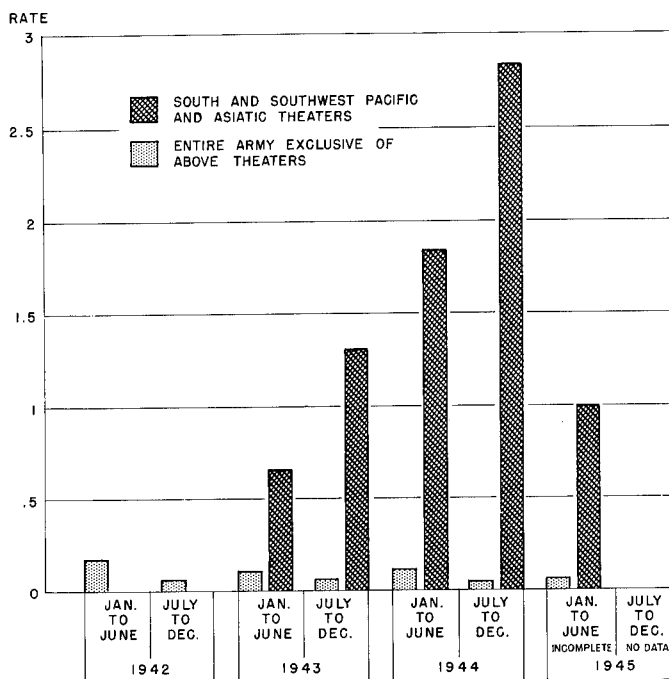
Source: Custer, R. P.: Aplastic Anemia in Soldiers Treated With Atabrine (Quinacrine). Am. J.M. Sc. 212: 211–224, August 1946.

to June 1945, the incidence of aplastic anemia in the entire Army—exclusive of the South Pacific, Southwest Pacific, and China-Burma-India—remained below 0.18 cases per 100,000 troops; whereas, in the areas just cited, it rose steadily from early 1943 to the end of 1944, reaching a peak of 2.84 cases per 100,000 troops in the period from July to December 1944, at a time when the rate for the rest of the Army was 0.04 cases per 100,000.

[15] Bull. U.S. Army M. Dept. 4: 653–659, December 1945.
[16] See footnote 13, p. 400.

The beginning of this increased incidence in the South Pacific and Southwest Pacific Areas and in the China-Burma-India theater in 1943 coincided with the period of the increased use of Atabrine in these areas. The peak in 1944 coincided with the period when suppressive-drug therapy was in extensive and widespread use. The incomplete figures for the first half of 1945 are of dubious significance. If borne out by complete data, they might reflect the diminished use of Atabrine as other measures to control malaria became effective and might reflect as well a smaller number of persons taking Atabrine as a result of troops being moved out of the more malarious areas in these theaters.

The cases of aplastic anemia occurring in 1943 and 1944 were further analyzed.[17] Among the 20 cases from nonmalarious regions, 2 followed arsenical treatment for syphilis, 3 occurred after irradiation of malignant tumors, 4 were ascribed to sulfonamide medication, and in 11 patients no cause could be demonstrated. The 47 cases that occurred in the South Pacific and Southwest Pacific Areas and in the China-Burma-India theater had all received suppressive doses of Atabrine over periods ranging from 1 to 34 months; the majority ranged between 4 and 9 months. The 34-month case was unique, however, and the patient apparently had not adhered to the prescribed regimen, as his record showed repeated attacks of tertian malaria which required active treatment.

There was specific mention of overdosage before the onset of illness in six cases. Four men had increased the dose to 0.2 gm. daily, one for 3 weeks, another for 6 months, a third for 8 months, and the last for an unspecified time. Another soldier took between 20 and 30 tablets during the 4 days preceding onset of symptoms; still another was said to have ingested massive doses for 3 weeks before. Other instances of overdosage probably occurred, but were either not known or not recorded. For example, men on patrol or detached service were given supplies of Atabrine adequate for estimated time away from their units and, although instructions in its use were given, its administration was unsupervised.

Seven of the group treated with Atabrine had also taken sulfathiazole or sulfadiazine. In two instances, it was not possible to exclude sulfonamide drugs as a precipitating factor, but in the others it was obvious that the drugs were administered only after the onset of the anemia and in two cases aggravated the purpuric manifestations.

Atabrine dermatitis complex, the term proposed to designate atypical lichen planus, preceded aplastic anemia in 20 patients. In these, topical applications of various sorts were used—and light roentgenologic treatment was given in one instance—but were not regarded as significant causal factors.

A few patients had taken aspirin for headache, which was frequently a feature of the prodromal period. The others had received no drugs, nor could a history of exposure to other etiological agents be elicited.

The study of case records of soldiers who developed aplastic anemia after taking Atabrine revealed no significant differences in the manifestations from those encountered in aplastic anemias of varied etiology.

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[17] See footnote 13, p. 400.

The most common complaint of the prodromal period was weakness, often associated with headache, vertigo, and dyspnea. A hemorrhagic tendency was frequently noted early, evidenced by bleeding gums after brushing teeth, nosebleed, "bruising easily," or the spontaneous appearance of ecchymoses in the skin. Dimness of vision, noted first by two of the patients, was found to be the result of intraocular hemorrhage. In the majority of cases, the onset was gradual, several weeks to a month or even more elapsing before the man reported to sick call. The prodrome was of brief duration in six cases and the onset precipitous in three in which an acute febrile state was the first indication of illness.

The early manifestations of aplastic anemia were often unnoticed in the group of 25 patients who were being treated for skin lesions until individuals among them were observed to be rather pallid and a blood count disclosed a reduction in the formed elements of the blood. In no instance did the anemia precede the dermatitis.

Almost invariably the course was marked by fever and hemorrhagic phenomena, the location and extent of the hemorrhages accounting for differences in symptoms. For example, hemiplegia, convulsions, and coma were noted in patients with intracranial bleeding; in contrast, hematuria and sometimes pain were associated with hemorrhage of the urinary tract. Of four patients, one was known to have survived at least 2 months; a second, 4 months; and the other two, 7 months.

Hematological findings.—Rather complete series of blood counts were submitted in most cases, and the diagnosis of aplastic anemia was confirmed by sternal biopsy in 25.

In four patients, blood counts were performed very soon after the onset and showed that the number of erythrocytes was fairly well maintained (4.0 to 5.0 million per cubic millimeter), whereas the numbers of leukocytes and platelets had fallen sharply, the lowest being 1,500 and 40,000 per cubic millimeter, respectively. This is to be expected when one recalls the relatively long life (120 days or more for erythrocytes as opposed to from 3 to 5 days for neutrophils and platelets) of the mature erythrocytes and that most of the residual cells found in the bone marrow at necropsy are their progenitors.

The other 21 patients were already anemic when first examined, and initially the erythrocytes numbered as few as 600,000 per cubic millimeter, although the average range was from 1.5 to 3.0 million per cubic millimeter. The anemia was generally of the normocytic, normochromic type. In some cases, it seemed to be macrocytic, but this is questionable since it was reported only in instances where the anemia was severe; that is, in the range where hemoglobin readings are apt to be very inaccurate. Furthermore, no hematocrit values were available in these cases as a check on the presence of macrocytosis. Nucleated erythrocytes almost never appeared in the peripheral blood. Reticulocyte counts over 1 percent were rarely recorded and they were frequently reported as either none or less than 0.1 percent. Anisocytosis and poikilocytosis were seldom marked except in the few cases showing evidence of regeneration. It was possible with frequently repeated blood transfusions to restore the number of erythrocytes and the amount of hemoglobin to normal or nearly so in 16 patients and to effect

an improvement in nearly all. A few patients became progressively more anemic despite transfusions, and the majority did not maintain their improved status.

The initial leukocyte count was seldom over 3,000 per cubic millimeter and usually fell between 1,000 and 3,000 being normal (7,200) in only one case. Values below 1,000 per cubic millimeter were noted in five instances. The counts fluctuated somewhat, and occasionally rose following transfusions, but the general trend was toward lower levels as the disease progressed, with little tendency to increase significantly even during clinical remissions. The leukopenia was due primarily to failure of the bone marrow to produce granulocytes, but when the total count was greatly reduced the relative lymphocytosis actually represented a lymphocytopenia. This was also the case with respect to the monocytes. Absolute agranulocytosis was frequently recorded, but a general scan of the blood films usually disclosed a few neutrophils, most of them mature forms. Immature granulocytes were occasionally seen early in the course of the disease, but rarely thereafter.

The number of platelets was significantly low in all but 4 of the 49 cases in which counts were done. In three of these exceptions, the platelets were counted once and it was then early in the course of the disease. In the fourth, two counts were recorded as 263,000 and 154,000 per cubic millimeter. Necropsy disclosed extensive visceral hemorrhages in every one of these cases, however, and the marrows were devoid of megakaryocytes, indicating that platelets must have been subsequently much reduced. In general, the counts ranged between zero and 100,000 per cubic millimeter, with most of them below 50,000 at some time during the disease.

The coagulation time of the blood was but little altered, but clot retraction was either slow or absent. Bleeding time was sometimes normal even though the tourniquet test was positive. In other cases, the bleeding time was prolonged; in one patient, blood oozed for several days from the prick caused by the lancet.

Examination of the bone marrow in all cases showed the marrow to be markedly depleted of all normal hematopoietic elements. Usually the residual cells of the marrow belonged to the erythropoietic series and were in the late erythroblastic and normoblastic stages. The few granulocytes were generally stab or segmented forms, although occasionally small foci of myelocytes or even younger elements were encountered. Megakaryocytes were either absent or very sparsely distributed and when present often showed evidence of degeneration.

Although the evidence now makes it appear that Atabrine was etiologically significant in the production of bone marrow aplasia, it must be pointed out most emphatically that even the highest rate, 2.84 cases of aplastic anemia per 100,000 troops, was of trivial significance in comparison with both malarial morbidity and mortality before the introduction of suppressive-drug therapy.

INFECTIOUS MONONUCLEOSIS

Infectious mononucleosis has been a commonly diagnosed disorder among troops both in the continental United States and in theaters overseas. During 1944, the rate of admission for this disease was 97 per 100,000 troop strength. This high incidence of the disease may be explained by a number of factors. First, a routine examination of the blood was made on all Army patients admitted to hospitals, while in civilian life many of these patients would have been treated at home without the benefit of a hematological study and, therefore, their disease would have gone undiagnosed. Secondly, infectious mononucleosis is a disease which has the highest incidence in youth.

Contratto [18] found that 1.5 percent of the total medical admissions to Stillman Infirmary, Harvard University, Cambridge, Mass., were due to mononucleosis, whereas only 0.36 percent of the total medical admission to the Peter Bent Brigham Hospital, Boston, Mass., were so diagnosed. The disease was definitely epidemic in certain areas. In the Caribbean Defense Command during the last 4 months of 1944, 92 cases of infectious mononucleosis were admitted to the 368th Station and the 262d General Hospitals.[19] In the United States, 300 cases were observed within a period of 20 months at several large hospitals of the Army Air Forces.[20] At the Station Hospital, Camp McCoy, Wis., between December 1943 and May 1944, 340 subclinical cases were discovered while 26 clinical cases were being treated.[21]

No evidence was accumulated during the war which would indicate that the severity of infectious mononucleosis was increased when it appeared in epidemic form. However, spontaneous rupture of the spleen, a complication which has been reported only three times in civilian life,[22] occurred at least seven times in the Army.[23] A total of 44 instances of spontaneous rupture of the spleen have been collected by the Army Institute of Pathology from 7 December 1941 to 2 September 1945.[24] The cause of rupture could not be determined in 5 patients; in 22, it was due to malaria; in 7, to mononucleosis; in 5, chronic congestive splenomegaly (Banti's syndrome) ; in 3, to torsion; and in 2, to leukemia.

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[18] Contratto, A. W.: Infectious Mononucleosis; A Study of One Hundred and Ninety-Six Cases. Arch. Int. Med. 73: 449–459, June 1944.

[19] Essential Technical Medical Data, Caribbean Defense Command, for January 1945, dated 20 Feb. 1945. Inclosure 1, "Epidemic of Infectious Mononucleosis."

[20] Read, J. T., and Helwig, F. C.: Infectious Mononucleosis; An Analysis of Three Hundred Cases With Three Characterized by Rare Hematologic Features. Arch. Int. Med. 75: 376–380, June 1945.

[21] Vander Meer, R., Lutterloh, C. H., and Pilot, J.: Infectious Mononucleosis; Analysis of 26 Clinical and 340 Subclinical Cases. Am. J.M. Sc. 210: 765–774, December 1945.

[22] (1) King, R. B.: Spontaneous Rupture of Spleen in Infectious Mononucleosis; Report of a Case. New England J. Med. 224: 1058–1060, 19 June 1941. (2) Ziegler, E. E.: Infectious Mononucleosis; Report of a Fatal Case With Autopsy. Arch. Path. 37: 196–201, March 1944. (3) Darley, W., Black, W. C., Smith, C., and Good, F. A.: Spontaneous Splenic Rupture in Infectious Mononucleosis; A Case and Pathologic Report. Am. J.M. Sc. 208: 381–384, September 1944.

[23] Smith, E. B., and Custer, R. P.: Rupture of the Spleen in Infectious Mononucleosis; A Clinicopathologic Report of Seven Cases. Blood 1: 317–333, July 1946.

[24] See footnote 23.

AGRANULOCYTOSIS

During 1942 and 1943, agranulocytosis was not separately indexed, and therefore data bearing on its incidence are not available. In 1944, a rate of only 1.0 per 100,000 troop strength was reported with a total of 8 deaths. During the entire period of hostilities, only 37 accessions diagnosed as agranulocytosis were received by the Army Institute of Pathology. Although precise figures were not available on how many soldiers received sulfonamide drugs, it has been estimated that over 80 percent of the wounded were so treated and often for considerable periods of time. The 15th Medical Hospital Center, in the European theater, reported on 300 to 400 admitted casualties of whom 75 percent received local sulfonamide and over 80 percent received oral sulfonamide medication. This low incidence of agranulocytosis was therefore rather remarkable. One explanation offered was that repeated examinations of blood were made routinely on patients receiving sulfonamides in hospitals, and medication was stopped at the first indication of leukopenia.

NITROGEN MUSTARDS

Mustard gas, bis (β-chloroethyl) sulfide, which was extensively employed as a poison gas in 1918 and which was known to have remote effects on hematopoietic tissues, was studied further after World War I. Its adverse effect on leukopoietic tissues and on the growth of experimental tumors was demonstrated. With the advent of World War II, biological research on gases used in war was resumed and attention directed to the nitrogenous analogs of mustard gas, the bis- and tris- (β-chloroethyl) amines, known as nitrogen mustards.

It was soon determined that these compounds owed their biological activity to their ability to undergo intramolecular cyclization in a polar solvent to form the highly reactive ethylenimonium cation.[25] This cation alkylates the functional groups of many compounds of biological importance, and it is likely that the basic mechanism of the cytotoxic action of the mustards is through such a reaction with a vital cellular constituent.

In general, it may be stated that the susceptibility of cells to the mustards is proportional to the proliferative activity of the cells. Thus, the blood-forming organs and the gastrointestinal mucosa are first and most profoundly affected (as is also the case with irradiation, see p. 412). Following the intravenous administration of the nitrogen mustards to experimental animals and to man, lymphocytopenia, granulocytopenia, and thrombocytopenia occur and, to a less extent, anemia. Marked effects on the blood may be obtained with doses of such a small size that nausea and vomit-

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[25] Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the β-chloroethyl Amines and Sulfides. Science 103: 409–415, 5 Apr. 1946.

ing are the only gastrointestinal effects. Larger doses lead to diarrhea which may become hemorrhagic. The outstanding pathological lesions after a mustard has been administered consist of (1) lymphatic fragmentation (as early as 10 hours after injection), leading to atrophy of lymphatic structures, and (2) the early disappearance of all mitotic activity in the bone marrow, leading to depletion. With larger doses or prolonged administration, there was almost complete aplasia, and necrosis and desquamation of the gastrointestinal mucosa.

The marked effects of the mustards on lymphoid tissue coupled with the finding that actively proliferating cells are selectively vulnerable to the cytotoxic action of the mustards suggested the therapeutic use of these compounds in the treatment of neoplasms of lymphoid tissue. Because of its undesirable physical properties and extreme chemical reactivity, sulfur mustard is not suitable for parenteral administration. However, nitrogen mustards in the form of their hydrochloride salts are water-soluble crystalline compounds that can be readily dissolved in sterile saline for intravenous administration. Experiments on transplanted lymphosarcoma in mice revealed that dissolution of such tumors could be effected rapidly although the dose required bordered on the toxic, and the tumor invariably returned.[26] The first clinical trial of the nitrogen mustards [27] was conducted on a group of six patients in the terminal stages of various neoplastic diseases. In two cases of lymphosarcoma in which roentgenologic therapy had been discontinued, a rapid dissolution of large tumor masses followed a course of injections. The results were sufficiently encouraging to warrant further clinical experimentation. Since then, much clinical experience with nitrogen mustard has accumulated.

Although sporadic temporary remissions of symptoms, sometimes associated with regression of primary or metastatic lesions, have occurred in a variety of malignancies—including some of neural origin—the only statistically significant results were observed in undifferentiated bronchogenic carcinoma and in malignant lymphoma, particularly of the Hodgkin's type. In bronchogenic carcinoma, striking remissions of fever, pain, weakness, cough, and anorexia have occurred. At times, these conditions were accompanied by regression of pulmonary infiltrations and of the signs of obstruction of the superior vena cava. In general, individual remissions were of relatively short duration, measured in weeks rather than months, but often repeated courses of treatment have continued to produce remissions (figs. 42 and 43).

In Hodgkin's disease, rapid improvement in the patient's general condition—disappearance of fever, gain in weight, and increase in the number of erythrocytes and hemoglobin—was accompanied by regression in the

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[26] Dougherty, T., Gilman, A., Goodman, L., and Dougherty, J.: 1942–43. [Unpublished work cited by Gilman and Philips, see footnote 25, p. 406.]

[27] Gilman, A., Goodman, L., Lindskog, G. E., and Dougherty, J.: 1942–43. [Unpublished work cited by Gilman and Philips, see footnote 25, p. 406.]
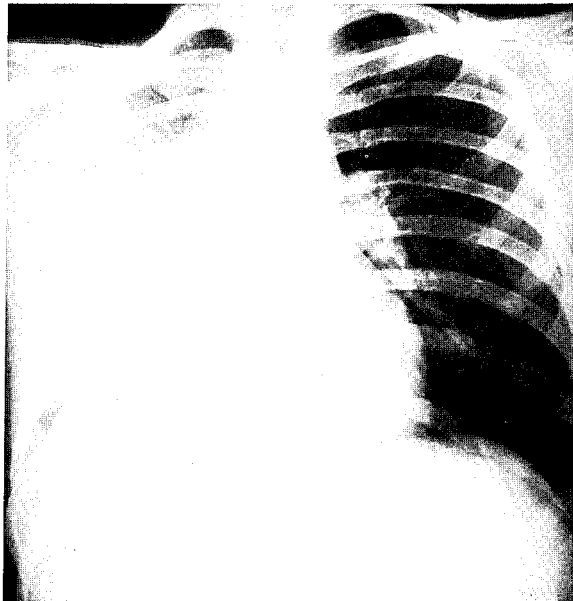
FIGURE 42.—Roentgenogram of chest of 24-year-old male with bronchogenic carcinoma before therapy with nitrogen mustard.
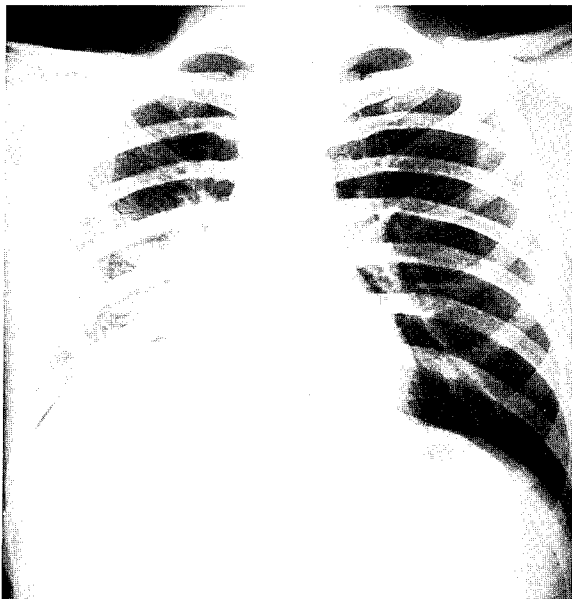
FIGURE 43.—Roentgenogram of chest of 24-year-old male (fig. 42), 52 days later, after three courses of nitrogen mustard at intervals of 4 weeks. Each course was followed by a remission of fever and constitutional symptoms. The first two courses consisted of 0.4 mg. of nitrogen mustard per kilogram of body weight; the third, of 0.6 mg. per kilogram. The duration of each remission was from 2 to 3 weeks.

size of palpable lymph nodes, by reabsorption of pleural effusions, and by dramatic disappearance of enlarged mediastinal tumors. Figures 44, 45, 46, and 47 show the roentgenographic appearance in a case of Hodgkin's granuloma and a case of lymphosarcoma before and after a course of treatment consisting of 0.1 mg. per kilogram of body weight daily by intravenous injection on 4 consecutive days. Remissions occurred more rapidly after therapy with mustard than following irradiation, but these remissions seemed to be of shorter duration, although this was not demonstrated in a large enough group to be of statistical significance. The response to repeated courses of treatment appeared to be the same as to the first course, although the duration might be longer, of similar length, or shorter.

Patients who have had repeated courses of irradiation, and who no longer obtain remissions from the largest dose of roentgen rays which the radiologist gives, might respond very well to the mustards and subsequently regain sensitivity to irradiation.

In contrasting mustard to roentgenologic therapy, it should be pointed out that nausea and vomiting seem to be more frequent and severe after the former and that leukopenia is less often seen after irradiation.

Mycosis fungoides responded in dramatic fashion to nitrogen mustard with relief of itching and involution of the skin lesions, leaving pigmented areas as the only clinically detectable residuum.

Although some remissions were observed in lymphosarcoma, mustard therapy has been disappointing in other types of lymphoma, both of the lymphoblastic and lymphocytic type. Acute leukemias and plasmoma (including myeloma) have not been benefited. Clinical results in both chronic myelogenic and lymphatic leukemia have not been satisfactory, although the peripheral blood and the picture of the bone marrow may show improvement.

Results similar to those just presented were reported by other investigators.[28]

Although some patients receiving nitrogen mustards were observed for a period of several years, the evaluation of the clinical status of this group of compounds will require many more years of careful study. As yet, there is no basis for assuming that the therapeutic efficacy of the nitrogen mustards is any greater than that of irradiation.

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[28] (1) Ap Thomas, M. I. R., and Cullumbine, H.: Nitrogen Mustards in Hodgkin's Disease; Report on 21 Cases and 4 of Other Reticuloses. Lancet 1: 899–901, 28 June 1947. (2) Goodman, L. S., Wintrobe, M. M., Dameshek, W., Good, M. J., Gilman, A., and McLennan, M. T.: Nitrogen Mustard Therapy. Use of Methyl Bis (β-chloroethyl) Amine Hydrochloride and Tris (β-chloroethyl) Amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders. J.A.M.A. 132: 126–132, 21 Sept. 1946. (3) Jacobson, L. O., Spurr, C. L., Barron, E. S. G., Smith, T., Lushbaugh, C., and Dick, G. F.: Nitrogen Mustard Therapy. Studies on the Effect of Methyl Bis (β-chloroethyl) Amine Hydrochloride on Neoplastic Disease and Allied Disorders of the Hemapoietic System. J.A.M.A. 132: 263–271, 5 Oct. 1946. (4) Osborne, E. D., Jordon, J. W., Hoak, F. C., and Pschierer, F. J.: Nitrogen Mustard Therapy in Cutaneous Blastomatous Disease. J.A.M.A. 135: 1123–1128, 27 Dec. 1947. (5) Philpott, O. S., Woodburne, A. R., and Waldriff, G. A.: Nitrogen Mustard in the Treatment of Mycosis Fungoides. J.A.M.A. 135: 631–633, 8 Nov. 1947. (6) Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Disease. J.A.M.A. 131: 656–658, 22 June 1946.
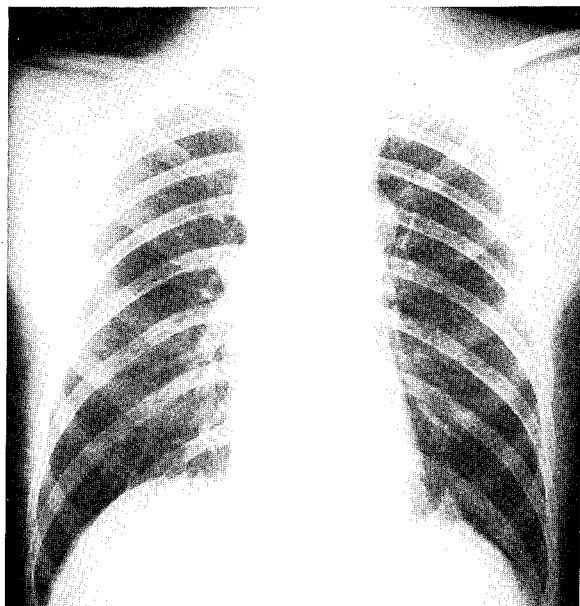
FIGURE 44.—Roentgenogram of chest of a 23-year-old male with Hodgkin's granuloma, before therapy with nitrogen mustard. Note the enlarged mediastinal and hilar nodes.
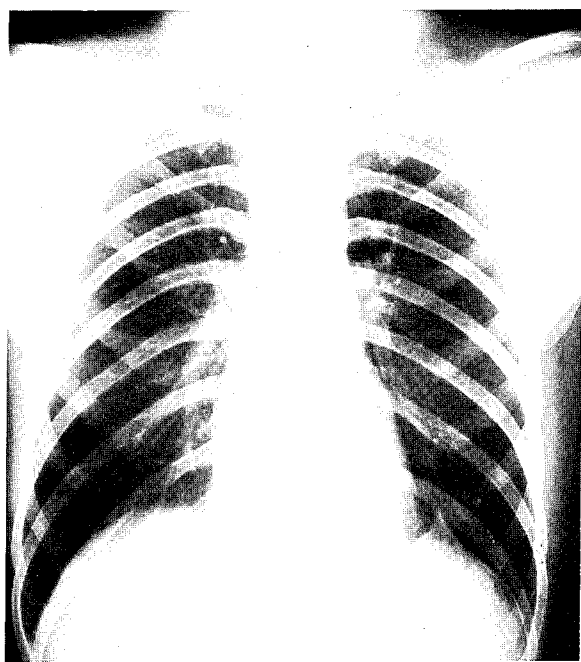
FIGURE 45.—Roentgenogram of chest of a 23-year-old male (fig. 44), 2 months after a single course of 0.4 mg. of nitrogen mustard per kilogram of body weight.
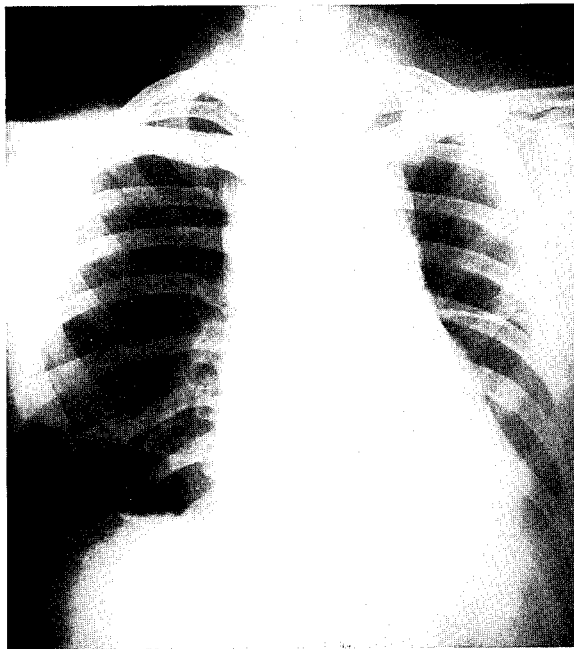
FIGURE 46.—Roentgenogram of chest of a 29-year-old male with lymphosarcoma, before therapy with nitrogen mustard.
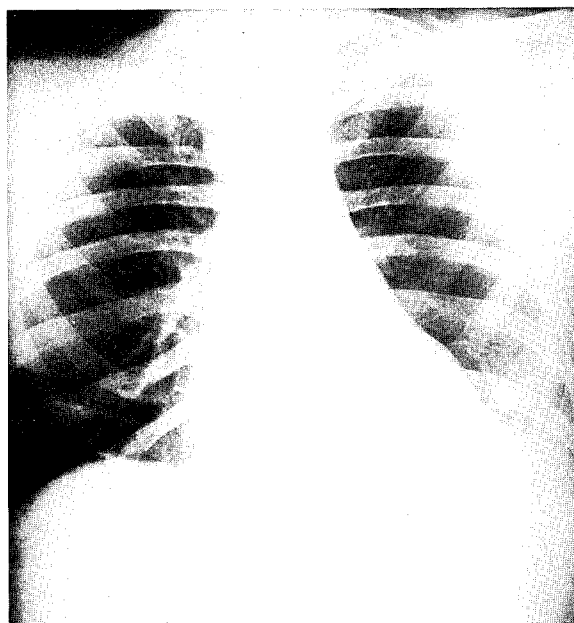
FIGURE 47.—Roentgenogram of chest of a 29-year-old male (fig. 46), 2 weeks after a single course of 0.4 mg. of nitrogen mustard per kilogram of body weight.

ATOMIC BOMB AND APLASTIC ANEMIA

The medical complications of exposure to the atomic bombing of Hiro-shima and Nagasaki were reported in part by the Joint Commission for the Investigation of the Effect of the Atomic Bombs in Japan and abstracted by LeRoy.[29]

There were approximately 120,000 casualties in Hiroshima and 65,000 in Nagasaki, about one-sixth of whom were either killed instantly or died under circumstances in which no medical care was possible. These people were burned to death by the direct heat of the bomb, were crushed under demolished buildings, or were burned in the fires started by the bombing. It has been estimated that about one-seventh of the total number of casualties escaped significant mechanical injuries or burns but received sufficient ir-radiation to produce significant effects on the blood and blood-forming organs as well as on the germinal epithelium and the intestinal epithelium. It appeared that the effect of this extremely brief exposure (probably no longer than 1 second) was similar to that observed following massive roentgen irradiation of animals or the administration of nitrogen mustard gas; that is, the destruction of tissues in which active cell division occurred, such as the bone marrow, the gastrointestinal epithelium, and the germinal epithelium. In addition to ionizing radiation, consisting principally of gamma rays harder than those produced by any known electrical apparatus, alpha particles, beta particles, and neutrons were also produced, but the relation of these to the casualties is not clear. The intensity of the gamma radiation emitted by the bombs decreased as the inverse square of the distance from the source of irradiation. It is accordingly presumed that the most severe casualties were probably those closest to the center of detona-tion, although other factors, such as shelters, played a role.

Persons who were subjected to intense exposure and who were not immediately killed or who did not die shortly thereafter of burns or other injury began to have nausea and vomiting within a few hours after ex-posure. Fever, diarrhea, and leukopenia began from the second to the seventh day. Purpura and thrombocytopenia generally did not appear until at least the fourth day. Death usually occurred in from 4 to 10 days. Exam-ination of the blood in some cases was stated to have shown a total absence of leukocytes and platelets. Red urine was also reported. At necropsy, wide-spread ulcerative, necrotic, and hemorrhagic lesions were found in the gastrointestinal tract, together with degeneration of all bone marrow ele-ments. A photomicrograph of the spleen of a 24-year-old man who died 5 days after exposure is shown in figure 48. This shows disappearance of lymphocytes from the Malpighian corpuscles, cytolysis of lymphocytes, and fibrinoid changes in the subendothelial portion of the central artery. Figure

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[29] LeRoy, G. V.: The Medical Sequelae of the Atomic Bomb Explosion. J.A.M.A. 134: 1143–1148, 2 Aug. 1947.

FIGURE 48.—Photomicrograph of spleen of 24-year-old man who died 5 days after exposure to the atomic bomb. The field shows disappearance of lymphocytes from Malpighian corpuscles, cytolysis of lymphocytes, and fibrinoid changes in subendothelial portion of central artery. X 400. (LeRoy, G. V.: J.A.M.A. 134: 1143–1148, 2 Aug. 1947.)

49 shows a section of the bone marrow of a 39-year-old man who died 7 days after the bombing. It will be noted that few normoblasts remain and that there is proliferation of reticuloendothelium and of many plasma cells and lymphocytes. These observations resemble those of Shouse, Warren, and Whipple [30] in dogs receiving large, single doses of roentgen rays.

Individuals who received a less severe dose of irradiation had early nausea and vomiting but then presented no symptoms for at least a week, with the possible exception of diarrhea which occasionally began as early as 4 days after exposure. Leukopenia, anemia, and epilation generally began sometime between the end of the first week and the end of the first month; fever, thrombocytopenia with purpura, and ulceration of the mucous membrane of the mouth occurred in the third or fourth week; and anemia became manifest in from 1 to 4 weeks after the detonation. Death occurred

[30] Shouse, S. S., Warren, S. L., and Whipple, G. H.: Aplasia of Marrow and Fatal Intoxication in Dogs Produced by Roentgen Radiation of All Bones. J. Exper. Med. 53: 421–445, 1931.
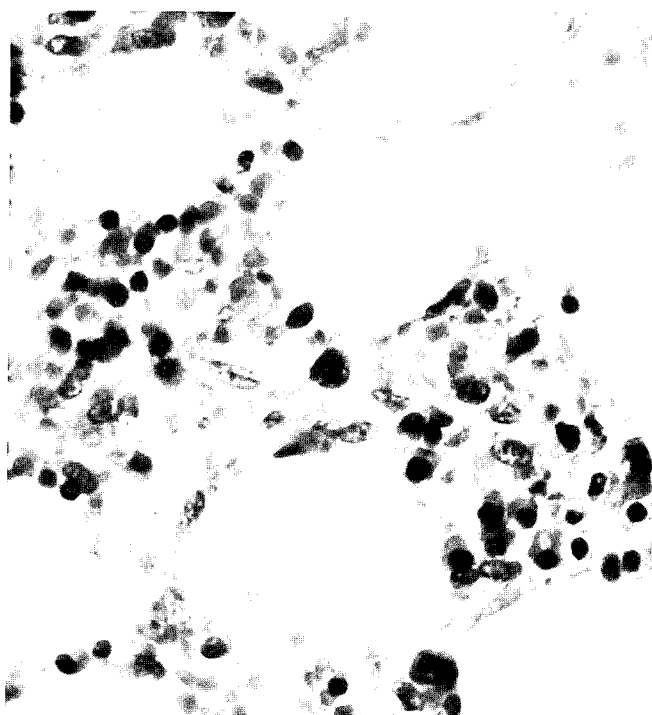
FIGURE 49.—Photomicrograph of bone marrow of 39-year-old man who died 7 days after bombing. The section shows a proliferation of reticuloendothelium and many plasma cells and lymphocytes. There are a few normoblasts remaining. X 654. (LeRoy, G. V.: J.A.M.A. 134: 1143–1148, 2 Aug. 1947.)

in approximately 50 percent of the cases between 10 days and 6 weeks after the bombing. Laryngitis, pharyngitis, tonsillitis, gingivitis, and tracheal and female genital ulcerations developed in many of these patients and presented essentially the same appearance as that seen in malignant neutropenia from any cause. Petechiae and purpura appeared in the skin of almost all the patients, together with epistaxis, melena, metrorrhagia and hematuria in many. The loss of hair was particularly marked in the scalp. Regrowth of hair did not begin for several months in those patients who recovered. Leukocytes numbering as few as 100 cells per cubic millimeter were reported. Recovery was rare in those whose leukocytes numbered less than 600 per cubic millimeter, essentially all of which were lymphocytes. Anemia was present in all such patients and became progressively more pronounced but did not occur until several weeks after the maximum leukopenia was observed. Presumably, the anemia was due, partly, to bleeding. In association with the leukopenia, serious infection and septicemia were common. Apparently, the chief causes of death were pneumonia and infection. The
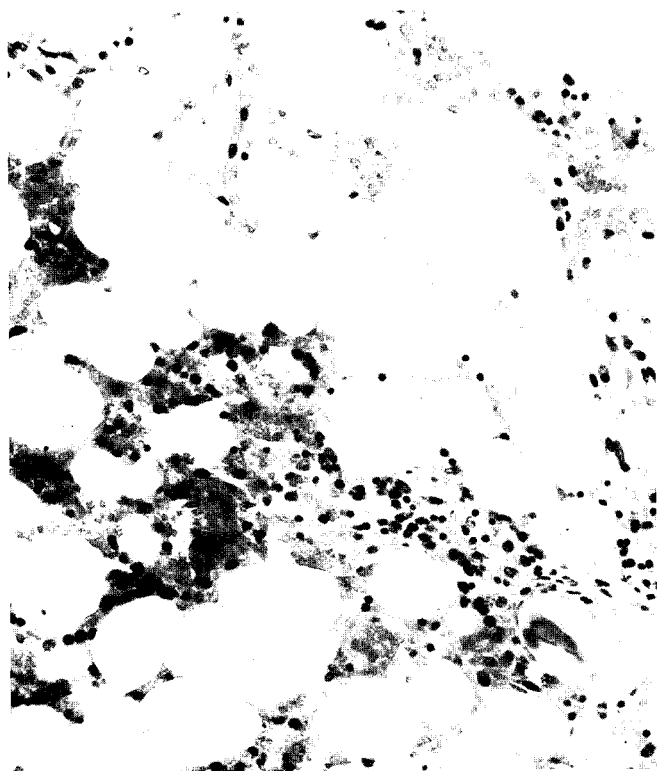
FIGURE 50.—Photomicrograph of bone marrow of 29-year-old man who died 29 days after the bombing. The section shows hypoplasia, a necrotic area, and bacteria. The majority of the cells are reticulum cells, plasma cells, and lymphocytes. X 230. (LeRoy, G. V.: J.A.M.A. 134: 1143–1148, 2 Aug. 1947.)

bone marrow (fig. 50) of a 29-year-old man who died 29 days after the bombing shows marked hypoplasia, a necrotic area, and bacteria. The cells were mostly reticulum cells, plasma cells, and lymphocytes. The spleen (fig. 51) of a 35-year-old woman who died 19 days after the bombing shows atrophy of the lymphoid tissues with karyolysis of some of the cells in the vicinity of the central arteriole. Hyalinlike material is deposited beneath the arteriolar endothelium.

Individuals with still less exposure may or may not have vomited on the day of bombing. They then were asymptomatic from 1 to 3 weeks. Diarrhea generally began from 2 to 5 weeks after the explosion as did epilation. Leukopenia was noted from the second to the fourth week, ulceration of the mucous membrane in the third and fourth weeks, and anemia from the third to fifth week. Death occurred in the second or third month. It is uncertain what proportion of these individuals succumbed, but those who died appeared to have an aplastic type of anemia. The hemorrhagic tendency in
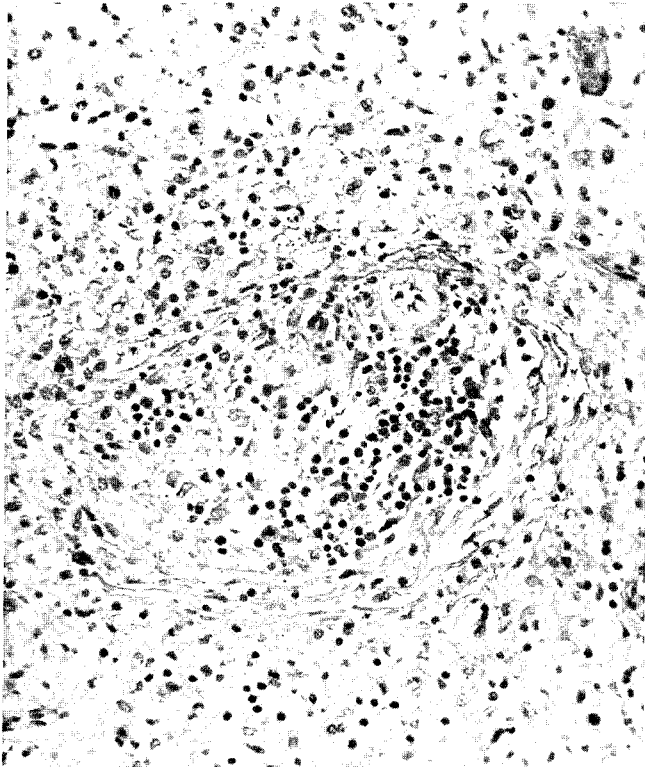
FIGURE 51.—Photomicrograph of spleen of 35-year-old woman who died 19 days after the bombing. The section shows atrophy of the lymphoid tissue, with karyolysis of some of the cells in the vicinity of the central arteriole. The arterioles show a deposition of hyalinlike material beneath the endothelium. X 135. (LeRoy, G. V.: J.A.M.A. 134: 1143–1148, 2 Aug. 1947.)

these patients was never severe, leukocytes numbering less than 1,500 cells per cubic millimeter were rare, and ulceration of the mucous membrane tended to be transitory and not severe. Figure 52 is of the bone marrow of a 31-year-old man who died of bronchiectasis 14 weeks after the bombing. The section shows gelatinous marrow from the rib with a large focus of regenerating cells replacing the fat.

LeRoy (p. 412) has summarized the important pathological changes as follows: The bone marrow was badly damaged with an almost complete disappearance of all cells of the myelopoietic and erythropoietic series. In all but the most severely irradiated patients, regeneration commenced within a week to 10 days after injury. The type of regeneration of tissue varied considerably, and often the marrow appeared to be producing mainly macrophages, plasma cells, and lymphocytes 3 to 4 weeks after the injury with very few cells of the granulocyte or erythrocyte series, although in
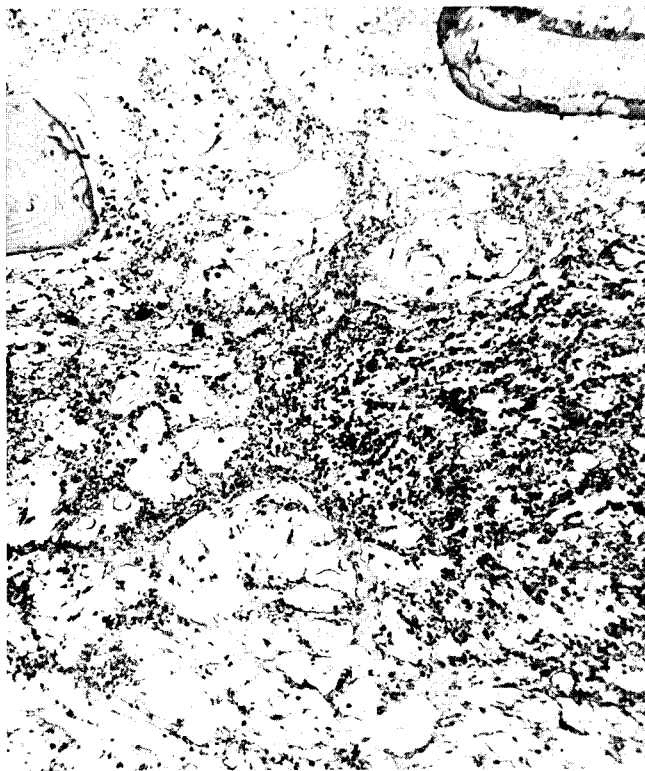
FIGURE 52.—Photomicrograph of bone marrow of 31-year-old man who died of bron-chiectasis 14 weeks after the bombing. The section shows gelatinous marrow, from the rib, in which there is a large focus of regenerating cells replacing the fat. X 115. (LeRoy, G. V.: J.A.M.A. 134: 1143–1148, 2 Aug. 1947.)

other cases well-marked hyperplasia of these elements occurred. Tissue from patients dying early showed an almost complete absence of lymphocytes in the lymph nodes, the spleen, and the thymus. Recovery of the lymphatic elements was evident after a few weeks although, in many patients who died several months after irradiation, the lymphatic tissues contained only a fraction of the usual number of adult-type lymphocytes.

It seems probable that, had adequate measures been available at Hiro-shima and Nagasaki to combat serious infection by the use of antibiotics and to combat anemia with blood transfusions, the early death rate might have been considerably lessened. The evidence suggests that some of the very early deaths occurred from an overwhelming dose of gamma irradia-tion without conspicuous morphologic change at necropsy.

The sequence of events in those who survived this immediate effect appears to be: First, a destruction of the marrow and lymphoid elements; then, following the destruction of marrow, the development of leukopenia

and severe infection and the onset of thrombocytopenia and hemorrhagic phenomena; and finally, the development of anemia, with the destruction of the circulating erythrocytes by normal processes. Thus, some of the early deaths resulted from leukopenia and sepsis before conspicuous bleeding occurred. Others died with hemorrhagic manifestations (subarachnoid hemorrhage was commonly reported in one group) after the onset of thrombocytopenia but before the development of anemia. Finally, late deaths were generally due to anemia associated with aplasia of the bone marrow.

A preliminary report was issued by Tullis and Warren[31] on the observations of animals exposed to the atomic detonation at Bikini. The earliest lesions to appear were hemorrhages—involving almost any tissue of the body and apparently associated with radiation injury—dilatation and congestion of the small blood vessels of the brain, heart, lungs, mesentery, bowel, and subcutaneous tissue. Hemorrhages into the kidney, often filling the kidney pelves, were occasionally seen. The lymph nodes became extremely hemorrhagic; the lungs in 80 percent of the fatal cases were mottled, dark red, and pink. The cut surface was wet and the bronchi were filled with abundant pink or white froth. The gastrointestinal tract showed ulcerative lesions of the large intestine. The bone marrow sometimes was pale and sometimes hyperemic. The lymphocytes in the peripheral blood were the first to fall, within a matter of a few hours. After a few days, the granulocytes decreased and at the end of from 1 to 2 weeks the erythrocytes declined. Microscopic examinations were not yet available when this paper was written.

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[31] Tullis, J. L., and Warren, S.: Gross Autopsy Observations in the Animals Exposed at Bikini. J.A.M.A. 134: 1155–1158, 2 Aug. 1947.

CHAPTER XVI

Heart Disease

Edward F. Bland, M.D.

During World War II, the fevers and fluxes of previous wars were largely replaced by the hazards of high altitudes and by the devastation of blasts and bombs—circumstances where physical fitness assumed special significance. It was, therefore, inevitable that the stability of the circulation, its diseases and its disorders, should have attracted particular attention and detailed study. The Army Medical Corps, superbly equipped and augmented manifold by experienced physicians and able investigators from civilian life, was presented with an unparalleled opportunity to study disease and to acquire new knowledge in far and unfamiliar areas of the world. It is with the activities and contributions of these men in the field of cardiovascular disease that this report is concerned.[1] It is a record of achievement and progress which testifies to their devotion to duty and to the diligence with which they pursued their studies, at times under difficult and dangerous circumstances.

SELECTION FOR SERVICE

Following the passage of the Selective Training and Service Act of 1940, there immediately arose the problem of standards for the new recruits. With the world again at war and with the contemplated requirements of the service, defects and disorders of the cardiovascular system assumed an important role in the selection of men for the fighting forces. The existing standards for acceptability as outlined in the early mobilization regulations before 1940, seemed, in the opinion of the Medical Corps of the Army, to warrant revision, and those pertaining to the heart and circulation were referred to a special committee [2] on cardiovascular diseases appointed in 1940 as a subcommittee of the National Research Council.

The range of normal, as always, posed a problem, especially in terms of acceptable blood pressure and pulse rates. It was at first suggested by

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[1] This chapter on the heart has been prepared at the invitation of The Surgeon General, 10 years after the war. The lapse of a decade has been in some respects an advantage in providing a perspective of the contributions of the war years in terms of their later significance.—E. F. B.

[2] This committee consisted of Dr. Paul D. White (Boston, Mass.), chairman, and Drs. Edgar V. Allen (Rochester, Minn.), E. Cowles Andrus (Baltimore, Md.), Ashton Graybiel (Boston), Robert L. Levy (New York, N.Y.), and William D. Stroud (Philadelphia, Pa.). Later, in 1943, the services of some of the committee members were required in the Armed Forces, and other members were added. (Personal communication from Dr. Paul D. White.)

this committee that the blood pressure should be determined in all cases, but it was soon recognized that great difficulties would arise in the case of healthy young candidates who under the excitement of the occasion might have temporary elevations above the normal standards. Therefore, the Army wisely decided not to follow this earlier suggestion, and a more practical compromise in dealing with this troublesome problem was provided by the recommendation that the blood pressure will be determined only in those cases in which it appears indicated. Likewise, considerable leeway was recommended in dealing with pulse rates, but special scrutiny was advised of those above 100 per minute after a reasonable rest and of those under 50 per minute.[3] These important variants of uncertain significance were subjected later to careful study during the war.

The earlier observations of Lewis [4] and his collaborators, in World War I, on the soldier's heart and the effort syndrome had emphasized the importance of determining the response of each recruit to effort rather than of relying on instrumental methods of examination. In this connection, it was also early recognized that routine electrocardiograms would be of little or no value from the military standpoint in demonstrating cardiac abnormalities not evident on physical examination,[5] although some useful data in terms of the range of normal were later recorded in electrocardiograms on large numbers of airmen in the United States [6] and in Canada.[7]

Thus, during the summer of 1940, the simplified and revised recommendations [8] were completed and incorporated in MR (Mobilization Regulations) 1–9, War Department, "Standards of Physical Examination During Mobilization," 1 August 1940, and the buildup of the new army acquired momentum.

It soon became evident from the early tabulation available in 1942 that diseases and disorders of the cardiovascular system by these standards had rendered unacceptable for general military service an alarming proportion of the eligible population. A summary of a statistical survey carried out by Selective Service and appearing as Medical Statistics Bulletin No. 1 indicated that, of the first 2 million men examined up to 31 May 1941, examining boards disqualified for general military service approximately

[3] White, P. D.: The Soldier and His Heart. War Med. 1: 158–167, March 1941.

[4] (1) Lewis, Thomas: Report Upon Soldiers Returned as Cases of Disordered Action of the Heart (D.A.H.) or Valvular Disease of the Heart (V.D.H.). Medical Research Committee, National Research Council, Special Report No. 8. London: His Majesty's Stationery Office, 1917. (2) Lewis, Thomas: The Soldier's Heart and the Effort Syndrome, 2d edition. London: Shaw and Sons, Ltd., 1940.

[5] Wood, F. C., Wolferth, C. C., and Miller. T. G.: Electrocardiography in Military Medicine, With Special Reference to Its Lack of Value in the Study of Recruits. War Med. 1: 696–709, September 1941.

[6] Graybiel, A., McFarland, R. A., Gates, D. C., and Webster, F. A.: Analysis of the Electrocardiograms Obtained From 1,000 Young Healthy Aviators. Am. Heart J. 27: 524–549, April 1944.

[7] (1) Hall, G. E., Stewart, C. B., and Manning, G. W.: The Electrocardiographic Records of 2,000 RCAF Aircrew. Canad. M.A.J. 46: 226–230, March 1942. (2) Stewart, C. B., and Manning, G. W.: A Detailed Analysis of the Electrocardiograms of 500 RCAF Aircrew. Am. Heart J. 27: 502–523, April 1944.

[8] The procedure for determining the blood pressure only in those cases in which it appears indicated was rescinded in MR 1–9, 15 March 1942, by requiring that blood pressure be routinely measured. This became standard requirement beginning with the March 1942 revision of MR 1–9.

1 million (50 percent). Of these rejectees, 10 percent (96,000) had cardio-
vascular defects, a figure exceeded only by deficiencies of the teeth (188,000)
and the eyes (123,000) and by illiteracy (100,000).[9] A subsequent and
somewhat more detailed report from the same source [10] on the causes for
disqualification for general service in 18- and 19-year-old registrants indi-
cated that 23.8 percent of the white youths were so disqualified, whereas,
of Negroes, twice as many (45.5 percent) were disqualified. Cardiovascular
defects were in fourth place for the white group and in third place for the
Negro group. Valvular disease and hypertension in particular were more
prevalent among the Negroes. Experience with the older registrants showed
a similar distribution.[11]

These rejection rates during the early phases of the war were disturb-
ing and seemed excessive for the age period covered. Therefore, a confer-
ence was called in Washington, D.C., on 27 June 1942, for a discussion of
the problem. In attendance were members of the Subcommittee on Cardio-
vascular Disease of the National Research Council (p. 419), as well as
representatives of the Army, Navy, Public Health Service, Selective Serv-
ice, Veterans' Administration, the National Research Council, and the Com-
mittee on Medical Research. As a result of this conference, a letter was sent
to Maj. Gen. Lewis B. Hershey, Director, Selective Service System, pro-
posing that in each of five cities special boards of experienced cardiologists
reexamine 1,000 registrants rejected for cardiovascular reasons. The project
was approved and thus was launched one of the most important and practical
cardiovascular studies of the war years—a study which in turn led to fur-
ther investigations of considerable significance. Boston, Mass., Chicago, Ill.,
New York, N.Y., Philadelphia, Pa., and San Francisco, Calif., were desig-
nated as the five centers; the objectives of the program were (1) to deter-
mine the problems in diagnosis that particularly concern the range of the
normal cardiovascular system with respect to service, (2) to determine the
possible salvage of men for the Army by reclassification as 1A, and (3) to
compare the opinions of cardiovascular experts with those of the examiners
of local boards and induction stations to determine the desirability of such
reexaminations in this or other special medical fields throughout the coun-

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[9] Rowntree, L. G.: Rehabilitation and Prehabilitation. J.A.M.A. 119: 1171–1175, 8 Aug. 1942.

[10] Rowntree, L. G., McGill, K. H., and Edwards, T. I.: Causes of Rejection and the Incidence of
Defects Among 18 and 19 Year Old Selective Service Registrants. J.A.M.A. 123: 181–185, 25 Sept. 1943.

[11] In view of this high overall rejection rate, it is of interest to recall comparable data from World
War I. An official report of the Cardiovascular Section of the Office of the Surgeon General, U.S. Army
(Connor, L. A.: Report of Cardiovascular Section. *In* Medical Department of the United States Army
in the World War. Washington: U.S. Government Printing Office, 1923, p. 377) indicated that in one
million recruits 1.15 percent were rejected for cardiovascular reasons, whereas 0.88 percent with cardiac
disorders were accepted for limited service only. The causes of disqualification of the 11,562 rejected
were: Valvular disease, 49 percent; other organic diseases, 19 percent; and functional disorders, 23 percent.
The belief was expressed that the number rejected for organic heart disease was too high, because of
the tendency of the examiners to classify functional conditions, such as irritability of the heart, as
instances of organic disease. In the German and British official reports covering World War I, there were
no features worthy of special note in this connection (cited by Levy, R. L.: The Stimulus of War to Cardi-
ology. Bull. New York Acad. Med. 22: 237, May 1946).

try. The results of this study, published in 1943, by Levy, Stroud, and White [12] are noteworthy. These are summarized as follows:

Of the total number of 4,994 rejectees examined, there were 863 (17.3 percent) resubmitted as 1A and 4,131 (82.7 percent) whose rejection as 4F was confirmed. It was suggested that the low salvage rate might have been due to the already free use of cardiovascular experts in these communities in connection with doubtful cases, but in any event the wisdom of extending these reexaminations for the sake of the salvage alone seemed questionable.

The chief cause for rejection was rheumatic heart disease, found in 2,476 (50 percent) of the total 4,994 men.

The second most common cause for final rejection was hypertension, found in 1,059 cases (21 percent).

Third in frequency was neurocirculatory asthenia (204 cases, 4 percent) and fourth was sinus tachycardia (189 cases, 3.8 percent). Congenital heart disease was found in 183 cases.

In conclusion, Levy and his associates pointed out that there remained eight problems of special interest as yet unsettled but concerning which tentative opinions were expressed, as follows:

1. The interpretation of apical systolic murmurs—may they, if very slight or even slight, in the absence of any other abnormal or doubtful finding be considered inadequate reason for rejection?

2. The upper limits of the normal blood pressure—may the systolic pressure in very nervous young men be set perhaps as high as 160 mm. of mercury or even a shade more, provided the diastolic pressure does not exceed 90 mm.?

3. The limits of the normal pulse rate at rest—may there not be a wider range, perhaps 40 to 120 per minute, than that given in the current criteria?

4. The heart size—especially in relation to body build.

5. The electrocardiogram of which the wide range of normal has not been explored adequately.

6. Neurocirculatory asthenia—difficult to diagnose in mild degree, but probably rejectable even when slight, unless there is an obvious correctable cause.

7. Recent rheumatic fever—a hazard even when the heart seems normal.

8. Exercise tests—the usefulness of which in cardiovascular examination for military service is open to question.

The ensuing 4 years provided ample opportunities to observe the effectiveness of the screening program, and reports from medical officers in the Zone of Interior and from those overseas are available in this connec-

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[12] Levy, R. L., Stroud, W. D., and White, P. D.: Report of Reexamination of 4,994 Men Disqualified for General Military Service Because of the Diagnosis of Cardiovascular Defects. J.A.M.A. 123: 937–944, 11 Dec. 1943; 1029–1035, 18 Dec. 1943; Am. Heart J. 27: 435, 1944.

tion. An early survey of the fate of selectees previously passed by their local draft boards revealed, upon later examination at the induction station at Camp Shelby, Miss., an additional rejection rate of 25 percent of which cardiac defects accounted for 1.9 percent—an indication, it was thought, of the initial confusion and variance in interpretation of the regulations prescribed by the War Department.[13] The remarkable success of the overall program is borne out, however, by subsequent experience. Reports from the station and general hospitals at Fort Devens, Mass., covering a 1- and 2-year period, respectively,[14] indicated an expected high incidence of functional complaints relating to the heart and the circulation and a low incidence of organic disease, with a ratio of approximately 10:1.

A reexamination for aircrew training of 344,134 men previously passed by other Army medical facilities and already in the service sheds some further light on the incidence and nature of the more frequently missed cardiovascular defects (fig. 53).[15] As a result of this second screening, an additional 2,033 (5.9 per 1,000) were disqualified for cardiovascular defects. The majority, however, were for defects of conduction and for disturbances in blood pressure and circulation of psychogenic origin— variants quite understandably overlooked or considered less significant for general service.

In the South Pacific Area, Sprague and McGinn [16] undertook a similar study with reference to the cardiovascular system. During the 12 months from 1 July 1942 to 1 July 1943, there were 22,085 patients (Army, Navy, and Marine) admitted to two hospital facilities. In that year, 143 patients (0.65 percent) were found to be suffering from valvular disease, degenerative heart disease, or important functional disorders of the heart. During the same period, 36 patients with rheumatic fever (0.16 percent) were evacuated. Typical effort syndrome (neurocirculatory asthenia), although important, appeared to be less common than in World War I, owing in part to this syndrome being absorbed in neuropsychiatric diagnoses without as much emphasis as in the past on the circulatory system. Sprague and McGinn believed that the elimination of men with heart ailments was being satisfactorily accomplished in enlistment, recruiting, induction, and training areas in the United States.

In concluding this review of the standards employed in the selection of men for service in World War II and of the results in terms of later reports from the United States and overseas, it is with great admiration

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[13] (1) Saslaw, M. S.: Medical Aspects of the Selective Service System. War Med. 1: 486–492, July 1941. (2) Saslaw, M. S., and Jundermann, C. S.: Medical Aspects of the Selective Service System; Follow-Up Study. War Med. 2: 99–101, January 1942.

[14] (1) Brown, M. G.: Cardiac Problems in a Station Hospital. Am. Heart J. 27: 565–567, April 1944. (2) Porter, R. R.: Cardiovascular Experiences in an Army General Hospital. Am. Heart J. 27: 559–564, April 1944.

[15] Leach, J. E.: Diseases and Defects in Aircrew Trainees. I. Cardiovascular System. War Med. 8: 1, 1945.

[16] Sprague, H. B., and McGinn, S.: Heart Diseases and Disorders as Causes for Evacuation From the South Pacific Combat Area. Am. Heart J. 27: 568–574, April 1944.

that one contemplates the long hours, the inherent difficulties, and the extraordinary efforts of our medical colleagues, on the induction boards, who so conscientiously sought and succeeded in providing the Armed Forces with men remarkably free of defects of the heart and circulation.

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TOTAL EXAMINED   344,134
TOTAL DISQUALIFIED  2,033
TOTAL DEFECTS        2,275
DISQUALIFIED PER 1,000 EXAMINEES 5.9
DEFECTS PER 1,000 EXAMINEES    6.6
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3.92 BLOOD PRESSURE AND CIRCULATION

.89 DEFECTS OF RATE RHYTHM AND CONDUCTION

.83 VALVULAR HEART DISEASE

.46 RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

.34 ARTERIES AND VEINS

.11 CONGENITAL HEART DISEASE

.05 DISEASES OF MYOCARDIUM

.01 DISEASES OF AORTA AND PULMONARY VESSELS

.01 DISEASES OF PERICARDIUM

FIGURE 53.—Distribution of defects of the cardiovascular system in aircrew trainees. (Leach, J. E.: War Med. 8: 1, 1945.)

INFECTIONS AND DEFICIENCIES

Rheumatic fever and infections likely to injure the heart [17] received careful study during World War II. In most instances, the observations served to extend existing knowledge, but occasionally an unusual opportunity was presented to acquire new and detailed information, notably in tsutsugamushi fever (scrub typhus), where earlier studies had been scant and sketchy. The availability and full use of electrocardiograms and roentgenograms in the field and the expert processing and study of the specimens

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[17] In this section, a discussion of these infections is restricted to those aspects of the various diseases as they relate to the cardiovascular system.

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in laboratories overseas with subsequent assembly and analysis in the United States provided reliable and revealing data of lasting importance.

Furthermore, the harassing experiences and consequent debilitation of U.S. personnel in the prison camps of the Far East and of the inmates of the concentration camps in Germany presented medical officers with a keener insight into the untoward effects of deficiency states upon the circulation.

Rheumatic Fever and Rheumatic Heart Disease

In the early months of the war, the assemblage of large groups of men from civilian life in the crowded buildings and barracks of the training centers provided a favorable medium for the spread of respiratory infections, which at times reached epidemic proportions. This led, inevitably, to the appearance of rheumatic fever cases in considerable number. Thus, early in the war, a situation was created which, fortunately, proved far less troublesome later in the field, where more rugged but less crowded conditions prevailed. This early experience served as the basis for a number of important bacteriological and epidemiological studies concerning the role of the streptococcus and for the testing of preventive programs of early detection, intelligent isolation, and mass protection with chemotherapy (sulfonamides) and later with antibiotics (penicillin). It even provided the basis for a new and less conservative approach to the management of rheumatic fever than had hitherto been recommended, of merit perhaps under such special circumstances, although generally not acceptable in the younger age groups where the heart is more susceptible.

An extensive study [18] of the protective effects of daily sulfadiazine (1.0 gm.) in 250,000 trainees at a large base, between December 1943 and April 1944, indicated that sulfadiazine could (1) check a well-advanced streptococcal epidemic, (2) repel a streptococcal outbreak at its onset, and (3) protect 85 percent of susceptible recruits from implantation with bacterial respiratory pathogens. Untoward effects were minimal, with evanescent rashes in 0.5 percent and dangerous constitutional disturbances in only 0.01 percent. All these factors are of special significance in the prevention and control of rheumatic fever.

Likewise, the Army Air Forces inaugurated a broad program [19] in the spring of 1943 at 40 of the larger hospitals, representing 25,000 beds and 800,000 troops. The posts chosen were in areas where the incidence of rheumatic fever was high and intermediate, as well as low. At some airbases, the rates of incidence for 1943 were in excess of 25 per 1,000 troops, and, during the peak of the rheumatic fever season, one

[18] Coburn, A. F.: The Prevention of Respiratory Tract Bacterial Infections by Sulfadiazine Prophylaxis in the United States Navy. J.A.M.A. 126: 88–92, 9 Sept. 1944.

[19] Holbrook, W. P.: The Army Air Forces Rheumatic Fever Control Program. J.A.M.A. 126: 84–85, 9 Sept. 1944.

large post experienced rates in excess of 100 per 1,000 troops. It was concluded from this extensive study that acute rheumatic fever occurring in high incidence was invariably preceded by a high incidence of hemolytic streptococcal infection. A 50- to 75-percent reduction was accomplished by the use of sulfadiazine prophylaxis (1.0 gm. daily) under careful conditions on a significantly large troop population. No serious drug reactions occurred, and from these data it appeared that the reduction in rheumatic fever paralleled that in streptococcal respiratory diseases.

The thesis that early physical activity might be of value in the treatment of rheumatic fever was explored by the Army Air Forces at the Regional Station Hospital, Orlando, Fla.[20] The patient's comfort was employed as the principal determining factor in prescribing strict bed rest or in permitting early ambulation. In this program, apparently, the incidence of anxiety neurosis was considerably lessened, and at the same time satisfactory clinical results were obtained in 200 patients.[21]

A survey of the overall problem of preexisting valvular disease and the prevalence of acute rheumatic fever in the U.S. Army overseas was made in the Mediterranean (formerly North African) theater from November 1942 to the end of hostilities in May 1945.[22] These data were obtained largely from the 17 general hospitals in that theater and from those station hospitals functioning in a like capacity. Approximately 1,400 patients were hospitalized, of whom more than one-half had rheumatic fever and the remainder inactive, preexisting rheumatic valvular disease. In addition, a review of the records of 1,507 consecutive post mortem examinations at the 15th Medical General Laboratory and from the 2d and 4th Medical Laboratories disclosed only 13 instances of healed valvulitis (all unrelated to the cause of death) and 2 instances of active carditis—an overall incidence of 9.9 per 1,000. This extraordinary low post mortem incidence, in terms of civilian experience, was thought to be due to careful preinduction screening and to the prompt evacuation to the Zone of Interior of patients with valvular defects or rheumatic activity.

From this study, it was noted also that rheumatic fever and rheumatic heart disease accounted for 3.9 percent of the patients returned to the Zone of Interior from the medical services of the general hospitals and that, if those patients with preexisting (and detectable) heart disease and those who had had recognizable rheumatic fever within 1 year of entry into the

[20] Robertson, H. F., Schmidt, R. E., and Feiring, W.: The Therapeutic Value of Early Physical Activity in Rheumatic Fever: Preliminary Report. Am. J.M. Sc. 211: 67–73, January 1946.

[21] This interesting report is open to the general objection that such a program is contrary to the well-established precepts of the beneficial effects of rest in combating inflammation and more specifically that it lacks clinical and laboratory details, adequate control studies, and followup data. Furthermore, the material concerns acute rheumatic fever in previously healthy young adults, where the duration of the disease is apt to be shorter and injury to the heart less common than in younger age groups. Nevertheless, it was evident that such a program had merit under the special circumstances.—E. F. B.

[22] Bland, E. F.: Rheumatic Fever and Rheumatic Heart Disease in the North African and Mediterranean Theater of Operations, United States Army. Am. Heart J. 32: 545–559, November 1946.

service had been excluded, the problem presented to the Army overseas would have been reduced by 37 percent. Nevertheless, a scrutiny of the details in individual cases also indicated that the measures then in force to exclude from oversea service individuals with chronic valvular disease and those especially susceptible to rheumatic fever had been, with occasional evident exceptions, highly effective. Contrary to the earlier experiences in the training centers, no frank epidemics were encountered, and no mass protection with chemotherapy was undertaken.

Somewhat at variance with the foregoing studies are two reports from the postwar era which are provocative in their implication in terms of future planning. They concern the fate of known rheumatic fever subjects, in military service during the war, from two well-known series with long-term followups.[23] In both instances, the recurrence rate was actually less in the service groups than in their civilian counterparts; furthermore, those with rheumatic heart disease (usually of minor degree) tolerated strenuous activity in basic training and under combat conditions without difficulty or detriment, and some even received decorations for outstanding service. This documented experience may well require further consideration should the Nation again be faced with a serious manpower shortage in some future crisis.

Scrub Typhus (Tsutsugamushi Fever)

Involvement of the heart and failure of the circulation in the course of severe scrub typhus had been recognized but only briefly described before World War II.[24] This acute and serious disease was widely encountered by the Army in the Southwest Pacific Area and in Burma, where over 5,000 cases were reported. Three major epidemics occurred in northern Burma and in Netherlands New Guinea in 1944, and, as a direct result of the Army experience, ecologic concepts of this rickettsial disease were changed (it was found that there were no typical scrub typhus areas), a wider geographic distribution of the disease became evident, the etiology was confirmed, vector species were proved, strains were isolated, a new complement fixation test was evolved, and the clinical pattern and pathological features became established.[25] Among the extensive studies completed during the war were a number of important reports of cardiovascular significance.

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[23] (1) Wilson, M. G., Payson, J. W., and Lubschez, R.: Experience of Rheumatic Patients Who Served in the Armed Forces, 1942–1946. Am. J. Pub. Health 38: 398–405, March 1948. (2) Bland, E. F., and Jones, J. D.: Rheumatic Fever and Rheumatic Heart Disease: A 20 Year Report on 1,000 Patients Followed Since Childhood. Circulation 4: 836–843, December 1951.

[24] (1) Lewthwaite, R.: Pathology of the Tropical Typhus (Rural Type) of the Federated Malay States. J. Path. & Bact. 42: 23–30, January 1936. (2) Kouwenaar, W.: Investigations on Rickettsial Diseases in Sumatra; Pathological Anatomy of Human Mite Fever. Geneesk. tijdschr. v. Nederl.-Indie 80: 1119–1140, 30 Apr. 1940.

[25] Developments in Military Medicine. Bull. U.S. Army M. Dept. 7: 594, July 1947.

Two early studies at the 1st Evacuation Hospital, New Guinea, based on 200 cases indicated a mortality of nearly 10 percent.[26] As regards the cardiovascular system, it was found that a sustained pulse rate above 120 per minute was of grave significance and was frequently a precursor of myocardial failure. In the severely ill patients (20 percent of the series), abnormalities referable to the circulatory system were noted, as follows: Extrasystoles were numerous; a soft, blowing, apical systolic murmur was not uncommon; a pronounced accentuation of the pulmonary second sound was frequent; and cyanosis of the lips, mucous membranes, and nail beds was often present without dyspnea or clinical evidence of pulmonary congestion. In those with a fulminating form of the disease, one or more of the following were noted: Cyanosis, severe dyspnea, profound tachycardia, atrial fibrillation, gallop rhythm, pulsus alternans, cardiac dilatation with signs of congestive failure, harsh pulmonary systolic murmur, thrombophlebitis, and pulmonary emboli. Subsequent reports by others attested to the severity of the acute illness.[27]

Although Kouwenaar[28] had earlier demonstrated that myocarditis may complicate scrub typhus and be a frequent cause of death, the pathological features of the disease were more definitely described than ever before by the reports from the 3d Medical Laboratory overseas.[29] The study was based on an analysis of 55 fatal cases in American troops in New Guinea and adjacent islands. In these cases, the heart on inspection exhibited relatively mild changes and was usually of normal weight, but the myocardium at times appeared flabby and in a few instances contained minute, pale, brownish-gray areas of degeneration and, more rarely, small focal hemorrhages. No valvular involvement was demonstrated. Microscopically, however, the heart was involved more seriously than any other organ of the body, since the dominant lesion in all cases was an acute, nonsuppurative myocarditis, focal as well as diffuse, varying in severity, patchy in distribution, and usually most severe in the interventricular septum and the left ventricle. The most marked and constant finding was a perivascular infiltration of mononuclear cells, chiefly plasma cells with lesser numbers of large mononuclear cells, occasional lymphocytes, and sometimes large multinucleated cells with vesicular nuclei and basophilic cytoplasm (fig. 54). The more diffuse type of myocarditis was characterized by columns of mononuclear cells, chiefly plasma cells, lying in the connective tissue interstices between individual muscle fibers and in close relationship to capillaries (fig.

[26] Lipman, B. L., Byron, R. A., and Casey, A. V.: Clinical Survey of Scrub Typhus Fever. Bull. U.S. Army M. Dept. 72: 63–70, January 1944.

[27] (1) Logue, J. B.: Scrub Typhus: Report of Epidemic in the Southwest Pacific. U.S. Nav. M. Bull. 43: 645–649, October 1944. (2) Berry, M. G., Johnson, A. S., Jr., and Warshauer, S. E.: Tsutsugamushi Fever: Clinical Observations in One Hundred and Ninety-Five Cases. War Med. 7: 71–75, February 1945. (3) Likoff, W.: Changes in the Cardiovascular System in Scrub Typhus in Early Convalescence. Am. J.M. Sc. 211: 694–700, June 1946.

[28] See footnote 24(2), p. 427.

[29] Settle, E. B., Pinkerton, H., and Corbett, A. J.: A Pathologic Study of Tsutsugamushi Disease (Scrub Typhus) With Notes on Clinicopathologic Correlation. J. Lab. & Clin. Med. 30: 639–661, August 1945.
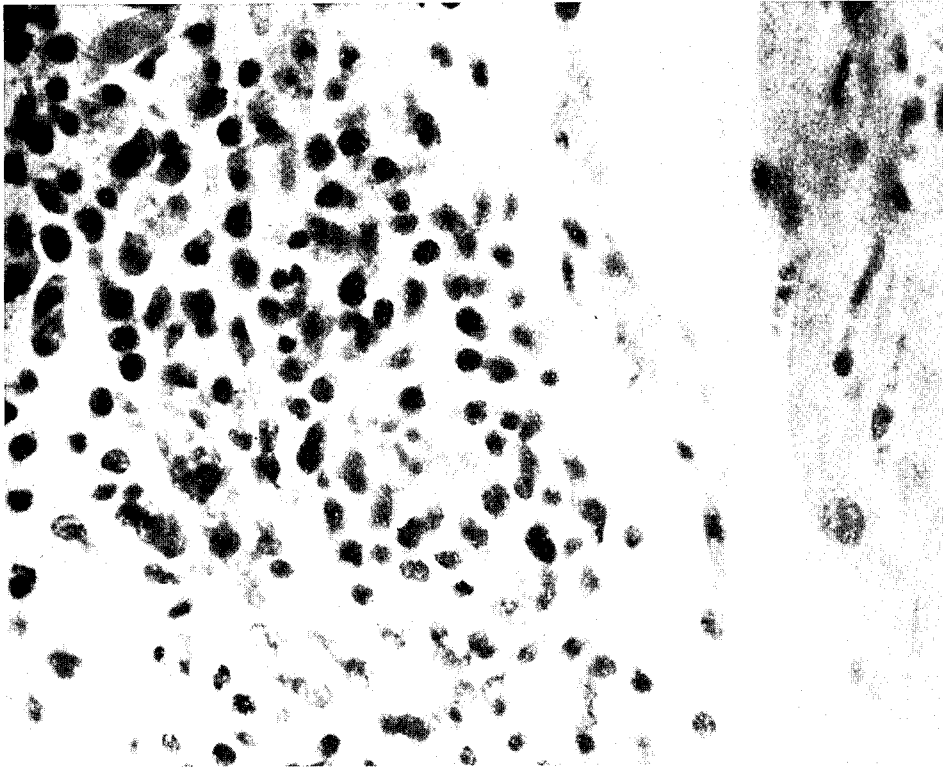
FIGURE 54.—Photomicrograph, tsutsugamushi disease. Perivascular mononuclear cell infiltration around a small damaged vessel in a fibrous septum in the myocardium. (Settle, E. B., Pinkerton, H., and Corbett, A. J.: J. Lab. & Clin. Med. 30: 639–661, August 1945.)

55). The capillary endothelium often showed swelling and proliferation. Areas of focal hemorrhage were not unusual where this inflammatory reaction was severe. Degenerative changes in the cardiac muscle fibers varied from cloudy swelling, loss of striation, and fatty degeneration, to actual necrosis.

In summarizing their clinical and pathological correlations, Settle and his coworkers concluded:

Circulatory failure, evidenced by increasing pulse rate and falling blood pressure, rapid shallow respirations, cyanosis, sweating, and cold clammy skin, generally appears in the second week. This syndrome, usually diagnosed clinically as peripheral vascular collapse, closely resembled that seen in surgical shock. Less frequently circulatory embarrassment occurs which is referable to acute myocarditis. * * * The myocarditis is difficult to evaluate as a cause of death. We do not believe it is of great importance when mild. In the more severe cases, however, with degenerative changes in the myocardial fibers, death may be due to myocardial failure.

Clinically, death was ascribed to circulatory failure in about one-third of the patients, to respiratory failure in about one-third, and to cerebral
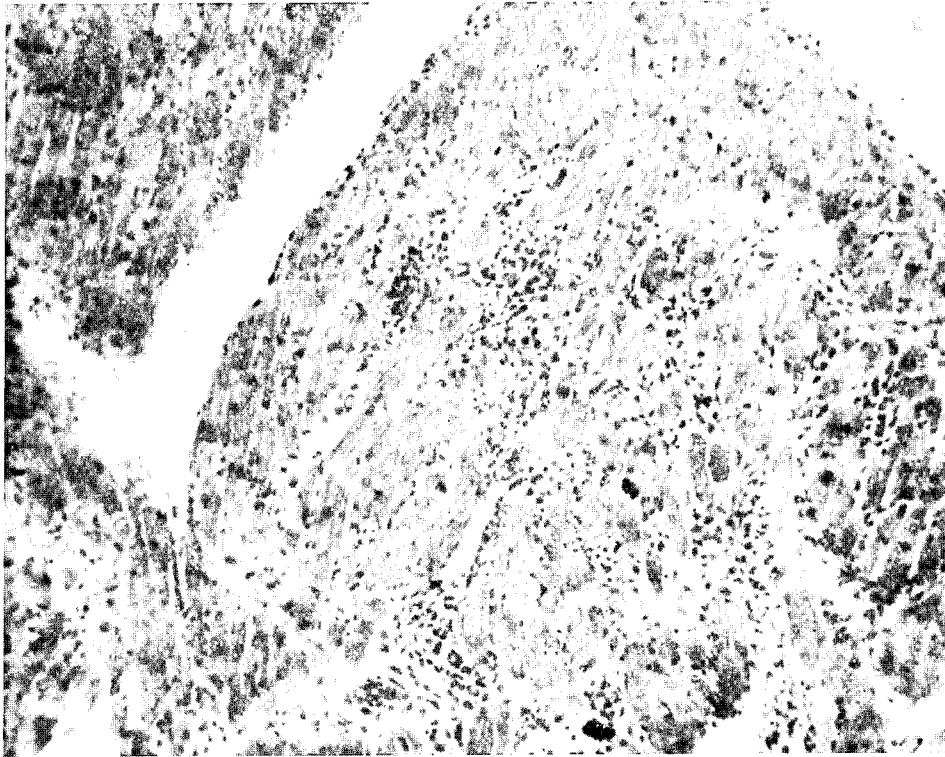
FIGURE 55.—Photomicrograph, diffuse myocarditis in tsutsugamushi disease. (Settle, E. B., Pinkerton, H., and Corbett, A. J.: J. Lab. & Clin. Med. 30: 639–661, August 1945.)

involvement and miscellaneous complications in the remaining third. Generalized acute vasculitis was a constant finding. Woodward and Bland [30] have emphasized the importance of myocarditis as a cause of death in typhus fever, and their conclusions may apply equally to tsutsugamushi disease.

The cardiac status during convalescence was the object of a special investigation for evidence of residual injury at a general hospital in the Southwest Pacific Area from July 1942 through February 1944.[31] Electrocardiograms on 118 patients were normal in 109; striking, though transient abnormalities were noted in 7; and minor changes in 2. From the available clinical and laboratory data, Levine concluded:

The evidence for persistent myocardial damage following tsutsugamushi fever is not convincing. In its effect on the heart, this disease is rather like diphtheria. If the patient survives the acute phase of the disease, his heart eventually shows complete return of function.

[30] Woodward, T. E., and Bland, E. F.: Clinical Observations in Typhus Fever; With Special Reference to the Cardiovascular System. J.A.M.A. 126: 287–293, 30 Sept. 1944.

[31] Levine, H. D.: Cardiac Complications of Tsutsugamushi Fever (Scrub Typhus); An Investigation of Their Persistency. War Med. 7: 76–81, February 1945.

Other Infections

Typhus fever.—In spite of fears to the contrary, and the wide distribution of American troops in many areas where typhus fever was endemic, this disease was rare in U.S. personnel. Shortly after the landings in North Africa and because of the known prevalence of the disease in that area, a special project was organized in French Morocco under the auspices of the United States of America Typhus Commission with the aid of the 6th General Hospital and the cooperation of the municipal authorities in Casablanca. A ward in the local infectious disease hospital was made available for the study and treatment of the disease in the local population (Arab and European). Later, in 1944, certain phases of the study were extended to the epidemic among civilians in Naples, Italy. Inasmuch as previous descriptions of the disease had emphasized circulatory collapse and the possible usefulness of cardiotonic drugs, the cardiovascular system was the object of special consideration and study.[32] From detailed observations on patients with severe epidemic typhus, it was concluded, as follows:

The altered physiological state, probably owing to widespread endothelial damage in severe cases, consists primarily of an inadequate circulating blood volume, hypoproteinemia (especially the albumin fraction), hypochloremia, hemodilution without blood destruction, or an azotemia.

The circulatory collapse frequently encountered under these conditions is primarily of peripheral origin.

General supportive measures to increase circulating blood volumes are not beneficial.

Cardiac drugs (digitalis and allied preparations) are probably of benefit only in exceptional cases with clear evidence of congestive heart failure. This was not encountered in the study.

Further investigation is needed to clarify: (1) The blood electrolytes and tissue analysis to determine the fate of chloride, (2) carbon dioxide combining power and the general alkali reserve picture, and (3) blood volume studies with the use of both whole blood and plasma in support of the reduced volume.

Diphtheria.—During World War II, diphtheria was an important epidemic disease among the civilian population of both Europe and Asia, and numerous cases occurred in the American, British, and German Armies. In 1943, an estimated one million cases occurred among civilians on the European Continent, excluding the U.S.S.R., with a probable fatality rate of at least 5 percent. In 1945, there were 2,079 reported cases with at least 53 deaths among U.S. troops in Europe.[33] Myocarditis was a frequent complication; in an analysis of 100 fatal cases in U.S. Army hospitals from 1943 through 1947, abnormal electrocardiograms were reported in 90 per-

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[32] See footnote 30, p. 430.

[33] Diphtheria in American Troops in Europe. Bull. U.S. Army M. Dept. 5: 504, 1946.

cent.[34] Cutaneous diphtheria also was encountered, in which a 5-percent incidence of myocarditis was reported in 141 cases in American soldiers from a general hospital in the India-Burma theater from July through December 1944. In an additional 5 percent, myocarditis could not be definitely excluded. The electrocardiograph proved to be more reliable than the clinical examination in detecting cardiac involvement.[35] A report on wound diphtheria in the German Army indicated myocardial involvement (by electrocardiogram) in 20 percent.[36]

Malaria.—It is generally agreed that malaria is the most widespread and serious disease in the world, and heavy plasmodial infection (especially *Plasmodium falciparum*) can cause death from myocardial inflammation or capillary thrombosis. However, in Sprague's experience [37] based on several thousand cases occurring in members of the Armed Forces, mostly in the Southwest Pacific Area, there was no instance of an acute cardiac death or of a proved chronic cardiac disease. Likewise, in another, detailed study of 50 cases, including roentgenograms and electrocardiograms, Tumulty and his associates [38] could detect no cardiac injury. Merkel,[39] however, reported two cases of death resembling coronary thrombosis where, at autopsy, there was noted widespread obstruction of the coronary vessels by the parasites of falciparum malaria.

Dengue.—A large number of cases of dengue occurred among the naval and marine personnel in the combat area of the Southwest Pacific during the summers of 1942 and 1943, and the studies reported by Hyman [40] indicated certain cardiovascular manifestations of interest. The disease was characterized by a slow pulse rate, low blood pressure, leukopenia, high temperature, and slow recovery from extreme physical and mental depression. The slow pulse rate was found to be due to a simple sinus bradycardia. Disturbances of conduction were discovered by electrocardiographic examination; these consisted of a delay in the P-R interval (up to 0.34 seconds) and a widening of the QRS complexes in three cases up to 0.12, 0.14, and 0.16 seconds, respectively. There were a few minor changes in the T waves and the R-T segments of the electrocardiogram.

Irregularities of rhythm were chiefly due to extrasystoles, for the most part ventricular in origin. The heart sounds were of poor quality, and systolic murmurs of varying intensity and localization appeared in many cases

[34] Edwards, W. M.: Analysis of Fatal Cases of Diphtheria. U.S. Armed Forces M. J. 2: 217–227, February 1951.

[35] Kay, C. F., and Livingood, C. S.: Myocardial Complications of Cutaneous Diphtheria. Bull. U.S. Army M. Dept. 4: 462–464, October 1945.

[36] Moser, H.: Wound Diphtheria. Deutsche med. Wchnschr. 70: 5, 7 Jan. 1944.

[37] Sprague, H. B.: The Effects of Malaria on the Heart. Am. Heart J. 31: 426–430, April 1946.

[38] Tumulty, P. A., Nichols, E., Singewald, M. L., and Lidz, T.: An Investigation of the Effects of Recurrent Malaria: An Organic and Psychological Analysis of 50 Soldiers. Medicine 25: 17–75, February 1946.

[39] Merkel, W. C.: Plasmodium Falciparum Malaria; Coronary and Myocardial Lesions Observed at Autopsy in 2 Cases of Acute Fulminating P. Falciparum Infection. Arch. Path. 41: 290–298, March 1946.

[40] Hyman, A. S.: The Heart in Dengue; Some Observations Made Among Navy and Marine Combat Units in the South Pacific. War Med. 4: 497–501, November 1943.

(these all disappeared after convalescence). Roentgenograms showed no cardiac dilatation. The blood pressure was consistently low in almost every case and remained low for some time after the attack. There were no striking changes in venous pressure.

It was suggested that the slow pulse and other cardiovascular signs were due to an excessive vagal or autonomic response to viral infection.

Infectious mononucleosis.—A study of an epidemic of infectious mononucleosis from the Station Hospital, Fort Bliss, Tex., based on 556 cases observed during 15 months included some unusual features.[41] The finding of electrocardiographic changes in 23 percent of 223 patients in the series was surprising. There was little else to differentiate this group from those with normal electrocardiograms. No cardiac symptoms were encountered except for precordial pain in an occasional patient, and abnormal physical findings were scant and unimpressive. All patients recovered.

Amebiasis.—The cardiovascular effects of emetine administration for amebiasis were studied in the Panama Canal Zone [42] and at the Schick General Hospital, Clinton, Iowa.[43] In the latter series, cardiovascular manifestations were observed in 83 percent of 93 subjects, but in most instances they were mild and transient. A significant fall in blood pressure occurred in 36 percent, precordial pain in 36 percent, dyspnea (of doubtful origin) in 15 percent, and tachycardia (at rest) in 13 percent. No instance of heart failure or of residual myocardial injury was observed.

Schistosomiasis.—The effects on the electrocardiogram of antimony compounds (tartar emetic and Fuadin) used in the treatment of schistosomiasis were studied at the Harmon General Hospital, Longview, Tex.,[44] and at the Moore General Hospital, Swannanoa, N. C.[45] In the former series, variations from the control records were found in all patients receiving tartar emetic and from 57 up to 80 percent in those receiving Fuadin, depending on the dose. The findings in the two series were similar and were confined for the most part to alterations in the T waves. The commonest finding was a decrease in amplitude, but actually negative T waves appeared in from 6 to 10 percent following tartar emetic. The S-T segment and other portions of the record (including cycle length) showed no significant change. In no instance was there evidence of cardiac weakness or persistent injury.

[41] Wechsler, H. F., Rosenblum, A. H., and Sills, C. T.: Infectious Mononucleosis: A Report of an Epidemic in an Army Post. Ann. Int. Med. 25: 113, July 1946; 236, August 1946.

[42] Dack, S., and Moloshok, R. E.: Cardiac Manifestations of Toxic Action of Emetine Hydrochloride in Amebic Dysentery. Arch. Int. Med. 79: 228–238, February 1947.

[43] Klatskin, G., and Friedman, H.: Emetine Toxicity in Man. Ann. Int. Med. 28: 892–915, May 1948.

[44] Tarr, L.: The Effect of Antimony Compounds, Fuadin and Tartar Emetic, on the Electrocardiogram of Man. Ann. Int. Med. 27: 970–988, December 1947.

[45] Schroeder, E. F., Rose, F. A., and Most, H.: The Effect of Antimony on the Electrocardiogram. Am. J.M. Sc. 212: 697–706, December 1946.

Beriberi and Deficiency States

Deterioration of the cardiovascular system and circulatory failure during prolonged starvation and deficiency states was the fate of large numbers of allied personnel in the prison camps of the Far East. A remarkable and distressing on-the-spot study of beriberi in a Japanese camp by a medical officer, himself a prisoner, was reported following his release in 1945.[46] The observations were made over a period of 34 months on approximately 8,000 Americans from Bataan and Corregidor and extended from their surrender on 9 April 1942 to their release on 30 January 1945. As Hibbs modestly points out, the study was handicapped by meager laboratory facilities, a complete lack of cooperation by the Japanese officials, lack of supplies for records, inability to maintain followup reports, and the poor state of health of most of the medical officers involved. In spite of these almost insurmountable obstacles, important data were obtained, and the observations and conclusions are noteworthy. These are summarized as follows:

Beriberi was probably the most important vitamin deficiency disease encountered for several reasons: (1) Beriberi had the highest incidence— everyone in the camp having some form of beriberi at one time or another; (2) beriberi had the highest morbidity—the disease was chronic in nature, incapacitating a soldier for months; (3) beriberi had complications and sequelae which were considered to be permanently disabling; and (4) beriberi was directly responsible for more deaths than any other vitamin deficiency disease; it was observed with many novel features far removed from the textbook picture.

In conclusion, Hibbs states that (1) enlargement of the heart is not to be expected in the majority of cases of beriberi heart disease, (2) thiamine deficiency may be the cause of almost any type of cardiac arrhythmia, (3) both left and right ventricles are involved in congestive heart failure, (4) digitalis is without benefit in the treatment of beriberi heart failure, and (5) beriberi heart disease is an acute medical emergency which must be treated energetically to prevent secondary irreversible damage or death.

Further observations on the released soldiers after the active phases of their avitaminosis had been relieved were more encouraging than the preceding paragraph suggests, since there were relatively few residua of a serious nature.[47] However, an occasional instance of otherwise unexplained cardiac enlargement and chronic congestive failure has been described as a probable aftermath of wartime beriberi.[48]

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[46] Hibbs, R. E.: Beriberi in a Japanese Prison Camp. Ann. Int. Med. 25: 270–282, August 1946.

[47] Fischbach, W. M.: Cardiac and Electrocardiographic Observations on American Prisoners of War Repatriated From Japan. U.S. Nav. M. Bull. 48: 69–75, January–February 1948.

[48] Alleman, R. J., and Stollerman, G. H.: The Course of Beriberi Heart Disease in American Prisoners-of-War in Japan. Ann. Int. Med. 28: 949–962, May 1948.
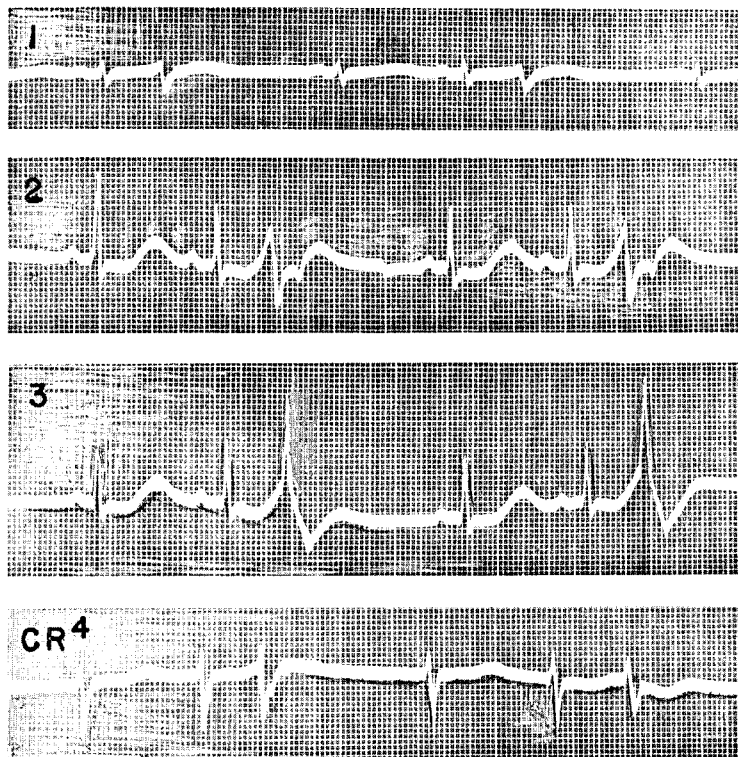
FIGURE 56.—Electrocardiogram in severe malnutrition, showing broad high T waves and a long Q–T interval. (Ellis, L. B.: Brit. Heart J. 8: 53–61, April 1946.)

The striking electrocardiographic abnormalities reported from Europe by Ellis [49] on four freed prisoners of war suffering from severe and prolonged malnutrition are of interest in this connection. These abnormalities consisted of marked prolongation of the Q–T interval, unusually well marked but not persistent U waves, and, less constantly, depression of the S–T segment, alterations in T waves, and increase in the P–R and QRS intervals (fig. 56). Although the available data did not permit definite conclusions on the cause of these changes, they were thought to represent a composite picture of prolonged protein and carbohydrate starvation and electrolyte imbalance. There was no evidence in these patients of a significant degree of anoxia of cardiac muscle or of clinical avitaminosis. Vitamin deficiency, however, could not be entirely ruled out as an etiological factor in spite of the absence of clinical symptoms or signs. That the electrocardiograms returned to normal within 2 to 3 weeks after the institution

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[49] Ellis, L. B.: Electrocardiographic Abnormalities in Severe Malnutrition. Brit. Heart J. 8: 53–61, April 1946.

of an adequate regimen suggests that the changes were due to functional and not to structural causes.[50]

HYPERTENSION

The importance of hypertension in determining fitness for active military duty is indicated by the fact that in World War II one-fourth of those rejected for cardiovascular defects were disqualified for this reason (p. 422). As was stressed by Levy and his associates, the range of the normal, both systolic and diastolic, was not clearly defined, and critical levels above which it is unsafe or unwise to accept a candidate had not been established on a sound factual basis. Transient emotional elevations of blood pressure were recognized and properly discounted by the Army. The guiding principles employed were set forth in MR 1–9, 15 October 1942, as follows: "If the blood pressure appears to be abnormally high, it will be measured after the subject has rested in the recumbent position." A cause for rejection is: "Persistent blood pressure at rest above 150 mm. systolic or above 90 diastolic, unless in the opinion of the medical examiner the increased blood pressure is due to psychic reaction and not secondary to renal or other systemic disease."

The high rejection rate led to a series of conferences early in the war from which evolved a carefully planned program of study for the primary purpose of obtaining information useful to the Army, but there was also a desire to contribute to the general knowledge of the problems involved. This important project was conceived and organized in 1942, and the subsequent results were published between 1944 and 1947.[51] Because of the significance of the data and of the circumstances involved, certain details of this project, as recorded by Hillman, Levy, Stroud, and White,[52] warrant special recognition in this account of World War II events. These details are as follows:

At a meeting of the Subcommittee on Cardiovascular Diseases of the National Research Council, held in Washington in June 1942, * * * the advisability of modifying certain of the existing criteria of physical fitness was considered. The urgent need for

[50] In view of postwar recognition of the profound and similar effects on the electrocardiogram of severe alterations of potassium concentration in the blood, this seems, in retrospect, to be the most likely explanation.

[51] (1) Hillman, C. C., Levy, R. L., Stroud, W. D., and White, P. D.: Studies of Blood Pressures in Army Officers; Observations Based on Analysis of the Medical Records of 22,741 Officers of the United States Army. J.A.M.A. 125: 699–701, 8 July 1944. (2) Levy, R. L., Hillman, C. C., Stroud, W. D., and White, P. D.: Transient Hypertension: Its Significance in Terms of Later Development of Sustained Hypertension and Cardiovascular-Renal Diseases. J.A.M.A. 126: 829–833, 25 Nov. 1944. (3) Levy, R. L., White, P. D., Stroud. W. D., and Hillman, C. C.: Transient Hypertension; The Relative Prognostic Importance of Various Systolic and Diastolic Levels. J.A.M.A. 128: 1059–1061, 11 Aug. 1945. (4) Levy, R. L., White, P. D., Stroud, W. D., and Hillman, C. C.: Transient Tachycardia; Prognostic Significance Alone and in Association With Transient Hypertension. J.A.M.A. 129: 585–588, 27 Oct. 1945. (5) Levy, R. L., White, P. D., Stroud, W. D., and Hillman, C. C.: Overweight; Its Prognostic Significance in Relation to Hypertension and Cardiovascular-Renal Diseases. J.A.M.A. 131: 951–953, 20 July 1946. (6) Levy, R. L., White, P. D., Stroud, W. D., and Hillman. C. C.: Sustained Hypertension; Predisposing Factors and Causes of Disability and Death. J.A.M.A. 135: 77–80, 13 Sept. 1947.

[52] See footnote 51(1).

manpower made it imperative to recruit all eligibles who could serve with safety to themselves and with advantage to the armed forces. With respect to the upper limits of blood pressure, it was suggested by some that these might be raised, whereas others claimed that the existing levels were too high. As a result of the discussion, it became clear that a change in either direction was not justified on the basis of the evidence at hand; for there was no large series of observations carried out over long periods of time. To obtain the lacking information as quickly as possible seemed highly desirable.

It was known that, in the Office of the Surgeon General of the Army, there were filed abstracts of the medical records of some 23,000 officers, on which were noted the results of annual physical examinations made between January 1924 and December 1941. Appended to many of these were the detailed reports of special examining boards, submitted on the occasion of promotion or retirement or of examination incident to hospitalization. Often electrocardiograms and teleroentgenograms were made at such times, and other laboratory procedures were employed. In many cases the record began with the admission of the young man, as a cadet, to West Point. Annual examinations were discontinued in 1941 owing to the pressure of work essential to the war. No examinations were made after an officer had retired unless he applied for reinstatement for active duty. Samples of these records were inspected, and it was at once apparent that here was a valuable storehouse of material.

To supplement the histories in the Surgeon General's Office, Col. Albert G. Love, Medical Corps, United States Army, kindly offered to place at our disposal his notes on the medical records of 5,000 officers who were in the service on Jan. 1, 1901 and also those commissioned between that time and Dec. 31, 1916. These had been analyzed in collaboration with Professor Lowell J. Reed of the Johns Hopkins University, and the results published in 1931 and 1932 in a series of papers dealing with "Biometric Studies on U.S. Army Officers."

The availability of this material appeared to offer an unusual opportunity to study variations of blood pressure during the passage of a number of years and to relate them to various other factors. Of particular immediate importance was the significance of transient hypertension. Additional topics for consideration which at once came to mind were the later course of those who developed sustained hypertension, the relationship between body weight and hypertension, and the significance of tachycardia, both transient and sustained. These could all be correlated with disability retirement and mortality rates at various ages, with the causes of retirement and death and, in those who died, with the findings at necropsy.

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On Sept. 12, 1942 a contract, recommended by the Committee on Medical Research, was made between the Office of Scientific Research and Development and Columbia University, providing funds for this study. Dr. Levy was appointed chairman of the project.

From this study and analysis of the long-term records of 22,741 officers of the U.S. Army, the following findings of significance were established:

1. Transient hypertension or transient tachycardia or overweight, each by itself, increased the probability of the later development of sustained hypertension and of retirement or death with cardiovascular-renal disease. The presence of two of these conditions was of greater importance, in these respects, than that of any one alone. The presence of all three was of major prognostic importance.

2. In the group in which sustained hypertension developed, the leading causes of retirement because of cardiovascular-renal diseases were hypertension itself, coronary heart disease, and cerebral arteriosclerosis, including

hemorrhage and thrombosis. These three conditions together accounted for 84 percent of such retirements. Coronary heart disease and cerebral hemorrhage together were responsible for 66 percent of the deaths from cardiovascular-renal conditions during the period of observation.

It was suggested that, in revising standards for the selection of those physically qualified for military service, factors predisposing to the later development of sustained hypertension and cardiovascular-renal diseases should be taken into account. When making disposition of men in whom sustained hypertension develops while they are in service, consideration may well be given to the high incidence and disabling nature of the circulatory and renal complications associated with this condition. The extent to which the conclusions derived from these studies are applied can be varied according to the need for manpower.

Furthermore, it seems probable that the facts obtained from this analysis hold true also for the general male population of comparable physical fitness and similar age groups.

Thus ended a unique undertaking, based on the exigencies of the war and combining the accumulated experience of the Army and the resources of the Government with the services of an expert civilian committee.

CORONARY DISEASE

The stress and strain of the war upon carefully screened young men in service made it possible to study the potential effects of these factors upon latent and unsuspected coronary arteriosclerosis. Furthermore, the results of this study may be, in part, responsible for the existing suspicion that coronary disease is more prevalent in young men of this generation than in those of the past.

Relatively early in the war, an analysis was undertaken of the clinical and pathological features in 80 fatal cases in soldiers from 20 to 36 years of age. This material from the Army Medical Museum, Washington, D.C., revealed that coronary disease occurred in men of various racial and national origins without predilection for any particular stock.[53] The most striking, and presumably predisposing, factor was overweight, present in 91 percent of the cases. Vigorous effort and the activities of early morning chores brought on the fatal attacks in over 50 percent of the cases. Sudden death or the onset of the fatal attack occurred during sleep in 10 percent. The basis of the occlusion in every case was arteriosclerosis, and a scar of previous infarction was found in 59 percent.

A subsequent and more extensive study of sudden and unexpected death in young soldiers, based on material received at the Army Institute of Pathology, Washington, D.C., during the 4 years between January 1942 and

[53] French, A. J., and Dock, W.: Fatal Coronary Arteriosclerosis in Young Soldiers. J.A.M.A. 124: 1233–1237, 29 Apr. 1944.

January 1946, contributed further significant data.[54] Among the 40,000 autopsy protocols, there were approximately 1,000 which concerned young and apparently healthy soldiers whose collapse and death were so sudden and unexpected that there was little or no opportunity to make an ante mortem diagnosis. The most frequent conditions responsible for death under these circumstances were heart disease, intracranial hemorrhage, and meningococcemia. Among these 1,000, there were approximately 350 sudden deaths from previously unrecognized heart disease; almost 300 were due to coronary arteriosclerosis. The following additional facts and opinions were derived from a detailed analysis of the data on 115 who died of coronary disease: There were 8 percent under 25 years of age, and 22 percent under 30. White and Negro soldiers were represented in proportion to their numbers in the Army. The body weights were significantly greater than those for healthy inductees; however, this was equally true of the weights in autopsy protocols of soldiers dead of accidental injuries. This important control observation was not considered in the earlier report by French and Dock (p. 438); its possible significance is weakened somewhat, as Moritz and Zamcheck noted, by the fact that the body weights were mostly estimates and hence cannot be used without reservation in appraising the relation of obesity to any given disease.

The frequency with which the onset of the fatal attack of coronary insufficiency occurred during a period of strenuous physical exertion supports the plausible opinion that violent exercise is probably dangerous for persons with severe coronary disease. Moritz and Zamcheck further suggest, however, that this information would be of little practical value to the Army in the prevention of such casualties, since none of these soldiers was suspected of underlying heart disease before death, and even in retrospect less than 25 percent of them had a history of symptoms that might have been of cardiac origin.

In addition to the two foregoing reports assembled during the war, a third and important study, based in part upon the material from the Armed Forces Institute of Pathology but expanded during the early postwar years to include further data from the Veterans' Administration, has been reported in papers by Yater and his associates.[55] These reports dealt with initially nonfatal coronary disease in World War II soldiers. The earlier communications concerned the younger men, from 18 to 39 years of age, and the later study the age group over 40. The 1951 report included data

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[54] Moritz, A. R., and Zamcheck, N.: Sudden and Unexpected Deaths of Young Soldiers; Diseases Responsible for Such Deaths During World War II. Arch. Path. 42: 459–494, November 1946.

[55] (1) Yater, W. M., Traum, A. H., Brown, W. G., Fitzgerald, R. P., Geisler, M. A., and Wilcox, B. B.: Coronary Disease in Men Eighteen to Thirty-Nine Years of Age: Report of Eight Hundred Sixty-Six Cases, Four Hundred Fifty With Necropsy Examinations. Am. Heart J. 36: 334–372, September 1948; 481–526, October 1948; 683–722, November 1948. (2) Yater, W. M., Welsh, P. P., Stapleton, J. F., and Clark, M. L.: Comparison of Clinical and Pathologic Aspects of Coronary Artery Disease in Men of Various Age Groups: Study of 950 Autopsied Cases From Armed Forces Institute of Pathology. Ann. Int. Med. 34: 352–392, February 1951.

on 950 autopsied cases. This formidable undertaking was approached as follows:

During 1945–46, a study was made of 866 male patients, ages 18 through 39, for whom the principal diagnosis was coronary artery disease. These included 416 who had survived typical attacks of acute myocardial infarction and whose case histories were obtained from the Veterans' Administration and 450 who died while in the Army and whose autopsy protocols were in the files of the Armed Forces Institute of Pathology.

Following completion of the study of the younger age group, research was begun to determine what similarities or differences might exist in the clinical and pathological aspects of coronary artery disease in older men as compared to those under 40 years of age. For this purpose, selection was made of 500 additional autopsy records of men 40 years of age and over.

That the 635 fatalities from coronary artery disease among World War II soldiers in this series do not represent, either numerically or percentagewise, the total picture of its incidence among military personnel is shown by the fact that as of 30 June 1948, 6,075 World War II veterans were receiving service-connected disability pension awards principally because of coronary artery disease.

From these two related studies, it was found that Negroes comprised only 4 percent of the World War II soldiers in the series, although they constituted approximately 10 percent of the Army during that period.

No definite conclusions could be drawn as to the role of army life in precipitating fatal attacks; however, generally shorter length of service of these men as compared with the average in the World War II Army suggests that they were not in condition to withstand the stress of army life. In contrast to the findings of French and Dock (p. 438) and of Moritz and Zamcheck (p. 439), the etiological importance of obesity as a predisposing factor in coronary disease could not be definitely established in any age group, although a tendency to overweight appeared to accompany advancing age. The onset of the coronary attack occurred in a higher percentage of the younger men while they were engaged in strenuous activity and in a higher percentage of the older men while they were in bed. The data also suggested that coronary disease carried a more serious prognosis for men under 40 than for those of 40 and over.

The relation of unusual or extreme effort to acute myocardial infarction is of considerable practical as well as theoretical importance, since legal decisions and line-of-duty determinations are often vitally affected thereby. Blumgart [56] cited some striking examples and summarized his Army experience in this connection. He discussed the clinical criteria which he considered necessary to establish this relation and the pathological mechanisms involved.

These extensive data acquired during the war have emphasized the mounting incidence of coronary disease in otherwise vigorous young men and have indicated the need for broader and more basic studies in its causes and its prevention. In conclusion, a final lesson of the war years

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[56] Blumgart, H. L.: The Relation of Effort to Attacks of Acute Myocardial Infarction. J.A.M.A. 128: 775–778, 14 July 1945.

should not pass unheeded: Industry, faced with a manpower shortage incident to the war, demonstrated that individuals with healed infarcts and those with lesser degrees of angina, although unsuited for the Armed Forces, are capable of pursuing useful and productive lives under proper training and supervision without added risk to themselves or to their fellow workers. Their zeal and energy more than compensate for their physical handicaps. It is unfortunate that with the passing of the emergency the rules and practices of peacetime economy often force such useful workers into the ranks of the unemployed. This practical demonstration as a corollary of the war presents a challenge to the medical profession and to the legislators in planning future programs for the welfare of the United States and its citizens.

NEUROCIRCULATORY ASTHENIA

(Soldiers' Heart, Effort Syndrome, Shellshock, Anxiety Neurosis)

A wide variety of names had been used to identify the syndrome which, in 1918, The Surgeon General officially designated as "neurocirculatory asthenia," a term considered moderately descriptive and yet adequately noncommittal.[57] In 1871, DaCosta,[58] an army physician in the Civil War, proposed the term "irritable heart." Another early American description of the disorder was given by Beard,[59] in 1880, using the terms "neurasthenia" and "nervous exhaustion." The name "anxiety neurosis" was substituted later for neurasthenia by Freud.[60] In World War I, the terms "shellshock" and "effort syndrome" were employed, the latter chiefly by British investigators under Sir Thomas Lewis. A group of American workers [61] in World War I devised the term "neurocirculatory asthenia," and this term was adopted for use in the American Army and was the title of the report by Brooks [62] in the official Army history of World War I. Studies of civilians with the disorder were carried on between World Wars I and II by Craig

[57] This section on neurocirculatory asthenia has been prepared, at my request, by Dr. Mandel E. Cohen, Boston, Mass., whose long interest and extensive studies qualify him to speak with authority concerning this controversial but important symptom complex, especially troublesome during the stress of war.—E. F. B.

[58] DaCosta, J. M.: On Irritable Heart; A Clinical Study of a Form of Functional Cardiac Disorder and Its Consequences. Am. J.M. Sc. 61: 17, January 1871.

[59] Beard, G. B.: A Practical Treatise on Nervous Exhaustion (Neurasthenia): Its Symptoms, Nature, Sequences, Treatment. New York: William Wood and Co., 1880.

[60] Freud, S.: Ueber die Berechtigung von der Neurasthenia einen Bestimmten Symptomencomplex als "Angstneurose" abzutrenn. Neurol. Centralbl. 14: 50, 1895.

[61] (1) Oppenheimer, B. S., Levine, S. A., Morison, R. A., Rothschild, M. A., St. Lawrence, W., and Wilson, F. N. (cited by T. Lewis): Report on Neuro-Circulatory Asthenia and Its Management. Mil. Surg. 42: 409, April 1918. (2) Oppenheimer, B. S., Levine, S. A., Morison, R. A., Rothschild, M. A., St. Lawrence, W., and Wilson, F. N.: Illustrative Cases of Neurocirculatory Asthenia. Mil. Surg. 42: 711, 1918.

[62] Brooks, Harlow: Neurocirculatory Asthenia. In The Medical Department of the United States Army in the World War. Washington: U.S. Government Printing Office, 1928, vol. IX.

and White.[63] In World War II, British studies under Wood [64] were reported as DaCosta's syndrome or effort syndrome. In the American Army, official terminology was shifted somewhat to fit certain etiological and psychological theories, and terms, such as "anxiety state," "somatization reactions," "psychogenic reactions," and "combat fatigue," were introduced. German Army terminology was even longer, such as "personalities with mixed psychic * * * constitutionally labile * * * organ systems." World War II investigations, however, were mainly reported under the term "neurocirculatory asthenia" (anxiety neurosis, neurasthenia, effort syndrome, nervous exhaustion) in an effort to reach physicians of various interests and specialties.

Research During and After World War II

Because of the importance of neurocirculatory asthenia in World War I, further organized research was conducted during and after World War II under the leadership of White and his associates, with Army support.[65] The plan of study was based on applying the best quantitative techniques of the day to the problem of explaining the symptoms and the other phenomena of the disorder. For instance, because patients complained of troubles while working, studies in work physiology were done. Because of such symptoms as nervousness, psychological studies were done. Because patients said other members of the family had symptoms similar to theirs, genetic studies were done. This is, then, simply the method of scientific investigation in contrast to a method used so often in fields such as psychology, for instance, of applying the theories and conclusions of a special school or authority to a given problem.

Studies of breathing and dyspnea

Patients with neurocirculatory asthenia commonly complain of shortness of breath, of inability to draw a satisfactory breath, and of inability to do hard work because of breathlessness. Such patients sigh, have difficulty in wearing a gas mask, and find it extremely difficult to run while wearing the mask. They may complain of difficult breathing during swimming and of shortness of breath for as far back as they can remember.

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[63] Craig, H. R., and White, P. D.: Etiology and Symptoms of Neurocirculatory Asthenia; Analysis of One Hundred Cases, With Comments on Prognosis and Treatment. Arch. Int. Med. 53: 633–648, May 1934.

[64] Wood, P.: DaCosta's Syndrome (or Effort Syndrome). Brit. M. J. 1: 767–772, 24 May 1941.

[65] (1) Cohen, M. E., White, P. D., and Johnson, R. E.: Neurocirculatory Asthenia, Anxiety Neurosis or the Effort Syndrome. Arch. Int. Med. 81: 260–281, March 1948. (2) Cohen, M. E., Johnson, R. E., Consolazio, F. C., and White, P. D.: Low Oxygen Consumption and Low Ventilatory Efficiency During Exhausting Work in Patients With Neurocirculatory Asthenia, Effort Syndrome, Anxiety Neurosis. J. Clin. Invest. 25: 920, 1946. (3) Cohen, M. E., Johnson, R. E., Chapman, W. P., Badal, D. W., Cobb, S., and White, P. D.: A Study of Neurocirculatory Asthenia, Anxiety Neurosis, Effort Syndrome. Final Report to the Committee of Medical Research, Office of Scientific Research and Development. Washington: National Research Council, 1946.

Quantitative studies of respiration showed that, while resting and breathing oxygen, patients with neurocirculatory asthenia have more rapid respiratory rates and more shallow breathing than do healthy control subjects. The ventilation index was abnormally high in patients for four speeds of exercise; the more severe the exercise, the greater the discrepancy between patients and controls. This was due to a high ventilation factor and not to vital capacity. (The mean vital capacity for 54 healthy men was 2,387 cc. per square meter of body surface and for 73 patients with neurocirculatory asthenia, 2,362 cc.)

The ventilation index is usually an objective correlate of the subjective phenomenon of dyspnea. When the level of ventilation index was the same, more patients than healthy controls complained of dyspnea. Furthermore, the degree of dyspnea complained of was greater in patients than in healthy controls doing the same amount of exercise and with the same ventilation index.

Drury,[66] in 1919, had demonstrated that intolerant hyperpnea developed in these patients at a lower level of concentration of inspired carbon dioxide than in control subjects. It was noted that patients complained of choking or smothering and had undergone anxiety attacks in crowded places, such as subways, bargain basements, and theaters. This suggested a study in which 43 patients and 27 control subjects first breathed oxygen for 12 minutes; then, a second test of 12 minutes of rebreathing was done in which carbon dioxide had accumulated to about 4 percent of inspired air. This showed that an increase of sighs to a mean of 7.5 per 12-minute period took place in patients as contrasted with 2.8 in comparable controls. It was concluded that intolerable hyperpnea, increased sighing, and symptoms of the disorder identical with anxiety attacks can be produced by rebreathing a mixture containing an excess of carbon dioxide. It was not clear, however, that a natural stimulus for the disorder was reproduced experimentally. Nor did this observation show whether the entire abnormal response was set off by carbon dioxide, by nonspecific discomfort (this seemed unlikely), or by the awareness of the sensation of disturbed breathing or by something else.

Cardiovascular studies

Cardiovascular studies showed only a few significant deviations from the normal. The pulse rate at rest, during exercise, and after exercise was higher than average by 8 to 10 beats per minute as compared with healthy controls. The size of the heart, as determined by measurements of the diameter and area of the heart in roentgenograms, was not significantly different in the two groups (50 subjects in each group). These findings did not confirm the conclusion of others that neurocirculatory asthenia is

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[66] Drury, A. N.: The Percentage of Carbon Dioxide in the Alveolar Air, and the Tolerance to Accumulating Carbon Dioxide in Cases of So-Called "Irritable Heart of Soldiers." Heart 7: 165, April 1920.

characterized by the presence of a small heart. The electrocardiogram, made with the patient at rest and after mild exercise (Master's tolerance test), was within normal limits.

Other normal findings were related to responses of the blood pressure and the pulse to changes of posture on a tilt table, resting venous pressure, blood volume, vital capacity, circulation time, and resting cardiac output as measured by the acetylene method of Grollman and compared with normal standards. Measurement of the cardiac output by the direct Fick method, employing catheterization of the right auricle of the heart, gave mean values that were within the limits of those reported for normal subjects with evidence of anxiety. Patients seemed tense and apprehensive during the procedure. Values obtained by the Grollman method were lower than those obtained by the direct Fick method.

Studies of muscular work

Studies of muscular work were of special interest because (1) patients say they cannot do hard work; (2) the symptoms of the illness have been compared with the feelings of hard work, this being the basis for the concept of the effort syndrome; and (3) patients with this disorder say that they are made worse by doing hard work.

White,[67] in 1920, had described an abnormal performance of and response to a test which combined work, respiration, and discomfort (a 100-meter run, wearing a gas mask) as compared with control subjects. Hence, patients and controls were studied during and after muscular work in the laboratory. Moderate work consisted of walking on a treadmill, and hard work consisted of running on a treadmill, of stepping up and down on a 20-inch (50.8 cm.) step, and of stepping up and down with a pack on the back.

In the basal condition, the pulse and respiratory rates are slightly abnormal in neurocirculatory asthenia, but there was no difference between patients with neurocirculatory asthenia and controls in regard to oxygen consumption and the blood lactate concentration while resting. When one compares groups of subjects who work hardest and longest with those who work least (women, men in poor training, and patients with neurocirculatory asthenia), differences between the two groups become more apparent as the intensity and duration of the work tests are increased. In other words, the more the work is stepped up, the more clearly does a "poor work group" separate itself from a "good work group." When the subjects are at rest, the measurable differences appear consistently. During a hard-work test which all subjects perform for a comparable length of time at a fixed pace and grade, all the differences seen in walking are accentuated. In addition, oxygen consumption is lowest in groups who do not run well. When subjects run at a fixed pace until they reach their stopping point, those who run

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[67] White, P. D.: Observations on Some Tests of Physical Fitness. Am. J.M. Sc. 159: 866, June 1920.

longest have higher oxygen consumption, higher pulmonary ventilation, higher blood lactate levels, higher ventilatory efficiency, and lower pulse.

It was concluded that with either moderate or exhausting muscular work, during which patients and controls alike perform for the same duration and at the same rate, there are many measurable abnormalities in patients with neurocirculatory asthenia. The findings are consistent with the hypothesis that aerobic metabolism is abnormal in these patients. The high blood lactate concentration suggests reciprocal high oxygen debt. It cannot be stated whether these findings apply specifically to patients with neurocirculatory asthenia or whether they are the general signs of poor health, chronic illness, poor runners, or poor state of training.

The results of further studies showed that painful stimuli could produce abnormal responses, also responses at unusually low stimulus levels in some systems, in patients with neurocirculatory asthenia.[68]

It was concluded from the studies and the general experience in World War II that there are fairly definite quantitative abnormalities in neurocirculatory asthenia. The disorder has many recurring symptoms, is never monosymptomatic, and can be diagnosed on the basis of symptoms. The laboratory abnormalities furnish objective evidence related to patients' subjective complaints. It is also clear that several functions seem normal under basal conditions, but under stress, for instance, work or discomfort, measurable differences appear between patients and controls.

The question remains, once the diagnosis is made, what is the military future of the patient with neurocirculatory asthenia? It was believed that the automatic rejection or discharge of these patients may not be the right answer and that the favorable course of most of the patients in civilian life, and of some in army life, suggests that although neurocirculatory asthenia is a handicap and difficulty it is not necessarily a disabling disorder.

Finally, it should be pointed out that, as yet, the answers to many of the problems posed by neurocirculatory asthenia are unsettled and that more scientific investigation is needed.

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[68] In a 20-year followup of 173 civilian patients with neurocirculatory asthenia, Wheeler and his associates (see *Journal of American Medical Association*, vol. 142, 25 Mar. 1950, pp. 878–889) showed the following:

1. Significant amounts of handicap and disability were present in 15 percent of the patients, the others reporting that the disorder and its symptoms produced little or no disability.

2. The number of children, divorces, marriages, employment problems, adequate income, and reasonably happy lives was not obviously different from that of the general population.

3. Hospitalizations, surgical operations, the development of other diseases, and mortality are not excessive in patients over 20 years when compared with the general population.

4. Although these patients showed "anxiety" as a characteristic phenomenon, they did not develop to any unusual extent diseases such as hypertension, peptic ulcer, asthma, diabetes, which some authors have speculated are caused by "anxiety."

5. A comparison of the condition of these 173 patients who received only a thorough examination and a simple explanation and reassurance compared favorably with the published therapeutic results after sanitarium psychotherapy, out-patient psychotherapy, Freudist psychoanalysis, sanitarium care, electroshock procedure and frontal lobotomy.

6. Veterans showed more disability as compared with others of the followup study.

WOUNDS AND FOREIGN BODIES

In World War II, it was estimated that the heart and pericardium were injured in 3.3 percent of intrathoracic wounds in casualties arriving at the forward installation.[69] Occasionally, the heart or lungs were involved secondarily by missiles migrating in the bloodstream from elsewhere in the thorax or the abdomen. Serious wounds were detected earlier and treated more effectively than ever before, and from this experience evolved new techniques and an attitude of confidence which have contributed significantly to the remarkable success of the operations for acquired valvular disease developed in the postwar decade. This important and inspiring facet in the progress of the war years is worthy of special consideration here.

In spite of the dramatic and often singular features incident to wounds of the heart and great vessels, it is well to remember, as pointed out by Barrett [70] in his excellent review, that the unique cases recorded during each World War usually have had their counterparts in previous conflicts. This is well illustrated by three case histories from the early 19th century. The first describes an unusual foreign body (embolic) in the chamber of the right ventricle, reported first by Davis,[71] in 1834, and commented upon later by Bland-Sutton,[72] in 1919, as follows:

A boy, aged 10, made a gun of a telescopic toasting fork. To form the breach of the gun he drove a plug of wood three inches long into the hollow handle of the fork and made a touch-hole. When the gunpowder exploded the stick was forced into his chest between the third and fourth costal cartilages, to the right of the sternum. Immediately after the accident the boy walked a distance of 40 yards to his home. He survived the accident thirty-seven days. After death, a piece of wood 3 in. long and as thick as a cedar pencil was found in the right ventricle of the heart encrusted in a clot. Thomas Davis reported these facts in 1834; he found no wound in the pericardium or the heart, and expressed the opinion that the stick, after wounding the lung, had passed into the vena cava and was carried by the bloodstream into the right auricle and then into the right ventricle, where it was found. On reading this report for the first time, I was skeptical in regard to the emboli theory that Davis advanced to explain the presence of the stick in the ventricle, for at the date of the accident surgeons knew nothing of the transport of bloodclot either to or from the heart. It was at least a quarter of a century later that the word "embolus" was coined by Virchow, and the dangers underlying the movement of clot began to be understood.

The second case cited by Barrett dates from the Napoleonic Wars and demonstrates that a large object may enter the aorta near the heart without causing the patient to die of primary hemorrhage:

Mr. Beunton, Assistant Surgeon on board the hospital ship in the Mediterranean, says that a boat's crew, detached to cut-out a French vessel, met with such determined

[69] Samson, P. C.: Battle Wounds and Injuries of Heart and Pericardium; Experiences in Forward Hospitals. Ann. Surg. 127: 1127–1149, June 1948.

[70] Barrett, N. R.: Foreign Bodies in the Cardiovascular System. Brit. J. Surg. 37: 416–445, April 1950.

[71] Davis, T. D.: Cited by Bland-Sutton (see footnote 72) and Barrett (footnote 70). Trans. Prov. Med. Surg. Assoc. 2: 357, 1834.

[72] Bland-Sutton, J.: A Lecture on Missiles as Emboli. Lancet 1: 773, 10 May 1919.

resistance that several were killed or wounded, and amongst the latter was a seaman who affirmed that a musket-ball, striking his oar, had run along it and entered his side; he bled a good deal and then, almost completing the third day from the injury, he died.

The post-mortem examination showed that the missile entered the body between the eighth and ninth ribs, it had wounded the diaphragm and passed into the pericardium, which was full of blood; a hole in the aorta had been made by the shot, and this had been closed up by a firm coagulum. Much blood had escaped into the chest and abdomen, not only from the vessels wounded in the course followed by the ball, but from the heart itself. The ball was found adhering to the inner side of the aorta, and there it is now. (The ball measured 1½ inches in diameter.)

A third case of historical interest mentioned by Bland-Sutton concerns a foreign body which entered the left side of the heart by penetrating a pulmonary vein:

At the storming of the Great Pagoda, Rangoon, 1852, a round leaden bullet entered the chest of a soldier between the third and fourth ribs near the anterior fold of the left axilla. Blood and air issued from the wound for several days, and the surrounding tissues became emphysematous. The man was attended in the field hospital by Dr. J. Fayrer (the late Sir Joseph Fayrer), the symptoms abated, and the patient came under the care of Dr. W. White. The soldier died 72 days after being wounded. An examination of the body revealed a pint of pus in the left pleural cavity and a piece of cloth from his jacket. The lung was solid. The track of the missile ran through the chest to the left pulmonary veins. The rifle ball lay in the left ventricle of the heart near its apex. There was no wound of the heart. It appeared from these facts that the ball perforated one of the left pulmonary veins, entered the left auricle, and finally passed into, and settled in, the left ventricle. The heart is preserved in the Museum of the Medical College, Calcutta.[73]

Others had recognized in the 19th century that patients could survive for years with foreign bodies (usually needles) in their hearts without apparent harm, and by 1900, although it was known that the heart could survive serious wounds and heal well, cases of weak scar with aneurysm formation had been recorded and the risks of sepsis appreciated. Suture of heart wounds was known to be possible and was accepted as indicated in certain emergencies.

The experience provided by World War I with heart wounds was extensive. Numerous operations for the removal of foreign bodies from in and around the heart were recorded between 1914 and 1918, for which the French surgeons deserve especial credit. Delorme,[74] in 1917, reviewed 13 operations (Beaussenat (2), Beloit, Laurent, Bichat, Dujarrior (2), Chauvel, Hallopean, LeFort, Gaudier, Fredet, and Delbet), in France, of which the results were known with only 3 deaths. Of special interest were four operations for the removal of intraventricular (right) foreign bodies, all of which were successful. The following year, LeFort[75] reported the first

[73] White, W.: Case of Lodgment of a Musket Ball in the Left Ventricle of the Heart. Indian Ann. M. Sc. 1: 294, 1853–54. Cited by Bland-Sutton (see footnote 72, p. 446) and by Barrett (see footnote 70, p. 446).

[74] Delorme, E.: Contribution à l'étude de la Chirurgie Cardiaque. Bull. Acad. de méd., Paris 78: 243, 18 Sept. 1917.

[75] LeFort, R.: Extraction d'un Eclat de Grenade de la Cavité du Ventricle Gauche; Guérison: Présentation du Malade. Bull. Acad. de méd., Paris 80: 147, 6 Aug. 1918.

case in France of a fragment successfully removed from the left ventricular chamber. He also recorded a consecutive series of nine cardiotomies for the removal of foreign bodies with only one death.

Nonetheless, as Barrett (p. 446) points out, opinion was still divided at the start of World War II. An extensive survey by Decker,[76] in 1939, indicated that the late mortality from foreign bodies in the heart was 20 percent and that the mortality from operations for their removal was no less, with the probability that many unsuccessful attempts had escaped publication and that therefore the risk was understated. Likewise, Turner [77] at this time (1941) advised caution, with the admonition: "It would seem to be a good rule to leave the foreign body alone unless the heart continues to rebel against its presence."

On the other hand, after World War I, a considerable group of well-informed surgeons, including Leriche,[78] Delorme (p. 447), Tuffier,[79] and Sauerbruch,[80] advocated the removal of all foreign bodies lodged in the heart. Sauerbruch recorded in 1941 a series of 105 patients from whose hearts foreign bodies had been taken to control late complications, with a mortality of 8 percent. Further, he concurred with Stephens (cited by Barrett), who stated that, although 95 percent of people who survive cardiac injuries and who have foreign bodies in their hearts are symptomless, only 13 percent continue to be well indefinitely.

Since these conflicting opinions were expressed by able observers, the experience gained in another war has added to our knowledge. It was the author's privilege during World War II to assemble and review on behalf of the Mediterranean theater surgeon (and his medical and surgical consultants [81]) the total experience with wounds and injuries of the heart in the North African, Sicilian, and Italian campaigns from November 1942 until the end of hostilities in May 1945.[82] This material consisted of 94 cases (of which 15 were personally observed) and included the cases recorded in the report of the 2d Auxiliary Surgical Group and additional cases encountered by others in the Mediterranean theater. The pertinent features of the total experience are as follows:

Wounds of the ventricular wall occurred in 53 cases; of the auricular wall, in 5; and of the pericardium alone, in 22. The remaining 14 patients presented a variety of conditions, including 3 with retained missiles for 9,

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[76] Decker, H. R.: Foreign Bodies in the Heart and Pericardium—Should They Be Removed? J. Thoracic Surg. 9: 62–79, October 1939.

[77] Turner, G. G.: A Bullet in the Heart for Twenty-Three Years. Surgeon 9: 832–852, June 1941.

[78] Leriche, R.: Sur un Cas d'ablation de Corps Etranger du Coeur Suivie de Guérison. Rev. de chir., Paris 51: 274, 1916.

[79] Tuffier, T.: Surgery of the Heart. Cinquième Congress la Societe International de Chirurgie Rapports Proces-Verbaux et Discussions. Bruxelles: M. Hayez, 1921, pp. 5–75.

[80] Sauerbruch, F.: Steckgeschosse in Herz und Lunge. Deutsche Ztschr. f. Chir. 255: 152–170, 1941.

[81] Col. Perrin H. Long, MC, and Col. Edward D. Churchill, MC, respectively.

[82] Bland, E. F.: War Wounds of the Heart: A Report of 94 Cases With a Note on Foreign Body Emboli. [Unpublished data, The Surgeon General's Office, U.S. Army, 1945.]

13, and 20 years, respectively, and 4 others in whom metallic shell fragments migrated in the bloodstream from distant wounds.

Cardiac tamponade occurred in 12 cases. It was relieved by early surgical intervention in 10 but was an unexpected post mortem finding in the remaining 2. In an additional eight patients, active hemorrhage of serious proportions was encountered at operation, but the escape of blood into the pleural cavity through the pericardial laceration prevented the development of tamponade.

Pericardial effusion of clinical significance occurred in seven cases. Its delayed appearance from 2 to 6 weeks after injury in one-fourth of those with retained foreign bodies was of special interest. Pneumopericardium was a complication in three, and in one additional patient purulent pericarditis was successfully relieved by surgical drainage.

Intracardiac mural thrombi were found post mortem in three cases, and thrombosis of an injured left coronary artery was noted in another fatal case. Peripheral emboli from the heart were not encountered.

Missiles were removed at operation from the myocardium in 11 patients, in 1 of whom it extended into the ventricular cavity, and from the pericardium in 3 others. All made good recoveries. In 18 cases, foreign bodies remained within the heart or pericardium and, in 2 additional cases, against the ascending aorta. The subsequent progress of these patients should be followed carefully in connection with the unsettled question of future hazards from retained missiles. The intravascular migration of metallic fragments was recorded in four cases.

The mortality figure of 24.4 percent for this series, as contrasted with 45.5 percent for 428 cases collected from the literature in 1934 by Ramsdell,[83] is noteworthy. Probably three factors were chiefly responsible for this striking reduction: (1) Early administration of plasma and blood, (2) chemotherapy and antibiotics, and (3) expert surgical intervention close to the frontlines.

Complete perforation of the heart with survival is unusual. In the Mediterranean theater series, there were four cases with two survivors. In one of these (Samson's case),[84] in addition to a diagram of the operative findings (fig. 57), electrocardiograms were available during the recovery phase and are reproduced here as a matter of interest (fig. 58).

The migration of metallic fragments in the bloodstream is a bizarre complication, not necessarily fatal. The fragments usually enter by way of the great veins in the thorax, by the hepatic veins from liver wounds, or through the inferior vena cava, pass with the bloodstream to the chambers of the right side of the heart and, occasionally, on into the pulmonary circulation to lodge finally in a major pulmonary artery. Thus, a foreign body

[83] Ramsdell, E. G.: Stab Wounds of the Heart. Ann. Surg. 99: 141–151, January 1934.

[84] Samson, P. C.: Two Unusual Cases of War Wounds of the Heart. Surgery 20: 373–381, July-September 1946.
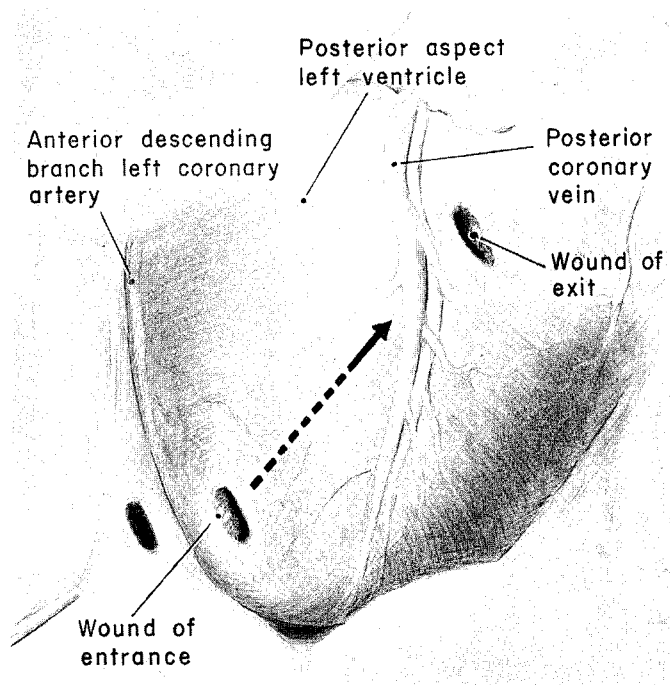
FIGURE 57.—Diagram of the operative findings in a patient with through-and-through perforation of the left ventricle. (Samson, P. C.:   Surgery 20: 373–381, July-September 1946.)

at the hilum of the lung is sometimes found at operation impacted in a pulmonary artery. Harken and Williams [85] encountered this in patients in the European theater, and a striking example of a casualty of the Italian campaign (in the Mediterranean theater series) is recorded herewith:

On 12 April 1944, an infantryman of the 45th Infantry Division received multiple severe penetrating wounds of the *right* thorax, right leg, and both feet. Roentgenogram showed a large metallic body at the hilum of the *left* lung. On 28 April, after transfer to a general hospital, his condition seemed good except for moderate dyspnea. Further X-ray study confirmed the presence of the foreign body in the left lung (fig. 59). On 10 May (4 weeks after injury), dissection of the left hilar region by Maj. Thomas H. Burford, MC (2d Auxiliary Surgical Group), failed to reveal the foreign body, and the chest was closed. Recovery was uneventful. Postoperative roentgenograms revealed the foreign body now at the right hilum (fig. 60). On 9 July (3 months after injury), a right thoracotomy revealed the foreign body impacted in the right pulmonary artery. The circulation to the lung seemed entirely adequate, and a palpable thrill was felt over the artery for a short distance distal to the foreign body. A complete dissection of the hilar structure did not mobilize the artery sufficiently to permit an arteriotomy, since the involved segment was directly beneath the superior pulmonary vein anteriorly and rested upon the right

[85] Harken, D. E., and Williams, A. C.: Foreign Bodies In, and In Relation To, the Thoracic Blood Vessels and Heart; Migratory Foreign Bodies Within the Blood Vascular System. Am. J. Surg. 72: 80–90, July 1946.

stem bronchus posteriorly. Furthermore, since there was no evidence of aneurysmal dilatation of the artery or of inadequacy of the pulmonary circulation, it was decided not to sacrifice the superior pulmonary vein. The chest was closed, and convalescence was uneventful except for a disproportionate degree of dyspnea for a few days after operation. On 16 August 1944, the patient was transferred to the Zone of Interior, ambulant and in good condition. A followup letter in October (6 months after the injury) reported no further studies or operative procedures and no symptoms other than dyspnea on fast walking.[86]
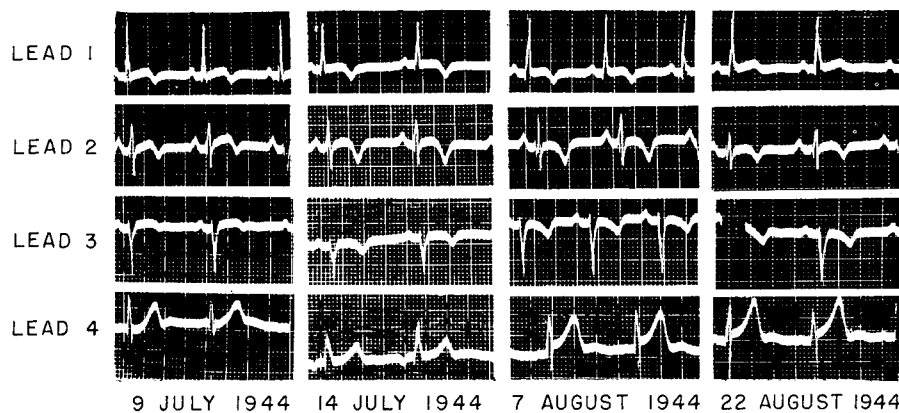
FIGURE 58.—Electrocardiograms during recovery from the through-and-through wounds of the left ventricle in Samson's case (fig. 57). (Bland, E. F.: Am. Heart J. 27: 588, 1944.)

It is of interest that, during a review of this unusual case shortly after the first thoracotomy, Col. Edward D. Churchill, MC, suggested that the fragment had originally entered the superior vena cava and passed through the right heart chambers to the left pulmonary artery and later, just before or during operation, shifted intravascularly to the right pulmonary artery. In any event, the absence of infarction and significant impairment of respiratory function is remarkable.

A curious and further variant from the usual migration of foreign bodies in the direction of blood flow is represented by the infrequent case where the metallic fragment arriving in the right auricle passes down the inferior vena cava against the stream to lodge in the cava or in one of its main branches, as observed by Cutler [87] in World War I and by others [88] in World War II.

In contrast to the Mediterranean theater data where the emphasis was upon the management of cardiac wounds in the forward installations and

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[86] Burford, T. H.: Personal communication, 1945.

[87] Cutler, E. C.: Migration of Shell Fragment From Inferior Vena Cava to Right Pulmonary Artery. Mil. Surgeon 53: 264–267, September 1923.

[88] Davey, W. W., and Parker, G. E.: Surgical Pursuit and Removal of Metallic Foreign Body From Systemic Venous Circulation. Brit. J. Surg. 34: 392–395, April 1947.
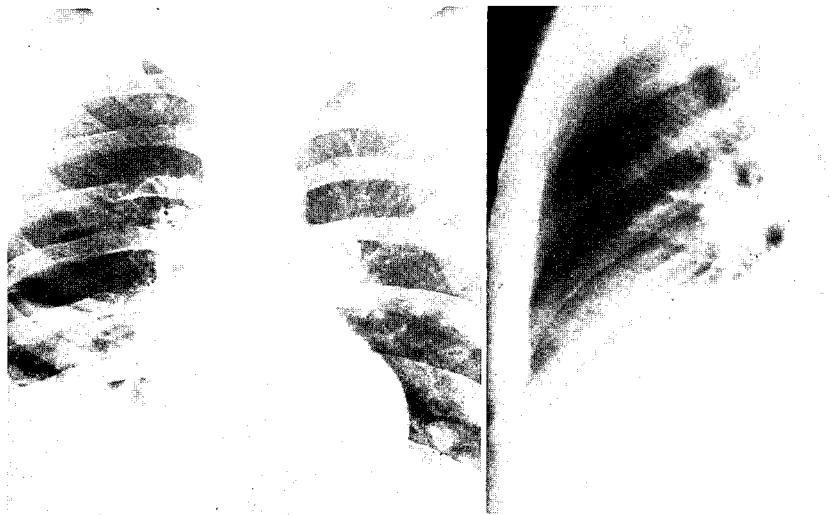
FIGURE 59.—Roentgenograms showing an embolic shell fragment in the left pulmonary artery.

early protective operations, the extensive experience of Harken and his collaborators [89] at the base center in England has a more direct bearing on the problems of later definitive and often elective surgery, in particular with the much discussed issue of retained foreign bodies. Their three reports cover a series of 134 fragments removed from within or adjacent to the heart and great vessels. The following tabulation shows the distribution of the 134 missiles in relation to the pericardium, heart, and great vessels:

	Number of fragments
Pericardial	26
Involving pericardium, but principally pulmonary	17
Intracardiac	13
On great vessels (and in walls)	35
Intravascular (three embolic)	7
On great vessels, but principally pulmonary	17
Mediastinal, but not directly on great vessels	19
Total	134

There were no deaths in the three cited reports.

In particular, the successful evacuation of 13 missiles from within the cardiac chambers without mishap represents a brilliant extension of the

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[89] (1) See footnote 82, p. 448. (2) Harken, D. E.: Foreign Bodies In, and In Relation To, the Thoracic Blood Vessels and Heart. Techniques for Approaching and Removing Foreign Bodies From the Chambers of the Heart. Surg., Gynec. & Obst. 83: 117–125, July 1946. (3) Harken, D. E., and Zoll, P. M.: Foreign Bodies In, and In Relation To, the Thoracic Blood Vessels and Heart. Indications for the Removal of Intracardiac Foreign Bodies and the Behavior of the Heart During Manipulation. Am. Heart J. 32: 1–19, 1946.
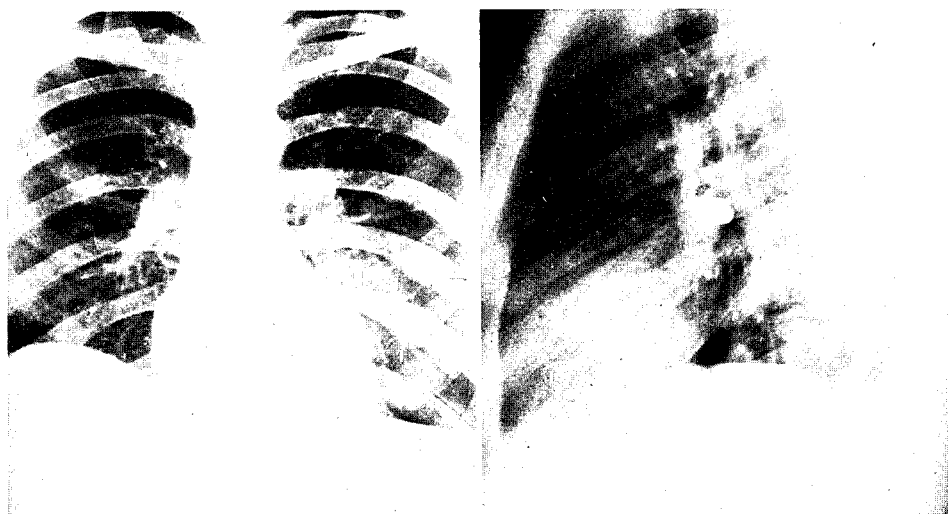
FIGURE 60.—Roentgenograms showing the foreign body illustrated in figure 59, now lodged in the right pulmonary artery.

earlier French experience in World War I. This, together with the equally favorable outcome in removing fragments from the heart wall, both in the European theater and in the Mediterranean theater series (11 cases) without a fatality, represents a real advance in heart surgery. It in turn strengthens the position of those who believe all foreign bodies had best be removed. In particular, Harken and his associates naturally and strongly recommend their removal, in order (1) to prevent embolus of the foreign body or associated thrombus, (2) to reduce the danger of bacterial endocarditis, (3) to prevent recurrent pericardial effusions, and (4) to diminish the incidence of myocardial damage. The additional factors of pain and cardiac neurosis are occasional indications.

It seems appropriate to end this discussion with the conclusions of Barrett (p. 446) who, after a thoughtful consideration of both sides of the issue, observed:

There are three clinical phases in the history of these patients in which a decision must be taken. In the emergency the concern is to save life and the presence of a foreign body in the heart is of secondary importance. During the period of convalescence and shortly after, the decision to operate depends upon the belief that late complications can be avoided, or that limitations of cardiac function can be ameliorated without exposing the patient to mortal hazard. Patients who have harboured a foreign body in the heart for years without apparent harm will not want it removed, but they may come to the surgeon when complications occur; some of these late complications can still be relieved by removal of the foreign body, but others are by now beyond surgical cure.

To the medically minded, and especially to those who have discovered by chance retained foreign bodies of many years' standing, the sentiments

attributed to Frank Jeans but quoted in this connection by Turner (p. 448) still have some appeal: "A living problem is better than a dead certainty."

SUMMARY

In summarizing this survey of diseases and disorders of the heart in the Second World War, it seems appropriate to commend again the wisdom and foresight of those responsible for the special Subcommittee on Cardiovascular Diseases. The wise counsel and sustained activities of this group throughout the emergency not only contributed directly to the war effort but, also, in various subtle ways afforded encouragement and aid to many doctors in uniform in their pursuit of useful knowledge. This coordination of military personnel, civilian consultants, and Government resources was of great practical benefit and lasting importance, and the lessons learned may serve well another generation should the need arise.

The special attention given to the circulatory system in the selection for service provided an insight into the strength as well as the weakness of our eligible population and, though it proved to be disturbing in certain respects, stimulated the thoughtful planning of special studies in the fields of hypertension and of latent coronary disease. The spread of respiratory infections in training centers led to a number of important epidemiological studies and, in turn, to effective programs of control and prevention, not only of streptococcal diseases but of rheumatic fever as well.

That traditionally troublesome complex, neurocirculatory asthenia (including shellshock) at best poorly understood, was again the object of careful analysis. Its apparent diminished incidence, in comparison with previous conflicts, was perhaps the result both of its earlier detection and of a shift in emphasis to its manifestations on other systems. In the oversea theaters, especially in the Southwest Pacific, the opportunity to observe and to delineate more carefully than ever before the cardiac lesions of tsutsugamushi fever was a noteworthy event. Elsewhere, our surgical colleagues, with the support of modern anesthesia, antibiotics, and blood, pushed forward in brilliant fashion to remove missiles from within the heart and great vessels more effectively than ever before. There still remains, moreover, an equal opportunity and obligation in this connection for the Army Medical Corps and the Veterans' Administration to trace and record the ultimate fate of that considerable number of soldiers who were discharged from the service with retained missiles in the cardiovascular system.

It is unlikely in future crisis of comparable magnitude that the United States can afford to write off one-half or even one-quarter of its eligible manpower as unfit for service by the standards of World War II. It now seems certain that future circumstances will require either broader standards or new categories whereby those with minor defects may serve with recognition, if not in the lines at least on the production front.

The preparation of this chapter on the heart has been a personal privilege. It is submitted as a token of gratitude to our patients of the war years—the men and women of the Armed Forces who in spite of illness and injury did all they could to help. For the members of the medical profession who shared a little in this great effort, the recollection of those eventful years has probably been dimmed by other interests and new responsibilities, but to them in quieter moments of reflection the words of that noble Irish churchman, Jeremy Taylor, written in equally turbulent times three centuries ago may have a special significance: "To preserve a man alive in the midst of chances and hostilities is as great a miracle as to create him." [90]

[90] Taylor, Jeremy (1613–67), cited by Hume, E. E.: Introduction to Military Medicine. Mil. Surgeon 102: 17–24, January 1948.

CHAPTER XVII

Peripheral Vascular Disorders

Fiorindo A. Simeone, M.D., **and**
Robert W. Hopkins, M.D.

Peripheral vascular disorders encountered in World War II have been described in considerable detail in earlier volumes of the official history of the U.S. Army Medical Department in World War II.[1] Trauma encountered in epidemic proportions during wartime provides a wealth of experience not found in civilian medicine, and accordingly, vascular abnormalities occurring subsequent to injury have provided most of the data for these volumes.

Work in the forward areas of theaters of operations provided an invaluable experience with early wounds of blood vessels and with such conditions as cold injury. From this experience, a number of earlier erroneous impressions were corrected, improved methods of prophylaxis and management of these injuries were suggested, and newer forms of therapy were evaluated. In the Zone of Interior, vascular centers were established to provide competent specialized care for large numbers of patients with vascular injuries and diseases. These centers provided not only facilities and personnel for optimum treatment, but also an unparalleled opportunity for study of the problems the patients presented. Significant improvements in the late management of arterial injuries and cryopathies resulted from work at these centers. Ideas and techniques were explored which forced the remarkable later advances in cardiovascular surgery.

Vascular disorders not directly the result of military action were observed in induction centers, in military medical units, and in the specialized vascular centers. These observations have provided data on the incidence and logistic significance of vascular disease in men of military age and on the effects of the military environment on men with these diseases. Insofar as the cases are documented by their military medical records, they constitute a group from which rosters can be developed for long-term followup studies. Such investigations can greatly benefit both military and civilian medicine and surgery.

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[1] (1) Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955. (2) Medical Department, United States Army. Cold Injury, Ground Type. Washington: U.S. Government Printing Office, 1958.

CENTERS FOR VASCULAR INJURY AND DISEASE

Experience with casualties returned to the Zone of Interior during the first year of the war suggested the need for specialized care of patients with certain injuries and diseases. However, the rapid increase in numbers of military hospitals precluded the assignment of adequate numbers of highly trained medical personnel to them. Nor could specialized equipment be made available to all general hospitals. Accordingly, specialized hospitals were designated for the treatment of such conditions by authority of War Department Memorandum No. W40–14–43, dated 28 May 1943.

Centers for the treatment of vascular disturbances first were established under this memorandum, in May 1943, in West Virginia at Ashford General Hospital and in California at Letterman General Hospital. In June 1944, a third center was established in the Middle West at Percy Jones General Hospital. Because of changing demands upon the facilities and of increased requirements for space, the center in California initially established at Letterman in San Francisco was transferred, in December 1943, to Torney General Hospital in Palm Springs, Calif., and from there, in June 1944, to DeWitt General Hospital in Auburn, Calif. The Middle West center was transferred in September 1944, shortly after its establishment (June 1944), from Percy Jones in Battle Creek, Mich., to Mayo General Hospital in Galesburg, Ill. Ashford General Hospital in White Sulphur Springs, W. Va., remained a center for vascular diseases throughout the war (May 1943–June 1946).

Referrals to the vascular centers, in accordance with the memorandum of 28 May 1943, included patients with the following disorders: "Major vascular injuries and their sequelae such as arteriovenous fistulae, aneurysms, and peripheral vascular disturbances such as chronic vasospastic conditions, those resulting from frostbite, immersion foot, and other conditions producing peripheral circulatory deficiency states; but not including minor disturbances such as varicose veins."

The advisability of providing centers for the study of vascular diseases not resulting from trauma was taken under consideration by the Office of The Surgeon General, in December 1943, and although the incidence of nontraumatic vascular diseases was not sufficient to warrant special centers, the advantages of the centers for study as well as for therapy provided strong argument in their favor. Therefore, centers for nontraumatic vascular diseases were established in association with the existing vascular centers, in August 1944. In accordance with War Department Circular No. 347, dated 25 August 1944, the designation of patients to be referred to the vascular centers was modified to include the following: "Patients with peripheral vascular disturbances, such as chronic vasospastic conditions, Raynaud's phenomenon, thromboangiitis obliterans, and the sequelae of trenchfoot, immersion foot, and frostbite; patients with peripheral vascular

injuries and their sequelae, such as arteriovenous fistulae and aneurysms. Does not include minor disturbances such as varicose veins."

At Mayo General Hospital, separate but closely cooperating medical and surgical sections were established with the activation of the vascular center on 15 September 1944. A similar organization was created in the vascular center at DeWitt General Hospital, in May 1945. At Ashford General Hospital, internists were assigned to the vascular service in the surgical section. The number of beds available at the three vascular centers varied during the hostilities, reaching a peak of 1,900 during the early months of 1945. In addition to providing an optimum in specialized care for these patients, the centers provided a unique opportunity for the study of patients with the vascular conditions cited in the directives of 1943 and 1944. The Annual Report of Ashford General Hospital for the year 1944, noting the 400 beds for vascular patients in use in the hospital and the 183 patients who had been operated upon for arterial aneurysm and for arterio-venous fistula, observed: "This is unquestionably the largest number of patients with these conditions treated in any clinic in a similar period of time and the largest number of aneurysms and arteriovenous fistulas treated by operation in one institution throughout any period of time." Publications from this experience and similar experiences in the other centers comprise an invaluable contribution not only to military surgery and the surgery of trauma, but to civilian medicine as well.

Clinical observations of the patients in the vascular centers provided much valuable information concerning the clinical course and management of vascular injuries, late sequelae of cold injury, and other vascular disturbances. The desirability of obtaining detailed physiologic studies on patients in the vascular centers was well recognized by the medical personnel in charge. Difficulties and delays were encountered in procurement of proper equipment, however, and when these did become available, adequate numbers of trained personnel were no longer available to carry out the studies.[2] The numbers of physiologic studies of the circulation made in these patients were, therefore, regrettably few.

Although the detailed organization of the vascular services in the several hospitals differed, the cooperation of the various disciplines involved in the care of the patients in these services was an essential factor in the success of the centers. Internists and surgeons participated jointly in the management of the vascular problems encountered. Collaboration of the departments of roentgenology supported the programs at all centers. Departments of physical therapy and reconditioning and departments of occupational therapy were invaluable for the long-term management of the patients with vascular disease.

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[2] (1) Annual Report, Mayo General Hospital, 1945. (2) See pp. 11–16 in publication cited in footnote 1(1), p. 457.

ACUTE VASCULAR INJURIES

The most significant progress in the surgery of wounds in the U.S. Army in World War II was made in the prevention and control of infection. The principles of adequate debridement of wounds with removal of devitalized tissue and foreign debris followed by delay in closure of wounds became well established. Improvement in the prevention and control of infection by the employment of these advances in wound surgery and by the use of chemotherapeutic and antibiotic agents was reflected by the relative increase in the importance of arterial occlusion as an indication for amputation. While figures indicate that amputation was required for infection 5 times as often as for arterial injury in the German Army and 16 times as often in the Russian Army, data from American battle casualties show arterial injury to be nearly twice as frequent a reason for amputation as infection (table 80). Additional benefit from improved control of infection was observed in the decrease in secondary hemorrhage from wounds. Freeman [3] reported an incidence of 1 percent of secondary hemorrhage among 2,168 patients with wounds of the neck and extremities treated at the 20th General Hospital in Assam, India. In World War I, Waugh [4] reported an incidence of 14 percent from wounds in which long bones were involved.

TABLE 80.—*Indications for amputation among German, Russian, and American casualties, in World War II*

Amputation	Casualties		
	German	Russian	American
Cause:			
Extensive trauma_____percent__	64.3	16	68.6
Clostridial myositis or other infection_____percent__	29.7	79	11.9
Arterial injury_____percent__	6	5	19.5
Number studied_____	1,359	_____	3,177

NOTE.—Percentages are based on the total number of amputations studied.

Source: DeBakey, Michael E., and Simeone, Fiorindo A.: Acute Battle-Incurred Arterial Injuries. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, text pp. 66–67.

The nature and location of arterial wounds in relation to the incidence of amputation were studied by DeBakey and Simeone.[5] Amputation was

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[3] Freeman, N. E.: Secondary Hemorrhage Arising From Gunshot Wounds of Peripheral Blood Vessels. Ann. Surg. 122: 631–640, October 1945.

[4] Waugh, W. G.: Secondary Hemorrhage. *In* Bailey, Hamilton (editor): Surgery of Modern Warfare. Baltimore: Williams & Wilkins Co., 1941, vol. 1, pp. 328–332.

[5] DeBakey, Michael E., and Simeone, Fiorindo A.: Acute Battle-Incurred Arterial Injuries. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, chart 12, p. 81.

required in approximately 30 percent of cases in which simple laceration of the artery occurred and in about 50 percent when the artery was transected. Injury associated with arterial thrombosis carried a much poorer prognosis, with loss of limb occurring in 70 percent of these patients.

The incidence of amputation with wounds of specific arteries (table 81) was noted to be at variance with previous observations and reports. In general, wounds of the arteries in the lower extremity were more likely to be followed by amputation than those in the upper extremity. The highest proportion of gangrene occurred following injury to the popliteal artery, a finding in marked contrast to some earlier impressions.[6] Injury to more than one major artery in an extremity was also followed by decreased salvage of the limb.

TABLE 81.—*Incidence of amputation following arterial injuries, U.S. Army casualties, World War II*

Artery	Total injuries (number)	Amputations	
		Number	Percent
Brachial	601	159	26.5
Subclavian	21	6	28.6
Radial and ulnar	28	11	39.3
Axillary	74	32	43.2
External iliac	30	14	46.7
Common iliac	13	7	53.8
Femoral	517	275	53.2
Anterior and posterior tibial	91	63	69.2
Popliteal	502	364	72.5
All others	594	64	10.8
Total	2,471	995	40.3

Source: DeBakey, Michael E., and Simeone, Fiorindo A.: Acute Battle-Incurred Arterial Injuries. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, modified table 3, p. 69.

While the usual treatment for arterial wounds was ligation of the artery, restoration of blood flow by suture of lacerations, anastomosis of the severed ends of vessels, or vein grafting was attempted in a few instances. Unfortunately, the military situation and other considerations usually precluded attempt to repair the artery. The timelag between injury and arrival at a field hospital in a sample of 104 first-priority patients in the Mediterranean theater averaged 12½ hours, considerably over the maximum safe time for arterial repair. In addition, the time required for the meticulous surgery involved was rarely justified, nor were sufficient experi-

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[6] National Research Council, Division of Medical Sciences: Burns, Shock, Wound Healing and Vascular Injuries. Prepared under the auspices of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Military Surgical Manuals, vol. 5. Philadelphia: W. B. Saunders Co., 1943.

enced personnel available in most hospitals in the field. Results in cases where repair was attempted were not uniformly good, although specific instances where salvage of a limb could be attributed to restoration of arterial flow were observed. Satisfactory evaluation of the indications and overall usefulness of methods for direct repair could not be made from this series.

POSTTRAUMATIC ARTERIAL ANEURYSMS AND ARTERIOVENOUS FISTULAS

The policy of management of aneurysms and arteriovenous fistulas in the oversea areas was entirely conservative. Usually, these lesions did not become manifest for several weeks. When they were observed, delay was warranted for several reasons: to allow complete disappearance of any initial infection, to diminish the likelihood of secondary infection or secondary hemorrhage, to allow collateral circulation to develop, and to allow the aneurysm in the rare instance to heal spontaneously.

At the vascular center at Mayo General Hospital,[7] spontaneous thrombosis with apparent cure was observed in 10 of 119 traumatic arterial aneurysms. Flow apparently continued through the artery involved in five of the nine cases where the observation was recorded. At this center, also, spontaneous closure of the fistula was observed in 8 of 245 arteriovenous fistulas. Three of these required operation for an associated saccular aneurysm. At operation, thrombosis of the vein in all three was observed as the mechanism of obliteration of the fistula. Although of considerable interest, these spontaneous "cures" did not appear with sufficient frequency to indicate per se a prolonged period of observation before institution of surgical therapy.

Circulatory Studies of Patients With Arteriovenous Fistulas

Data concerning circulatory dynamics in patients with arteriovenous fistulas studied at Ashford General Hospital are summarized in table 82.

The cardiac output was studied preoperatively and postoperatively in 47 patients by means of a low frequency, critically damped ballistocardiograph.[8] The accuracy of the method was checked against comparative studies by the direct Fick technique. None of the patients in this group had evidence of frank heart failure.

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[7] Shumacker, Harris B., Jr.: Arterial Aneurysms and Arteriovenous Fistulas: Spontaneous Cures. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 361–374.

[8] Starr, I., Rawson, A. J., Schroeder, H. A., and Joseph, N. R.: Studies on Estimation of Cardiac Output in Man, and of Abnormalities in Cardiac Function, From Heart's Recoil and Blood's Impacts; Ballistocardiogram. Am. J. Physiol. 127: 1–28, August 1939.

TABLE 82.—*Summary of preoperative and postoperative observations of 47 patients with arteriovenous fistulas*

Observation	Preoperative	Postoperative
Average duration of fistula_____months__	6.7	_____
Heart rate_____beats per minute__	73.2	71.1
Stroke volume_____milliliter__	118.1	92.8
Cardiac index_____liters per minute per square meter__	4.9	3.7
Change in transverse diameter of heart_____centimeter__	_____	.45
Change in whole blood volume_____milliliter per square meter__	_____	229

The preoperative resting cardiac output was found to range from 21 percent below to 127 percent above the postoperative (normal) value. A 25-percent variation in cardiac output was considered within a normal range. Of the 47 patients, 25 exceeded this range and were therefore considered to have had a significantly elevated cardiac output before surgery. The decrease in cardiac output after surgery was attributed chiefly to a change in stroke volume rather than to heart rate. The basal heart rate preoperatively was above 85 in only 7 of the 47 patients.

Studies were also carried out on 25 patients with temporary occlusion of the arteriovenous fistula effected by means of a pneumatic tourniquet. In 17 of the 25 patients, a prompt decrease in heart rate, ranging from 4 to 32 beats per minute, was observed (Branham's (Nicholadoni's) sign). In 19 patients, the stroke volume decreased by more than 10 ml. with sudden occlusion of the fistula. A decrease of the cardiac index of 0.5 to 3.6 liters per square meter of body surface was observed in 22 of the 25 patients. In five patients, additional tests were carried out following the administration of atropine. The pulse rate rose, and in some instances, the cardiac index increased. Occlusion of the fistula at this time was not followed by a change in pulse rate greater than 4 beats per minute, while the cardiac index declined in amounts ranging from 1.0 to 2.2 liters per square meter.

Determinations of the plasma and whole blood volume were made using the blue dye T–1824 (Evans blue) in 41 patients at Ashford General Hospital. Measurements were made preoperatively and 10 or more days postoperatively in all patients. In 23 patients, the change in blood volume was less than 200 cc. per square meter, considered to be within the range of normal variation. In 18, there was a postoperative decrease in blood volume, ranging from 200 to 1,060 cc. per square meter of body surface. Preoperative and postoperative determinations of hematocrit varied only slightly, indicating that parallel changes occurred in the volumes of plasma and of whole blood.

Studies on the effects of arteriovenous fistulas on heart size were carried out at the vascular centers. The data obtained at Mayo General Hospital[9] include measurements of cardiac frontal area from teleroentgenograms of 185 patients. The predicted and actual frontal areas of the cardiac silhouette were calculated according to the method of Ungerleider and Gubner.[10]

Preoperative measurements were in excess of 105 percent of predicted values in 55 percent of 153 of the 185 patients and in excess of 125 percent of predicted values in 12 percent. Postoperatively, no patient had measurements in excess of 125 percent of the predicted values and 27 percent exceeded 105 percent of the predicted size. Although definite conclusions could not be drawn, fistulas of long duration appeared to be associated with a greater increase in heart size than were those of shorter duration. Patients with larger fistulas also tended to have larger cardiac silhouettes.

There were two instances of frank congestive failure in this group. One of these with two arteriovenous fistulas had been in failure before resection of an external iliac fistula prior to his admission to a vascular center. The other was a patient with a *Streptococcus viridans* infection of a femoral arteriovenous fistula. The case history of this patient, the fourth with bacteremia of this origin to be reported, has been presented in detail elsewhere.[11] This patient was relieved of all his symptoms following resection of the arteriovenous fistula.

The findings in these patients tended to confirm previous impressions of abnormal circulatory dynamics drawn from relatively isolated cases in civilian experience. The numbers of patients studied here, however, added a wealth of preoperative and postoperative data in patients in whom the fistulas were successfully closed by surgery.

Surgical Management of Aneurysms and Arteriovenous Fistulas

Two technical considerations may be noted here briefly in the light of their influence on subsequent developments in vascular surgery. The first is the improvement of techniques for surgical exposure of major vessels, especially in the mediastinum. Further use and extensions of these procedures developed for managing traumatic lesions have stimulated the remarkable developments in the surgery of lesions of the great vessels. The second is the development of a policy favoring restoration of normal arterial and venous blood flow instead of interruption of the affected vessels.

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[9] Shumacker, Harris B., Jr.: Arterial Aneurysms and Arteriovenous Fistulas: Alterations in the Cardiac Size in Arteriovenous Fistulas. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 206–224.

[10] Ungerleider, H. E., and Gubner, R.: Evaluation of Heart Size Measurements. Am. Heart J. 24: 494–510, October 1942.

[11] Elkin, Daniel C., and Shumacker, Harris B., Jr.: Arterial Aneurysms and Arteriovenous Fistulas: General Considerations. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 165–173.

Because of the presence of collateral circulation adequate to maintain viability of a limb in the presence of aneurysms and arteriovenous fistulas, ligation was considered the safest procedure, and repair of the artery was not commonly attempted until the last months of the war. It became increasingly evident, however, that although a viable limb was maintained, the function of the extremity was often seriously impaired.

During the latter part of the war, therefore, repair of the artery with preservation of its lumen became the rule in appropriate cases.[12] While only 4 reparative procedures had been performed in the first 138 cases at Mayo General Hospital, 30 of the last 57 cases were handled in this manner. Similarly, restoration was attempted for 23 of 67 patients operated upon at DeWitt General Hospital from June to November 1945. Of these 57 attempts at repair, 46 (81 percent) were successful in preserving normal blood flow. Largely as a result of these successes, surgeons were no longer content with the previous goal of maintaining a viable limb. The importance and feasibility of restoring normal arterial flow and normal function of the limb became established.

COLD INJURY

The ravages of cold injury in warfare have seldom been effectively anticipated. Serious consequences in terms of significant losses of military manpower and subsequent chronic disability to individual soldiers have occurred through the centuries of military operations forced upon commanders in severe cold and in wet terrain. Yet, in each war, the lesson has had to be learned anew. It is especially regrettable that these losses occur in spite of the fact that cold injury is a preventable disease. With proper indoctrination of troops and adequate provision of proper footgear, the condition can virtually be eliminated.

The nature of the problem makes effective preventive measures a responsibility of command rather than of the Medical Department. However, this responsibility historically has not been recognized by higher command and staff echelons until loss of combat manpower brought the problem acutely to the foreground.

In World War II, the first experience with cold injury among American troops occurred on the Aleutians. Here, a high incidence of injury occurred among men exposed to cold and wet with inadequate indoctrination and improper clothing. In sharp contrast was the paucity of cold injury in a single unit which had had earlier experience on maneuvers in cold weather.[13]

These lessons were not immediately transferred to the Mediterranean theater, and the first winter of fighting under difficult circumstances, that

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[12] Freeman, Norman E., and Shumacker, Harris B., Jr.: Arterial Aneurysms and Arteriovenous Fistulas: Maintenance of Arterial Continuity. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 264–301.

[13] Orr, R. D.: Report on Attu Operations. May 11–June 16, 1943, dated 30 July 1943.

of 1943–44, saw a distressing number of casualties from cold injury. Preventive measures were instituted too late to be effective during this first winter, but their value was well demonstrated during the subsequent winter, 1944–45.

A consideration of vital statistics emphasizes the military significance of this preventable disease. The incidence of cold injury in World War II is summarized in table 83. A total of 7,514,000 man-days were lost during the period of 1942–45. This is equivalent to the loss of an entire division, 15,000 strong, for 16 months. Disregarding the time factor and calculated on the basis of loss of combat troops in the European theater alone in 1944–45, it can be said that about 5 divisions (derived from approximately 70,000 cases) were lost to combat. However, since about 90 percent of all cold injury casualties were riflemen and since some 4,000 riflemen were in each infantry division, the loss of effective fighting strength could be interpreted as more nearly 16 divisions than as 5 divisions. This loss of combat manpower was in addition to the huge logistic cost in terms of transportation, hospital occupancy, and professional and nursing care.

The experience with cold injury in World War II provided a wealth of material from which clinical and pathologic observations could be made.

TABLE 83.—*Incidence* [1] *of cold injury in the U.S. Army (including the Army Air Forces), by specific diagnosis and theater, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]

Theater or area	Total cold injuries	Trench-foot	Frostbite	Immersion foot (or hand)	Chilblains	Other effects of cold
All theaters and areas_____	90,535	64,590	19,559	1,451	971	3,964
Continental United States_____	5,203	315	4,342	36	335	175
Total outside continental United States_____	[2] 85,332	64,275	15,217	1,415	636	3,789
Europe_____	71,038	53,911	13,134	506	204	3,283
Mediterranean [3]_____	11,192	9,778	765	322	272	55
Middle East_____	33	22	11	_____	_____	_____
China-Burma-India_____	35	7	12	_____	15	1
Southwest Pacific_____	578	351	10	214	3	_____
Central and South Pacific_____	139	26	36	68	1	8
North America [4]_____	2,225	145	1,230	295	141	414
Latin America_____	28	25	1	1	_____	1

[1] Consists of both admissions for cold injury and cases in which admission was for other conditions but in which cold injuries appeared as secondary diagnoses. Data on secondary-diagnosis cases are not presently available for 1942 and 1943, and for these 2 years, only admissions have been included in this table. It should be noted that cold injury admissions in 1942 and 1943 constituted but a small proportion of the World War II admissions for cold injury. For 1942 and 1943, admissions may be considered an approximation of incidence. During 1944–45, in the total Army, the incidence of cold injury exceeded admissions by 11 percent.

[2] Includes 64 cases among admissions on board transports.

[3] Includes North Africa.

[4] Includes Alaska and Iceland.

Source: Medical Statistics Division, Office of The Surgeon General, Department of the Army.

These are recorded in detail in the volume on cold injury [14] and will be summarized only briefly here.

Cold injury may be caused by exposure to dry cold or wet and cold in various combinations. Frostbite results from actual freezing of tissues. Wet and cold combine to cause injury in immersion foot with wetness predominating. In trenchfoot, wet and cold are relatively equal in importance as etiologic factors. Cold injury resulting from these factors may be considered basically the same pathologic process, with the extent and nature of the injury dependent upon the intensity and duration of the cold stimulus. In World War II, fought predominantly in temperate climates, trenchfoot was most common.

Other factors relating to the production of frostbite were considered extensively. Most important were factors classified as socioeconomic. These included (1) the intensity of combat activity, (2) the availability of proper clothing, especially footgear, (3) the attitude of those in command, (4) adequate training and discipline of troops in prevention of cold injury, (5) previous experience with cold weather, and (6) rotation of troops.

Although pathologic material in trenchfoot is generally limited, Friedman's [15] study of 14 specimens at various stages may be regarded as definitive. The histologic pattern was common to all cold injury. The essential early change was circulatory. There was marked engorgement of the vascular tree with extravasation of red blood cells. Agglutinative erythrocytic thrombi, poor in fibrin, of the type seen in stagnant blood, were commonly observed. Endothelial damage was not striking in early stages. Later, arteritis obliterans of varying degrees was present in arteries and veins.

Changes in fatty tissue were profound. Early leukocytic infiltration of the deeper subcutaneous tissues and proliferation of adventitial cells of prominent capillaries and smaller vessels in the interlobular fibrous septa were seen. Later, fat lobules were diffusely infiltrated with foam cells laden with fat, and fibrous replacement of adipose tissue was notable. Muscle tissues exhibited degeneration, necrosis, and inflammation but no atrophy in specimens of early trenchfoot. Atrophy, however, was extensive in all specimens of late cases. In early specimens, nerves in the area of inflammation were swollen and edematous, and degeneration of both axis cylinders and myelin was present. Damage was severe in areas of gangrene in late cases, and demyelinization and perineural fibrosis were marked. Many small vessels in the nerves were thickened, and lipoid phagocytosis was pronounced. Most of the changes observed, whether superficial or deep, were regarded as secondary to vascular occlusion. It was also thought that structures rich in lipoids, especially adipose tissue and myelinated nerve fibers, might sustain a direct thermal effect from cold trauma.

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[14] See footnote 1 (2), p. 457.
[15] Friedman, N. B.: Pathology of Trench Foot. Am. J. Path. 21: 387–433, May 1945.

Clinical picture.—Three separate phases in the clinical course of cold injury were described in World War II, as follows:

1. The preinflammatory stage, without blisters or gangrene. The skin was cold and might still be wet.

2. The inflammatory stage, characterized by vasodilatation, blisters with or without gangrene, and by edema and dryness of the skin. The skin was hot to palpation, except in the gangrenous areas.

3. The postinflammatory stage, characterized by coldness, cyanosis with or without gangrene, and by hyperhidrosis.

The preinflammatory stage (the ischemic or prehyperemic stage) usually lasted only an hour or two beyond the period of exposure except in cases with intense vascular involvement. The vasodilatation of the inflammatory stage became apparent almost immediately after the patient was removed from the cold environment. In cases where this was mild or almost undetectable, prompt return to duty was possible. More frequently, the vasodilatation was obvious and lasted for a week or more. Small patchy areas of ecchymosis were present at pressure points, and areas of superficial thrombosis were sometimes present. In severe cases, early blister formation was evident. Impending gangrene might be apparent, progressing to frank gangrene within 48 hours.

Pain was a prominent symptom in trenchfoot in all stages beyond the preinflammatory. This was in contrast to frostbite where pain was surprisingly absent. It persisted through the inflammatory, postinflammatory, and late stages, frequently lasting for months following evacuation to the continental United States. In specimens available for histologic study, it was often possible to relate pain to excessive perineural fibrosis.[16] Late in the postinflammatory stage of trenchfoot, the skin was delicate and waxy. Ambulation was considerably delayed by the long period of time before callus formation developed sufficiently to permit weight bearing. Claw foot and pes cavus deformities sometimes developed. Gangrene in cold injury, short of frostbite, was relatively uncommon, appearing in less than 10 percent of cases. In many instances, gangrene was less extensive than it originally appeared to be. Deep gangrene requiring amputation of any extent was rare. These observations indicated a conservative approach to excision of tissue, especially in the early stages of the disease process.

Efforts to find specific therapeutic measures applicable to cold injury were unrewarding. Initial treatment during World War II consisted chiefly in the avoidance of further trauma. The patient was most comfortable with the feet exposed at room temperature. No local applications appeared helpful. Drugs were not effective. A trial of early sympathetic block proved disappointing. Surgical treatment was limited to measures to maintain cleanliness, and with few exceptions, amputation of any sort was deferred

16 White, J. C., and Warren, S.: Causes of Pain in Feet After Prolonged Immersion in Cold Water. War Med. 5: 6–15, January 1944.

until the patient was evacuated to the Zone of Interior. In later stages, sympathectomy proved to be of some value in minimizing tissue loss and accelerating healing. When hyperhidrosis and maceration were prominent, sympathectomy was beneficial. It was of questionable value in limiting pain of weight bearing and in relieving the "burning" neuritic type of pain observed late in the disease.

The most significant advance in rehabilitation after cold injury was probably the demonstration of the value of early supervised exercise. The feet of patients from hospitals where this had been insisted upon were in much better condition, when the patient reached installations in the Zone of Interior, than were the feet of patients who did not participate in such early exercise. Radiographic evidence of osteoporosis of metatarsals and phalanges, often quite extensive, was maximal when early exercise had not been practiced. Weight bearing for these patients was often long delayed.

The importance of cold injury in terms of loss of manpower was also emphasized by the high recurrence rate among men returned to duty. Early estimates anticipated recurrences of about 15 percent. Experience with recurrences and recognition of the insidious and prolonged nature of the injury led the staffs of most hospitals in the Mediterranean theater to conclude that less than 10 percent of men who had suffered attacks of cold injury could be returned to combat duty.

THROMBOANGIITIS OBLITERANS

In World War II, 1,030 admissions of patients with a diagnosis of thromboangiitis obliterans were recorded, a rate of 4 per year per 100,000 average strength (table 84). Of these patients, 274 were admitted to the special vascular centers.[17] According to a study of 152 male patients with thromboangiitis obliterans seen in the vascular centers, the majority (122 patients) were between the ages of 26 and 40. The race of 2 was not recorded, 7 were Negroes, and 143 were Caucasians of whom 32 were Jews. Among the 152 patients, intermittent claudication was the most common symptom and was present in 67 percent. Many complained of pain or numbness in the foot. Migratory phlebitis was present in one-third of the patients, and ulceration was present in 20 percent. Gangrene was unusual and was found in only 4.4 percent of the cases treated in the vascular centers.

In addition to a complete history and physical examination, special procedures were used to study the patients at the vascular centers where constant-temperature rooms were available. Using skin temperature as an index of blood flow, measurements were recorded before and after thermoregulatory vasodilatation and nerve block with procaine hydrochloride.

[17] Freeman, Norman E.: Peripheral Vascular Disturbances: Thromboangiitis Obliterans, Arteriosclerosis, and Arterial Thrombosis and Embolism. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 375–382.

TABLE 84.—*Morbidity data on selected vascular diseases, U.S. Army, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]

Cause of admission	Admissions [1]		Noneffective rate [2]	Separations for disability [3]	
	Number	Rate [4]		Number	As a percent of admissions
Arteriosclerosis [5]	6,230	0.25	4.29	2,856	45.8
Thromboangiitis obliterans	1,030	.04	1.33	774	75.1
Raynaud's disease	650	.03	.49	297	45.7
Varicose veins	54,383	2.15	15.27	4,061	7.5
Thrombophlebitis	14,733	.58	6.24	3,001	20.4
Hemorrhoids	221,289	8.73	46.08	1,588	.7
Other vascular diseases	10,688	.42	6.32	4,008	37.5
Total	309,003	12.20	80.02	16,585	5.4

[1] The term "admissions" refers to cases newly admitted to medical treatment facilities for the indicated disease as the primary cause of admission.

[2] Expressed as average number noneffective daily per 100,000 average strength.

[3] This category refers to disability separations for any cause among admissions for the specified disease during 1942–45.

[4] Expressed as number of admissions per year per 1,000 average strength.

[5] Excludes arteriosclerosis of coronary artery, kidney, and eye.

Source: Medical Statistics Division, Office of The Surgeon General, Department of the Army.

Oscillometric measurements were also made. Arteriographic studies with Thorotrast in four patients with normal peripheral pulses demonstrated that circulation was maintained by means of collaterals. The diagnosis of thromboangiitis obliterans was substantiated by biopsy in four other patients.

Nonmedical therapy consisted chiefly of attempts to eliminate smoking. Only 4 of 274 patients with thromboangiitis obliterans at the vascular centers did not smoke. Nonsmoking wards with special privileges, group therapy, occupational therapy, and sedation appeared to help. Of 93 patients whose subsequent habits were known, 77 did not smoke. Only two of these had persistent symptoms. Of the 16 who continued to smoke, 8 were observed to have progression of vascular obliteration. Indifferent results were secured by use of conservative measures other than elimination of smoking. These included Buerger's exercises, intermittent venous occlusion, and intermittent suction and pressure (pavex boot).

Sympathectomy was performed for 75 extremities in 53 of the 152 patients from whom data were available. Results were felt to be good in all but three patients. Two of these came to major amputation. Minor amputations were required in 12 other patients.

In spite of the generally good results obtained in this group of patients, only 24 of 274 patients (9 percent) recovered sufficiently to continue in service, and most of these in a limited duty capacity. The overall statistics compiled by the Medical Statistics Division, Office of The Surgeon General,

reveal that 75 percent of the men with a recorded diagnosis of thromboangiitis obliterans were separated from the service for disability.

It was noted that thromboangiitis was encountered in the early stages of the disease. This may relate to the fact that more advanced disease was detected in induction centers, as reported by Jahsman and coworkers,[18] and, therefore, such men were not inducted into military service. It is also true that men living under stress of military life may have sought medical aid sooner than in civilian life. These men constitute a group from which long-term followup studies on the causative factors and the natural history of Buerger's disease can be done.

ARTERIOSCLEROSIS OBLITERANS

Arteriosclerosis of peripheral vessels with symptoms of arterial insufficiency was observed in 55 patients seen in the vascular centers.[19] The majority of patients in this group were from 40 to 55 years of age. The youngest was 30; only one was over 60. Intermittent claudication was present in 27 of them. Twenty complained of pain and eleven of abnormal coldness in the extremities. Ten patients had cardiac disease, five hypertension, three diabetes, and one nephritis.

Special attention in diagnosis was paid to evidences of calcification on roentgenograms of the extremities. Calcification was observed in all patients studied at Ashford General Hospital and in two-thirds of those seen at the other vascular centers. Other studies in constant-temperature rooms included skin temperatures and oscillometry. Lumbar sympathectomy was performed on four of these patients with satisfactory results reported in all. One minor amputation was performed; no major amputation was done. With the exception of five patients who were returned to limited duty, all men in this group were separated from the service for disability.

An additional 10 men were studied at Ashford General Hospital because of the incidental finding of calcification in peripheral blood vessels noted in films taken elsewhere for other purposes. No abnormality of the circulation could be detected clinically or by study in the vascular laboratory. None of the roentgenograms demonstrated spotty, mottled calcifications; all showed smooth, uniform shadows fading into normal vessels proximally and distally. These findings were consistent with earlier studies [20] revealing that men with the smooth type of calcification demonstrated by X-ray were relatively symptom free as compared with those with calcification of the mottled type.

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[18] Jahsman, W. E., Durham, R. H., and Dallis, N. P.: Recognition of Incipient Thromboangiitis Obliterans in Young Draftees. Ann. Int. Med. 18: 164–176, February 1943.

[19] See footnote 17 p. 469.

[20] Huyler, W. C.: Calcification in Arteries of Leg. Am. J. Roentgenol. 41: 784–788, May 1939.

ARTERIAL EMBOLISM

Arterial embolism was relatively uncommon in the Army. Sixty-seven patients with this diagnosis were admitted to hospitals during the war; of these, six went to the vascular centers. For only 3 patients are case histories available, and the source of the embolus is not known for any of the 67 patients. One underwent a successful popliteal embolectomy overseas. Two patients required major amputation because of gangrene of the leg. Of the total 67 patients, only 8 (12 percent) were separated from the service as a result of the arterial embolus.

RAYNAUD'S DISEASE

The war provided an unusual opportunity to observe the manifestations of Raynaud's disease, and this diagnosis was recorded for 650 admissions during this time (table 84). Those admitted were predominantly men; however, in relation to the number of men and women in the Army, the admission rate for women was about five times the rate for men. One hundred and eighty-four patients with Raynaud's disease with digital syncope were observed at the three vascular centers. Data were available for analysis of 127 of these.[21] At the centers, 111 were male and 16 female, ranging in age from 21 to 51 years. There was no evidence for occlusive vascular disease in any of these patients.

The digital syncope was observed in all patients included in the series from the three vascular centers. Of 57 patients studied at Mayo General Hospital, 20 exhibited the classical triphasic color changes characteristic of Raynaud's disease. The involved digits, immediately on exposure to cold, would turn "dead white," and the patient would experience in them the sensation of intense coldness, numbness, and stiffness. A clear-cut line of demarcation was generally present between the portion of the digit showing the pallor and that portion retaining the normal color. After a variable interval following return to a warm environment, the digits would become cyanotic. Cyanosis was followed by a period of rubor which was succeeded, in turn, by return to normal color. During the late stages of the attack, most patients complained of tingling, throbbing, and burning sensations or other paresthesias. In the remaining patients, the blanching occurred, but the phase of rubor or cyanosis or both was not perceptible before the return to normal color.

About half the patients were asymptomatic in the interval between attacks. The remainder experienced varying degrees of hyperhidrosis, cool-

[21] Shumacker, Harris B., Jr., and Abramson, David I.: Peripheral Vascular Disturbances—Vasospastic Disorders—Raynaud's Syndrome and Raynaud-Like Disorders. *In* Medical Department, United States Army. Surgery in World War II. Vascular Surgery. Washington: U.S. Government Printing Office, 1955, pp. 383–394.

ness, or mild cyanosis. Trophic changes, usually minimal, occurred in 20 of the 127 patients. In five instances, scleroderma or sclerodactylia was present, and one patient had areas of gangrene of the fingertips in both hands. The majority of the patients seen in the vascular centers were separated from the service without active treatment. Sympathectomy was performed for those with incapacitating or severe symptoms. Sympathectomy was usually bilateral, with three extremities denervated in four patients and four extremities denervated in five. A total of 100 sympathectomies were performed in 46 of the 127 patients. At Mayo General Hospital, 21 sympathectomies were performed on 9 patients and the immediate results were considered excellent in all but 1, who had all 4 extremities denervated in stages. In this patient, digital syncope was abolished, but some tingling sensations persisted in cold weather. He also complained of annoying hyperhidrosis of the trunk. The fingertips of the one patient with gangrene healed promptly following sympathectomy.

Other disorders involving the vasomotor system were seen at the vascular centers. Some presented the picture of acrocyanosis. Others presented a picture similar to that of Raynaud's disease with increased sensitivity to cold but without digital syncope or with only a vague history of blanching. These patients were treated according to the severity of symptoms. Some were separated from the service; others returned to duty. Sympathectomy was performed in 6 of the 55 patients from whom data were available. Immediate results were good in all.

At the vascular centers, the presence of digital syncope was used as a necessary criterion for the diagnosis of Raynaud's disease in the cases reported. Six percent of these patients were observed to have symptoms and digital syncope in one extremity only, instead of the bilateral disturbances characteristic of Raynaud's disease. It may be that unilateral symptoms were an early manifestation of Raynaud's disease in these individuals and that the men in the service sought medical aid sooner than they would have in civilian life. Patients with digital syncope differed from the group without digital syncope in that hands were involved alone or more severely than were the feet. About one-third of the patients without digital syncope had involvement of the feet alone. Although the syndromes may in many instances be quite similar, the opinion was developed at the centers that the diagnosis of Raynaud's disease should be reserved, at least for those patients in whom pallor (or cyanosis) occurs on exposure to cold.

VENOUS DISEASE

Problems encountered with disorders of the venous system were similar to those in civilian life. Specific studies were not undertaken of individuals with varicose veins and thrombophlebitis, and as a rule, they were not sent to the vascular centers. Of interest, however, are the effects of

these diseases on the individual as a soldier and on military manpower, and
the effect of the military situation on the disease.

Statistics compiled by the Medical Statistics Division, Office of The
Surgeon General, show 54,383 admissions to medical treatment facilities
for varicose veins and 14,733 for thrombophlebitis, a combined incidence
of 2.73 per 1,000 average strength per year (table 84). With an average
duration of stay of 26 days for the former condition and 39 days for the
latter, the loss in military manpower came to approximately 2 million man-
days, equal to the loss of 5,500 men for a year. Approximately three-fourths
of the patients were admitted in the continental United States. Among the
patients with a diagnosis of thrombophlebitis, the secondary diagnoses were
investigated in a sample of 1,597 patients.[22] A diagnosis of pulmonary
embolus or pulmonary infarction was made in 36 (2.25 percent). The pro-
visional mortality due to varicose veins was 0.02 percent and that due to
thrombophlebitis was 0.17 percent per year per 100,000 average strength.
Of men admitted for varicose veins, 92 percent were returned to duty.
Nearly all of the remainder, over 4,000 men, were separated from the service
for disability. Of men admitted for thrombophlebitis, 21 percent were re-
turned to civilian life.

Methods of management of patients with thrombophlebitis were simi-
lar to those used in civilian practice. Conservative measures included bed
rest, elevation of the legs, and elastic support. Venous surgery consisted
largely in ligation of superficial or deep veins in the leg as appeared to be
indicated. Anticoagulation with heparin or Dicumarol (bishydroxycouma-
rin) or both was used. Statistical and followup data are not available for
these patients. Sympathectomy was tried because of sweating, diminished
peripheral circulation, cyanosis, and pain in seven of the patients referred
to the vascular centers for longstanding thrombophlebitis. Although sweat-
ing and vasoconstriction were relieved and pain sometimes improved, the
venous congestion and edema were not helped and in some instances ap-
peared to be worse following surgery. It was believed, therefore, that
sympathectomy was not of value in treatment of the late residuals of
thrombophlebitis.

HEMORRHOIDAL VARICES

Although not generally considered among the vascular diseases, hemor-
rhoidal varices caused a rather significant loss in military manpower and so
will be mentioned briefly. There were over 220,000 admissions to medical
treatment facilities for hemorrhoids (table 84) with an average duration of
stay of 19 days. The resulting loss in manpower was 4,265,000 man-days,
equivalent to the loss of a hypothetical 15,000-man division for 9.5 months.

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[22] Data compiled by the Medical Statistics Division, Office of The Surgeon General, Department of
the Army.

Data such as these indicate to some extent the significance of a seemingly minor illness in the progress of the military effort. The importance of managing such problems with minimal loss of duty time must repeatedly be stressed.

SUMMARY

The results of observations on certain aspects of peripheral vascular disease and injury during World War II broadened our understanding of the nature and logistic or economic significance of vascular disorders and provided a stimulus for the remarkable subsequent advances in cardiovascular medicine and surgery. The appalling loss of limbs after acute interruption of major arteries and the apparent impairment of function after arterial interruption for acute or chronic lesions stimulated interest in exploiting reconstructive vascular surgery as opposed to obliterative surgery in the management of both acute and chronic arterial lesions.

Much was learned about the mistakes which permitted the catastrophic incidence of cold injury in one theater of war after another; unfortunately, too little cognizance was taken of the experience gained in antecedent operations of other theaters in this war, as well as in previous wars. The recognition of the responsibility of command with regard to prevention of cold injury should prove of inestimable value for possible future operations in cold environments. The information collected has provided a clearer picture than heretofore of the natural history of cold injury and of the results of conservative management. This is of value not only for the military but also for the civilian surgeon who encounters this condition not infrequently during the winters of temperate climates.

Although little that is new was discovered with regard to such civilian conditions as phasic vasospasm and cold sensitivities, thromboangiitis obliterans, and arteriosclerosis, some idea was gained of the prevalence of these conditions in a selected and fairly homogeneous group of subjects. Much was learned of the clinical characteristics of these vascular diseases in their early stages, and their significance as a drain on military resources is better known than heretofore. But of greatest import and broadest implication for medical science is the fact that records are available of groups of individuals with certain diseases of the peripheral circulation and contain baseline data, disappointingly scant as they may be in many instances, for future reference. From these groups, rosters can be developed for followup studies.

A review of the available records with regard to peripheral vascular disease has emphasized the rather obvious fact that relatively little of value for subsequent clinical studies can be achieved without effort. Records prepared without anticipation that they would be of special value for subsequent investigation of a particular condition have been of relatively little

use. Perhaps the greatest single achievement in this connection was the establishment of vascular centers in the Zone of Interior. Had nontraumatic vascular disturbances been referred to these centers earlier than the summer of 1944, unquestionably more would have been learned about these diseases. The credit for the unequaled achievements in the physiologic studies and in the surgical approach to chronic arterial and arteriovenous lesions must go to the establishment of these centers. One regrets that lack of equipment and of personnel made it impossible to take truly full advantage of the extraordinary opportunity for study of these vascular conditions.

Finally, it is well to emphasize here that the effort expended in the centers and by individual investigators in the field bore fruit not alone for this and subsequent military operations but for medical science as a whole. Indeed, the great potential of valuable information from clinical research based upon data recorded during the war has barely been touched and remains a challenge for the future.

CHAPTER XVIII

Rheumatic Diseases

Richard T. Smith, M.D.

The importance of arthritis and other rheumatic diseases as a cause of disability and noneffectiveness in military personnel was recognized by the War Department in 1942, for although arthritis did not account for a large percentage of illnesses in the Army, it had been found to be one of the most disabling. In anticipation of a formidable number of cases of rheumatic diseases, and in an effort adequately to diagnose, treat, and salvage as many military personnel as possible, not only for the World War II period but also for the long-range national economy, tentative steps were taken in the latter part of 1942.

The Surgeon General and his staff, with the cooperation of the American Rheumatism Association, formulated a plan for the establishment of one or more rheumatism centers for the Army when the need for them should arise. These were to be designated as centers for chronic rheumatic diseases and centers for rheumatic fever, specifically for the care of the difficult or progressive cases and the handling of diagnostic problems.

Toward the end of 1943, it became apparent that a center for the treatment of chronic arthritis would be needed. Therefore, on 17 December 1943,[1] the Army and Navy General Hospital at Hot Springs, Ark., was designated as a center for the diagnosis and treatment of rheumatic diseases. A second center for chronic rheumatic diseases was authorized on 25 August 1944, at Ashburn General Hospital, McKinney, Tex., to relieve the flow of patients at the first center.[2] At the same time, the following three centers were designated for the care of soldiers with rheumatic fever: Birmingham General Hospital, Van Nuys, Calif.; Foster General Hospital, Jackson, Miss.; and Torney General Hospital, Palm Springs, Calif.

CENTERS FOR RHEUMATIC DISEASES

Army and Navy General Hospital

The first rheumatic disease center had its beginning as a general hospital, established in 1882. On 20 June 1882, Congress passed an act appro-

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[1] Letter, Headquarters, Army Service Forces, Washington, D.C., to Commanding Generals, all service commands and Military District of Washington, 17 Dec. 1943, subject: General Hospitals Designated for Specialized Treatment.

[2] War Department Circular No. 347, 25 Aug. 1944.

priating $100,000 for the erection of an Army and Navy Hospital on a Government reservation near Hot Springs, Ark. War Department General Orders No. 72, 5 July 1882, officially established the Army and Navy General Hospital.[3] The cornerstone was laid in 1883 on a site of approximately 15 acres. The hospital was opened for occupancy on 17 January 1887.[4] From that time until the last additional building was added on the hospital grounds in 1927, there was a daily average of 300 patients.

A new building for the Army and Navy General Hospital was started in 1941 and completed in 1943, costing approximately $1,500,000. It was a six-floor modern building with a total bed capacity of 518.

A short time after war was declared in 1941, the hospital underwent new expansion which more than doubled its bed capacity to a total of 1,220. The Eastman Hotel situated across the street from the hospital was purchased by the War Department on 13 October 1942. Considerable rehabilitation was required in the hotel but it was ready for occupancy as the hospital annex, connected to the main building by an overhead passageway across Reserve Avenue, on 5 December 1943. The annex contained 466 rooms. It was planned to be used exclusively for the housing and care of convalescent patients, which would minimize any fire risk although the building had been "fireproofed" throughout. In addition, other properties were purchased, including the Eastman Hotel garage and the Hot Springs Hotel.

The reservation of 24.24 acres on the southwest slope of North Mountain, approximately 650 feet above sea level, overlooked the main intersection of Hot Springs. By utilizing the barracks and quarters which were established, before the beginning of World War II, for a technicians' school, a rehabilitation center for ambulatory patients was also established. In addition, there were quarters for nurses, Wacs, and enlisted men; seven homes for officers; and quartermaster and all other facilities for a self-contained army post.

When the Army and Navy General Hospital (fig. 61) was designated a center for the diagnosis and treatment of rheumatic diseases among American soldiers, it and any others that might be established in the future were designed, as previously mentioned, for the care of difficult or progressive cases, or for the handling of diagnostic problems.

It was believed that the majority of soldiers who developed rheumatism would not be transferred to a center such as the Army and Navy General Hospital. Patients with transient muscular rheumatism, mild rheumatic fever without carditis, or acute traumatic or specific infectious arthritis could be handled effectively in adjacent station or regional hospitals.

The designated aims for a rheumatism center were—

1. Accurate diagnosis: to provide a diagnostic center where difficult

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[3] Unless otherwise indicated, all data on the Army and Navy General Hospital are from "Annual Reports, Army and Navy General Hospital, 1941–45."

[4] The Army and Navy General Hospital was closed on 30 November 1959.
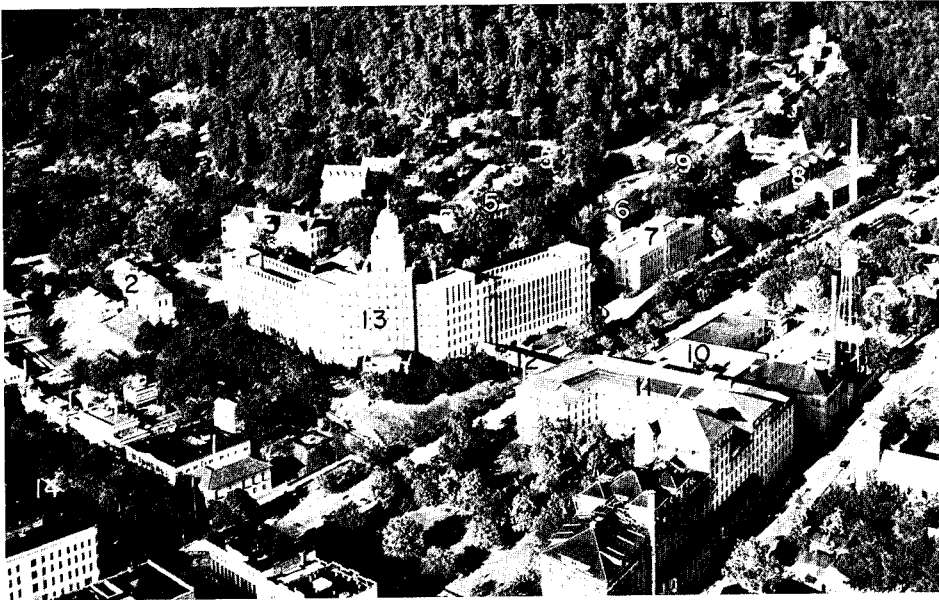
FIGURE 61.—Army and Navy General Hospital, Hot Springs, Ark. (1) Public bath-houses. (2) Army and Navy General Hospital bathhouse and physical therapy depart-ment. (3) Nurses' and Wacs' quarters. (4) Advanced reconditioning. (5) Homes for staff officers. (6) Enlisted men's recreation hall. (7) Rehabilitation area. (8) Quartermaster and utilities. (9) Enlisted men's barracks. (10) Fire station in Eastman Hotel garage. (11) Eastman Hotel Annex. (12) Walkway across Reserve Avenue, connecting 2d floor of hospital to 4th floor of annex. (13) Army and Navy General Hospital. (14) Central Avenue, Hot Springs, Ark.

cases can be studied by special methods and by medical officers with a special knowledge of rheumatic diseases.

2. Intensive treatment: to provide special facilities for the treatment of the more severe or progressive cases.

3. Prompt disposition: to accomplish as great a reduction in hospitali-zation time as is consistent with adequate treatment.

4. Increase salvage: to restore to duty, if possible, all men with "cured" or "arrested" disease.

5. Rehabilitation: to educate or rehabilitate for civilian life those whose disability necessitates discharge from the Army.

6. Application of newer advances in treatment.

7. Appropriate clinical studies of patients while under treatment.

8. Long-range economy, an incidental, but important aim: to reduce the costly need for disability pensions and prolonged hospitalization in veterans' facilities.

The Army and Navy General Hospital, the Army's oldest general hos-pital, was chosen because of its past history and excellent facilities. The

adjacent Hot Springs which, since 1887, had been a mecca for rheumatic personnel of the Army, was a natural choice. An outstanding advantage of establishing a rheumatism center in a large general hospital provided varied medical and surgical specialties which were necessary for proper knowledge and complete treatment of rheumatic diseases. This provided specialists in all fields of medicine to support the extreme specialization in the rheumatic diseases.

The rapid growth of the rheumatism center is evidenced by the daily census of the rheumatic disease section, which rose from 56 patients in January 1944 to a total of 704 patients in October 1944. This is well demonstrated in table 85 where the total admissions to the rheumatic disease section in 1943 was 556 patients, or 29 percent of the total admissions for that year. In 1944, it had increased to 3,105 rheumatic patients, 63.8 percent of the total 4,868 admissions in the year. Between 1 January and 30 June 1945, an additional 2,210 rheumatic patients were admitted, or a total of 5,315 in 18 months.

TABLE 85.—*Total admissions and admissions for rheumatic diseases, U.S. Army personnel, Army and Navy General Hospital, 1941–45*

Year	Total admissions	Rheumatic diseases	
		Number	Percent
1941	907	584	64.4
1942	985	516	52.4
1943 [1]	1,930	556	28.8
1944	4,868	3,105	63.8
1945	6,041	3,542	58.6
Total	14,731	8,303	57.0

[1] Hospital designated a specialized center for treatment of rheumatic diseases, 17 Dec. 1943.

Source: Annual Reports, Army Navy General Hospital, 1941–45.

Another evidence of the activity of the rheumatic disease section is seen in table 86. In 1942, of the 15 officers of the medical service, 2 were assigned to the care of rheumatism patients, utilizing 111 beds. For 1944 and 1945, the professional personnel for the section increased to 9 and 18, respectively, with an allotment of 600 beds for these special patients. Other facilities, such as the physical therapy department, the occupational therapy department, a braceshop, and the physical rehabilitation area, also were expanded.

Organization of the rheumatic disease section.—During 1944–45, the rheumatic disease section of the Army and Navy General Hospital reached its maximum in space and function. With a total of 600 beds allocated to this section (exclusive of beds for female patients), 90 percent of these

were for ambulatory patients and were situated in the Eastman annex. Ambulatory enlisted rheumatic patients were housed in seven complete wards in the annex while nonambulatory patients were housed in one complete ward in the hospital building proper. Ambulatory rheumatic officers were housed in two complete wards in the annex, while nonambulatory rheumatic officers were cared for in the officers' ward in the main building. Female rheumatic patients were assigned to the female ward. There were actually eight complete wards ranging from 60 to 83 beds, and parts of five other wards that were utilized for patients assigned to this section.

Between 1 July 1944 and the end of 1945, the daily census ranged between 500 and 700 patients present in the section. In addition, there were between 150 and 350 rheumatism patients on furlough at all times.

TABLE 86.—*Number of Medical Service officers and bed allotments assigned to the Rheumatic Disease Section, Army and Navy General Hospital, 1942–45*

Year	Rheumatic Disease Section		Total officers in Medical Service
	Officers	Beds	
1942	2	111	15
1943	2	45	14
1944	9	600	22
1945	18	600	35

Source: Annual Reports, Army and Navy General Hospital, 1942–45.

The ratio of only 60 beds for nonambulatory patients and 540 for ambulatory patients occurred partly owing to necessity and partly by design. The Eastman annex, containing 90 percent of all the beds in the rheumatic disease section was not considered a suitable building for completely bedfast patients. This constituted the necessity. It was the philosophy of the staff of the rheumatic disease section, and the design, that (1) less disability and permanent crippling would occur if joints were not severely limited by excessive rest; (2) less rehabilitation and reconditioning would be required if patients were forced to be active; and (3) morale would be higher if the severely ill bed patients were physically separated from the ambulatory patients. An additional benefit also occurred in that the period of hospitalization was considerably shortened.

Despite the fact that more than half of the patients transferred to the Army and Navy General Hospital arrived as litter patients or had been only semi-ambulatory at the time of admission, most of them were informed that they were now ambulatory and were assigned to wards in the annex. As might be expected, many of those newly designated ambu-

latory patients were most unhappy with their new status. This rapidly changed when they realized that only in this category were they eligible for afternoon or evening passes, or for furloughs.

All special areas of the hospital were utilized for the best treatment of the patients. Constant and frequent consultation with the orthopedic department was essential in providing the best treatment to the patients. Where necessary, corrective or diagnostic operative procedures were carried out. The physical therapy department participated in the treatment of most patients. All laboratory and diagnostic services were utilized for the best benefit of the patients.

The personnel of the section on rheumatic diseases in 1944 consisted of nine medical officers. Three officers were qualified as specialists in rheumatic diseases, one of whom was the chief of the section; one was a partially trained officer; and five officers were undergoing training (table 86). The director of the rheumatism center was also the chief of the medical service.

In 1945, the staff of the section (fig. 62) was increased to 18 officers. These included five qualified specialists in rheumatic diseases, four partially trained officers, and nine officers undergoing training.

Ashburn General Hospital

Within the first few months of 1944, it became apparent that an additional rheumatism center would be needed. The second rheumatism center, as already mentioned, was established at the Ashburn General Hospital.[5] This hospital became operative as a rheumatism center, on 1 September 1944. There were 729 beds allocated for arthritis. On 1 January 1945, by converting regular barracks into wards, the bed capacity for rheumatic disease patients was increased to a total of 1,661. This hospital reached its peak of admissions to all sections of the hospital on 29 August 1945, when there was a total of 2,852 patients. Thereafter, there was a steady decline of admissions and census in the hospital until 12 December 1945, at which time, with only 17 beds occupied, the hospital was declared surplus. During the first 8 months that Ashburn General Hospital functioned as a rheumatism center, admissions to the rheumatic disease section averaged more than 400 a month. During 1945, a total of 3,534 patients were admitted to the section.

The rheumatic disease section consisted of 14 wards when it first began operation on 1 September 1944. The medical personnel consisted of a chief of the section, assisted by four medical officers. This was an inadequate staff for the size of the section, requiring the chief of the section to take personal charge of wards in addition to his other duties.

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[5] Unless otherwise indicated, all data on Ashburn General Hospital are from "Annual Reports, Ashburn General Hospital, 1944–45."

FIGURE 62.—Members of the Medical Service, Rheumatic Disease Section, Army and Navy General Hospital, Hot Springs, Ark., with Brig. Gen. Hugh J. Morgan, Chief Consultant in Medicine, SGO, Brig. Gen. Ralph H. Goldthwaite, Commanding General, Army and Navy General Hospital, and Col. Walter Bauer, MC, Consultant in Medicine, Eighth Service Command, at a meeting, 22 January 1945, at the Army and Navy General Hospital. Front row (left to right) : General Goldthwaite, General Morgan, Colonel Bauer, and Lt. Col. Philip S. Hench, MC, Chief of Medical Service and Director, Rheumatism Center, Army and Navy General Hospital. Back row (left to right) : Lt. Edward F. Rosenberg, MC, Capt. Richard T. Smith, MC, Maj. Edward W. Boland, MC, Chief, Rheumatic Disease Section, Maj. James O. Finney, MC, Capt. Nathan E. Headley, MC, Maj. Howard C. Coggeshall, MC, and Lt. Harley E. Cluxton, MC.

The following objectives were the guide for organizing the section:

1. To facilitate the prompt and proper care of patients upon admission to the hospital.

2. To give all patients received from overseas a convalescent furlough as soon as it could be determined such would not aggravate their physical condition.

3. Definitive treatment, to emphasize teaching all patients the nature of their disease and the way to care for themselves in their homes.

4. To bring all patients with interesting or puzzling features of disease before conferences of the entire group of medical officers, and particularly to utilize the services of the orthopedic surgeon and the neuropsychiatrist in this connection.

5. To keep adequate records of each patient in order to contribute as much as possible toward increasing knowledge of the type of rheumatic diseases observed.

During 1945, the rheumatic disease section increased in size to four groups of six to eight wards. Each group of wards was under the direction of one officer trained in the care of rheumatic diseases, who supervised and taught the ward officers under his charge.

When patients were admitted to the hospital, they were placed in classification wards. The type and severity of their disease was estimated. Then, within 48 hours, they were transferred to another ward where definitive treatment was started. Frequently, patients were permitted to proceed on their initial oversea furlough directly from these classification wards.

The officers' and women's section of the hospital consisted of seven wards with three to six medical officers. Most of the patients had a rheumatic disease. One of the officers assigned to the section, trained in the care of rheumatic diseases, acted as consultant for the entire section.

EPIDEMIOLOGY

The conditions imposed upon military personnel by military combat operations influenced the probabilities of an increased incidence of many of the rheumatic diseases. The factors which would increase the hazards of fibrositis, psychogenic rheumatism, and rheumatoid arthritis are emotional disturbances, repeated and prolonged exposure to extremes of temperature and dampness, poor personal hygiene, exposure to respiratory and other infections, musculoskeletal strain, fatigue, and joint trauma. An increased prevalence of respiratory infections would tend to increase the incidence of rheumatic fever. The rate of traumatic arthritis would increase, since injuries to joints would be more common. Increased exposure to, and the occurrence of, gonorrhea would produce more gonorrheal arthritis. Infectious arthritis with penetrating injuries to joints would be more common.

Climatic conditions, often thought to be an important factor in the frequency and distribution of the rheumatic diseases, were of little import. The total incidence and that of the various rheumatic conditions was essentially the same for those theaters and areas with wide differences in climate, such as the continental United States, the Mediterranean theater,

and the Southwest Pacific Area (table 87). The highest rate of admissions (21.21) was for the North American theater (including Alaska and Iceland), while the lowest rate (10.72) was for the European theater, with a comparable climate. The next highest admission rates were found in the Middle East (18.61) and the Southwest Pacific theaters (15.24).

TABLE 87.—*Admission rates for rheumatic diseases in the U. S. Army, by theater or area, 1942–45*
[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as number of admissions per annum per 1,000 average strength]

Theater or area	Total	Acute arthritis	Chronic rheumatoid arthritis	Osteoarthritis	Other arthritis	Synovitis	Tenosynovitis	Ankylosis	Rheumatic fever	Gout and gouty arthritis	Tuberculosis, bone and joint	Bursitis	Myositis	Muscular rheumatism [1]
Continental United States	15.41	0.87	0.77	1.39	3.30	1.34	0.71	0.18	0.96	0.06	0.03	1.37	2.27	2.16
Overseas:														
Europe	10.72	0.75	0.59	0.88	1.04	0.88	0.96	0.05	0.46	0.03	0.02	1.16	2.35	1.55
Mediterranean [2]	16.38	1.16	.87	1.13	2.10	1.24	.71	.05	.50	.03	.02	1.62	4.18	2.77
Middle East	18.61	1.43	.35	.47	2.06	1.10	.33	.05	.45	.01	.02	2.14	5.07	5.13
China-Burma-India	10.86	.73	.58	.80	.93	.89	.30	.02	.25	.05	....	1.27	3.02	2.02
Southwest Pacific	15.24	.78	1.15	1.52	1.43	1.08	.39	.06	.36	.03	.02	2.00	3.72	2.70
Central and South Pacific	13.26	.88	.67	.93	1.73	.95	.42	.03	.27	.02	.01	1.65	3.37	2.33
North America [3]	21.21	1.96	.45	.54	2.68	1.34	1.20	.09	.44	.06	.02	2.05	5.47	4.91
Latin America	11.63	1.02	.39	.47	1.03	1.12	.23	.09	.16	.03	.01	1.70	2.27	3.11
Total overseas [4]	12.98	0.90	0.69	0.95	1.41	0.99	0.69	0.05	0.40	0.03	0.02	1.48	3.12	2.25
Total Army	14.37	0.88	0.74	1.21	2.51	1.19	0.50	0.12	0.72	0.05	0.02	1.41	2.62	2.20

[1] Includes certain other diseases of muscles.
[2] Includes North Africa.
[3] Includes Alaska and Iceland.
[4] Includes admissions on transports.

STATISTICAL DATA

Anticipated Incidence

When the original planning for rheumatism centers was undertaken, there was no guide by which a possible need could be determined. Much of the future need had to be arrived at by considering an "anticipated incidence" based upon World War I and various peactime studies. There were many pitfalls in attempting to compare civilian rates with the Army rate; namely, the relative vagueness and unreliability of the diagnostic groupings and the differences in age groups being considered since the Army consisted of young males. In addition, the Army diagnostic criteria differed considerably in the two wars, making a direct comparison impossible.

The first civilian study, the Hagerstown Morbidity Study, begun in 1921, showed a rate of 20.8 cases for 1,000 population per year.[6] At this

[6] Hagerstown Morbidity Study, U.S. Public Health Service, Hagerstown, Md.

rate, a total of 530,000 cases of rheumatic disease would have occurred during the war. The U.S. Public Health Service survey, 1933–36, developed a rate of 22.7 cases per 1,000 population per year,[7] or a possible 578,000 cases for the duration of the war. On the other hand, a rate of 14 per 1,000 per year, arrived at by the Massachusetts survey in 1933,[8] suggested a total of 357,000 for the same period of hostilities.

During World War I, there were no special centers for rheumatic diseases, although there were 84,550 admissions with a primary diagnosis of one of the rheumatic diseases.[9] However, with the addition of those patients having a rheumatic disease as the secondary diagnosis, the total incidence was approximately 107,000, or 26 per 1,000 average strength per year.[10] On this basis, the incidence of rheumatic diseases for World War II would have amounted to approximately 659,000.

It is quite evident that any effort to arrive at a realistic rate on the basis of the preceding figures would have been impossible. An average of the four rates amounts to 21.25 per 1,000 per year. The rate which more nearly approximated the actual figure was the Hagerstown rate of 20.8. The true incidence rate for World War II was 20.7 cases per year per 1,000 average strength, or 528,300 cases during the years 1942–45.[11] This consisted of those patients primarily admitted to hospitals for a rheumatic condition, as well as those cases secondary to or concurrent with other admission diagnoses.

Disqualification for Military Service Because of Rheumatic Diseases

Any direct comparison between rejection rates of applicants for enlistment in World War I and World War II must be considered with caution. Some of the more important sources of error are: (1) Differences in ages in the two wars, (2) differences in diagnostic criteria, and (3) differences in the prevailing medical standards. These data should not be used to draw definite conclusions in regard to trends in the prevalence of the rheumatic diseases.

The examinees of World War I were younger than those in World War II. Therefore, table 88 shows a comparison between those rejected for military service in World War I and the age group of 20–24 years in World War II. It is clearly seen from this table that the medical standards were different in the two wars; for instance, gonococcus infection of a joint, limitation of motion, and sacroiliac deformities were reasons for

Preliminary Reports, The National Health Survey: 1935 to 1936, Sickness and Medical Care Series. Bulletins Nos. 1 to 6, U.S. Public Health Service, Washington, D.C.

[8] Bigelow, George H., and Lombard, Herbert L.: Cancer and Other Chronic Diseases in Massachusetts. Boston: Houghton Mifflin Co., 1933.

[9] The Medical Department of the United States Army in the World War. Washington: Government Printing Office, 1925, vol. XV, pt. 2.

[10] See footnote 9.

[11] Medical Department, United States Army. Medical Statistics in World War II. [In preparation.]

disqualification in World War II but not in World War I. The increase
in the number of disqualifying defects should not be interpreted as an
increase in their incidence, but rather improvement in the diagnostic
criteria at the time of World War II.

TABLE 88.—*Disqualification for military service because of rheumatic diseases in World War I and World War II (ages 20–24)*

[Rate expressed as number of disqualifications per 1,000 examinees]

Diagnosis	Disqualified for World War I [1]	Disqualified for World War II,[2] ages 20–24
Ankylosis	3.79	0.52
Arthritis	1.71	1.41
Bursitis	.04	.17
Gonococcus infection of joint		.02
Limitation of motion		5.22
Muscular rheumatism	.32	
Myositis	.02	.02
Sacroiliac deformities		.56
Tenosynovitis	.02	
Total	5.90	7.92

[1] Love, Albert G., and Davenport, Charles B.: Defects Found in Drafted Men. Washington: Government Printing Office, 1920, table V.

[2] Karpinos, B. D.: Defects Among Registrants Examined for Military Service, World War II (in manuscript form). Medical Statistics Division, Office of The Surgeon General, U.S. Army.

Hospital Admissions for Rheumatic Conditions

The disparity in the diagnostic terms for the rheumatic diseases in
World War I and World War II interferes with a direct comparison of
hospital admissions by diagnoses (table 89). In World War I, all arthritis,
including osteoarthritis, was grouped under the single term "arthritis,"
while six different classifications for "arthritis" (acute, chronic rheuma-
toid, osteo, other, tuberculosis, and gouty) were employed in World War II.
In addition, data for "bursitis" separately are not available for World
War I.

The term "admissions" in the various tables refers to the specified
diseases reported as the primary cause for the patient's admission to a
medical treatment facility. There were, in addition to those admissions
indicated in table 89, other diagnoses of specific rheumatic diseases, sec-
ondary to or concurrent with some other admission diagnoses. If these
additional diagnoses were added to the primary rheumatic hospital admis-
sion rates, the total incidence rate for World War I would have been 25.9
per 1,000 per year and for World War II, 20.7.

TABLE 89.—*Comparison of admission rates for rheumatic diseases (excluding rheumatic fever),*
World War I [1] and World War II [2]

[Rate expressed as number of cases per annum per 1,000 average strength]

World War I		World War II	
Diagnosis	Admissions	Diagnosis	Admissions
Arthritis	8.14	Arthritis	5.34
([3])		Acute (type unspecified)	.88
([3])		Chronic rheumatoid	.74
([3])		Osteoarthritis	1.21
([3])		Other and unspecified	2.51
Myositis	1.00	Myositis	2.62
Synovitis	.87	Synovitis	1.19
Tenosynovitis	.65	Tenosynovitis	.70
Ankylosis	.46	Ankylosis	.12
Muscular rheumatism and certain other diseases of joints	3.32	Muscular rheumatism and certain other diseases of joints	2.20
		Tuberculosis of bone or joint	.02
Gout	.02	Gout and gouty arthritis	.05
		Bursitis	1.41
Total	20.46	Total	13.65

[1] The Medical Department of the United States Army in the World War. Washington: U.S. Government Printing Office, 1925, vol. XV, Statistics, pt. 2.

[2] Preliminary data based on sample tabulations of individual medical records, 1942–45.

[3] In World War I, all arthritis, including osteoarthritis, was grouped under the single term "arthritis."

The admission rates for rheumatic diseases in the various theaters is shown in table 87. Some isolated but incomplete reports of the incidence of certain rheumatic diseases are available from a few theaters; namely, a portion of the Latin American area, the North African theater, and the western portion of the Central and South Pacific theater.

In the Panama Canal Department, of the Latin American area, Gorgas General Hospital had a total of 23 patients with rheumatoid arthritis between 1 January 1940 and 1 October 1945; an additional eight cases were reported from other military hospitals of the Department for the period 1 January 1941 to 31 December 1945.[12] Most of the patients had mild arthritis; 14 of the 23 from Gorgas General Hospital were returned to the United States for full evaluation and treatment.

In the Antilles Department,[13] also of the Latin American area, from 1942 to 1 October 1945, a total of 225 patients were admitted with rheumatoid arthritis to the 161st General Hospital, San Juan, Puerto Rico. The majority of these patients were separated from the military service.

[12] Professional History of Internal Medicine in World War II, 1 January 1940 to 1 October 1945, The Panama Canal Department, vol. I, p. 73. [Official record.]

[13] Professional History of Internal Medicine in World War II, The Antilles Department, pp. 39–40. [Official record.]

The 359th Station Hospital, on Trinidad, however, had only 100 admissions with a primary diagnosis of arthritis and 35 admissions in which arthritis was a secondary diagnosis. Fifty-two of the first group and 15 of the second group, or a total of 67, were transferred to general hospitals. The remaining 68 patients were returned to duty. Only 15 of the 135 patients were diagnosed as rheumatoid arthritis.

In the Mediterranean theater, in a group of 10 general hospitals up to 1 December 1944, 3,260 patients were admitted with a diagnosis of arthritis, or 1.8 percent of the total 177,317 hospital admissions.[14] With respect to a comparison between those patients admitted for a diagnosis of arthritis versus the total number of admissions to the medical services of three general hospitals (70th, 45th, and 12th), there were 1,157 patients with a diagnosis of arthritis, or 4.1 percent of the 28,251 medical patients.

Disposition of patients with arthritis in selected general hospitals from the Mediterranean theater is presented in table 90. The data collected from the 10 general hospitals were obtained by written questionnaires. The information from the 45th General Hospital, Rabat, French Morocco, came from an examination of the records of the medical service. These are compared with the dispositions of the remainder of medical patients in the 45th General Hospital, as well as with the dispositions for all patients hospitalized for medical reasons in the entire theater. An inference can be drawn from this table that slightly less than half of those patients with arthritis reaching a general hospital in that theater were evacuated, and approximately another one-fourth were reclassified for limited service. When compared with the medical admissions for the entire

TABLE 90.—*Disposition of patients with arthritis in general hospitals in the Mediterranean theater, U.S. Army*

Source of patients	Total	Duty		Limited service		Evacuation	
		Number	Percent	Number	Percent	Number	Percent
Ten general hospitals (up to 1 December 1944)_____	2,938	956	32.6	692	23.4	1,290	44.0
45th General Hospital (Medical Service)_____	329	63	19.1	130	39.6	136	41.3
Remainder of 45th General Hospital Medical Service___	5,222	3,341	64.1	534	10.2	1,347	25.7
Cases hospitalized for disease in theater, January 1943– April 1945_____	703,320	618,921	88.0	53,079	7.6	31,320	4.4

Source: Short, C.L.: Arthritis in the North African and Mediterranean Theater of Operations, table 6. [Official record.]

[14] Short, C. L.: Arthritis in the North African and Mediterranean Theater of Operations, table 3. [Official record.]

theater, it is quite evident that the arthritic is much more vulnerable in these respects.

A geographic distribution of admissions for arthritis and arthralgia in five islands of the Western Pacific Base Command of the Central and South Pacific theater is shown in table 91, as compared with the total medical admissions for the same islands. Most medical officers believed that the symptoms causing hospital admission were directly related to the high humidity in this area of the Pacific regardless of whatever the underlying process might have been.[15] This is of particular interest, for Iwo Jima, the driest of the islands in the Western Pacific Base Command, had the lowest incidence of arthritic conditions. No specific data were presented in regard to the disposition of these patients. In general, the criteria for evacuation were the severity of symptoms and the persistence of sedimentation rate elevation, further influenced by such factors as the amount of time spent overseas and the amount of combat duty. Patients for evacuation were usually classed as "arthritis," therefore, statistics of diagnosis may be considered as unreliable.

TABLE 91.—*Geographic distribution of admissions for arthritis and arthralgia in certain islands of the western Pacific, 1945*

Island	Total medical admissions	Admissions for arthritis and arthralgia	
		Number	Percent of total admissions
Angaur_____	1,756	37	2.1
Guam_____	3,909	119	3.0
Iwo Jima_____	988	9	.9
Saipan_____	8,602	241	2.8
Tinian_____	2,700	50	1.9
Total_____	17,955	456	2.5

Source: Turner, Glenn O.: History of Internal Medicine of the Western Pacific Base Command, table 4a. [Official record.]

Disposition of Rheumatic Diseases

During the period 1942–45, 64,619 enlisted and commissioned personnel were released from the Army because of rheumatic diseases (table 92). Of this number, there were 50 deaths. During this same period, 886,127 soldiers were separated from the service because of nonbattle disability. The 64,569 rheumatic patients separated comprised only 7.3 percent of the total for nonbattle causes.

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[15] Turner, Glenn O.: History of Internal Medicine of the Western Pacific Base Command, 1945. [Official record.]

The daily average noneffective rate during 1942–45, due to nonbattle causes was 36.68 per 1,000 per average strength. The noneffective rate for rheumatic diseases was 1.28, or 3.5 percent of the total. The diseases "acute arthritis," "chronic rheumatoid arthritis," "hypertrophic arthritis," and "other and unspecified arthritis" caused more noneffectiveness than all other rheumatic diseases.

TABLE 92.—*Disability separations, deaths, and noneffectiveness due to rheumatic diseases* [1] *in the U.S. Army, 1942–45*

[Preliminary data based on sample tabulations of individual medical records]
[Rate expressed as average daily number of noneffectives per 1,000 average strength]

Diagnostic category	Number of disability separations [2]	Number of deaths [2]	Noneffective rate [2]
Arthritis, acute (type unspecified)	262	0	0.05
Arthritis, chronic rheumatoid	9,310	0	.16
Osteoarthritis	15,756	1	.19
Arthritis, other and unspecified	22,299	0	.26
Synovitis	2,373	0	.09
Tenosynovitis	146	0	.03
Ankylosis	4,355	0	.02
Rheumatic fever	5,544	29	.19
Gout and gouty arthritis	372	0	.01
Tuberculosis of bone or joint	422	17	.01
Bursitis	543	0	.07
Myositis	1,185	0	.10
Muscular rheumatism and certain other diseases of muscles	2,002	3	.10
Total	64,569	50	1.28

[1] Includes rheumatic diseases directly attributable to traumatisms.
[2] With respect to the disability separation data, the specified condition was the cause of separation from service; regarding deaths, it was the underlying cause of death; and for noneffectiveness, it was the cause of admission.

One of the outstanding purposes of the rheumatism centers of the U.S. Army was to conserve personnel, not only for military service but also for civilian life. Of 894 dispositions by certificates of disability for discharge at the Army and Navy General Hospital in 1944, 501 (approximately 50 percent) were due to rheumatic diseases that made the individuals unfit for further service. In 1945, 1,030 of 1,576, or about 56 percent, were also lost from service through certificate of disability for discharge. Every consideration was given to the possibility of conserving each of these soldiers for further military service, on limited service if full duty was not possible. However, even limited duty can prove strenuous for military personnel with musculoskeletal deformities or disabilities. None of those separated from service was considered suited to work as much as 8 hours a day.

Most of the patients with fibrositis, "psychogenic rheumatism," rheumatic fever, or gonorrheal arthritis were returned to duty, while the majority of those with rheumatoid arthritis, osteoarthritis, or gout were separated from service. Generally, those patients with osteoarthritis were older commissioned or noncommissioned officers who had had long service in the Army. Soldiers suffering from gout or gouty arthritis were unsuitable for military life because of the impossibility of following a medical or dietary regimen, and of the ever-present danger of provocative physical trauma. The impracticability of continuing in military service would be particularly true if there were frequent recurrences of acute gouty arthritis even in persons on limited military service.

The disposition of rheumatic patients by diagnosis at the Army and Navy General Hospital is shown in table 93. These are not consecutive admissions but rather groups of patients including enlisted men and officers with various diagnoses. No final statistics are available regarding the disposition of patients with rheumatic diseases from Ashburn General Hospital. Its 1944 Annual Report, however, contained the following statement: "* * * the disposition of by far the greater number of patients with rheumatoid arthritis has been separation from the Service upon certificate of disability and it is probable that this will continue to be the case."

TABLE 93.—*Disposition of 1,300 soldiers with rheumatic disease, Rheumatism Center, Army and Navy General Hospital, 1945*

Condition	Number of patients	Returned to duty (full or limited duty)		Separated from service, medical discharge or retirement	
		Number	Percent	Number	Percent
Rheumatoid arthritis, including rheumatoid spondylitis	500	76	15.2	424	84.8
"Psychogenic rheumatism"	200	128	64.0	72	36.0
Fibrositis, primary	150	123	82.0	27	18.0
Osteoarthritis	100	38	38.0	62	62.0
Rheumatic fever	50	39	78.0	11	22.0
Gonorrheal arthritis	20	13	65.0	7	35.0
Gout	10	1	10.0	9	90.0
Miscellaneous and unclassified cases of arthritis and "rheumatism"	270	171	63.4	99	36.6
Total	1,300	589	45.3	711	54.7

Source: Hench, P. S., and Boland, E. W.: The Management of Chronic Arthritis and Other Rheumatic Diseases Among Soldiers of the United States Army. Ann. Int. Med. 24: 822, May 1946.

CLINICAL PICTURE

In the early period of World War II, most of the rheumatic disease patients admitted to the Army and Navy General Hospital had been received from various military establishments throughout the continental United States, but by early 1944, the majority of patients were arriving from oversea hospitals. Many were returned by ship from the South Pacific Area or from the European theater. Others were transported by ambulance planes of the Military Transport Command. Some patients had arrived by plane within 4 to 6 days after leaving hospitals in the South Pacific (for example, within 4 days from Saipan to Hot Springs) ; others within 3 to 7 days from England, Italy, or France (for example, from Paris to Hot Springs in 3 days). This rapid evacuation of rheumatic soldiers from oversea hospitals to a hospital equipped especially for their needs was a strong morale builder among the military personnel and their very anxious relatives. In addition, the promptness of diagnosis and disposition and the adequate treatment programs also raised and maintained morale.

Unfortunately, no official final figures on the relative incidence of the rheumatic diseases are available from the Army and Navy General Hospital. From 1942 to 1945, there were 7,719 rheumatic disease admissions, of which 86.1 percent (6,647) occurred during 1944–45 (table 85). Very definite information can be gleaned from a survey of the first 2,000 consecutive admissions to the rheumatic disease section and the first 5,000 admissions (table 94). Since the patients sent to the rheumatism centers are selected, a census from such installations does not reflect a relative incidence of the rheumatic diseases in the Army as a whole. All the common forms of rheumatic diseases, as well as most of the rarer types, were seen at this rheumatism center.

As might be anticipated, rheumatoid arthritis presented the largest group of patients, affecting approximately one-third of all those admitted to the section. Approximately one-fifth of the patients admitted as "rheumatic" had no evidence of organic skeletal disease. These patients were suffering from a psychoneurosis which was manifested by musculoskeletal symptoms, a condition which had been termed by some as "psychogenic rheumatism," [16] and by others as "psychoneurotic rheumatism," [17] or "psychosomatic rheumatism." [18] The relative use of soldiers was largely responsible for the low incidence of gout and gouty arthritis. The highest incidence for gout was 1 percent as compared with approximately 4 to 5 percent frequently seen in civilian rheumatism clinics. The incidence

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[16] Boland, E. W., and Corr, W. P.: Psychogenic Rheumatism. J.A.M.A. 123: 805–809, 27 Nov. 1943.

[17] Halliday, J. L.: Psychological Factors in Rheumatism; a Preliminary Study. Brit. M.J. 1: 213–217, 30 Jan. 1937; 264, 6 Feb. 1937.

[18] Halliday, J. L.: Concept of Psychosomatic Rheumatism. Ann. Int. Med. 15: 666–677, October 1941.

TABLE 94.—*Incidence of the various rheumatic diseases based on the first 2,000 and 5,000 admissions to the Rheumatic Disease Section, Army and Navy General Hospital*

Diagnosis	2,000 cases [1]		5,000 cases,[2] percent
	Number	Percent	
Rheumatoid arthritis	686	34.3	35.2
Peripheral	390		
Spondylitis	209		
Both	87		
Psychogenic rheumatism	375	18.8	14.8
Pure (without organic disease)	231		
Superimposed (with organic disease)	101		
Residual (following organic disease)	43		
Fibrositis primary	272	13.6	14.6
Osteoarthritis	249	12.4	11.4
Primary	210		
Secondary	39		
Rheumatic fever	41	2.0	1.6
Gonorrheal arthritis	27	1.4	.8
Gouty arthritis	18	.9	1.0
Specific infectious arthritis	9	.5	.3
Rarer types of arthropathies	43	2.1	3.0
Joint tumors	8	.4	.3
Miscellaneous conditions	176	8.8	9.9
Nonclassified rheumatism and arthritis	96	4.8	8.2

[1] Annual Report, Army and Navy General Hospital, 1944.
[2] Annual Report, Army and Navy General Hospital, 1945.

of gonorrheal arthritis was quite low because of the chemotherapy which was available.

Approximately one-third of the patients with rheumatoid arthritis had rheumatoid spondylitis. This relative incidence was surprisingly high and in considerable contrast with experiences in civilian practice. For many months at a time, there were between 70 and 100 cases of rheumatoid spondylitis in the hospital. This rather high incidence was probably due to three factors: (1) Rheumatoid spondylitis affects males much more often than females and especially young males of military age (18–30 years); (2) the early symptoms of the disease, including vague intermittent low back pain, are difficult to evaluate and an early diagnosis had frequently not been made, including failure to recognize it in young men as they were being inducted into the Army; and (3) the strenuous physical exertion of army life and the training to which they were exposed probably soon aggravated the symptoms and revealed the early previously undiagnosed patients. The incidence of the various rheumatic diseases at the Army and Navy General Hospital and at Ashburn General Hospital are within about the same limits (table 95).

TABLE 95.—*Comparison of incidence of various rheumatic diseases among first 2,000 cases at Army and Navy General Hospital* [1] *and first 800 cases at Ashburn General Hospital* [2]

Diagnosis	Army and Navy General Hospital (Percent)	Ashburn General Hospital (Percent)
Rheumatoid arthritis	34.3	38.3
Psychogenic rheumatism	18.8	16.1
Fibrositis	13.6	4.8
Osteoarthritis	12.4	26.7
Rheumatic fever	2.0	
Gonorrheal arthritis	1.4	1.4
Gouty arthritis	.9	.6
Specific infections	.5	.2
Joint tumors	.4	.7
Miscellaneous conditions	15.7	11.2

[1] Annual Report, Army and Navy General Hospital, 1944.

[2] Personal communication from Col. J. B. Anderson, Lt. Col. John Harvey, Maj. David M. Kydd, and Lt. Charles W. Fogarty, Jr., Ashburn General Hospital.

PROBLEMS OF DIAGNOSIS

The first stated aim of the rheumatism centers was to provide "accurate diagnosis" (p. 478). The absolute necessity of this aim was indicated by the first admissions to the centers and emphasized and reemphasized with each succeeding group of admissions. The commonly stated transfer diagnoses of "acute arthritis," "chronic arthritis," or simply "arthritis" were inadequate for instituting proper therapy, estimating prognosis, or planning for the disposition of the patients. In fact, these terms often constituted no diagnosis at all. There were scores of patients with a diagnosis of "arthritis" who had no arthritis at all. There were patients who were presumed to have "osteoarthritis" when they really had rheumatoid arthritis or vice versa. Very few patients with gout were correctly diagnosed. A large proportion of soldiers transferred because of "muscular rheumatism," "myositis," or "fibrositis" were suffering from "psychogenic rheumatism." These errors were not reflections on individual medical officers but rather revealed the inadequate diagnostic level of the medical profession in rheumatologic matters, pointing up the extreme need for a wider and more critical understanding of the fundamentals of diagnosis in disease of the joints.

There were also several special problems relating to differential diagnosis. These included post-gonorrheal rheumatoid arthritis versus gonorrheal arthritis and psychogenic rheumatism versus fibrositis.

Post-Gonorrheal Rheumatoid Arthritis Versus Gonorrheal Arthritis

That rheumatoid arthritis could be precipitated by gonorrheal infection, just as by tonsillitis, influenza, or some other acute infection, was not

well understood. In addition, the possibility that a very mild or non-symptomatic rheumatoid arthritis could be aggravated by an acute genital gonorrhea was usually overlooked. Neither of those instances should have been considered as intimately involved with a venereal disease, but simply as rheumatoid arthritis precipitated by an acute infection which just happened to be a venereal disease. It was reported in the First World War by Pemberton and his associates [19] that approximately 1 percent of the cases of chronic arthritis seen among soldiers began in close relationship with the onset of gonorrhea.

Proved gonorrheal arthritis among American soldiers was apparently rare. Many more patients with a rheumatoid arthritis, precipitated or aggravated by a gonorrheal infection, were seen at the arthritis centers. Unfortunately, the majority of these patients were improperly labeled gonorrheal arthritis. They were unsuccessfully treated for this condition, before transfer, with sulfonamides, penicillin, or fever therapy, then sent to the center with a diagnosis of "gonorrheal arthritis resistant to penicillin and/or sulfonamides." Almost invariably those so-called cases of "gonorrheal arthritis resistant to chemotherapy" turned out to be rheumatoid arthritis, as shown by their subsequent course, their response to therapy, and in some cases, by articular biopsy.[20]

Many of these soldiers were on a limited pay status, in keeping with the regulations regarding treatment of a venereal disease. Prompt correction of the diagnosis improved the morale of the patient by reinstating his normal pay; it also permitted a realistic prognosis and the institution of proper therapy.

Psychogenic Rheumatism

Most physicians were familiar with psychoneurosis as it could manifest itself by symptoms referable to the gastrointestinal tract, the cardiovascular system, et cetera. Apparently, a large proportion of the medical profession was not familiar with psychoneurosis as it affected the locomotor system.

"Psychogenic rheumatism," a musculoskeletal expression of a functional disorder, tension state, or psychoneurosis, was one of the most common causes of generalized or localized aches and pains in muscles and in joints, not only in military life but also in civilian life. It was possible for it to exist alone or it could occur as a functional overlay of a true rheumatic condition, particularly fibrositis or rheumatoid arthritis. Probably the terminology "psychoneurosis manifested by musculoskeletal complaints" would have been more proper than the term "psychogenic rheu-

[19] Pemberton, R., Buckman, T. E., Foster, G. L., Robertson, J. W., and Tompkins, E. H.: Studies on Arthritis in the Army Based on 400 Cases. Arch. Int. Med. 25: 231–282, 335–404, March–April 1920.

[20] Hench, P. S., quoted by Harrell, W. E.: Penicillin and Other Antibiotic Agents. Philadelphia and London: W. B. Saunders Co., 1945, p. 348.

matism," or "psychosomatic rheumatism." However, it was found expedient to use the term "psychogenic rheumatism," because of its compactness and its understandability. Many individuals who were inadequate or unable to adapt to military life unconsciously found some solution to their problems by musculoskeletal complaints which were often misinterpreted as "rheumatism" or "arthritis." Those patients did have symptoms, although they were not objective or constitutional, nor could roentgenographic or biochemical manifestations of disease be found. It was most unusual for them to have any real rheumatism, synovitis, arthritis, or organic muscular lesions. On the other hand, if some minor musculoskeletal condition did exist, it was insufficient to account for the severity of the disability. Many times, those patients would have functional complaints referable to other systems as well. The severity of the psychoneurosis could vary from that of a very mild tension state to a major conversion hysteria; not unusual were bizarre gaits, peculiar articular postures and camptocormia (a forward bending of the trunk of the body, often a symptom of some traumatic neurosis), or flexed fingers caused by hysteria.

It is notable that from 16 to 19 percent of the rheumatism patients admitted to the several rheumatism centers had no significant organic rheumatic disease (table 95). A prompt recognition of the presence of "psychogenic rheumatism" soon after the complaint was first made could have gone a long way in reversing this condition before it had become well established by a long period of complaining. This might very well have provided better conservation of manpower, as well as reduction of pension payments after separation from the military service for neuropsychiatric conditions.

Psychogenic Rheumatism Versus Fibrositis

The greatest problem in the differential diagnosis of "psychogenic rheumatism" was with fibrositis. Generally speaking, fibrositis puts its victims at the mercy of alterations in external environment; therefore, weather, heat, cold, humidity, rest, and exercise would influence the condition for better or for worse. In contradistinction, the person with "psychogenic rheumatism" is a victim of his internal environment: the symptoms vary depending upon mood or psyche, pleasure, excitement, mental distraction, worry, or fatigue. The differentiation proved very difficult if a patient had a mild fibrositis with a marked functional overlay.

TREATMENT OF THE RHEUMATIC DISEASES

When the first rheumatism center was established, The Surgeon General, Maj. Gen. Norman T. Kirk, said, "Don't make the center a rheumatism repository." This was outstanding advice, since nothing could

destroy a soldier's potentialities for salvage (his morale, his will to recover and to return to duty) more readily than the atmosphere of a "chronic hospital," or a "rheumatic old soldiers' home." The majority of the personnel admitted to the center had already been hospitalized for prolonged periods of time, evacuated great distances around the world, and in a state of uncertainty. They had no idea whether they would be returned to duty, even limited duty, or whether they would be discharged from the Army. The most immediate question in their minds was what the future might hold for them.

Certainly, for the best interests of the military, as well as the country as a whole, no hasty disposition could be made. It was important, however, that, to develop an estimate of the situation for each patient, a prompt examination of the patient with a definite diagnosis was necessary at the earliest possible moment. The soldier was informed whether a prolonged period of treatment was going to be necessary, whether he would remain in the hospital only a short time, and what the possibilities were for him to return either to military duty or to civilian employment. An overlong hospitalization could easily turn an individual into a soldier with a hospital habit and decrease his salvageability. Even though previously well oriented, he might beome a hospital-engendered psychoneurotic with a fixation on illness and a functional overlay that could be more difficult to treat than the original organic condition upon which it was superimposed.

It was a policy, therefore, that immediately upon arrival at the hospital the patient was informed that he could be certain his period of hospitalization would not be indefinite; that after a few days of thorough initial physical examination and study a progressive, well-oriented program of intensive treatment would be initiated; and that, if he had been serving overseas for a prolonged period of time, a furlough would be arranged as soon as possible. Under any circumstances, he would be informed that his intensive treatment, either before or after furlough, would probably continue for 3 to 8 weeks or longer, if necessary, but he would be told the possibilities for reconditioning him to a useful way of life. Every effort was made to maintain a pleasant atmosphere in the hospital and annex which would be conducive to high morale and optimism rather than pessimism.

The comprehensive schemes of treatment used at the rheumatism center for the various rheumatic diseases were those approved by the American Rheumatism Association,[21] and used by the leading rheumatologists of the country. Although the rheumatism center did have unusual facilities for physical therapy and hydrotherapy, these facilities were used properly but without undue emphasis and certainly not to the

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[21] Hench, P. S., Bauer, W., Boland, E. W., Dorsan, M. H., Freyberg, R. H., Holbrook, W. P., Key, J. A., Lockie, L. M., and McEwan, C.: Rheumatism and Arthritis; Review of American and English Literature for 1940. Ann. Int. Med. 15: 1002–1108, December 1941.

exclusion of any other useful measure. For the most part, rheumatic patients were gentle, docile, and well behaved. They really asked very little of their physicians; they apparently were aware that no elusive "rapid cures" were available but they did look for a diagnosis and a man-to-man understanding of what they were up against, what they could do for themselves, and what they should do to prevent making themselves worse. This type of patient had very little respect for a physician who tended to brush them off with an incomplete diagnosis or who gave them a fancy diagnosis in medical terms and a "few well chosen words."

To orient these rheumatic patients in the best possible way, a regular rotating series of group consultations or lectures on rheumatism were given in layman's language. There were 12 different lectures. Two or three of them were oriented on general topics for all patients; others were given only to the appropriate group, depending upon the particular disease with which they suffered. Patients with one diagnosis were not admitted to the specific lecture designed for those with a different diagnosis. Very particularly, patients with "psychogenic rheumatism" were not permitted to attend the lectures for patients with rheumatoid arthritis or fibrositis, simply to prevent them from developing misinterpretations of their own conditions. There were special talks designed for this particular group of patients and their needs which were given jointly by rheumatologists and a psychiatrist. Each patient was given a card (fig. 63) with the assignment of the lectures he was to attend.

The lectures were on the following subjects:

1. The meaning of rheumatism and arthritis.
2. Facts, fads, and false concepts about rheumatism.
3. Fibrositis—its meaning and management.
4. Rheumatoid arthritis and its management.
5. Rheumatoid spondylitis and its management.
6. Facts about osteoarthritis.
7. Gout and gouty arthritis.
8. Shoulder disabilities and their management.
9. Body mechanics in relation to disability of joints.
10. Home physical therapy (motion picture and demonstration).
11. Emotional tension and its relation to "rheumatism."
12. The management of rheumatic fever.

These group lectures were not a substitute for but rather supplemental to individual consultations with ward officers. The lectures were designed to project the individual beyond his period of Army hospitalization and actually into his home and to indicate at least some of the benefits that he might derive from the more formal treatment received in the hospital. They also served as an introduction to the advice which each patient would receive from his home physician. These lectures were

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NAME   RANK   WARD

     The Rheumatism Center at the Army and Navy General Hospital offers a series of lectures on arthritis and rheumatism. These group consultations are considered as part of your treatment program. You are to attend only those lectures (marked "X" on reverse side of card) which pertain to your condition.

     Place -- Red Cross Game Room, Basement Eastman Annex.
     Hour -- 1:00 P.M.
     Day -- Consult ward bulletin board for lecture schedule.

     Please feel free to ask questions.

A&NGH 2-7-45

To Attend	Lecture Number	SUBJECTS	Have Attended
☐	1.	The types of arthritis and rheumatism and their meaning.	☐
☐	2.	Fads, fancies and false concepts in rheumatism and arthritis.	☐
☐	3.	Mechanics of the body and joint disability.	☐
☐	4.	Home physiotherapy: Demonstration and motion picture.	☐
☐	5.	Emotional tension and its relation to rheumatism.	☐
☐	6.	Rheumatoid arthritis: Its nature and its treatment.	☐
☐	7.	Rheumatoid spondylitis and its management.	☐
☐	8.	Fibrositis: Its meaning and management.	☐
☐	9.	Shoulder disabilities and their management.	☐
☐	10.	Osteoarthritis: Its meaning and management.	☐

FIGURE 63.—Card presented to each rheumatic patient upon completion of diagnosis, indicating which lectures he should attend. (Top) Front of card. (Bottom) Back of card.

well received and proved to be a great timesaver for the busy medical officers. The recipients of the lectures were encouraged to ask qustions at the end of each lecture, particularly on points that bothered them or that they did not understand. They were informed at the time for questions that any question, no matter how trivial it might seem, was a valid question. It was found that these lectures tended to improve morale. Probably, this was because each individual discovered that he was not alone with

his own problem but that others were as bad as or worse than he was and that he had every reason to take courage.

Rheumatoid Arthritis

The treatment for peripheral rheumatoid arthritis was quite standard and included, among other things, the removal of obviously infected foci, the providing of highly nutritious diets (but no food fads, "antirheumatism vitamins," or specific diets), foreign protein fever therapy in selected cases, simple analgesics, physical therapy, occupational therapy, orthopedic measures to prevent or correct deformities, and gold salts carefully administered to selected patients whose rheumatoid arthritis was progressive despite the use of other more conservative measures. These various measures were blended along with physical reconditioning to restore the best function that could be achieved for each patient.

Rheumatoid Spondylitis

The characteristic posture of patients with rheumatoid spondylitis dictated the stress that was placed on posture training. It was a highly successful part of the total treatment program, producing correction or near correction of the posture in all but those patients whose spines were ankylosed in an abnormal posture. Probably much of the success of posture training was due to generally successful relief of pain by roentgen therapy.

X-ray therapy appeared to relieve pain and probably halt the progression of the disease. For the purpose of treatment the spine was divided into four areas; namely, (1) the sacroiliac joints and lumbar spine; (2) the lower half of the thoracic spine; (3) the upper half of the thoracic spine; and (4) the cervical spine. A total of 450r to 600r in three or four divided doses was administered to each segment of the spine involved clinically. Treatments were given every other day, with all areas treated within 9 or 10 days. A second course of therapy would be given after an interval of 3 months if symptoms persisted.

All the adjunctive therapy, with the exception of gold therapy, mentioned in the treatment of peripheral rheumatoid arthritis, was also employed in these patients.

Osteoarthritis

Despite the X-ray evidence of osteoarthritis, most of the patients had a moderate to severe secondary fibrositis with muscle atrophy. The treatment program was directed against both conditions.

These patients were given salicylates and heat treatments for the relief of pain. Weight-bearing joints were stabilized by improving muscle strength and orthopedic supports when required. The patients were instructed in ways and means of modifying their living habits to decrease the further wear and tear in the involved joints.

The treatment of osteoarthritis of the cervical spine, in addition to the general treatment already outlined, received intermittent Sayre halter cervical traction and posture training. The traction was very effective in relieving the radicular pain of this type of osteoarthritis.

Fibrositis

One of the most important elements in the treatment of either primary or secondary fibrositis was the assurance that this was not a type of arthritis and that it was a self-limited condition with no residual deformity. Salicylates and heat were given for relief of pain. Muscle rehabilitation and posture training exercises were prescribed and carefully supervised.

Psychogenic Rheumatism

The treatment of psychogenic rheumatism, although very interesting, posed a most difficult problem, second only in importance to the treatment of rheumatoid arthritis. Although it was a pleasure to be able to reassure soldiers with psychogenic rheumatism that they had no arthritis or muscular rheumatism and that they need not fear that they had a crippling disease, it was always tempered by the difficulty of helping them to develop insight and accept the diagnosis, at least to the point of submitting wholeheartedly to a trial of psychotherapeutic reconditioning. Of course, the latter was much more important than physical reconditioning for this group of patients. Any attempt to use physical reconditioning alone in this type of patient accomplished little or nothing.

Those particular patients were not generally given formal courses of physical therapy or other treatments that would be used for "organic rheumatism," except as diagnostic or therapeutic tests. This was because many treatments of this type tended to fix more firmly in their consciousness the belief that they had a true organic disease.

Gouty Arthritis

The acute attacks of gouty arthritis were treated with colchicine. These patients were carefully instructed in the constitution and use of low-purine diets as a means of decreasing the serum uric acid level and to decrease the number of acute attacks. Large doses of aspirin for three

to four successive days each week were administered for the uricosuric effect. Concomitant with the aspirin administration, sufficient sodium bicarbonate was given to maintain the urine in an alkaline state to prevent, as far as possible, the formation of uric acid stones.

Miscellaneous Therapy

Acute gonorrheal arthritis and other specific infectious arthritis were treated with penicillin, followed by rehabilitation. Bursitis and tenosynovitis were treated with heat, rest of the part and splinting if necessary, followed by rehabilitation and restoration of function when possible. Joint tumors, villus synovitis, and joint biopsies were transferred to the orthopedic department for the surgery required.

RECONDITIONING

The task of getting a convalescing soldier physically and mentally prepared to return to military duty is generally spoken of as reconditioning.[22]

A soldier with rheumatic disease who was considered to be salvageable was "reconditioned" in several steps. He was first reconditioned in the hospital by means of a medical program, followed by a supplemental period of 2 or more weeks during which time he lived in a convalescent barracks and participated in a daily program of physical activity carefully measured to his abilities. Before his transfer to the reconditioning barracks, he was frequently assigned, along with three to five other soldiers with essentially the same needs for reconditioning, to a noncommissioned officer patient who had already transferred to the convalescence barracks or was about to do so, who would periodically gather his squad together and supervise the performance of the reconditioning exercises assigned on the ward.

The ability of these patients to participate in reconditioning and convalescent programs was determined by the ward officer. Some, of course, with transient rheumatic disease could participate in very strenuous programs. Other patients who could only be expected to return to limited service at the most were recommended for less strenuous activities. In every instance, however, an attempt was made to apply the reconditioning program on an individual prescription basis.

REHABILITATION

If the type of rheumatic condition from which the soldier suffered precluded the possibility of his return to duty within a reasonable period

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[22] Hillman, C. C.: The Reconditioning Program in Army Service Forces Hospitals. Mil. Rev. 24: 10–12, April 1944.

of time, particularly if his disease was essentially progressive and disabling, he would be considered ready for a discharge to civilian life and for subsequent followup treatment by his civilian physician or, if necessary, by a veteran's facility. The Army acknowledged an obligation to a soldier in this category, just as for one who might return to some form of duty. It was necessary to prepare soldiers, not only physically but mentally, to return to a useful civilian life despite the rheumatic disability. This was spoken of as rehabilitation.

Since, after discharge from the Army, the arthritic patient may find it necessary to modify the pattern of his life to a considerable extent to avoid certain factors that might aggravate his disease, it was necessary to instruct him to make only those alterations in his life that were unavoidable but not to the extent of engendering defeatism. The educational program, including the group lectures, and the individual consultations with the ward officers were the chief weapons against the dangers of a wheelchair or crutch psychology. Every attempt was made to have each discharged arthritic patient continue to regard himself as a vital unit of his community. Every effort was made to teach him to live with his disease, not for it. This was the only possible way to make him consider his rheumatism as an avocation rather than a vocation. If he should prematurely or needlessly consider the disease a vocation, then he had taken too long a step toward the sterile existence of the pensioner's rocking chair.

It was the policy of the rheumatism centers to consider patients with rheumatoid arthritis, particularly when it was progressive, as eligible for discharge. However, even many of those patients were salvageable, particularly if they had a good insight into their disease and were only mildly affected.

On the other hand, the disposition of patients with psychogenic rheumatism required even more individual consideration. Many soldiers affected with psychoneurosis of a mild or moderate degree could be expected to render effective service. When, despite conscientious treatment, psychogenic rheumatism persisted to the extent that its victim no longer represented a unit of manpower, there was no other recourse but to recommend him for discharge.

The standing order was "to conserve manpower." The mission of the rheumatism center was to diagnose and treat chronic rheumatic illnesses in an effort to salvage as many men as possible. Despite the most dedicated attempts, only about 45 percent could be returned to some type of duty.

TRAINING

From the time that the rheumatism centers became functional, there was a need for training medical officers in the diagnosis and treatment

of rheumatic diseases. All ward officers had frequent conferences with the chief of the rheumatic disease section to present their findings on all new admissions, to discuss progress of patients receiving therapy, and to plan for dispositions of patients. In addition, there were weekly staff conferences and X-ray conferences to discuss the rheumatic diseases.

The director of the rheumatism center conducted a weekly clinic as a part of the educational program for officers assigned to the section, and for visiting officers, local physicians, and other interested members of the staff.

It was very fortunate that the medical consultant for the Eighth Service Command was an eminent rheumatologist. At the time of his periodic visits, several days were devoted to the presentation and discussion of cases, methods of therapy, ward rounds, and stimulating roundtable discussions.

CLINICAL INVESTIGATION

"It is hoped to make this hospital a source of extensive knowledge on arthritis for the whole medical profession. Studies will be carried on in the use of special drugs, such as sulfonamides and penicillin, in the treatment of arthritis." This is an excerpt from the War Department announcement of the establishment of the first rheumatism center at the Army and Navy General Hospital. It was evident that the Army realized there was an obligation, not only to the soldier with arthritis as an individual, but also as a representative of all human beings with the same problems. The physicians in the various rheumatism centers were encouraged to improve their clinical knowledge and, if possible, the methods of treatment for the benefit of the entire medical profession. A constant effort was made to fulfill these obligations by clinical investigations carried out in all centers. Despite the newness of these centers, they rapidly became the largest rheumatism facilities in the world. They were both treatment centers and supervised schools of rheumatology for physicians assigned temporarily for instruction. They provided a unique opportunity to benefit the rheumatic soldier, his medical officer, the medical profession, and humanity as a whole.

The clinical investigations at the Army and Navy General Hospital during the year 1944 were as follows:

1. Penicillin was found to be ineffective against rheumatoid arthritis.

2. Penicillin was found to be an important adjuvant in the treatment of agranulocytosis resulting from chrysotherapy; that is, as a treatment for the infections which may complicate an agranulocytosis.

3. Studies on the incidence of various types of rheumatic diseases admitted to the facility, as well as pertinent observations on the military aspects of the common rheumatic diseases.

4. Studies on psychogenic rheumatism and its differentiation from fibrositis.[23] In the course of this study, differentiation between fibrositis and "psychogenic rheumatism" was developed (table 96).

TABLE 96.—*Differentiation between fibrositis and "pyschogenic rheumatism"*

Generalities	Fibrositis, primary type	"Psychogenic rheumatism"
General attitude_____	Cooperative, earnest, "objective."	Tense, anxious, "subjective," defensive, antagonistic.
Chief complaint_____	"Joints hurt and feel stiff"__	"Can't quite describe it, doctor. It's like * * *."
Chief symptoms_____	Aching, soreness, stiffness, fatigue.	Burning, tightness, weakness, numbness, tingling, queer or tired sensations.
Time of day when symptoms are worse.	Morning and/or late afternoon.	Inconstant—often continuous day and night.
Aggravation or amelioration dependent on:	External or physical environment.	Internal or mental environment.
Effect of mental preoccupation (theater, movie, bridge, etc.).	No definite relief, symptoms intrude.	Often marked relief but perhaps "pays for it afterwards."

Symptom analysis:
1. Pain:
     Amount_____
     Constancy_____
 	
     Duration_____
 	
     Location_____
     Migration_____
 	
2. Stiffness_____
 	
3. Fatigue_____
	
	+ to + +_____
	Varies in intensity during day; worse in morning, better at noon, often worse again later in day.
	Hours or days, remissions, exacerbations.
	
	Anatomical_____
	May not migrate; if so, migrates in anatomical fashion.
	Worse after much rest (jelling); more marked in early morning; better after mild exercise.
	A.M. on waking: 0 to +; P.M. +; "disability causes fatigue."
		
		+ to + + +
		Tendency to be constant, "bad all the time."
		
		Momentary or constant, "no different," getting worse.
		Often not anatomical.
		Bizarre, hemalgia, etc.; may follow no anatomic pattern.
		Minimal or not present; jelling not characteristic.
		
		Early A.M. + to + + +; may be constant; "fatigue causes disability."

[23] Hench, P. S., and Boland, E. W.: Management of Chronic Arthritis and Other Rheumatic Diseases Among Soldiers of the United States Army. Ann. Rheumat. Dis. 5: 106–114, June 1946.

TABLE 96.—*Differentiation between fibrositis and "pyschogenic rheumatism"*—Continued

Generalities	Fibrositis, primary type	"Psychogenic rheumatism"
Effect of rest_____	After prolonged rest— worse (jelling).	Improvement or no effect.
Effect of exercise_____	Better "limbers up"_____	Worse during and after.
Effect of applied heat_____	Temporary relief—hours____	Variable—often worse.
Effect of weather_____	Worse when cold and damp; "weather prophet."	Variable.
Effect of therapy: In general_____ Patient's attitude_____ Aspirin_____ Physical therapy_____	Temporary relief_____ Admits relief_____ Temporary relief—hours____ Temporary relief_____	"Nothing helps me, doctor." Defies finding a cure. Usually no relief (aspirin futility), or "never tried it" (aspirin inutility). Variable—often worse.
Response to examination_____	Cooperative; tenderness; consistent.	Fearful, resistant; "touch me not" reaction.
"Extras" (associated functional complaints).	0 to +_____	+ to + + + +; bizarre limps and postures; headaches; globus hystericus; sighing respirations; precordial pains; insomnia; nervousness; tremor; etc.

The factors underlying psychogenic rheumatism were determined to be different kinds of fears and frustrations. More specifically they consisted of (1) combat fatigue—less stable soldiers reached the saturation point when the subconscious demand for self-preservation caused the development of musculoskeletal symptoms to save the man's life or his mind; (2) maladjustment to discipline, criticism, or a menial job; (3) lack of privacy caused by military herding; (4) homesickness and loneliness; (5) worry about family finances or illness; (6) worry about lack of promotion; and (7) worry over fidelity of wife, fiancee, or even himself.

Successful treatment was dependent upon the awareness that the soldier had psychogenic rheumatism and that psychiatric treatment was necessary. This type of individual could frequently be salvaged since the result of psychiatric treatment was often most gratifying.

5. Differential diagnosis between post-gonorrheal rheumatoid arthritis and gonorrheal arthritis.

The joint lesion of gonorrheal arthritis was known to be a severe, rapidly destructive infectious arthritis. Without specific therapy to overcome infection, it completed the destruction of the articular cartilage and "burned out" within a period of 3 to 4 months, leaving a useless, often ankylosed, joint. It responded well to penicillin intra-articularly.

Many patients transferred to the Army and Navy General Hospital were seen 3 to 6 months after the onset of the arthritis. Adequate penicillin and sulfonamides, or both, had been administered previously with no benefit to the joint involvement. Instead of the hot, inflamed, excruciatingly painful joint of an acute infection, these patients had a chronic, mild to moderately painful joint or joints. Differentiation of a rheumatoid arthritis precipitated by the acute infection of a venereal gonorrheal arthritis was made by (1) the subsequent course of a chronic rheumatoid-like arthritis often with additional joints becoming involved; (2) therapeutic tests with penicillin when indicated; and (3) biopsies of the joints when indicated.[24]

6. Further studies on palindromic rheumatism. The clinical characteristics of palindromic rheumatism as first reported [25] were confirmed. Various therapies were tried, including purine-free and low-purine diets, colchicine, intravenous and oral calcium preparations, and search for and eradication of foci of infection and febrile reactions with intravenous typhoid vaccine. The last seemed to have a measure of success, but often only of a temporary nature for a few months.

During the year 1945, the investigative program at the Army and Navy General Hospital was more extensive, largely because the rheumatism center was more firmly established; more trained rheumatologists were assigned to the rheumatic disease section; and more medical officer trainees, who were interested in assisting in the various studies, were assigned to the hospital. The clinical investigations for that year were:

1. Cardiac changes occurring in rheumatoid arthritis—a clinical and electrocardiographic study.

2. Further studies on palindromic rheumatism. This investigation was a continuation of the one begun in 1944. Atypical forms of palindromic rheumatism and various types of onsets and clinical courses of the disease were becoming apparent. Some of these patients appeared to have bouts of rheumatoid arthritis which cleared within a few weeks, leaving no residuals. This latter type of arthritis was differentiated into "episodic rheumatoid arthritis." [26]

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[24] See footnotes 20, p. 496, and 23, p. 506.

[25] Hench, P. S., and Rosenberg, E. F.: Palindromic Rheumatism. Arch. Int. Med. 73: 293–321, April 1944.

[26] Hench, P. S.: Episodic Rheumatoid Arthritis. Arizona Med. 4: 62, 1947.

The studies of palindromic rheumatism and the failures of the various forms of treatment, as well as the gradual development of a chronic rheumatoid arthritis in some cases, raised the question as to whether it might not be an atypical form of rheumatoid arthritis. These impressions led to a trial of gold therapy in these patients.[27] Three patients were treated with a favorable response to gold thioglucose.

3. The diamidines in the treatment of rheumatoid arthritis.

4. The clinical and pathologic features of psoriatic arthritis and psoriatic arthropathy.

5. Rheumatoid spondylitis—a study of 100 cases with special reference to diagnostic criteria.[28] This was a study as a followup to one done at Hoff General Hospital, Santa Barbara, Calif. The purpose of this study was to determine early diagnostic criteria for the disease. Patients with unequivocal evidence of the disease were included. Each patient was questioned in detail in order to determine the symptoms which occurred prior to the finding of definite spinal involvement. It was determined that the onset was insidious. By a correlation of the symptoms as the disease progressed, with X-rays, it was determined that the earliest roentgenographic changes appeared in the sacroiliac. It was recommended that rheumatoid spondylitis should be suspected in young men with recurrent or persistent low back aching and stiffness, and that the sacroiliac joints should be examined for the characteristic changes which they had found of a bilateral sacro-illiitis.

6. Rheumatoid spondylitis—correlation of clinical and roentgenographic features.[29] A group of 50 soldiers with definite X-ray evidence of rheumatoid spondylitis were studied. In two-thirds of these patients, the clinical findings were advanced to a greater degree than the roentgenographic changes. Attempts were made to find explanations for all the symptoms in relation to the extent of involvement. Since clinical involvement was at least one or two spinal segments higher than the roentgenographic evidence, if X-ray therapy was to be administered it should be chosen on the basis of the clinical involvement.

7. The cerebrospinal fluid in rheumatoid spondylitis.[30] Since rheumatoid spondylitis must be differentiated from other causes of chronic low back disability, this study was undertaken to determine whether biochemical studies of cerebrospinal fluid might afford data upon which clear and early differentiations could be made.

[27] Boland, E. W., and Headley, N. E.: Treatment of So-Called Palindromic Rheumatism With Gold Compounds. Ann. Rheumat. Dis. 8: 64–69, March 1949.

[28] Boland, E. W., and Present, A. J.: Rheumatoid Spondylitis; Study of 100 Cases With Special Reference to Diagnostic Criteria. J.A.M.A. 129: 843–849, 24 Nov. 1945.

[29] Boland, W. E., and Shebesta, E. M.: Rheumatoid Spondylitis; Correlation of Clinical and Roentgenographic Features. Radiology 47: 551–561, December 1946.

[30] Boland, E. W., Headley, N. E., and Hench, P. S.: Cerebrospinal Fluid in Rheumatoid Spondylitis. Ann. Rheumat. Dis. 7: 195–199, December 1948.

Moderate increases in protein content of the spinal fluid were found in patients with rheumatoid spondylitis. The increase was due largely to the severity of the disease rather than the duration. The elevation of spinal fluid protein was found to be of little value in differentiating rheumatoid spondylitis from other spinal conditions. When, however, the protein content was elevated above 100 mg. per 100 cc., some other cause should be sought, even though spondylitis was also present.

8. The use of penicillin in the treatment of agranulocytosis—report of a study resulting from chrysotherapy in rheumatoid arthritis.

9. The management of chronic arthritis and other rheumatic diseases among soldiers in the U.S. Army.

10. Precipitating and predisposing factors in rheumatoid arthritis among soldiers.

11. The incidence of rheumatic diseases among soldiers—a study of 6,000 cases at an Army rheumatism center.

12. Roentgen therapy in the treatment of rheumatoid spondylitis.[31] Although roentgen therapy had been administered for rheumatoid spondylitis, there was considerable doubt about its efficacy. This study was designed as a blind triple crossover to determine the benefit of X-ray therapy. Twenty-five patients received roentgen therapy to the area (one or more courses) of the spine clinically involved over a period of 6 months. A second group of 25 patients were exposed to the roentgen therapy equipment but no roentgen rays on one or more occasions for 6 months. The third group of 25 received physical therapy. All received salicylates as needed. Between the sixth and the ninth months, the groups were crossed over. At the end of 9 months, all had received one or more courses of 600r to each area of the spine clinically involved; many had had a "psychic" X-ray treatment; and all had been given physical therapy, particularly posture training. There was a 92-percent response to the roentgen therapy.[32]

13. Post-gonorrheal rheumatoid arthritis.

Ashburn General Hospital functioned as a rheumatism center for 15 months and 18 days, beginning on 1 September 1944. It was declared surplus on 12 December 1945. All patients were disposed of by 18 December 1945.

The officers assigned to the section on rheumatic diseases had very fine opportunities to study these conditions in all their manifestations. Despite the limited time this center was in operation, various types of research in rheumatic diseases were carried out:

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[31] (1) Smith, R. T., Boland, E. W., Shebesta, E. M., and Hench, P. S.: Roentgen Therapy in the Treatment of Rheumatoid Spondylitis. Presented at American Rheumatism Association Annual Meeting, New York City, June 1946. (2) Boland, E. W.: Medical Progress: Rheumatoid Spondylitis; Its General Features and Management. California Med. 65: 285–292, December 1946.

[32] Roentgen therapy became the treatment of choice for rheumatoid spondylitis until 1954, when the question was raised of a possible increase in the incidence of blood dyscrasia occurring in patients with rheumatoid spondylitis who had received X-ray therapy. This has not been resolved to the present.—R. T. S.

1. Arthritis resembling Reiter's syndrome.[33]

2. The penetration of penicillin into joint fluid following intramuscular administration.[34]

3. The effect of Prostigmine (neostigmine) on the muscle spasm in rheumatoid arthritis.[35]

4. The diagnosis and treatment of Reiter's syndrome.[36]

5. Gold therapy in the treatment of rheumatoid arthritis. Only 21 patients were considered suitable for gold therapy before the investigation was summarily terminated by the closure of the center.

Although chrysotherapy enjoyed a measure of popularity in civilian medical circles, it had not been an approved method of treatment in the rheumatism centers. Approval was lacking because of (1) the prolonged period of weekly injections required (up to 24 or more) ; (2) the general belief that gold was highly toxic; and (3) the lack of definite evidence to show that gold was capable of producing remissions of the disease.

The possible benefits which might be achieved with gold therapy in 1945 were severely limited by the fear of the severe toxic effects of agranulocytosis, exfoliative dermatitis, and renal damage, particularly since there was no known antidote for gold. Consequently, treatment programs were arbitrarily limited to 20 to 24 weekly injections; to an overall total dosage of 800 to 1,000 mg. of the drug; or were administered in courses with rest periods without gold following each remission. These limitations produced an unspectacular remission rate of approximately 35 percent.

The discovery of the dramatic changes that could be produced in rheumatoid arthritis by ACTH and cortisone and its derivatives directed the attention of many rheumatologists from chrysotherapy. On the other hand, the beneficial effect of the adrenocorticosteroids in the treatment of gold toxicity encouraged others. With the further revelation that BAL (British anti-lewisite)[37] was a specific antidote for gold toxicity, much of the stigma attached to gold was removed.

Investigators, no longer hampered by the arbitrary limiting of gold to a dose that produced the least toxicity in the greatest number of patients, began to increase the remission rate to as high as 65 percent by more prolonged treatment. They also eliminated the rest periods from

[33] Hollander, J. L., Fogarty, C. W., Jr., Abrams, N. R., and Kydd, D. M.: Arthritis Resembling Reiter's Syndrome; Observations on 25 Cases. J.A.M.A. 129: 593–595, 27 Oct. 1945.

[34] Balboni, V. G., Shapiro, I. M., and Kydd, D. M.: Penetration of Penicillin Into Joint Fluid Following Intramuscular Administration. Am. J.M. Sc. 210: 558–591, November 1945.

[35] Balboni, V. G., Hollander, J. L., and Kydd, D. M.: The Effect of Prostigmine (Neostigmine) on the Muscle Spasm in Rheumatoid Arthritis. Presented at American Rheumatism Association Annual Meeting, New York City, June 1946.

[36] Hollander, J. L.: Diagnosis and Treatment of Reiter's Syndrome. M. Clin. North America 30: 716–723, May 1946.

[37] (1) Regan, C., and Boots, R. H.: Treatment of Gold Dermatitides; Use of BAL. J.A.M.A. 133: 752–754, 15 Mar. 1947. (2) Cohen, A., Goldman, J., and Dubbs, A. W.: Treatment of Acute Gold and Arsenic Poisoning; Use of BAL. J.A.M.A. 133: 749–752, 15 Mar. 1947. (3) Margolis, H. M., and Caplan, P. S.: BAL in Treatment of Toxicity From Gold. Ann. Int. Med. 27: 353–360, September 1947.

gold and prolonged the remissions by giving a maintenance at 2- to 4-week intervals for months to years.[38]

SUMMARY

Of the more than 500,000 patients with rheumatic diseases admitted to hospitals between the years 1942–45, less than 20,000 of them were transferred to the arthritis centers at the Army and Navy General Hospital and Ashburn General Hospital. As had been recommended originally, not all patients were to be sent to the centers because those with acute and short-lived situations could be treated locally. Only those with the possibility of a need for prolonged treatment or diagnostic problems were considered eligible for admission to these hospitals. Even among those patients who were considered to be poor risks, approximately 45 percent could be returned to some type of military duty. The need for rheumatism centers has been well established from the experience in World War II.

It is conceivable that a greater conservation of manpower would be possible among military personnel with rheumatic diseases. Specific diagnosis at an earlier hospitalization could permit effective treatment and decrease the need for evacuation to the Zone of Interior. This would be particularly true of the second most common rheumatic condition, psychogenic rheumatism. Immediate recognition would permit adequate psychiatric therapy to prevent this conversion state from becoming a fixed disability.

Provision should be made in all theaters of operations to have at least one officer, trained in the care of rheumatic diseases, on the medical staff of each hospital facility. He would be responsible for making a prompt diagnosis, initiating therapy in all patients, and determining whether they could be treated there and returned to duty or would require more prolonged treatment and should, therefore, be evacuated.

Special rheumatic disease centers should also be available for the care of chronic rheumatic diseases and to handle diagnostic problems. Conservation of military manpower should continue to be an important consideration in these centers. An additional responsibility should be assigned; namely, conservation of civilian manpower for those patients where there is no possibility of further military duty. These centers should be staffed as fully as possible with well-trained rheumatologists, employing the latest refinements in the treatment of rheumatic diseases. Even more emphasis should be placed on clinical investigations which, carried out in the largest facilities of their type in the world, under the supervision of the top experts in our Nation, could lead to greater conservation of manpower.

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[38] Finally, in 1958, a remission rate of 82 percent was achieved by gradually increasing the weekly doses of gold in those patients who failed to respond to 50 mg. per week for 12 weeks. See Smith, R. T., Peak, W. P., Kron, K. M., Hermann, I. F., DelToro, R. A., and Goldman, M.: Increasing the Effectiveness of Gold Therapy in Rheumatoid Arthritis. J.A.M.A. 167: 1197–1204, 5 July 1958.

CHAPTER XIX

Peripheral Neuritis

George D. Gammon, M.D.

The incidence of neuritis in World War II was not high, and the condition, statistically at least, was of relatively minor concern among the medical and surgical problems of the Army. Practically, its importance arose chiefly from the severity of the invalidism it produced. Several new types were recognized, but no new causative agents were discovered. Ultimately, the greater number of cases were recognized as being due to diphtheria. This recognition was due to the growing familiarity with clinical manifestations, to the improvement in confirmatory diagnostic tests, and to the rising incidence of diphtheria toward the end of the war, particularly in Europe. Experience brought, too, a wider realization that an albuminocytologic dissociation in the spinal fluid could occur in a wide variety of neuritides and that this dissociation, of itself, did not establish a diagnosis of infectious polyneuritis of the Guillain-Barré type.

The first part of this chapter is an account of the problems as they appeared in the various theaters during the course of the war; the second part is an attempt to characterize the various syndromes and to emphasize the difference between them, in the conviction that clinical distinctions are themselves of value and must be maintained when causative agents cannot be defined.

Part I. Clinical Experience

Observations made early in World War II, cited by McGuinness,[1] indicated that from 10 to 76 percent of American servicemen were susceptible to diphtheria, depending on their prior residence. Since it was known that they would enter foreign areas in which the disease was endemic, the reports of cases in U.S. troops from the Pacific areas and the China-Burma-India and Mediterranean theaters were not unexpected. In these regions, however, the problem of proving a suspected diagnosis was fraught with difficulties. The demonstration of virulent micro-organisms in lesions of the throat or the skin was not easy, nor was the environment of forward combat areas favorable for doing such work. In all, 5,724 cases of diphtheria, with 125 deaths, were reported from January 1942 through December 1945.

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[1] McGuinness, Aims C.: Diphtheria. *In* Medical Department. United States Army. Preventive Medicine in World War II. Volume IV. Communicable Diseases. Washington: U.S. Government Printing Office, 1958, pp. 167–189.

DIFFERENTIAL DIAGNOSIS

Correspondingly difficult, particularly during the early years of the war, was the differential diagnosis of the nature of a neuritis. In the Tropics, paralysis was associated with cutaneous ulcers and with malaria, conditions generally unfamiliar to American medical officers. In Africa and Italy, the albuminocytologic dissociation was a frequent finding. Cases were sometimes ascribed to infectious polyneuritis on this basis alone until the same dissociation had been repeatedly demonstrated in proved cases of diphtheria, in late poliomyelitis, and in other conditions, poorly defined. In some syndromes, the etiology was, and remains, obscure.

Typical diagnostic problems are illustrated in Bronson's report [2] on two series of patients; the first, from the 4th General Hospital in Melbourne, Australia, in 1943, dealing with 13 cases of neuropathy in marines who had invaded Guadalcanal, and the second, from Moore General Hospital, Swannanoa, N.C., in 1945, dealing with 60 "similar cases" with skin diseases. The marines, without much contact with natives or foe, had developed severe sore throat and later a polyneuritis. There was no evidence to substantiate the diagnosis of diphtheria from cultural studies, Schick tests, or the titration of diphtheria antitoxin in their serums. Actually, the amounts of antitoxin found in the patients were identical with those found in the control cases. Attempts to isolate viruses were likewise unsuccessful, and pooled nasopharyngeal washings inoculated into embryonated eggs, spinal fluid inoculated intracerebrally into mice, and stools inoculated intraperitoneally into monkeys failed to provoke disease. The onset of the neuropathy in these 13 cases occurred from 3 to 60 days after the sore throat, reaching a maximum in 23 to 114 days, with recovery in 5 to 8 months (average 7 months).

In Bronson's second series of 60 "similar cases" with skin diseases studied in 1945, diphtheria was proved in 7 and suspected in 5; no evidence was produced to suggest that the other 48 cases were caused by diphtheria. The neuropathy was slow in developing and in subsiding to a complete recovery and was accompanied by increased amounts of protein in the spinal fluid. Although admitting that these findings were not consistent with the picture of diphtheritic neuropathy, Bronson concluded that they were, in fact, unrelated to diphtheria. Weighing against this view was the evidence that other marines fighting alongside the troops originally studied by Bronson, and evacuated to a naval hospital ship, were proved to have diphtheria and diphtheritic neuritis by Norris and his associates,[3] who identified *Corynebacterium diphtheriae* and who were among the first to recognize the character of the problem. Bronson's cases could not, in retrospect, be definitely

[2] Bronson, L. H.: Neurologic Disease Following Infections of Throat and Skin and Incidence of Diphtheritic Infections. Arch. Neurol. & Psychiat. 56: 558–566, November 1946.

[3] Norris, R. F., Kern, R. A., Schench, H. P., and Silcox, L. E.: Diphtheria in the Tropics; Report of 18 Cases on a United States Naval Hospital Ship. U.S. Nav. M. Bull. 42: 518–524, March 1944.

diagnosed, and they illustrated the difficulties in proving a diagnosis of diphtheritic neuritis.

Meanwhile Liebow, MacLean, Bumstead, and Welt [4] reported on cutaneous diphtheria seen in 1943 and 1944 at the 39th General Hospital, Auckland, New Zealand, with an extensive review of the literature, and described many cases of neuritis. Oppel, Smith, Montanaro, and Tompsett [5] of the 9th General Hospital, also in the Pacific, found virulent *C. diphtheriae* in various cutaneous lesions in one out of six individuals and noted that spread occurred from these patients regardless of isolation. They incriminated flies. These two studies, as well as others, emphasized the predominance of cutaneous over pharyngeal diphtheria. Oppel and his coworkers observed 9 cases of neuropathy in 210 cases of diphtheritic infection, an incidence of 4 percent.

In the China-Burma-India theater, an outstanding study of cutaneous diphtheria was made at the 20th General Hospital, Assam, India, by Livingood.[6] As described in his letter of 9 October 1944 to the commanding officer of that hospital, the ulcerous skin lesions were suspected as diphtheritic as early as June 1944, although cultural proof was lacking. The development of typical postdiphtheritic neuritis in one patient and the death of another in cardiac failure substantiated this suspicion, and confirmation by cultural studies finally came in October 1944. Livingood reported on 140 cases, 61 with neuropathy. Gaskill's description [7] on these neuropathic cases presented a clear and detailed summary which showed the neuropathy to be distinctive. In retrospect, this experience proved almost unique, since the cases were followed from onset to conclusion, and full advantage was taken of the opportunity to study and describe them (pp. 521 and 525). Many cases were also reported from the 69th General Hospital in this theater.[8] Other excellent reports of diphtheritic neuritis seen early in the war, in patients evacuated from various theaters, were made by Perkins and Laufer [9] with 21 cases, by Sampson [10] with 20 cases, and by Copsey [11] with 17 cases.

As troops with cutaneous diphtheria appeared in hospitals of the United States, the factor of contagion became a matter of concern. The Commission

[4] Liebow, A. A., MacLean, P. D., Bumstead, J. H., and Welt, L. C.: Tropical Ulcers and Cutaneous Diphtheria. Arch. Int. Med. 78: 255–295, September 1946.

[5] Oppel, T. W., Smith, J. J., Montanaro, A., and Tompsett, R. R.: Clinical Features of Diphtheria in the Tropics. [Official record.]

[6] Letters, Maj. Clarence S. Livingood, MC, Chief, Section of Dermatology and Syphilology, to Commanding Officer, 20th General Hospital, 9 Oct. 1944 and 25 Jan. 1945, subject: Cutaneous Diphtheria.

[7] Letter, Maj. Herbert S. Gaskill, MC, Chief, Neuropsychiatric Section, to Commanding Officer, 20th General Hospital, 18 Mar. 1945, subject: Preliminary Report on the Neuritis Complicating Cutaneous Diphtheria.

[8] Blumgart, H. L., and Pike, G. M.: History of Internal Medicine in India-Burma Theater. [Official record.]

[9] Perkins, R. F., and Laufer, M. W.: Clinical Study of Postdiphtheritic Polyneuritis. J. Nerv. & Ment. Dis. 104: 59–65, July 1946.

[10] Sampson, J. J.: Late Neuronitis Following Proved and Suspected Cutaneous, Faucial, and Wound Diphtheria. Am. J.M. Sc. 212: 432–448, October 1946.

[11] Copsey, H. G.: Symposium on Problems in Postwar Medicine; Postdiphtheritic Paralysis. M. Clin. North America 30: 445–450, March 1946.

on Meningococcal Meningitis, Army Epidemiological Board, from an exten-
sive survey at Letterman and Moore General Hospitals, concluded that
diphtheria was indeed a problem in the Pacific, that a large percentage of
cases of polyneuritis in general hospitals were postdiphtheritic, and that the
current clinical classification of polyneuritis was not satisfactory.[12] Mean-
while, the skepticism of physicians in the Southwest Pacific Area, based
upon failure to obtain laboratory confirmation of diphtheria, was gradually
yielding to growing experience, as reported by Col. Benjamin M. Baker,[13]
MC, in 1944. Subsequently, measures were taken that resulted in a steady
decline in the number of cases during that year. Liebow and his associates
(p. 515) noted that, after the diphtheritic nature of certain tropical
ulcers became apparent, there was not an instance of the neuritis of the type
just discussed that could not be related either to the ulcers, to sore throat, or
to proved diphtheritic pharyngitis or dermatitis. They concluded that the
vast majority of neuritis seen in the Tropics was diphtheritic in origin.
These views were incorporated in War Department Technical Bulletin (TB
MED) 143, "Cutaneous Diphtheria," February 1945.

There were other types of neuropathy in the Pacific areas, however,
that did not fit into this pattern. Harvey, Kuffler, and Tredway [14] reported
from the 118th General Hospital, Tolosa, Leyte, a group of 20 cases of un-
known cause in which the manifestations were quite unlike those of diph-
theritic neuritis but resembled the shoulder-girdle and peroneal paralysis
described by Spillane. (See page 534.) Harvey [15] also reported still another
type, associated with attacks of malarial fever (p. 532). This was overt in
16 cases and found in milder form in 18 of 100 consecutive cases of malaria.

Another group of 40 cases of neuropathy was reported from the Philip-
pines in 1945 by Pessin and Silverman.[16] These appear to have shown
diverse clinical manifestations and course. Over half the patients had gastro-
intestinal disturbances and 40 percent had infectious hepatitis; the authors
postulated that both infection and vitamin deficiency were responsible for
the paralysis.

Meanwhile, in Africa and Italy, the problem of neuropathy presented
itself chiefly as an outbreak of what appeared to be infectious neuritis of
the Guillain-Barré type. Maj. Joseph W. Johnson, Jr., MC, of the 300th
General Hospital, examined many patients, collected case records, and

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[12] Memorandum, Commission on Meningococcal Meningitis, Army Epidemiological Board, for The
Surgeon General (through Brig. Gen. S. Bayne-Jones, Preventive Medicine Service, Office of The Surgeon
General, 6 July 1945, subject: Diphtheria Infections at Letterman General Hospital, San Francisco, Cali-
fornia, and at Moore General Hospital, Asheville, North Carolina.

[13] Letter, Col. Benjamin M. Baker, MC, Consultant in Medicine, to Brig. Gen. Earl Maxwell, Head-
quarters, U.S. Army Forces, South Pacific Area, 16 Mar. 1944.

[14] Harvey, A. M., Kuffler, S. W., and Tredway, J. B.: Peripheral Neuritis; Clinical and Physiological
Observations on Series of 20 Cases of Unknown Etiology. Bull. Johns Hopkins Hosp. 77: 83–103, August
1945.

[15] Harvey, A. M.: Type of Neuritis Associated With Malarial Fever. Bull. Johns Hopkins Hosp. 75:
225-231, October 1944.

[16] Pessin, J., and Silverman, D.: Peripheral Neuritis in the Philippines. [Professional paper.]

analyzed the data, in a study that was finally embodied in two monographs. As a result of this focusing of attention upon the subject, the late Maj. Emanuel B. Schoenbach, MC, and the author were sent to Italy by the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board shortly after the end of the war in Europe. Almost concurrently, Lt. Col. Aims C. McGuinness, MC, and Dr. J. Howard Mueller studied diphtheria in the European theater.[17] In his report to the Surgeon, MTOUSA (Mediterranean (formerly North African) Theater of Operations, U.S. Army) of 2 February 1945, Major Johnson [18] outlined the problems encountered. Cases of the so-called Guillain-Barré syndrome had appeared in North Africa; five cases were reported by Lt. Col. Morton H. Hand (cited by Johnson) in January 1944. Many additional cases were observed widely throughout the theater as summarized from the literature by Johnson, who reported another 15 cases of Guillain-Barré syndrome in April and still more in June 1944. In September 1944, the Guillain-Barré syndrome was made reportable to the Surgeon, NATOUSA (North African Theater of Operations, U.S. Army). Weinstein and Gersten [19] had noted another type of shoulder-peroneal palsy. Lt. Col. Theodore J. C. Von Storch (quoted by Johnson) found after extensive investigation that neuropathy accounted for 1.5 percent of all the medical dispositions between Anzio and Casablanca in February 1944. Johnson [20] presented evidence, based on 119 cases of the Guillain-Barré syndrome, indicating that the diagnoses had been made as a result of the finding of albuminocytologic dissociation in the spinal fluid without much, if any other, relation to the syndrome described by Guillain, Barré, and Strohl. From his extensive data, he concluded that "a majority of these cases seen in Italy were probably attributable to post-diphtheritic polyneuritis (58.06 percent)." He noted "that the diagnosis of diphtheria is not easy, its substantiation even more difficult, and that diphtheria recently has been atypical." He pointed out the great difficulty of properly evaluating such cases during active combat.

Johnson made a second report,[21] 1 July 1945, to the Surgeon, MTOUSA, based on restudy of the records of 155 patients, 31 percent of whom had been observed on his own service in a general hospital in the theater. He reclassified them (table 97) on the basis of the total clinical findings rather than on spinal fluid or other tests and concluded that here, as in the Pacific, diphtheria accounted for the major portion of the neuritides. It is noteworthy that, in 20 of the 90 cases with a typical diphtheria neuritis, no history of a

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[17] See footnote 1, p. 513.

[18] Johnson, J. W., Jr.: Monograph on Infectious Polyneuritis, Part I, Report to the Surgeon, MTOUSA, 2 Feb. 1945.

[19] Weinstein, E. A., and Gersten, D.: An Unusual Type of Peripheral Neuropathy: Report of 13 Cases. M. Bull. North African Theat. Op. 1: 9–10, May 1944.

[20] (1) Johnson, J. W., Jr.: Infectious Polyneuritis—Diagnostic Criteria and Military Implications: Report of 15 Cases. M. Bull. Mediterranean Theat. Op. 2: 149–159, December 1944. (2) Johnson, J. W., Jr.: Some Unusual Complications of Diphtheria. J. Tennessee M.A. 40: 114–123, April 1947.

[21] Johnson, J. W., Jr.: Monograph on Infectious Polyneuritis, Part II, Report to the Surgeon, MTOUSA, 1 July 1945.

prodromal illness suggestive of diphtheria was recorded and that in 66 percent diphtheria had not been recognized until the development of the complication. Johnson commented on the British cases in the theater and on civilian cases in Italy. Of 397 patients with diphtheria in a hospital in Florence, neural complications developed in 90 to 95 percent, but myocardial complications in only 5 to 10 percent. He contrasted this with the very low incidence of neural complications (less than 1 percent) and the higher incidence (20 percent) of myocardial complications in the United States.

TABLE 97.—*Reclassification (final) diagnoses of neuropathies, U.S. Army personnel in Mediterranean theater, during World War II*

Original diagnosis	Number of diagnoses [1]	Percent of diagnoses	Reclassification diagnosis	Number of cases	Percent of cases
Guillain-Barré syndrome__	73	41.71	Guillain-Barré syndrome_	10	6.45
Landry's ascending paralysis_____	1	.57	Landry's ascending paralysis_____	0	0
Neuropathies due to—			Neuropathies due to—		
Sulfonamides_____	1	.57	Sulfonamides_____	1	.64
Alcohol_____	2	1.14	Alcohol_____	2	1.29
Nutritional deficiencies__	3	1.71	Nutritional deficiencies_	3	1.93
Diphtheria_____	46	26.28	Diphtheria_____	90	58.06
Virus of poliomyelitis___	1	.57	Virus of poliomyelitis__	14	9.03
Undetermined cause____	48	27.42	Undetermined cause___	18	11.61
No evaluation from available data_____	0	0	No evaluation from available data_____	17	10.96
Total_____	175	100.00	Total_____	155	100.00

[1] These were made on 155 cases in the chain of evacuation.

Source: Johnson, J. W., Jr.: Monograph on Infectious Polyneuritis, Part II, Report to the Surgeon, MTOUSA, 1 July 1945.

Major Schoenbach and the author,[22] arriving in the Mediterranean area when troop movements to the Pacific were underway, failed to find many new cases of neuropathy in visits to most of the American and British general hospitals in the theater. They therefore made a study of 70 patients with neuritis in a German prisoner-of-war base hospital in Merano, Italy. From clinical and laboratory evidence, diphtheria accounted for the majority, but a small number of the cases studied had a completely different clinical picture, the neuritis being caused by a sulfonamide, sulfamethylthiazole, used in the self-treatment of gonorrhea. Many soldiers had acquired tropical ulcers in Africa, and some of these had proved to be cutaneous diphtheria. Other types of neuritis were seen in smaller numbers. Diphtheria was observed in all its stages; indeed, the overall carrier rate of virulent micro-

[22] Report, Dr. George D. Gammon and Maj. E. B. Schoenbach, MC, to Surgeon, MTOUSA, 21 Aug. 1945, subject: Polyneuritis Studies in Mediterranean.

organisms was 17 percent throughout the hospital population. It will be recalled that a similar incidence was reported by Oppel and his associates (p. 515) among American troops in the South Pacific.

In the Mediterranean theater, the incidence of diphtheria in the Fifth U.S. Army was compared with that in the British 10 and 13 Corps and in the German *Heeresgruppe C*. The British incidence (expressed as monthly rates per 1,000 per annum) from September 1943 through the remainder of the year ranged from 4 to 20 and dropped to between 0.5 and 5 during 1944 and 1945. German figures during the same period were comparable but continued at 4 to 6 toward the end of the war. The American incidence was never so high but increased during the winter of 1944 to 5 per 1,000 per annum and dropped to 1 to 2 per 1,000 in early 1945. Italian civilian figures were unavailable, but it is known that Florence had severe epidemics in 1943 and 1944. In the German hospitals at Merano, the number of cases of diphtheria were as high as 34 per month. This is not surprising in view of the carrier rate (17 percent) found in the summer of 1945 in these hospitals.

The complications were noteworthy. Florentine physicians claimed an incidence of 5 to 10 percent myocarditis and of 90 to 95 percent neuritis and a mortality of about 18 percent. This extraordinary situation was suspected to be the result of poor antiserums. The Germans estimated polyneuritis as occurring in 12 percent, myocarditis in 3 percent, and death in 1 percent. These figures cannot be considered reliable and certainly underestimate the number of cases of diphtheria for, within the various armies and the civilian populations, diphtheria was rife.

Among the 70 cases of neuritis found at Merano, one group, due to diphtheria, consisted of 5 proved cutaneous cases and 21 proved pharyngeal cases followed by the complete typical neuritis with palatal accommodation and limb palsy. A second group of 14 patients had pharyngitis and typical neuritis without cultural evidence of diphtheria. A third group of two cases was similar except that a history of palatal and accommodation palsy could not be obtained, although the paralysis of extremities was identical with that found in the others. These two were classed as probable diphtheria. All three groups (42 cases) were combined and analyzed. The other types of neuritis (to be discussed) were clinically different, and in all but nine the distinction was great enough for a clear separation from diphtheritic neuritis. In these cases, along with a control group without sore throat or neuritis and with a group recovering from pharyngeal diphtheria without neuritis, cultures were made on 2 days, and the amounts of antitoxin in the serums were determined (table 98). Of the controls, approximately 17 percent had positive cultures, a figure exceeding the incidence in diphtheritic neuritis, which was approximately 12 percent. The patients with nondiphtheritic neuritis were positive in about the same percentage (18 percent) as the controls. No positive cultures were noted in the 13 cases due to sulfonamides. The amounts of circulating antitoxin did not differ significantly between the

groups, whether with positive or negative culture, but were higher in patients convalescent from diphtheria than in those with diphtheritic neuritis.

TABLE 98.—*Clinical classification and results of cultural and serologic studies of polyneuritis, Merano, Italy, July 1945*

Clinical classification	Number of cases studied	Number of cases cultured	Culture positive for virulent C. diphtheriae		Antitoxin content of serum				Culture negative for virulent C. diphtheriae, antitoxin content of serum			
					<0.01 unit		>0.01 unit		<0.01 unit		>0.01 unit	
			Number	Per-cent	Number	Per-cent	Number	Per-cent	Number	Per-cent	Number	Per-cent
Polyneuritis:												
Diphtheritic__	42	42	5	11.9	23	54.6	19	45.4	22	59.6	15	40.4
Sulfonamide__	13	13	0	.0	5	38.4	8	61.6	5	38.4	8	61.6
Postinfectious_	6	6	2		2		4		2		2	
Unclassified___	9	9	3		3		6		3		3	
Total_____	70	70	10	14.2	33	48.6	37	51.4	32	53.4	28	46.6
Control group: No diphtheria, no poly- neuritis_ ___	112	107	18	16.9	25	22.4	87	77.6	20	22.4	69	77.6
Convalescent diphtheria_____	17	17	9	52.6	5		12		1		7	
More than 4 weeks after therapy____	8	8	4	50.0	4		4		1		3	

These studies reflect Bronson's difficulty in establishing a retrospective diagnosis of diphtheria. Nevertheless, the neuritis of diphtheria is so characteristic that the author believes it can be diagnosed on clinical grounds with considerable assurance. By 1944, it had thus become evident that diphtheria was a major cause of neuritis in all theaters of operations. In the regions where factors conducive to ulceration of the skin prevailed, the cutaneous form of infection was most frequent; elsewhere, nasopharyngeal infection was dominant.

Part II.   Description and Comparison of Syndromes

DIPHTHERITIC NEURITIS

The essential effect of diphtheria toxin on the nervous system is to produce difficulty with speech, swallowing, and sight, followed by a slow, tin-

gling symmetrical palsy of the limbs. The paralysis develops and clears sequentially in one place after another in a leisurely pattern over many weeks, ending finally in complete recovery. The few fatalities result from myocardial failure, respiratory paralysis, or pneumonic complications of the latter. Paralysis of accommodation is a specific feature and results from weakness of the ciliary muscle. Pupillary reactions are unaffected.

Gaskill and Korb,[23] who had the exceptional opportunity to follow many patients throughout their illness, described the development of neurological changes in cutaneous diphtheria thus:

> The clinical course of the neuritis proceeded in regular sequence through certain definite steps, which were in some cases partially superimposed, and in others quite separate. The steps in order of their appearance were (a) cranial nerve, (b) peripheral nerve (sensory), and (c) peripheral nerve (motor) involvement.

Gaskill and Korb noted that the cranial nerve palsies lasted from 10 to 30 days and that as these were clearing up, or after an interval of a week or 10 days, the patient would then notice numbness and tingling of the hands and the feet, and in a short time objective sensory loss could be found. Motor paralysis did not appear until the end of the sensory involvement or after a latent period of 1 to 4 weeks. The motor phase lasted from 6 to 12 weeks. The average case lasted about 100 days.

Onset and Duration of Neuropathic Involvement

The evolution of neurological involvement and the structures affected in cutaneous and pharyngeal infections were somewhat different. Walshe,[24] in World War I, described a local paralysis related to the site of the ulcers; he considered palatal paralysis an example of local paralysis in pharyngeal infections. Gaskill and others, however, in their cases did not observe this local paralysis in cutaneous diphtheria and noted a longer interval before the onset of the neuritis than in pharyngeal diphtheria. Liebow and his associates (p. 515) observed neuritis from 2 to 7 months after the appearance of cutaneous lesions. It is quite possible that the ulcers might have become infected with *C. diphtheriae* secondarily at any time in their course, but these workers described two patients from whom virulent *C. diphtheriae* were cultured from cutaneous lesions 2 and 4 months before the onset of the neuritis. In Gaskill's patients, the onset of neuritis was quicker and averaged 70 days after the ulcers developed, with a range of 23 to 158 days.

In patients with pharyngeal diphtheria, the interval was somewhat shorter although there was much variation. Thus, Perkins and Laufer (p. 515), in 16 patients with faucial diphtheria and in 5 patients with cutaneous ulcers, noted that in the former the interval to onset of palatal or other

[23] Gaskill, H. S., and Korb, M.: Occurrence of Multiple Neuritis in Cases of Cutaneous Diphtheria. Arch. Neurol. & Psychiat. 55: 559-572, June 1946.

[24] Walshe, F. M. R.: Pathogenesis of Diphtheritic Paralyses. Quart. J. Med. 11: 191, April 1918; 12: 14, October 1918: 12: 32, January 1919.

cranial nerve palsy averaged 26 days, with a range of 14 to 41 days; the cranial nerve palsies lasted on an average of 15 days, with a range of 4 to 35 days. The sensory neuritis developed in an average of 5 weeks after sore throat, with a range of 3 to 11 weeks; it reached a maximum in 25 days, with a range of 1½ to 6½ weeks; and the time from the peak to recovery averaged 8½ weeks. Motor symptoms appeared at the same time as sensory change or a little later. In their patients with cutaneous diphtheria, the interval to onset averaged 3½ months, with a range of 2½ to 5 months.

Similar data were reported by Sampson (p. 515) in 20 patients, 10 of whom had cutaneous ulcers with the onset of neuritis from 4 to 9 weeks after the ulcers developed. Copsey (p. 515), in 17 patients, largely with pharyngeal diphtheria, found that the onset of neuritis was from 3 to 8 weeks after the appearance of sore throat. In Gammon and Schoenbach's 42 diphtheritic cases (p. 519), 5 of which were cutaneous, the palatal paralysis began from the 1st to the 12th week, most frequently in the 2d to 4th week (chart 5). Paralysis of accommodation appeared a little later, from the 2d to the 8th week, most frequently in the 3d to the 6th. The limbs were involved most often in the 5th and 6th weeks, with a range of 2 to 13 weeks (chart 6). (See also table 99 and chart 7.) The neuritis of the extremities reached a maximum in 1 to 20 weeks. Improvement began most frequently in 6 to 8 weeks after onset, with a range of 4 to 24 weeks (chart 8); a quarter had

TABLE 99.—*Week of onset of neurological involvement in 42 patients with diphtheria after pharyngitis*

Percent of cases involved (cumulative)	Palate	Ciliary	Limbs
Quarter	2	3	4
Half	3	4	5
Three-quarters	4	6	6

CHART 5.—*Onset and duration of paralysis, in weeks, after pharyngitis*
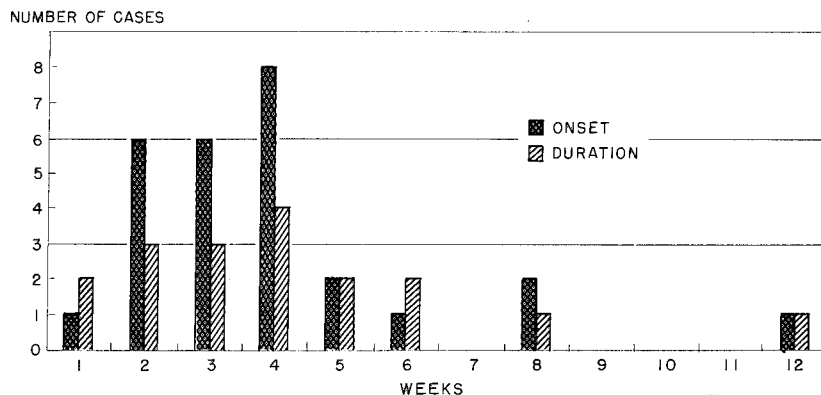
CHART 6.—*Onset of paralysis of the palate, of accommodation, and of the extremities, in weeks, after pharyngitis*

NUMBER OF CASES

WEEKS AFTER SORE THROAT

POLYNEURITIS OF EXTREMITIES
PALATAL PALSY
CILIARY PALSY
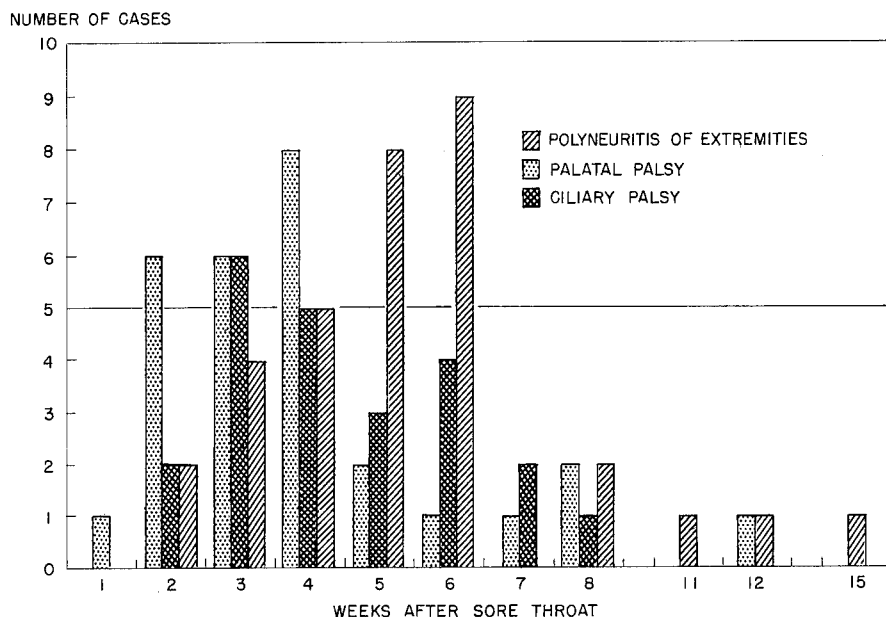
begun to improve by 6 weeks; half by 8; and three-quarters by 12 weeks. At the time of examination, only one patient had fully recovered.

These various reports emphasized the characteristic slow evolution of the process over many months and pointed out that its duration was a measure of the severity of the disease. Regardless of the time involved, the sequential steps were maintained, although the process might reverse itself at any stage and the full picture might never develop. On the other hand, in the most seriously sick, the paralysis progressed to involve the trunk, head, and neck, leaving the patients completely helpless. In these patients, disability was of the longest duration.

Structures Involved

The incidence of palatal paralysis in pharyngeal diphtheria was from 7 to 10 times greater than that in the cutaneous form, while the incidence of paralysis of accommodation was roughly the same. (See table 100.) Ciliary palsy occurred in between a third and a half of the patients with each type of disease, whereas palatal palsy was seen in only 10 percent of patients with cutaneous diphtheria but in 70 to 100 percent of those with pharyngeal infection. It should be noted, however, that the incidence of ciliary paralysis may actually be higher than reported for it is easily overlooked by the patient.

TABLE 100.—*Distribution of the neurological involvement in diphtheritic polyneuritis (in percentage)*

Area of involvement	Author							
	1	2	3	4	5	6	7	8
	Pharyngeal						Skin	
Motor:								
Palate	70	83	67	100	96	86	9	11
Accommodation	50	13	44	33	40	45	33	33
Esophagus	8	10	10	30	------	27	------	8
Pharynx	------	5	------	------	5	------	------	------
Larynx	------	------	9	21	------	------	------	2
Face	------	1	8	10	21	------	7	------
Squint	17	13	3	3	23	------	------	------
Limbs	ND	25	24	35	ND	39	100	52
Sensory:								
Limbs	ND	------	42	35	ND	------	100	99
Tongue, palate	------	------	7	7	------	------	------	11
Face	------	------	7	7	------	------	------	------
Trunk	------	------	3	------	------	------	------	------
Sphincter	------	2	3	------	------	------	------	------
Respiration	3	------	4	10	------	7	------	------
Total	477	209	144	30	53	74	30	61

NOTE.—The authors presented by numerals are as follows: (1) Rolleston, J. D.: Acute Infectious Diseases. New York: Phys. & Surg. Bk. Co. 1925. (2) Muhlenkamp, P.: Uber die nervosen Komplikationen bei Diphtherie. Beobachtungen an 4,937 Diphtheriekranken (1921–1933). Klin. Wchnschr. 13: 1424–1428, 6 Oct. 1934. (3) Hertz, M., and Thygessen, P.: Nervous Complications in Diphtheritic Paralysis. Acta Psychiat. et Neurol. Supp. 44: 3–66, 1947; Acta Med. Scandinav. (Supp. 206) 130: 541–546, 1948. (4) Sedallian, P., Mounier-Kuhn, P., Girard, P. F., and Monnet, P.: Diphtheritic Paralysis Clinical and Anatomical Data. J. Med. Lyon 28: 481–496, 1947. (5) Brown, M. R.: The Mechanism Involved in Polyneuritis as Exemplified by Post-Diphtheritic Neuritis. Ann. Int. Med. 36: 786–891, 1952. (6) Behr, W.: Post Diphtheritic Paralysis. Deutsche med. Wchnschr. 62: 771, 1936. (7) Walshe, F. M. R.: Pathogenesis of Post-Diphtheritic Paralysis. Quart. J. Med. 11: 191, 1917–18; 12: 14, 1918–19. (8) Gaskill, H. S., and Korb, M.: Occurrence of Multiple Neuritis in Cases of Cutaneous Diphtheria. Arch. Neurol. & Psychiat. 55: 559–572, 1946.

Source: Gammon, G. D.: Effects of Bacterial Toxins on the Nervous System. A. Res. Nerv. & Ment. Dis., Proc. (1952) 32: 506–525, 1953, Table 60.

Its great value as a specific sign demands special inquiry. The author was surprised to learn also that patients frequently forgot they had previously suffered from a palatal palsy that had disappeared.

The muscles innervated by other cranial nerves may also be affected in diphtheria. Esophageal paralysis occurred in 10 to 30 percent; pharyngeal paralysis, in 5 percent; and laryngeal paralysis, in 10 to 20 percent. Squint occurred in 10 to 20 percent; any of the ocular muscles may be affected. Sensory symptoms of the tongue and face, usually paresthesias, may affect some 10 percent, as may palatal anesthesia. Loss of taste has been noted by Gaskill and Korb (p. 521), but facial hypalgesia rarely occurred. Facial paralysis is of special interest. Since it is a feature of the Guillain-Barré

CHART 7.—*Course of diphtheritic neuritis after pharyngitis, illustrating time of onset and duration of paralysis of palate (dotted line), of accommodation (broken line), and of limbs (solid line)*
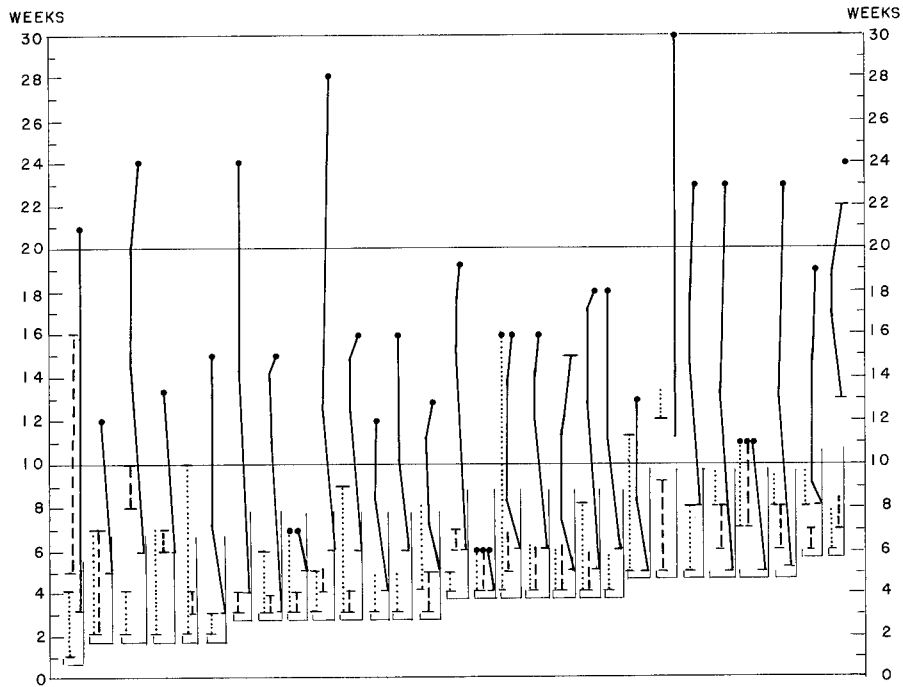
NOTE.—Termination of end of line in an upright line signifies end of event; termination in a dot, the time of observation. Each case is separated by a bracket. The onset of neural symptoms appeared in 1 to 5 weeks after pharyngitis.

syndrome, its presence in diphtheritic neuritis sometimes led to confusion in diagnosis. Usually unilateral, it reached an incidence of 20 percent in some series, varying from 0 to 10; Walshe (p. 521) found it in 7 percent of patients with cutaneous diphtheria. Johnson (pp. 516 and 517) reported it in 14 percent of patients, occurring unilaterally in half and bilaterally in half.

In Gaskill and Korb's patients with cutaneous diphtheria, 35 percent developed palsies of cranial nerves and all had involvement of peripheral nerves. Slightly fewer began with palsies of cranial nerves; some began with both simultaneously. The onset in the cranial nerves forecast a more severe neuritis in the patients with cutaneous diphtheria in contrast to the patients with pharyngeal involvement, many of whom had signs referable to cranial nerves but never developed the symptoms affecting the limbs. It is a question whether all cases that had involvement of cranial nerves only came under Gaskill's observation. No cases of hemiplegia due to embolism from the heart were reported in these series.

CHART 8.—*Time course of diphtheritic polyneuritis of extremities; time (in weeks) after onset when maximum disability was reached and when improvement began*

NUMBER OF CASES
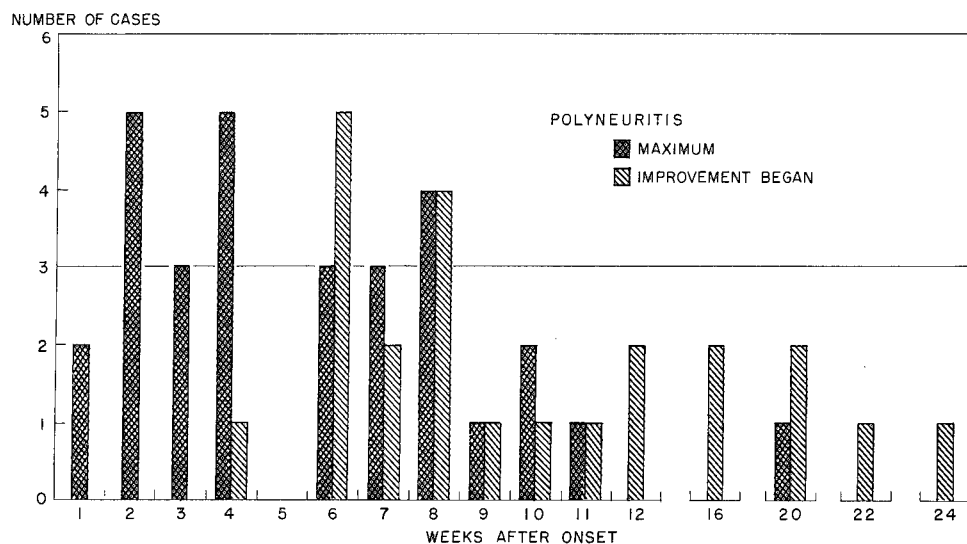
Symptoms and Signs of the Peripheral Neuropathy

A few patients with diphtheria in the first week or two of the illness, long before the ensuing neuropathic sequence, developed paresthesias in the limbs, suggesting a segmental or root arrangement. This in some involved the ulnar border of the forearms or hands; in others, there was tingling about the face and tongue. Commonly, however, symmetrical tingling paresthesias were felt in the distal parts, beginning in the fingers and hands, or toes and feet, or most often in both regions simultaneously and symmetrically on the two sides. Patients described this as "the tingles," a sense of the limb being "asleep" or numb. They seldom (in less than 10 percent of cases) spoke of pain. If present, it was described as a "pins and needles" sensation, never very severe nor necessitating analgesics. Very rarely, this mild pain replaced the tingles and rarely did paresthesias precede the weakness. At this stage of paresthesia, hyperreflexia, often mentioned but seldom seen, occurred, as well as tenderness of muscles, especially the small muscles of the hand. Walshe (p. 521) reported that this muscular tenderness anticipated all other signs of neuritis; the author was also impressed by this finding although most of the reports quoted previously minimized it.

The paresthesias ascended in 1 to 2 weeks to the forearms and legs; only occasionally did they reach the root of the limbs. At this time, examination disclosed sensory impairment, its character differing from patient to patient and from one group to another. Loss of vibratory or positional sense has been emphasized in the past. Perkins and Laufer (p. 515) in their

excellent report, which stressed the importance of the sensory findings, noted that the vibratory and the stereognostic senses were markedly affected; the tactile sense, moderately; and the perception of pain and temperature, only slightly. In contrast, all of Gaskill and Korb's series showed hypesthesia to pain, temperature, and light touch; only 8 patients out of 140 had a loss of vibration and sense of position, and in these alone was ataxia noted. In Gammon and Schoenbach's study (p. 518), in a series of 37 cases of nasopharyngeal diphtheria, 20 showed objective sensory involvement. Impairment of the perception of pain and of the tactile, but not of the vibratory or positional, sense was the most frequent combination (10 cases, 4 of which showed ataxia). No patient was observed with impaired vibratory and positional sense and normal tactile and pain sense. Ataxia was found eight times in 13 patients without objective impairment of sensory response to pinprick, touch, vibration, or position; 10 of these patients complained of tingling and 1 of pain.

Thus, a dissociation of sensory impairment has often been encountered, and ataxia has been observed without objective sensory loss. The lack of emphasis previously put on the sensory changes probably is due to the fact that *diminution* is much more frequent than complete loss. Also children, who predominate among patients reported in the literature, describe these symptoms less clearly. In distribution, these sensory changes are most often of the glove-stocking type, but many cases have shown a root or segmental or cord type. For example, Gaskill and Korb reported a loss of vibratory sense at the thoracic level; others noted a similar loss over the trunk. These data demonstrated that the process was not confined to nerve or root but involved the cord as well. In diphtheritic ulcers, the scar and a zone of 1 to 2 mm. around it are anesthetic. The paresthesia may cease in 1 to 4 weeks before weakness develops, or, more frequently, the two may overlap.

Motor signs developed with fatigability progressing to a flaccid palsy, more marked peripherally. The paralysis was usually symmetrical in onset and extent with minor differences in either. Atrophy developed if paralysis was severe. The lower limbs bore the brunt, and thigh as well as calf and foot were involved. The lower limbs were weak in twice as many cases as the upper limbs. The paralysis was much more marked than the sensory loss and at times it was complete in the extremities. In a smaller number of cases (10 percent), it involved the trunk and neck, leading to complete immobility. In such cases, loss of control of the sphincters ani sometimes occurred. In a small number of cases, there was intercostal and diaphragmatic paralysis. The degree of palsy varied enormously. Gaskill and Korb found the quadriceps and interossei especially susceptible. Loss of reflexes followed the distribution of the weakness. The ankle and knee jerks were most often affected; the biceps and triceps, less often. Loss of the abdominal reflexes was noted by Perkins and Laufer. The loss of reflexes may be permanent. Recovery in sensation preceded recovery from the weakness and both were usually

complete; however, Copsey commented on the painfulness of the feet in re-ambulation, and Liebow and his associates described one patient with permanent atrophy of the deltoid with a winged scapula.

Antitoxin in Relation to Diphtheritic Neuritis and Serum Neuritis

The experience of World War II confirmed the observations found in the older literature that antitoxin given early—within the first 3 days of infection—prevents or greatly diminishes the changes of neuropathy, but is valueless after its onset. In fact, it may induce a *primary* serum neuritis, which may be local in the limb of injection, or may be widespread. In either case, pain and hyperpathia are prominent symptoms and are often severe. This manifestation may occur in addition to a diphtheritic neuropathy. Cases of this kind are quite unlike the usual diphtheritic neuritis, as illustrated by the following:

A man, 44 years old, with proven nasopharyngeal dipththeria was given 5,000 units of antitoxin on the sixth and seventh days of disease. Serum sickness appeared a week later, with swelling of the feet and ankles. This subsided at the end of 1 week when tingling paresthesia of the feet occurred, accompanied by severe pain and weakness in both hands and forearms. All these symptoms regressed during the next 2 weeks with complete restoration to normal at the end of this period. During the height of the process, decrease in cutaneous sensation along the ulnar border of the hands was noted; the tendon reflexes were normal.

A 36-year-old male, with unproven but clinically typical pharyngeal diphtheria, was given 18,000 units of antitoxin on the second day of disease. Typical diphtheritic neuropathy ensued, with palatal palsy in the third week, following in the fourth week by tingling and weakness of the extremities, absence of knee and ankle jerks, hypesthesia, and loss of position sense. Evidence of myocarditis appeared, and antitoxin was again given 7 weeks after the first dose, in amounts of 9,000 units daily for 4 days. Two days later, severe pain and hyperpathia (requiring morphia) occurred in the legs, and all the limbs rapidly became weaker. Decreased awareness of temperature and pain and loss of tactile and vibratory senses were noted in the legs, and the patient had little use of his upper or lower extremities.

Spinal Fluid

All the observers quoted previously noted increased amounts of protein in the spinal fluid without increase of cells in diphtheritic paralysis. This fact had not been previously emphasized in the American literature and unawareness of it led to confusion with the Guillain-Barré syndrome. Guillain had originally stated that the amounts of protein in the spinal fluid in his syndrome must be very high—from 1 to 2 percent; however, this restriction is certainly not generally admitted as essential to a diagnosis of infectious polyneuritis (p. 531), for, in fact, many cases never have such large amounts. Older accounts reported an early slight increase in cells, but this was not a feature of the cases observed in World War II. Johnson (p. 516) reviewed the European literature and observed many cases. Gaskill and

Korb (p. 521), and Johnson as well, found that the protein increased early, within 2 weeks of the infection, and that the amount, according to Gaskill and Korb, was proportionate to the severity of the disease. Amounts as high as 400 to 500 mg. percent were found, although from 100 to 200 mg. percent or lower were more usual. The results of tests with colloidal materials were sometimes abnormal, and a midzonal curve was characteristic. In some cases, it was many weeks before the protein returned to normal; Gaskill and Korb found that, when the patients were clinically well, the spinal fluid protein had returned to normal.

Pathogenesis and Pathological Anatomy

In the author's review of the effects of bacterial toxins on the nervous system,[25] the recent literature was summarized, including German reports on their experience during World War II. In all species, diphtheria toxin is a general cellular poison affecting most tissues. It seems probable that the initial lesion is biochemical and, as with tetanus toxin, is undetectable by techniques now available. The changes seen are the results of parenchymal and vascular degeneration, the complications thereof, and the secondary processes of repair. Peripheral nerves show edema of endoneural and perineural tissue and the cells of origin show a chromatolytic change. The myelin sheath and zone degenerate. Nuclei in the spinal cord and brain stem are affected as well. Muscle is damaged secondarily or primarily. Minute cerebral vascular lesions due to endarteritis or embolic lesions from the heart have been described. Death results from cardiac or respiratory failure, from membranous bronchial obstruction, atelectasis, or from toxemia.[26]

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[25] Gammon, G. D.: Effects of Bacterial Toxins on Nervous System. A. Res. Nerv. & Ment. Dis., Proc. (1952) 32: 506–525, 1953. [Includes discussion by Harry M. Rose, pp. 518–519.]

[26] Pappenheimer's long study of the problem (see Pappenheimer, A. M., Jr.: Bacterial Toxins. Federation Proc. 6: 479–484, June 1947) has led him to suggest that the toxin is the protein moiety of the cytochrome B enzyme of C. diphtheriae and that its effect may result from interference with the synthesis or activity of this or related enzymes of the host. Direct proof, however, is lacking, as he found no action of the toxin in vitro or in vivo on preparations of cytochrome B. Indirect support, however, is given in the observation that, in the silkworm pupa, segmental muscle, containing the enzyme, is poisoned by the toxin, whereas cardiac muscle, lacking it, escapes. Ludwig has recently provided the first evidence of action of the toxin in vitro on the succinic dehydrogenase system; however, he attributed the effect to porphyrin present in the crude toxin. (Ludwig, G. D.: The Inhibition of the Succinic Oxidase System by Coproporphyrin. Proceedings of Physiological Society, Philadelphia, 17 Nov. 1953. Am. J.M. Sc. 227: 358–359, 1954.) It should be noted that cytochrome enzymes are all but universally distributed, and therefore interference with their action would be general, as is the case with this toxin. In poisoned skeletal muscle, phosphocreatine falls and inorganic phosphorus rises while adenosine triphosphate remains constant.

Wildführ has reported that the toxin can be found in the blood of patients a week or two before the onset of neuritis and in the spinal fluid of paralyzed patients. (Wildführ, G.: Uber Diphtherietoxingehalt im Patientenblut und Liquor bei Diphtherie-Spathlahmungen. Zentralbl. f. Bakt. (Abt. 1) 154: 18–26, 15 May 1949.) Presumably, therefore, all tissues are exposed and the susceptible ones poisoned. As yet, however, the manner of action of the toxin at a metabolic level is not clear. Rose, in commenting on Gammon's review (see footnote 25, above), pointed out that there is no actual proof that the toxin has a direct effect on the nervous system and the fact that the neuritis occurs so late raises the question whether one mode of action may not be the consequence of some type of antigen-antibody reaction. If this be so, an intrinsic antibody must be responsible, for many of these had no detectable antitoxin, and no increase in antibody was detected in serum or by Schick test in patients with diphtheritic neuritis. Furthermore, it is recognized that antitoxin can initiate a reaction, of one type at least, that is clearly different clinically from diphtheritic neuritis (p. 535).

There can be no doubt that diphtheria toxin has its own uniquely selective action on ciliary and on sensory and motor nerves quite unlike the equally unique effects of botulinus or tetanus toxins. It seems likely that investigation of its characteristic modes of action at metabolic levels will yield information concerning the makeup of the tissues that are specifically affected by these agents to produce specific clinical syndromes.

Diagnostic Proof of Diphtheritic Neuritis

If infection with *C. diphtheriae*, whether of nose, throat, skin, or elsewhere, is proved by isolation of virulent micro-organisms from the infected tissue, the subsequent neuritis, which has a characteristic clinical course, can with certainty be attributed to the original infection. The chances of recovering the micro-organism depend in part on whether it is suspected and sought in lesions, many of which do not at all resemble membranous sore throat nor fit other textbook descriptions. Furthermore, if the micro-organism is not sought early, it may have disappeared by the time of the onset of neuritis. By then, the frequency of recovery of organism approaches the rate in the general population of the carriers who are spreading the infections. Thus, 3 weeks after faucial diphtheria, the rate of recovery of organisms approximates 30 percent, and it falls off rapidly thereafter.

If recovery of the micro-organism fails, the next question is whether the amounts of circulating antitoxin found are of sufficient magnitude to prove infection. The Schick test is of no help, as many of the reports that have been quoted showed; at the time of the neuritis, patients with positive and negative Schick reactions were of about equal frequency. Determinations of two levels of antibody by Bronson (p. 514) failed to demonstrate any difference between the patients and their controls. Gammon and Schoenbach's data (p. 519) showed that patients convalescent from faucial diphtheria with neuritis had antibody levels lower than in those convalescent from diphtheria without neuritis or in controls. Furthermore, a lower carrier rate (12 percent) was found in the first group than in the control population (17 percent in patients with neither sore throat nor neuritis; 18 percent in patients with nondiphtheritic neuritis). Mueller (quoted by McGuinness, p. 513) has pointed out that the clinician must decide if the presence of the micro-organism indicates the disease or the carrier state. Thus, neither the amounts of antibody found nor the results of nasopharyngeal cultures could be used to prove the presence of past diphtheritic infection nor present diphtheritic neuritis. It is obvious therefore that the diagnosis must be made early. The only alternative as far as can be seen is discovering the toxin itself in blood or spinal fluid, as has been reported by Wildführ [27] but, so far as the author is aware, has not been confirmed.

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[27] See footnote 26, p. 529.

Actual proof of the diphtheritic origin of the neuritis is therefore often difficult and may be impossible. Nevertheless, the diagnosis can be made with some confidence on the basis of the clinical evolution. For the reasons given, the author does not agree with statements that, lacking the typical cranial nerve palsies, diphtheritic neuritis cannot be distinguished from infectious polyneuritis of the Guillain-Barré type.

INFECTIOUS POLYNEURITIS: THE GUILLAIN-BARRÉ SYNDROME

Confusion in diagnosis, as has been noted, arose principally over the distinction between diphtheritic neuropathy and the Guillain-Barré syndrome through the unwarranted emphasis on the albuminocytologic dissociation in the spinal fluid in the latter, and the difficulty of proving diphtheritic infection. There has, in fact, been some argument about the extent of the clinical range of the Guillain-Barré syndrome and whether it represents a disease, as Guillain contended, or a group of conditions. Americans have frequently considered the albuminocytologic dissociation as diagnostic of "the syndrome," but the English school of neurologists have considered increase of the protein in the spinal fluid indicative rather of the severity than of the type of neuropathy. The albuminocytologic dissociation may, in fact, occur in poliomyelitis; in mumps meningoencephalitis; in diabetic neuropathy; occasionally in alcoholic neuropathy; with compression of spinal cord; with brain tumor, especially posterior fossa tumors; in arachnoiditis; in meningeal carcinomatosis; in syphilis; in lead encephalopathy; possibly in sandfly fever; and in other conditions.

There is no doubt, however, that there does exist a group of cases fitting Guillain's criteria and showing a combination of facial diplegia, peripheral neuropathy, and increased amounts of protein without cellular increase in the spinal fluid. Typically, the onset in such cases is abrupt, and accompanied by pain, and the peak is reached within a short time—usually a week or 10 days; the prognosis for recovery is favorable if the acute phase is successfully passed. These patients often have a preceding pharyngeal, respiratory, or gastrointestinal illness which seldom causes much complaint, and the neurological symptoms appear, as in diphtheria, with little or no evidence of infection at the time. Around this basic syndrome, there are many variations. In some cases, the neuropathy develops more slowly over a period of weeks, frequently without any pain or paresthesia. Cranial nerves other than the facial may be involved, with or without peripheral neuritis. The motor findings frequently overshadow the sensory, and the weakness may be more proximal than distal. Paralysis of accommodation or pharyngeal paralysis is seldom reported. The cause of the polyneuritis is unknown, and the diagnosis rests on the clinical picture and examination of the spinal fluid.

Diagnostic uncertainties plagued medical officers in the Mediterranean theater where typical examples of the Guillain-Barré syndrome were unquestionably seen among the more numerous cases of diphtheritic neuritis. Johnson's final analysis of 155 cases (p. 517), however, showed that, although there were 73 diagnoses (approximately 42 percent) of the Guillain-Barré syndrome, this syndrome existed in only 10 patients (6 percent). These 10 patients showed the typical facial diplegia, but there were others that did not, only the limbs being affected. In certain patients, the course was that of an acute ascending paralysis of the Landry type, as in Johnson's Case 90, described as follows:

In this patient, a transient diarrhea was followed in 3 days by pains in the lower back and buttocks and down the back of the thighs and legs; 2 days later, severe weakness suddenly developed in the lower extremities and then in the hands. All deep tendon reflexes were absent. Sensation was intact, except for a slight decrease in vibratory sense, and cranial nerve function was normal. In the next 2 days, the trunk muscles were involved and the patient died with pneumonia 2 weeks after the onset of the diarrhea. Autopsy showed pulmonary atelectasis with bronchopneumonia. The spinal roots showed a primary inflammatory reaction with secondary degeneration of the anterior horn cells and patchy demyelinization of the roots. The spinal fluid protein measured 113 mg. percent.

A study of the cases reported in the war reveals that a rather small number were due to infectious polyneuritis of the type described by Guillain, Barré, and Strohl. The author agrees with Guillain that the clinical picture and course of disease distinguishes these cases from diphtheritic neuritis even if the latter shows bilateral facial involvement. It is important to make this distinction in order that such cases may be studied for causative agents. To combine all patients with peripheral neuritis on the basis of elevated protein without cellular increase in the spinal fluid would hinder such inquiry. We have already seen how it delayed the recognition of cases of diphtheritic origin. This view is discussed by Delp and his associates.[28]

POSTINFECTION NEURITIDES

With malarial fever.—Harvey and his coworkers (p. 516) described a series of 16 cases with neurological manifestations associated with recurrent attacks of malarial fever as follows: "The typical clinical picture was one in which 'irritative' phenomena were present, with sharp or stinging pain in the distribution of a peripheral nerve, followed by an * * * actual muscle contraction, intense hyperalgesia, and increased sweating." In the milder cases, numbness and tingling occurred. The symptoms were always increased with recurrence of the malaria. The nerves or roots were involved symmetrically, alone or in combinations in the lower thoracic, the trigeminal, or the sciatic regions. The axillary nerves as well as others

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[28] Delp, M. H., Sutherland, G. F., and Hashinger, E. H.: Post-Diphtheritic Polyneuritis; Report of 5 Cases With Albuminocytologic Dissociation Simulating Guillain-Barré Syndrome. Ann. Int. Med. 24: 618–628, April 1946.

of the upper extremities were also at times affected. During the acute attacks, the muscles of the limbs were usually flexed at the forearms and wrists, and attempts to straighten them greatly increased the pain. The hyperalgesia lasted several weeks. Occasionally, hypalgesia and hypesthesia were noted. It was suggested that the symptoms might be attributed to vascular lesions of the nerves. *Plasmodium vivax* was the common type of the associated infection, although mixed infections were suspected in some cases. Some 18 of 100 relapsing cases of malaria showed a milder form of the disability.

After other severe infections.—Neuropathy has also been described with severe sepsis, whatever the cause, as well as with diphtheria and other specific infections, such as the cases attributed to malaria by Harvey, and those ascribed by Wilke to dysentery in German patients following Shiga infections (noted by Johnson). These last had an albuminocytologic dissociation in the spinal fluid.

Neuropathy following pneumonia is illustrated by the course of disease in a 37-year-old man who had tropical ulcers of the legs, from August to October. On 23 March, bilateral bronchopneumonia developed, which was treated with a sulfonamide eubasin. About a month later, after the patient had improved but was still febrile, he awoke to discover weakness in the legs, hands, and fingers. There were no pains or paresthesias. The weakness increased for 3 weeks and he could barely walk. The small muscles of the hands and legs were wasted and the quadriceps were weak. The patient was ataxic and had a sensory loss of the glove-stocking type for pain, temperature, and touch. Position and vibratory senses were normal and the cranial nerves were normal. The process was symmetrical. The ankle and knee tendon reflexes were absent, but the biceps and triceps were normal.

In four other cases, septic wounds led to delirium and other signs of toxic psychosis and to a neuritis identical in course with the postdiphtheritic cases except for the lack of palatal or other cranial nerve involvement, symptoms of which, however, might have been undetected. Only one of the whole group of six patients had a slightly elevated cerebrospinal fluid protein (67 mg. percent). Diphtheria could not be ruled out in these cases, but similar ones have been noted in civil life where diphtheria was not a factor.

In a patient reported by Zimmerman and Lowry,[29] infectious hepatitis was followed by a typical motor and sensory polyneuropathy of the Guillain-Barré type, with unilateral involvement of facial nerve. The condition progressed for 17 days and then improved to the point of complete recovery in 4 months. The protein in the spinal fluid measured 192 mg. percent.

[29] Zimmerman, H. J., and Lowry, C. P.: Encephalomyeloradiculitis (Guillain-Barré Syndrome) as a Complication of Infectious Hepatitis—Case Report. [Professional paper.]

PERIPHERAL NEUROPATHY, MOSTLY PERONEAL AND AXILLARY, CAUSE UNKNOWN

Harvey, Kuffler, and Tredway (p. 516) described 20 cases of peripheral neuropathy, mostly peroneal and axillary, cause unknown. These cases were said to resemble the group described by Spillane [30] and were clearly distinguishable from the cases associated with recurrent malaria (p. 532). The authors described the conditions as characterized by the sudden onset of motor and sensory involvement, usually of a single nerve. Function, in most cases, returned within 4 to 6 months. In 15 cases, the common peroneal nerve was attacked; in 3, the axillary nerve; and in 1, the radial. Typically, the patient awakened to find weakness; this reached a peak within 1 to 3 days. About a quarter of the patients complained of pain, which was especially sharp and burning in the axillary type. This feature was emphasized by Spillane in a study of 46 patients, most of whom had served in the British MEF (Middle East Forces). Some patients had "pins and needles" paresthesias lasting from a few days to a few weeks. Sensory loss over the dorsum of the foot or lateral surface of the leg was noted in over half of the patients with peroneal involvement; the affected area was surrounded by a zone of intense hyperesthesia. In the patients with axillary involvement, sometimes other branches of the brachial plexus were affected. Spillane described pain in the chest wall. Electromyography was used to trace the degree of involvement and recovery. Two of the patients with axillary neuritis showed atrophy with no recovery in 6 months. The author has seen similar patients without recovery in over a year, and similar cases occurred among those described by Johnson in the Mediterranean theater. One of the patients with peroneal involvement relapsed without known cause after 3 months of improvement. The spinal fluid, when examined, was found normal.

Harvey considered this group distinct from a third group with polyneuritis accompanied by high protein in the spinal fluid without increase in cells, although he did not describe these last in detail. Atabrine (quinacrine hydrochloride) or quinine could not be implicated, and recurrent malaria did not affect these patients. Pressure appeared to play no role in the cause although the radial and peroneal nerves were notably susceptible. Harvey called attention to civilian cases in London reported by Mason [31] and to cases noted in Malta by MacPherson and Clark (1943). Weinstein and Gersten (p. 517), and Weinstein [32] alone, described patients with shoulder-girdle palsy resembling Harvey's cases and attributed them to vaccina-

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[30] Spillane, J. D.: Localized Neuritis of Shoulder Girdle: Report of 46 Cases in MEF. Lancet 2: 532–535, 30 Oct. 1943.

[31] Mason, R. W.: Brachial Neuritis Occurring in Epidemic Form. Lancet 2: 662–663, 29 Nov. 1941.

[32] Weinstein, E. A.: Delayed Appearance of Peripheral Neuropathy Following Serum and Vaccine Injection. [Professional paper.]

tion. An outbreak of peroneal palsy [33] occurred in 41 persons in a German prisoner-of-war camp at Alva, Okla., which bore some clinical resemblance to the disease described by Harvey; that is, one or both peroneal nerves and occasionally tibial nerves were affected by tingling parethesias and foot drop suddenly ensued. Occasionally, the fingers tingled. A blunting of sensation and decrease in ankle jerks and tone were noted. Improvement occurred in most instances. It is difficult to decide if these cases form a unity, and it is possible that the shoulder-girdle group differs from the peroneal type. Weinstein's suggestion that vaccination was the cause has not been widely accepted.

POSTVACCINATION NEURITIS

Postvaccination neuritis was observed by Sabin [34] in rare cases after immunization against Japanese B encephalitis. It was usually a segmental motor and sensory paralysis in the injected limb, or a complication of serum sickness. Note has been made of an allergic reaction to diphtheria antitoxin presenting as a local or general manifestation (p. 528).

The cases reported by Weinstein and Gersten were predominantly of the shoulder-girdle type. Thirteen cases seen in North Africa from July 1943 to January 1944 were reported. Later, Weinstein added six more cases and suggested that the cause was due to prior injections. He described the syndrome as "characterized by a rapid, often painless onset of motor involvement with frequently enduring paralysis and atrophy of the affected muscles, and a tendency for limitation to a single extremity with a predilection for the shoulder girdle." In most instances, there was multiple but local nerve involvement, which in some cases was asymmetrically bilateral. The onset was always rapid and at times sudden, the victim awakening to find paralysis of arm or shoulder. A sensation of numbness or deadness was frequent, but actual pain was present in only 7 of the 19 cases and was severe and persistent in only 2, each with involvement of the axillary nerve. In 16 cases, an upper extremity was affected, and in 4 patients both arms were involved asymmetrically. The brunt of the paralysis fell upon the shoulder girdle, usually with multiple neurological involvement. The following nerves were affected: Axillary, 6; long thoracic, 6; thoracodorsal, dorsoscapular, suprascapular, and radial, each 4; and musculocutaneous ulnar and spinal accessory, each 2. Isolated unilateral common peroneal palsy was noted twice. Sensory impairment was less conspicuous than palsy and was found chiefly in lesions of the axillary and radial nerves, confined

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[33] Report, Maj. Frank Kaminsky, MC, and Capt. Max E. Johnson, MC, to Medical Director, Eighth Service Command, Army Service Forces, Dallas, Tex., 26 Sept. 1945, subject: Investigation at Prisoner-of-War Camp, Alva, Okla.

[34] Sabin, A. B.: Epidemic Encephalitis in Military Personnel; Isolation of Japanese B Virus on Okinawa in 1945, Serologic Diagnosis, Clinical Manifestations, Epidemiologic Aspects and Use of Mouse Brain Vaccine. J.A.M.A. 133: 281–293, 1 Feb. 1947.

to the isolated sensory supply of the nerves involved. Palsy was maximal at onset and not progressive. Recovery was noted in about half the cases within 2 to 3 weeks, but the others remained paralyzed and atrophy ensued without fasciculations. The spinal fluids were normal.

Considering various possible causes, Weinstein commented on the absence of prior or current infection, although the late stage resembled poliomyelitis. No toxic agents, including sulfonamides, were implicated, and there was no suggestion that pressure had been operative. The only common factor was prior injection of vaccine, toxoid, or serum, which had been given to each of this group within 2 weeks to 3 months. None had serum sickness. For this reason and because the type of involvement resembled that of postvaccination neuropathy, Weinstein attributed the cases to this cause. He placed the incidence second to postdiphtheritic neuropathy. There is no doubt that postvaccination neuropathy occurs without serum sickness. The interval is longer after injection in Weinstein's cases than that usually recognized. Spillane (p. 534) did not associate his similar cases with this cause. Localization of poliomyelitis to an injected area has been noted. In most descriptions of postvaccination neuropathy, pain is however a prominent feature. It would thus appear that Weinstein's suggestion, while a valuable one, requires verification.

NEURITIDES CAUSED BY TOXIC AGENTS

After sulfamethylthiazole in gonorrhea.—Sulfamethylthiazole, which had been rejected in the United States when it was found to produce "anterior horn cell disease," was purchased surreptitiously in Italian pharmacies by German soldiers for the self-treatment of gonorrhea. It proved highly active for it "cured the gleet and dropped the feet."

Gammon and Schoenbach studied 13 patients in whom the onset was abrupt, with more or less severe pain in the legs and feet, followed in 1 to 7 days by the sudden onset of weakness. The maximum involvement was reached at the earliest in a week and in the other cases a few days later. All patients were paralyzed below the knees and in half of them the hands were also involved, usually at the same time or shortly thereafter. Here, the weakness was highly selective. The muscles of the thenar eminence, especially the short flexor of the thumb, were affected, and occasionally the weakness spread to the first and second interosseous muscles. The paralysis was flaccid and followed by atrophy and cessation of pain. The ankle jerks were lost, but the knee jerks and the triceps and biceps reflexes were unaffected. Sphincters were also unaffected. Only 2 of the 13 patients showed a slightly impaired sensory response to pinprick and light touch below the knees. The process was essentially a selective symmetrical paralysis with painful onset. Improvement was slow and incomplete with atrophy a permanent residuum in some cases, and only half the patients had shown any

improvement when examined. This began in the first to fifth months after onset. Two patients had a relapse, one after a second course of sulfonamide and the other after treatment with olobintin, a derivative of turpentine. The spinal fluid protein in these cases was not increased.

An interesting feature was the delayed onset of the palsy, which according to the German physicians might be several weeks after stopping the medicine. They also stated they had encountered the condition only during the treatment of gonorrhea and no other diseases. The condition resembled the neuropathy after Uleron, a disulfanilamide, and the triorthocresol "jake" paralysis. The symmetrical involvement distinguished these cases from the group studied by Harvey and his coworkers and by Spillane.

Trinitrotoluene toxicity.—Neuritis in munition manufacturers was reported in World War I. At the request of Dr. L. C. McGee, medical director of the Hercules Powder Company, the author, with Army ordnance and U.S. Public Health Service officials, saw eight patients suspected of this condition in a plant at Chattanooga, Tenn. Some of them showed an obviously hysterical sensory loss in the limbs and a few had tingling paresthesias of the limbs lasting several months. Sensory tests suggested an impairment of pain and temperature sense in a glove-stocking distribution, occasionally sparing the palms and soles. The motor weakness of which some complained was largely subjective. Tendon reflexes were unaltered. Cranial nerves were unaffected. The spinal fluid was not examined. The subjective nature of most of the complaints quite naturally led to conflicting interpretations of the evidence and prompted the question whether any disease at all was present. Physicians in the community had not observed similar cases in their practice. A sample survey of other plants by the U.S. Public Health Service failed to turn up other examples, a tribute to the effectiveness of industrial control methods for handling this undoubtedly toxic substance.

STARVATION NEURITIDES

This subject is discussed by Pollack (ch. X) and by Youmans [35] and is referred to only briefly here. Three principal syndromes were encountered —classical beriberi, burning feet, and the involvement of optic and auditory nerves with degeneration of spinal cord in lateral and posterior columns. Long-term followup studies have shown that recovery was often incom-

[35] Youmans, John B.: Malnutrition and Deficiency Diseases. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume III. Personal Health Measures and Immunization. Washington: U.S. Government Printing Office, 1955, pp. 159–170.

plete.[36] Similar British experience was summarized by Denny-Brown.[37] These neurological manifestations arose chiefly in prisoners, particularly in the Eastern theaters of war. Malnutrition as a cause of neuritis outside the prisons was unusual unless accompanied by other diseases, such as dysentery, and accordingly did not often present a diagnostic problem.

SPECIAL PROBLEMS IN DIFFERENTIAL DIAGNOSIS

Hysteria.—Hysteria, as well as other diseases of the nervous system, had to be distinguished in patients with neuropathy, just as the various types of neuropathy had to be distinguished from each other. Hysterical paralysis was frequently suspected until clear evidence of organic disease was uncovered. Findings indicative of toxic myocarditis and the discovery of elevated amounts of protein in the spinal fluid frequently clarified the diagnosis as did also the gradually growing acquaintance with the various syndromes.

Poliomyelitis.—Frequently, poliomyelitis had to be considered because, as a result of the transfers through various installations out of combat areas, adequate study was made late, at a time when the cells in the spinal fluid had diminished and the protein was still elevated. It is known that this rises several weeks after infection and may remain elevated for months. The pharyngitis or gastroenteritis of poliomyelitis is followed in a few days by paralysis, which reaches its peak in a few days at most. The onset may be painful, but sensory loss is not found with the exception of the rare case of transverse myelitis presenting a sensory level. The older clinical suspicion that poliomyelitis could cause such a condition has now been confirmed by means of the newer diagnostic tests. The Landry type of poliomyelitis ending fatally could not be distinguished from that of other causes unless there was sensory impairment. Bulbar poliomyelitis also proved difficult to distinguish from the Guillain-Barré syndrome. As a rule, however, the asymmetrical and patchy distribution of paralysis and atrophy permitted the differentiation from neuropathy.

Infectious mononucleosis.—This occasionally involves the nervous system and one form resembles the Guillain-Barré syndrome. Ricker, Blumberg, Peters, and Widerman [38] reported two fatal cases, with post mortem study at the Army Institute of Pathology (now the Armed Forces Institute of Pathology), Washington, D.C. These patients had a febrile illness with

[36] Report, prepared by the Department of Health, Education, and Welfare in cooperation with the Veterans' Administration, Department of Labor, and Department of Defense Pursuant to Public Law 744, 83d Congress, 2d Session, subject: Effects of Malnutrition and Other Hardships on the Mortality and Morbidity of Former U.S. Prisoners of War and Civilian Internees of World War II: An Appraisal of Current Information.

[37] Denny-Brown, D.: Neurological Conditions Resulting From Prolonged and Severe Dietary Restriction (Case Reports in Prisoner-of-War, and General Review). Medicine 26: 41–113, February 1947.

[38] Ricker, W., Blumberg, A., Peters, C. H., and Widerman, A.: Association of Guillain-Barré Syndrome With Infectious Mononucleosis, With Report of 2 Fatal Cases. Blood 2: 217–226, May 1947.

signs of rapidly advancing flaccid weakness of limbs, trunk, pharynx, and face with minor sensory impairment of a glove-stocking type. Death occurred from respiratory failure and atelectasis with pneumonia. Specimens of spinal fluid showed a modest pleocytosis and elevation of protein. Pathologically, the process was a widespread acute neuromeningomyeloencephalitis. Inoculation of specimens of the brain and of the spinal cord from one patient into mice and guinea pigs caused no disease. The authors pointed out that certain patients with peripheral paralysis have, unlike those with poliomyelitis, a good prospect for recovery.

Mumps.—Mumps meningoencephalitis with neuropathy was reported by Gellis, McGuinness, and Peters [39] in an outbreak in Army troops.

Compression.—Compression from tumors or herniated disks with Froin's syndrome in the spinal fluid gave rise to some confusion until collateral evidence of cord disease developed. Unrecognized shell fragments in the brachial plexus or compression by cervical rib, scalenus anticus muscle, or traction, or pressure from various sources were rare causes of confusion.

Alcoholic neuropathy.—This was not often a diagnostic problem. Alcoholic neuropathy evolves acutely with a good deal of pain and can be readily recognized.

Tabes dorsalis.—Tabes dorsalis was easily distinguished by serological and spinal fluid studies as well as by the slow course.

Sandfly fever.—This fever entered the diagnostic picture in Italy, owing to the aches in the limbs and the changes in the spinal fluid that were occasionally found. In such cases, there was usually a lymphocytic pleocytosis as well as a rise in the protein. Paralysis was not noted. A somewhat similar picture was seen in a group of German prisoners with quintana or Volhynia fever (trench fever). This entity has not been encountered since World War 1. The dramatic fever curve with a rise every 5 days for five or six episodes disclosed the diagnosis.

Beriberi neuropathy.—This was a differential problem in only a comparatively few instances involving prisoners or in association with other disease, particularly in the Far East.

One of the chief difficulties arose when multiple possible causes existed in the same person, such as malnutrition, in an area where diphtheria was endemic. It was not always possible to separate the influence of each, or the combined effect of all.

CONCLUSION

Two entities could be separated on the basis of their distinctive clinical course. One was found in groups of patients with shoulder-girdle or peroneal

[39] Gellis, S. S., McGuinness, A. C., and Peters, M.: A Study on the Prevention of Mumps Orchitis by Gamma Globulin. Am. J.M. Sc. 210: 661–664, November 1945.

palsy reported by Harvey and his coworkers and by Spillane. The protein in the spinal fluid was said to be normal in amount. The process was asymmetrical and frequently led to permanent atrophy. The other entity was the condition described by Harvey with severe pain and cramping phenomena in association with relapsing malaria.

The chief diagnostic problem was posed by the Guillain-Barré syndrome in relation to diphtheritic neuritis. Proof of prior infection with diphtheria frequently could not be reliably demonstrated by recovery of the microorganisms, by the Schick test, or by the amounts of serum antibody. Diagnosis was made more difficult by the fact that the pharyngeal infection need not be present since extrafaucial sites may exist, and the laboratory methods require great skill and experience. The Guillain-Barré syndrome, on the other hand, may occur in association with diphtheria, malaria, poliomyelitis, and other infections. Its presence did not constitute a definitive diagnosis in itself, nor is it constantly characteristic of any of these conditions, except infectious polyneuritis of unknown cause, and diphtheritic neuritis.

The diagnosis in the end rests on the clinical considerations. In both diphtheritic neuritis and the Guillain-Barré syndrome, the same region may be attacked. Thus, facial diplegia may occur in diphtheritic neuropathy and pharyngeal paralysis with the Guillain-Barré syndrome. But the incidence of the facial diplegia is very much higher in the latter condition and pharyngeal paralysis in the former. Ciliary palsy is considered specific for diphtheria, but it is discovered in only a third of the cases. Furthermore, it has been claimed that it may be found in the Guillain-Barré syndrome, though this is open to question.

There are, however, differences between the two which characterize the bulk of the cases. In diphtheritic neuritis, the course slowly evolves over weeks to reach its peak, while infectious polyneuritis is abrupt and quick in reaching its maximum. Pain is more typical of the latter and tingling paresthesias of the former. Based on these criteria, there are two typical syndromes that can be readily and reliably distinguished. Even lacking a history of the early cranial nerve palsies of diphtheria, the later tingling paresthesias followed by paralysis can be recognized. Although in the majority of cases the condition can be identified by the differences in the time of evolution, variations may be encountered in any toxemia, depending on the dose of the causative agent. Thus, Johnson reported a few cases with abrupt onset of paralysis of the limbs in diphtheria; but this is a great rarity. On the other hand, there are undoubtedly cases of polyneuritis with facial diplegia with slow subacute development over weeks; many of these patients have no paresthesias or pain while the paralysis is increasing. Such cases are customarily classified with the Guillain-Barré syndrome. Again, there are cases with abrupt onset of multiple neuritis of the limbs without facial involvement; these may be distinct or a variant of the Guillain-Barré

snydrome. Other cases with signs referable to cranial nerves but without involvement of limbs have also been grouped with it.

These clinical distinctions must accordingly be maintained until the various causative agents can be defined, when a reclassification can be made that embraces the full range of the clinical picture. If this is not done, there is danger that a specific causative agent may be mistakenly believed to be operative in producing the group as a whole. Thus, if viral studies were done in a case of unrecognized diphtheritic neuropathy, the erroneous conclusion might be reached that a virus was not responsible for any of the conditions falling in the wide spectrum of the whole group, while actually unrecognized viral disease might account for some of them.

In patients with diphtheria, antitoxin is not indicated after neuropathy has developed for it does no good and may add an allergic neuropathy to the other. Rest in bed in the presence of myocarditis must be enforced to avoid a fatal outcome. In patients with respiratory paralysis or pharyngeal-laryngeal paralysis, due to any cause, prevention of pneumonia is an equally serious problem. In the main, rest until beginning improvement is essential, along with general measures of physiotherapy and adequate diet. Supplementary vitamins apparently do not influence the course of disease.

CHAPTER XX

Dermatology

Donald M. Pillsbury, M.D., and
Clarence S. Livingood, M.D.

Part I. Administrative Considerations

GENERAL CONSIDERATIONS

Diseases affecting the skin, though not of great importance from the standpoint of the deaths they cause, are of major importance to an army operating in the field, because of the high morbidity and ineffectiveness that they can produce.[1] Hospital admission rates for these conditions give an incomplete and inaccurate picture of their potentialities for producing ineffectiveness for the reason that a very large proportion of them are treated in dispensaries and at sick call on a duty status.

When the "Manual of Dermatology,"[2] which was prepared under the auspices of the NRC (National Research Council), was published in 1942 (p. 548), the latest figures available for skin diseases in the U.S. Army were for 1940, which means that they were for peacetime and that they did not reflect the rapid increase to be expected—and that occurred—under conditions of military expansion and actual warfare. In 1940, nonetheless, diseases affecting the skin accounted for 9.8 percent of all entries on the sick list and for 10.41 percent of all man-days lost. Venereal diseases (exclusive of gonorrhea), that is, syphilis, chancroid, lymphogranuloma venereum, and similar diseases, accounted for an additional 3 percent of all hospital admissions. In the U.S. Navy, over the preceding 10 years, diseases of the skin produced 9.79 percent of all admissions to the sick list, and 8.65 percent of all man-days lost; venereal diseases (exclusive of gonorrhea) accounted for about 8 percent of all hospital admissions.

It was evident, well before the United States entered World War II, that dermatologic diseases would constitute a major cause of partial disability and lost man-days. In the Zone of Interior, where their impact was first felt, their incidence varied with the location of the troops and the season of the year. It was much higher, understandably, in the southern part

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[1] Appreciation is expressed to Dr. Robert Stolar for his work in assembling the source material upon which much of this chapter is based.

[2] Pillsbury, Donald M., Sulzberger, Marion B., and Livingood, Clarence S.: Manual of Dermatology. Military Medical Manuals. Issued under the auspices of the Committee on Medicine of the Division of Medical Sciences of the National Research Council. Philadelphia: W. B. Saunders Co., 1942.

of the country, particularly during hot, humid summer months, because of insect bites that became excoriated or infected, superficial pyogenic and fungal infections, severe miliaria, and dermatitis from plants and other contacts. It was far higher in some oversea theaters, such as the Pacific Ocean Areas, than in more temperate climates, such as the European theater. Everywhere, however, medical officers were confronted with active and latent dermatologic diseases, with all the circumstances favorable to recurrence, reinfection, and relapse, as well as to fresh infections in new hosts. These were superficial conditions, it is true, but they required an undue amount of attention when they were treated on an outpatient or sick call basis, and they accounted for undue bed occupancy in hospitals.

Many wartime hospital reports carry the statement that dermatologic disabilities could have been cut in half with improved methods of treatment and if the patients had been brought into contact, in the initial phases of their illness, with properly qualified dermatologists. It was also frequently noted, in hospital and other health reports, that, if battalion surgeons and other medical officers assigned to dispensaries had had adequate training in dermatology, there would have been significant decreases in the so-called overtreatment syndrome. These comments assume special significance if it is borne in mind that, in some tropical oversea areas, dermatologic diseases accounted for as much as 75 percent of all visits to dispensaries.

Obviously, these are diseases of serious military potentialities. Yet in spite of that fact, the statement may be made with considerable confidence that before the outbreak of World War II, and indeed until it was almost half over, diseases of the skin received less attention, both administratively and therapeutically, than any other major source of disability. Both civilian and military medicine contributed heavily to this situation for a number of reasons, some of which will be discussed in greater detail later in this chapter.

1. As late as 1942, diseases of the skin were still being cared for in Army hospitals on the urology service, an archaic arrangement that had been discontinued in civilian practice a quarter of a century earlier. This policy was not officially discontinued in the Army until 1943, except upon the initiative of commanding officers of a number of individual station and general hospitals. These officers organized dermatologic services and handled all patients with diseases affecting the skin on wards that ordinarily included both dermatology and syphilology. This plan was firmly established in all hospitals by the end of the war, though the changeover was accompanied by numerous administrative difficulties.

2. Before World War II, the United States had seldom had large bodies of troops in tropical areas for long periods of time. There was therefore little realization of the tremendous increases in the incidence of common skin diseases that would occur under conditions of prolonged heat and humidity. The attention given to unusual medical diseases peculiar to the

Tropics, fully justified though it was, far overshadowed the attention given to the remarkable exacerbation to be expected in frequently encountered but less exotic dermatologic conditions. The British, with their long and worldwide colonial and military experience, fully appreciated the situation. The United States, with its smaller and more limited experience, did not.

3. Little attention was paid to dermatology by the National Research Council.[3] In the prewar period, and well into the war, a single civilian physician was charged with all dermatologic problems in the Division of Medical Sciences. There was no subcommittee for dermatology, as there was for numerous other specialties, and no specific research was directed toward either the prevention or the management of diseases of the skin under military conditions. In fact, there was no national research program in depth set up to investigate physiologic and pathologic factors in dermatologic disability.

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[3] Lest the impression be created that little assistance was provided by the National Research Council in dermatological matters to the Army during World War II, it is desired to point out the very specific and valuable assistance given in the matter of control of fungal infections of the feet ("athlete's foot"). This was a chronic and perennial problem amongst troops forced to live close together in a barracks environment.

Prewar instructions for the prevention of athlete's foot required the use of chlorine solutions prepared daily (usually made from calcium hypochlorite) for footbaths in shower rooms, and the daily exchange and sun-drying of duckboards placed on the floor of such rooms. Moreover, responsibility for the supervision of such measures was made a command responsibility and therefore placed directly on the shoulders of the unit commander. Labor details were assigned to this task and many man-hours were expended daily throughout the Army in their execution.

Despite these vigorous measures over the years there appeared to be no appreciable impact upon the incidence of athlete's foot and the question of their continuing value was raised. To resolve this matter, the question was placed before the Division of Medical Sciences, National Research Council, during 1944. Opinion was divided amongst the dermatologists, but the most anyone would say on behalf of existing prophylactic measures was that they could do no harm. With this consensus, it was finally agreed that the Army could safely discontinue such measures, and action was initiated to that end by the Sanitation and Hygiene Division of The Surgeon General's Office.

At a talk given at the Service Command Medical Inspectors' Conference in Baltimore, Maryland, on 14 February 1945, Lt. Col. (later Col.) Arnold L. Ahnfeldt, MC, Director of the Sanitation and Hygiene Division, Preventive Medicine Service of The Surgeon General's Office, stated that widespread doubt concerning the value of present footbaths had now been confirmed by the National Research Council. As Colonel Robert J. Carpenter, the Executive Officer for The Surgeon General, reported in an indorsement to the Commanding General, Army Service Forces, on 29 March 1945, the comments of Colonel Ahnfeldt at the Medical Inspector's Conference were being translated into action. As a result, War Department Circular No. 146 of 17 May 1945 was prepared and published. Paragraph I, Athlete's Foot, directed that "The use of foot baths containing chemical solutions for the prevention of dermatophytosis of the feet is hereby discontinued."

This directive resulted in a substantial saving of calcium hypochlorite which was in critically short supply and was needed for other highly important purposes, such as water purification. Moreover, there was no further need to spend time on the daily preparation of chlorine solutions for footbaths.

A short while later, the publication of War Department Circular 262, dated 30 August 1945, made the use of "duckboards" in shower rooms *optional*, pointing out they "are of value only in the prevention of accidents" and thereby indicated their lack of value in the prophylaxis of athlete's foot. This circular led to the almost immediate discontinuation of the use of duckboards in showers and on aprons of swimming pools Army-wide.

Thus, the two War Department Circulars cited did away with long-standing practices within the Army mistakenly designed to prevent athlete's foot. Attesting to the wisdom of the recommendations of the Division of Medical Sciences, National Research Council, in this matter is the fact that there was no subsequent increase in the incidence of athlete's foot amongst troops with discontinuation of these prophylactic measures, and no increase since that time attributable to the change in policy. Instead, unit commanders were able to breathe a sigh of relief, and many man-hours expended in labor details Army-wide were diverted to other uses.—A. L. A.

4. The training of specialists in dermatology was, in many civilian centers, superficial and narrow. Trained dermatologists were in short supply throughout the war, and the shortages were increased by the lack of any system in the Army for assigning those with special training to areas or units with high admission rates for skin diseases (p. 571).

5. The consultant system, which operated so successfully in many other branches of medicine, was slow to operate in respect to dermatology, a situation that helped to explain the poor assignment of dermatologists just mentioned.

6. Numerous large general hospitals, including some affiliated hospitals, were sent overseas without a single medical officer on the staff who had even a cursory knowledge of diseases of the skin. The tables of organization for these units originally had no provision for a dermatologist, and the Personnel Division, OTSG (Office of The Surgeon General), apparently saw no need for providing one.

7. Tables of equipment were extremely inadequate, and often entirely deficient, in provision of agents necessary for topical medication.

8. Finally, as was true of other specialists, dermatologists failed to realize the potent sensitizing capacity of many new therapeutic agents, whether injected, ingested, or used topically. When the war began, the potentialities for harm of the sulfonamides were slowly being realized, but the story of penicillin, Atabrine (quinacrine hydrochloride), and many other compounds remained to be told.

EVOLUTION OF DERMATOLOGIC MANAGEMENT

By the fall of 1941, when it was evident that the United States would be drawn into the war and that dermatologic disability would be a considerable problem in the Army, many commanding officers, particularly of hospitals in training areas, began to request the assignment of medical officers with some experience in dermatology. Their requests were often based on the initial requests of chiefs of medical services, who found themselves unable to deal effectively with the numbers of patients with skin diseases who, under the existing arrangements, were occupying medical beds for long periods of time.

Improvement of the situation was accomplished, for the most part, by the individual efforts of individual medical officers and civilians rather than by any single centralized effort. Until late in the war, chief surgeons, medical consultants, and individual hospital commanders met the problem in various ways, and, as might have been expected, with varying degrees of success.

Action in National Research Council

The first general efforts to remedy the situation were made in the National Research Council, with the appointment of Dr. Donald M. Pillsbury, Professor of Dermatology, University of Pennsylvania School of Medicine, as Consultant in Dermatology to the Committee on Medicine, Division of Medical Sciences. His specific responsibility was to make recommendations concerning this specialty for the Armed Forces by way of this committee. It was a small beginning, but highly important; it was the first time any governmental or quasi-governmental organization had ever concerned itself specifically with diseases affecting the skin.

The previous lack of interest in this specialty was not hard to explain. The NRC Committee on Medicine, although composed of physicians of the highest ability and repute, was only mildly concerned with dermatology. Most of the members of the Committee on Medicine came from medical schools on the eastern seaboard, where skin diseases were regarded as minor problems and where, with occasional exceptions, dermatology had never achieved any special recognition. The appointment of a consultant on dermatology to the Committee on Medicine was an advance, but in retrospect, the additional appointment of a subcommittee on dermatology would have been a wiser move.

A development that was ultimately related to Dr. Pillsbury's activities was, as already mentioned, the initiative of the commanding officers of certain station and general hospitals in setting up sections of dermatology and syphilology headed by qualified dermatologists who were called to active duty from civilian practice. Col. Asa M. Lehman, MC, for instance, sponsored and actively encouraged the organization of such a section at the Indiantown Gap Station Hospital, Pa., which served a large training camp that had been set up early in 1941. Colonel Lehman, a veteran medical officer with a large oversea experience, was an extremely astute physician, who had a considerable knowledge of disability from dermatologic disorders, particularly in the Philippines. He was greatly disturbed by the lack of any organization within the Medical Corps, as well as the lack of personnel and supplies, to deal with this group of diseases. He solved the problem by setting up a dermatology and syphilology section, with Capt. (later Maj.) Clarence S. Livingood, MC, as chief of the section.

At Colonel Lehman's invitation, Dr. Pillsbury visited this hospital on numerous occasions and held long conferences with him and Captain Livingood. The latter soon accumulated an impressive body of statistics that showed very clearly that skin diseases were extremely frequent and that early mismanagement of even simple conditions could lead, at times, to prolonged disability and, on occasion, to separation from service. In a number of instances, key combat personnel, for this reason, had been unable to accompany their units overseas.

Preparation of Manual on Dermatology

The substance of these discussions was communicated to Brig. Gen. Charles C. Hillman, Chief, Professional Service Division, OTSG, who was then representing the War Department on the National Research Council. General Hillman brought the matter to the attention of Maj. Gen. James C. Magee, The Surgeon General, with the recommendation that special policies be developed to deal with dermatologic disability. He also recommended that a short technical directive be issued for the information and guidance of medical officers who had to deal with the more common dermatologic syndromes.

As the result of these recommendations, The Surgeon General invited Colonel Lehman, Captain Livingood, and Dr. Pillsbury to a conference with him and General Hillman early in 1942, to discuss the preparation of a manual on dermatology, which General Hillman proposed be carried out under the auspices of the National Research Council. The Surgeon General approved the plan, and the National Research Council concurred in the arrangement.

Dr. Pillsbury and Major Livingood had only just begun their work on the proposed manual when Capt. Charles S. Stephenson, MC, USN, who was representing the Navy on the National Research Council, became interested in the project and asked that it be pursued as a joint Army-Navy effort. Lt. Cdr. (later Capt.) Marion B. Sulzberger, MC, USNR, was therefore added to the authors. With the warm encouragement of General Hillman and Colonel Lehman, the work proceeded rapidly in spite of the transfer of Major Livingood, in May 1942, to the 20th General Hospital, Camp Claiborne, La.

Though the format was different, this manual became one of the series developed under the auspices of the Division of Medical Sciences, NRC, and designed to furnish the Medical Departments of the U.S. Army and Navy with compact presentations of essential information in the field of military medicine. While it is unfortunate that it was not ready when mobilization began in 1940 and 1941, in one sense the delay was an advantage: The whole text was written in the light of current, practical experience in military dermatology, with the most pressing needs of the general medical officer in mind. The subject matter was strictly limited. It concerned only the common skin diseases affecting males of military age. Methods of treatment were restricted to those expected to be available in the usual Army and Navy installations. The manual had a wide distribution, though it did not become available in many units overseas for a year or more after its publication. The total printing of 40,500 copies made it, in this respect, much the largest of all the NRC manuals published.

It is difficult to assess the real impact of any technical bulletin or manual upon medical practices in the Armed Forces. It is believed, however,

that this small, compact volume exerted a great deal of influence. For one thing, since it had the personal attention and backing of The Surgeon General in the Army Medical Department and the Navy Bureau of Medicine and Surgery, as well as of ranking officers in both services, attention was focused on the medical problems with which it dealt. There seems no doubt that, as the result of its publication, increasing efforts were made to achieve better professional care of dermatologic diseases. There were also improvements in the supply tables of drugs essential for the treatment of these diseases.

Recommendations for Development of Dermatology Service

Meantime, dermatology was receiving further attention in the Office of The Surgeon General. Shortly after Col. Arden Freer, MC, became Director of the Medical Practice Division, OTSG, in October 1942, he requested Lieutenant Colonel (later Colonel) Pillsbury, who had entered the Medical Corps and had been assigned to Walter Reed General Hospital, Washington, D.C., to submit recommendations for the organization and equipment of Army station and general hospitals, for the improved care of dermatologic patients.

Colonel Pillsbury regarded "the request for the opinion from a military medical neophyte" as presenting "a calculated risk," but, with the collaboration of Major Livingood, undertook the assignment. Their recommendations were based on the material included in the "Manual of Dermatology" and on data collected from various sources for the Committee on Medicine, NRC, during the previous year. In one way or another, the organization and facilities recommended were achieved in almost all station and general hospitals by the end of the war.

The substance of Colonel Pillsbury's reply to Colonel Freer, on 25 October 1942, was as follows:[4]

Incidence.—During 1940, skin diseases were responsible for about 8 percent of admissions to Army hospitals, but the proportion can be expected to vary widely under different conditions. Troops in warm climates will show sharp increases in fungal and pyogenic infections. Troops on maneuvers will show increases from extensive contact with plants. Parasitic skin diseases will increase in some theaters of operations.

Facilities.—On the basis of these estimates and projections, about 5 percent of all hospital beds should be kept regularly available for dermatologic patients, and provision should be made for the expansion that may be necessary.

Since most dermatologic patients are ambulatory and are treated on an outpatient basis, facilities for their examination and treatment, as well as for the maintenance of adequate records, must be correspondingly larger than for other dispensary sections. Figures from the Indiantown Gap Station Hospital show outpatient visits to the dermatology clinic to be two or three times more numerous than inpatient admissions. These figures are likely to be duplicated in other hospitals in isolated areas. In general hospitals serving large numbers of posts, outpatient dermatology visits will be at least 10 times as

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[4] Letter, Lt. Col. Donald M. Pillsbury, MC, to Col. Arden Freer, Services of Supply, Office of The Surgeon General, War Department, Washington, D.C., 25 Oct. 1942.

numerous as hospital dermatology admissions, and the disparity may be even greater. Statistics from Walter Reed General Hospital for August and September 1942 support these estimates.

Regular progress notes are particularly essential on dermatologic patients, and provision for storage of records must be adequate.

Complete examination of dermatologic patients is essential, and often it must be made with them stripped. Privacy and good lighting are therefore necessary in outpatient clinics. Examination of outpatients with skin diseases in open wards has a bad effect on both the outpatients and the occupants of the wards. Private examining rooms or cubicles must be provided.

Unit organization.—While policies of hospital organization vary from installation to installation, there is now rather general agreement that syphilis should be treated on dermatologic wards. Certainly, it is hard to justify its treatment on a surgical service. At the present time [October 1942], there is no specific provision for a dermatology section in the table of organization of a general hospital (TM 8-260, 13b), but there is such provision in the table of organization of a station hospital (TM 8-260, 275c). In some station hospitals, such as the hospital at Indiantown Gap, skin diseases, syphilis, and all other venereal diseases except gonorrhea are treated on a single section, a plan that requires about double the bed space necessary for dermatology alone. The advisability of combining the management of. these diseases has long been under discussion in the Army, and combined management is the established policy of the Navy. The plan also has the complete approval of Dr. Joseph Earle Moore and Dr. John H. Stokes, both members of the Subcommittee on Venereal Diseases, NRC. An argument in favor of the arrangement is the fact that all physicians trained in good dermatology clinics in recent years have also had adequate training in the diagnosis and treatment of syphilis.

Wards for dermatology and syphilis require the same facilities as are provided on any general medical wards. In recent years, dermatologists have been more and more inclined to study the systemic background of skin diseases as well as their surface aspects.

Personnel.—Whenever practical, a medical officer experienced in dermatology should be assigned to station and general hospitals, since there is no other branch of internal medicine in which general practitioners have as much difficulty in diagnosis and management. It is hoped that directives and other instructional efforts will enable medical officers untrained in dermatology to treat the more common skin diseases effectively, but these materials will not be helpful in the management of uncommon and chronic diseases. It would lessen disability from dermatologic causes, including overtreatment, if board-certified dermatologists were available for consultation on patients with such diseases.

The ward officer on a dermatology-syphilology section should preferably have had some special training in these fields. The assistant ward officer does not require it. Nurses and enlisted personnel who have had some training in dermatology greatly improve the efficiency of a dermatologic service. A noncommissioned officer, who is a keyman on such a ward, can be trained by a ward officer within a month, by reading assignments and demonstrations, to clean lesions, make topical applications, obtain scrapings, prepare solutions for injection, and assist at such minor surgical procedures as biopsy and electrodesiccation. Nurses, enlisted men, and officer personnel should not be rotated to other services; frequent changes of dermatologic personnel invariably mean less effective treatment. In military practice, as well as civilian, the difference between cure and chronicity can often be attributed to nursing care and attention to small details of treatment.

It is always desirable for the ward officer on the dermatology section to maintain good rapport with the laboratory. In the management of syphilis, regular comparisons of clinical and serologic findings redound to the good of the patient. Close cooperation on darkfield examinations is particularly useful.

Equipment and supplies.—Provision should be made for the performance on the dermatology section of minor surgical procedures such as biopsy; electrocoagulation of

warts, small papillomas, and epitheliomas; drainage of acne cysts; and similar procedures. The performance of biopsies by surgical consultants is often unsatisfactory because of the amount of paperwork involved as well as because the site is not always properly selected for the dermatologist's purposes. The treatment of small warts by X-ray is an uncertain and expensive method. Small electrocoagulation units, without cutting current, which cost no more than $30 or $40, are entirely adequate for their removal and, in fact, are less hazardous and more efficient than some of the larger obsolete units now in use. If space must be conserved, these units can be hung on the wall.

At the present time, the greatest obstacle to treatment of dermatologic conditions is the lack of certain common therapeutic agents. These basic preparations are essential and should be kept on all dermatologic wards ready for immediate use. The supply list is presently undergoing considerable revision, but the need for these agents is immediate and urgent.

Minimal organization.—Colonel Pillsbury closed his communication to Colonel Freer with recommendations for a tentative minimal organizational dermatology setup, with practical considerations in mind, for a thousand-bed station or general hospital. He made it clear that some additions would be necessary for a hospital like Walter Reed General Hospital, in which difficult cases were treated and to which newly inducted medical officers were sent for training.

Colonel Pillsbury's specifications were as follows:

1. Wards of 35 or 40 beds would be required for both the dermatology and syphilology sections, with, at a minimum, 1 or 2 examining rooms and 1 or 2 treatment rooms. Additional facilities would be required if a considerable number of outpatients were treated. Also required would be offices for the ward officer and the ward nurse; three cubicles for infectious patients on the dermatology section and six to eight (possibly less) for infectious patients on the syphilology section; and the usual closet and storeroom facilities required on any medical ward.

2. Standard items for ward and office equipment should include a sufficient number of filing cases; outpatient and other records should not be kept in desk drawers.

3. Equipment for the dermatology section should include a set of simple instruments (2 forceps, straight and curved scissors, scalpels, 2 ring curettes, a stilet, a biopsy punch, 2 syringes for skin tests and for local analgesia, and a microscope which, if there were difficulty in procuring it, could be dispensed with). The need for an electrodesiccation unit has already been mentioned. An ultraviolet unit should be provided unless treatment was readily available in the physical therapy department. The X-ray section of the hospital should provide the facilities for superficial X-ray therapy. If standard equipment was not available, the diagnostic units used in field hospitals could be calibrated and used for skin therapy.[5]

Special equipment for the syphilology section should include adequate numbers of syringes, needles, and mixing glasses; material for Frei and Ducrey tests; and anti-syphilitic drugs. The needles presently in use for intramuscular injection are usually too heavy and too short. A darkfield microscope is not considered necessary; ward officers can use the one in the laboratory.

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[5] This plan was widely used in oversea hospitals as well as in hospitals in the Zone of Interior during the war.

CONSULTANTS IN DERMATOLOGY

Zone of Interior

Early in the war, consultants in medicine, surgery, and neuropsychiatry were appointed in the Office of The Surgeon General. Later, consultants were appointed in various subspecialties, including orthopedic surgery, ophthalmology, otolaryngology, radiology, and physical medicine. Still later, consultants in medicine, surgery, and neuropsychiatry, as well as in some subspecialties, were assigned to all nine service commands, and, in time, to the headquarters of all oversea theaters, as well as to all armies and many base sections.

Office of The Surgeon General.—Consultant service in venereal diseases was provided in the Preventive Medicine Division, OTSG, early in the war, but a consultant in dermatology was not appointed in that office until April 1945, shortly before the end of the war in Europe and only 4 months before the end of the war against Japan. The position was filled by Major Livingood, who served from that time to January 1946.

A review of the various changes of policy by which the care of dermatologic patients was improved, chiefly by better utilization of medical officers with special training in this field, makes it clear that a large share of the credit for the improvement evident during the last year of the war should go to Brig. Gen. Hugh J. Morgan, Consultant in Medicine, Office of The Surgeon General. General Morgan requested the appointment of a consultant in dermatology, 18 months before the request was honored. The policies he introduced in internal medicine greatly influenced the correct utilization of all medical officers and encouraged their accurate classification on the basis of their training and experience. Through the use of consultants in internal medicine in the service commands and the ultimate addition of Major Livingood to his Medical Consultants Division, OTSG, General Morgan was able to direct increasing attention to dermatologic disability in the Zone of Interior. His efforts to assign consultants in this specialty to all major commands, both in the United States and overseas, were largely thwarted by the fact that there was no provision for them in tables of organization.

The following letter from General Morgan to all service command surgeons early in 1943 illustrates his broad point of view:

In my visits to army hospitals, overseas and in this country, I have been impressed by the fact that dermatological diseases are somewhat neglected. The reason for this is obvious—we haven't enough good dermatologists to go around (and a poor dermatologist is often worse than none) and the dermatologists assigned often must work in the medical service alone without the benefit of any exchange of ideas with fellow practitioners. I am perfectly certain that much good could be accomplished by good dermatological consultations. I believe that a great deal can be done in army hospitals to raise the level of dermatologic practice by providing occasional visits from an expert in the field. I realize

that our medical consultants are interested and that, in a general way, they keep their eyes on the dermatological problems; nevertheless, I suspect they adopt the same attitude that I do about the matter. Personally, in visiting army hospitals, I am very loath to put my opinion up against the opinion of the dermatologist on the ward. Moreover, I find it difficult to even evaluate his professional performance. Actually, my knowledge of, and experience with, dermatologic problems are limited and in the army, I make little or no contribution to hospital practice in this field. I expect a large majority of the medical consultants share my feeling in this regard. This letter is being written to the end of asking you to consider the suggestion that you select one of the best dermatologists in your service command and have him visit the hospitals throughout the service command to the end of stimulating better dermatological practice and bringing you information regarding the performance of personnel. You could do this of course, by having a dermatologist work out of your office from time to time on a temporary duty status. I am certain that many of our station hospitals would profit by such visits and I think that it is highly probable that regional, station, and general hospitals would also, and I am equally certain that the hospitals would welcome such a consultant. The system has been used successfully in the European and Southwest Pacific theaters as a supplement to the work of the permanently assigned medical consultants.

Service commands.—It was difficult, as just noted, to appoint consultants in dermatology in service commands because there was no provision for them in tables of organization. Some officers trained in dermatology were able to perform dermatologic duties on an informal basis, but the only consultant formally appointed was Maj. Herbert L. Traenkle, MC, who was assigned to the Fifth Service Command as venereal disease control officer and who was authorized to serve as consultant in dermatology in this command on 5 January 1945. The clear understanding, however, was that his dermatology assignment was strictly "in addition to other duties." He was the only consultant in dermatology who functioned as such in the Zone of Interior during the war. He made an extremely important contribution, and the standards of dermatologic care in the hospitals of the Fifth Service Command were raised as the result of his efforts.

The background of this odd situation should be emphasized: Venereal disease control had had a high priority in Army medicine for many years before the war, and control officers were therefore assigned at once to headquarters of all service commands as well as to oversea theaters and many base sections. The training and interests of these officers varied. Most of them were trained primarily in epidemiology and venereal disease prevention. Others were primarily dermatosyphilologists. It is unfortunate that the dermatologic abilities of this latter group of officers were not also utilized for dermatologic purposes. They were not so utilized. The officers were assigned to preventive medicine, and while their work in venereal disease control was extremely important and rewarding, a considerable part of it concerned matters far removed from medicine.

Oversea Commands

Consultants in dermatology were eventually appointed in ETOUSA (European Theater of Operations, U.S. Army) and in SWPA (Southwest

Pacific Area), but none was ever formally appointed in MTOUSA (Mediterranean Theater of Operations, U.S. Army) or in the CBI (China-Burma-India) theater.

European theater.—The consultant system in the European theater was unusually well developed early in the war. It included medicine, surgery, orthopedic surgery, plastic surgery, neurosurgery, otolaryngology, ophthalmology, and radiology.[6] In the summer of 1942, Brig. Gen. (later Maj. Gen.) Paul R. Hawley, Chief Surgeon, Headquarters, ETOUSA, requested the Office of The Surgeon General to make a consultant in dermatology available to him. In December of that year, Colonel Pillsbury joined General Hawley's consultant staff and functioned on it until the end of the war, with ultimate responsibility for deramtology and for diagnostic and therapeutic venereology.

The European theater differed from other commands in two important respects:

1. It was the only major Army command with a formal, full-fledged consultant system that received consistent and vigorous support from the theater surgeon. The system was distinctly on trial when it was institued, and it suffered in its early days from organizational and other growing pains. With General Hawley's unwavering support, however, it was able to function efficiently in the European theater, and by V-E Day, there was no doubt of its value.

2. The European theater was the largest of all theaters, and by 1945, it had a considerably greater number of medical installations and medical officers than the Zone of Interior itself.[7]

The appointment of a consultant in dermatology in the European theater provided the same advantages that were inherent in the total consultant system, as well as certain advantages peculiar to the specialty:

1. Personal visits by the consultant to hospitals and armies permitted him to keep abreast of current problems and to anticipate others long before he might have been alerted to them by reports through official channels.

2. Observation of therapeutic methods at the bedside and in outpatient dispensaries permitted prompt correction of poor techniques and deficiencies.

3. Contacts with large numbers of medical officers on a personal as well as professional basis had many advantages.

4. Personal observations permitted intelligent recommendations for transfer of specially qualified personnel to installations in which there was special need for their services.

[6] (1) Medical Department, United States Army. Radiology in World War II. Washington: U.S. Government Printing Office, 1966. (2) Medical Department, United States Army. Internal Medicine in World War II. Volume I. Activities of Medical Consultants. Washington: U.S. Government Printing Office, 1961. (3) Medical Department, United States Army. Surgery in World War II. Activities of Surgical Consultants. Volume I. Washington: U.S. Government Printing Office, 1962. (4) Medical Department, United States Army. Surgery in World War II. Activities of Surgical Consultants. Volume II. Washington: U.S. Government Printing Office, 1964.

[7] Medical Department, United States Army. Personnel in World War II. Washington: U.S. Government Printing Office, 1963.

5. Dissemination of information concerning improved methods of treatment, changes in methods which had not proved satisfactory, and other items was greatly facilitated.

6. Because of the short lines of communication between installations in the United Kingdom Base as well as on the Continent, at least until well into 1945, it was possible for all consultants to visit medical installations frequently, sometimes as many as four or five in a single day. These visits permitted a considerable amount of on-the-job training in dermatology for medical officers with no previous experience in skin diseases. This informal training was supplemented by seminars and by discussions at the Medical Field Service School at Cheltenham, England, and at the Eighth Air Force Provisional Medical Field Service School at PINETREE (High Wycombe, Headquarters VIII U.S. Bomber Command). In all discussions and classes, great emphasis was put upon the common diseases of the skin that could be treated in the field or in dispensaries if they were recognized early but that, if neglected or maltreated, could produce prolonged disability and sometimes require hospitalization.

Separate sections of dermatology were set up within the framework of the medical service in all hospitals in which the patient load justified such subdivision. With the introduction of intensive arsenical therapy for early syphilis and the later use of penicillin (p. 581), the diagnosis and treatment of all venereal disease became the responsibility of the section on dermatology. In installations of 500 beds or more, as a result, the patient load was sufficient to occupy the full-time attention of one medical officer and sometimes of two.

When it became evident that penicillin therapy for early syphilis would become available shortly after D-day, detailed plans were drawn up by the Consultant in Dermatology with the surgeons of the various armies for centralization of all patients with acute venereal disease; they were usually cared for in convalescent centers, in charge of specially qualified personnel. By this plan, all but a few patients in this large group were kept out of station and general hospital areas and were returned to duty as soon as their treatment was concluded. A great waste of manpower was thus prevented.

As of 1 January 1945, the number of dermatologists classified by MOS (military occupational specialty) ratings in the European theater was 47, while the number of fixed medical installations was 146. With the representation which dermatology had in the Office of the Chief Surgeon, ETOUSA, it was possible for Colonel Pillsbury to assign the limited number of well-qualified dermatologists in the theater, either formally or on an ad hoc basis, to the installations in which they were most needed. Difficulties arose later, of course, when the number of hospitals increased, casualties were heavy, and lines of communication lengthened. Then, with the support of the Chief Surgeon, the base surgeons, and the commanding officers of strategically located general hospitals, all dermatologic patients who presented difficult and resistant conditions were grouped in certain hospitals with competent dermatologists on the staffs. In addition, dermatologic officers with wide experience made regular rounds at adjacent hospitals without qualified dermatologists on their staffs. Among those who functioned in this informal

consulting capacity were: Capt. Frank E. Cormia, MC, 49th Station Hospital; Capt. (later Maj.) C. J. Courville, MC, 298th General Hospital; Maj. Emerson Gillespie, MC, 67th (later 5th) General Hospital; Maj. Herbert H. Holman, MC, 40th General Hospital; Maj. Adolph Loveman, MC, 49th Station Hospital; Capt. (later Maj.) Thomas W. Murrell, Jr., MC, 28th General Hospital (Major Murrell was later attached to dispensaries in London and in Paris); Maj. (later Lt. Col.) Maurice H. Noun, MC, 30th General Hospital; and Capt. (later Maj.) Samuel R. Perrin, MC, 58th General Hospital.

The service was not always easy to provide, but it was provided, and it seems fair to say that, by the plans just outlined, every patient with a skin disease of significant severity received prompt and adequate consultation service. The validity of this statement is borne out by the fact that, in spite of the large troop strength in the theater, not more than 30 or 40 patients per month were boarded to the Zone of Interior for skin disease. The maximum, 40, was reached only once, in June 1945.

Southwest Pacific Area.—In September 1943, General Morgan, noting the increasing number of dermatologic conditions in the Southwest Pacific Area, made a consultant in dermatology available to it on his own initiative, without a request from the area. When the consultant (Maj. (later Lt. Col.) John V. Ambler, MC) arrived, he found himself unable to function because of the indifference, bordering on hostility, of the area surgeon. When this incumbent was replaced, early in 1944, by Brig. Gen. (later Maj. Gen.) Guy B. Denit (Chief Surgeon, U.S. Army Services of Supply, SWPA), a general officer with a real understanding of the value of the consultant system, Major Ambler was able to function efficiently for the first time.

It is only fair to interpolate at this point that while some administrative officers took the attitude toward consultants just described, others welcomed them cordially. It is also only fair to note that the difficulties attendant on operation of the consultant system were often not helped by the habit of some consultants, fresh from civilian practice, of making recommendations without sending them through proper channels and by their lack of appreciation of the problems of commanding officers. In other words, attitudes on both sides sometimes furnished serious roadblocks to the achievement of better methods of prevention and treatment of diseases and injuries and also militated against the most profitable assignment of specially qualified personnel.

Once he was able to function unhampered, Major Ambler recognized the existence of certain problems:

1. Were some of the more unusual skin disorders encountered caused by infection by fungi?

2. Were the numerous cases being diagnosed as trichophytosis or epidermophytosis really fungal infections? There was little clinical, and no laboratory, support for these diagnoses.

At the direction of General Denit, an investigation to settle this point was undertaken by Dr. J. Gardner Hopkins, a mycologist of wide experience, Professor of Dermatology, Columbia University College of Physicians and Surgeons, Civilian Consultant in Dermatology to The Surgeon General, and investigator (dermatophytosis) for the Committee on Medical Research, OSRD (Office of Scientific Research and Development). Dr. Hopkins was not eligible for military service because of age and other reasons, but he devoted most of his time during the war in a civilian capacity to the Office of Scientific Research and Development. His numerous field studies were an outstanding contribution to the work of the Medical Corps.

Dr. Hopkins reached the Southwest Pacific Area on 2 September 1944, and after his survey made his report to General Denit on 13 March 1945.[8] By the time Dr. Hopkins reached the area, diseases of the skin had become an extremely serious problem. In some hospitals, 20 percent of the medical admissions were for this cause, and many hospitals had from 100 to 300 patients on the dermatology wards. The rate of evacuation to the Zone of Interior for skin diseases had reached 17 percent of all medical cases and was exceeded only by the rate for neuropsychiatry.

Under Major Ambler's guidance, Dr. Hopkins visited station and base hospitals in Brisbane, Australia; Oro Bay, Dobodura, Lae, Nadzab, Finschhafen, and Hollandia, in New Guinea; and Leyte and San Fabian in the Philippines. He also visited dispensaries at Lae (New Guinea) and Leyte, and battalion aid stations on the Rosario Front, in the Philippines. He was thus able to obtain a comprehensive view of dermatologic problems at different points in the line of evacuation, from the frontline to general hospitals in the rear. His observations are reported, under appropriate headings, elsewhere in this chapter.

China-Burma-India theater.—As already mentioned, there was no dermatology consultant in the China-Burma-India theater during the war, but Col. Herrman L. Blumgart, MC, served as Consultant in Medicine during the latter months of fighting.

Three general hospitals assigned to India had dermatology sections. The 20th General Hospital, which arrived in March 1943, was located in Assam, near the border of Burma. The 69th General Hospital, also assigned to Assam, arrived in June 1944, during the height of the intensive campaign being conducted by Merrill's Marauders at Myitkyina. The 142d General Hospital arrived in Calcutta in September 1944.

Each of these hospitals had from three to five wards set aside for dermatology and syphilology, and the two hospitals located in Assam also had wards for treatment of these conditions in Chinese soldiers. The experience of all three hospitals was essentially the same.

[8] Letter, J. G. Hopkins, M.D., Technical Observer, Office of Field Service, Office of Scientific Research and Development, to Brig. Gen. Guy B. Denit, Theater Surgeon, Headquarters, USAFFE, 13 Mar. 1945, subject: Report of Observations on Fungus Infections and Other Dermatoses in the SWPA.

PERSONNEL AND ASSIGNMENT

Before the beginning of mobilization in September 1940, there was not a single qualified (certified) dermatologist in the Regular Army Medical Corps, nor was there a section of dermatology in any Army hospital. With the mobilization of the members of the Medical Corps Reserve, in 1941, a few officers with special dermatological training came on duty, and some of them were assigned to hospitals in the Zone of Interior.

When maneuvers began, in the summer of 1941, it became abundantly clear that dermatologic admissions to station hospitals would be significant. The maneuvers in Louisiana were especially instructive in this regard (p. 572), for a continuing flow of soldiers were rendered ineffective by complications of insect bites, especially chiggers; primary or secondary bacterial infections; contact dermatitis caused by plants; miliaria; and the sensitizing effects of topical medicaments, particularly the sulfonamides. The commanding officers of the station hospitals that received these patients soon found it necessary to set up special dermatologic sections, even though in many instances they had no qualified dermatologists to put in charge of them.

Even though tables of organization did not provide for them, some affiliated general hospital units were able to recruit dermatologists by various methods. Other hospitals did not recruit them, and such university-sponsored units as the 2d General Hospital (Columbia University), the 18th General Hospital (Johns Hopkins University), and the 30th General Hospital (University of California) went overseas without dermatologists on their staffs.

Original Misassignments

Dermatologists called to active duty in 1941 were sometimes assigned to dermatologic duties but very frequently were not. Those who were not assigned as dermatologists communicated their dissatisfaction rather vigorously to civilians in high academic and organizational positions, and inquiries arising from these complaints were sent to appropriate authorities.

The first communication on the matter was a letter from Dr. (later Captain, Medical Corps) William B. Guy, Chairman, Section on Dermatology and Syphilology, American Medical Association, to The Surgeon General and to Maj. (later Brig. Gen.) Sam F. Seeley, MC, Chief, Office of Procurement and Assignment Service, War Manpower Commission, Office for Emergency Management. In this letter, dated 17 April 1942, Dr. Guy requested from Major Seeley specific information regarding (1) the need for dermatologists in the Armed Forces; (2) the official policy regarding the utilization of specialists in their own branches of medicine; (3) the routine by which dermatologists should proceed when they applied for commissions

in the Armed Forces, so that they would be utilized in their special field; and (4) the possibility of transfer of dermatologists presently assigned to nondermatologic duties in the Armed Forces.

Col. (later Maj. Gen.) George F. Lull, MC, replied for The Surgeon General, on 19 April 1942, in substance, as follows:

1. Because of the difficulty of assigning all specialists to positions in which they will do work they are accustomed to do in civilian life, many medical officers will have to adjust themselves in the Army and learn new occupations.

2. Dermatologists will be needed in the Armed Forces, but how many is not known. They can be utilized in the larger hospitals, but usually there will not be sufficient work to utilize them exclusively in their specialty.

3. An attempt will be made to assign dermatologists who volunteer for service to hospitals in which they will be used in the treatment of skin diseases and syphilis, but no promises can be made in this regard. Moreover, in many hospitals, skin diseases are treated in one department and syphilis in another.

4. If the names of those now in service who are not now doing dermatology and syphilology are provided, it may be possible to transfer most of them.

5. Dermatologists applying for commissions should state their preference for assignment, and every attempt will be made to grant their requests.

Major Seeley's reply to Dr. Guy was even less encouraging. In substance, he wrote:

1. The number of dermatologists needed by the Armed Forces would be so limited that he would be disinclined to encourage dermatologists to think their duties would be strictly in this field.

2. Those recognized in the specialty and now in service must continue to serve in their present capacities until such time as The Surgeon General had the advantage of an oversupply of medical officers. There would be no justification in asking him to make assignments until the rest of the profession had come forth for service and rearrangements were feasible.

3. Dermatologists applying for commissions should emphasize their training and ask for assignment to their specialty on the form for statement of preferences.

4. Many physicians who anticipated that military service would make specialists out of general practitioners must be satisfied with being made better practitioners if they were not engaged as specialists. "We must win this war," Major Seeley concluded, "and then enjoy our highly developed specialization in peacetime."

The replies to Dr. Guy's letter from Colonel Lull and Major Seeley are indicative of the misunderstandings and dissatisfaction that prevailed at this time. Newly inducted medical officers, without previous military experience, failed to understand the tremendous difficulties inherent in the assignment of personnel to the professional activities that would best utilize their previous training and talents. On the military side, it is clearly evident from these letters—entirely unrealistic in the light of later experience— that there was no anticipation of the volume and complexity of the dermatologic problems likely to be encountered in a global war. The lack of understanding before and early in the war led to a gross underestimate of the need for medical officers with special training in dermatology. For these and other reasons, adequate staffing for dermatologic diseases was never achieved. As the war progressed, it became clear that the Army alone

could have used every qualified dermatologist in civilian practice if they had become available.

After the formal declaration of war on 8 December 1941, an increasing number of dermatologists came on active duty and, almost without exception, requested dermatologic assignments. They did not always get them, one reason being, as mentioned several times already, that the table of organization of a general hospital did not provide for a dermatologist, though the table of organization of a station hospital did. The chief reason for the original misassignment of dermatologists, however, was that the Personnel Division, OTSG, had had no previous experience with the need for dermatologists in any type of hospital. Moreover, there was then no dermatologic consultant in the Office of The Surgeon General, no classification existed for medical specialists, and the need for medical officers was urgent without regard to specialty. Dermatologists were in the particularly unenviable position of having a specialty that had no official recognition.

Transfers

Some dermatologists, when they entered service, joined the AGF (Army Ground Forces), in which they did not function except at sick call. Some joined the AAF (Army Air Forces) which, during the first years of the war, did not operate enough hospitals to utilize the special experience of the dermatologists available to it. Since, however, neither of these groups came under the jurisdiction of The Surgeon General, it was impossible to change the assignments of the dermatologists in them. The ASF (Army Service Forces), in May 1945, had the responsibility for staffing some 108 general, regional, and station hospitals in the Zone of Interior, each with a bed capacity of 800 or more, and had available for them only 42 qualified dermatologists. At the same time, the Army Air Forces had 12 regional hospitals, each with the same bed capacity, and had some 28 qualified dermatologists available for them. Evident as was the disparity, it was impossible to effect a single transfer from the Air Forces in spite of the vigorous efforts of General Morgan and the Personnel Division. The only concession offered by the Air Forces personnel was the suggestion that ASF patients with dermatologic conditions be sent to their hospitals, an obviously impossible plan.[9]

There was similar difficulty in transferring dermatologists from one service command to another; the concurrence of all headquarters concerned had to be secured, and that was no simple matter. This lack of flexibility made it almost impossible to adjust changing situations in the dermatologic sections in the various hospitals.

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[9] This situation is an excellent illustration of the forced ineffectiveness of The Surgeon General occasioned by his subordination in the command structure to the Commanding General, Army Service Forces, early in World War II.—A. L. A.

Dermatologic situations were not static. Early in the war, during the training period, the greatest concentration of patients with skin conditions was in station hospitals. Later in the war, when patients with skin diseases were being evacuated from overseas, the concentration was heaviest in general hospitals. It was one of the principal functions of the Consultant in Dermatology, OTSG, once he had been appointed, to recommend assignments of personnel on a preferred basis. Though it was never achieved, the assignment of qualified dermatologists which he recommended in order of preference was to—

1. General hospitals designated as dermatology centers (p. 575).
2. General hospitals designated as neurosyphilis centers.
3. General hospitals designated as medical centers.
4. Regional hospitals.
5. Station hospitals.
6. General hospitals.

If this list had been prepared in 1941 rather than in 1945, high preference would have been given to the station hospitals that provided care for troops in training and on maneuvers, such as the station hospitals in Louisiana and the hospital at Indiantown Gap. A major factor in the change of preference was the large, active campaigns conducted overseas. To anyone who viewed the situation broadly, the changing hospital functions and the changes in the types of patients cared for in general and station hospitals were most impressive and instructive.

Another factor that complicated personnel assignments in dermatology was the necessity of utilizing a certain proportion of available dermatologists for the management of venereal diseases. Dermatologists furnished the principal professional reservoir of officers with training in syphilis and in other nongonorrheal diseases. Almost all neurosyphilis centers in general hospitals were staffed by dermatosyphilologists. It was possible to train general medical officers quite adequately in the management of early syphilis and other acute venereal diseases within a few months, and the plan was generally followed in the European theater, but trained dermatologists had to be kept available to provide the training.

Certification

At the close of the war, the Army Service Forces had 137 medical officers with recognized competence in dermatology. Of these, 107 were certified by the American Board of Dermatology and Syphilology, and the other 30 had demonstrated their competence and had had sufficient formal training to warrant their certification when and if they chose to apply to take the examinations for it.

Another group of 151 medical officers had had only a small amount of formal training but enough previous experience in civilian practice to

justify an MOS rating of C. Many in this group had increased their proficiency and experience in the Army. These officers were usually capable of serving as chiefs of dermatologic services in small hospitals or in hospitals whose primary mission was the care of battle casualties.

Still another group of officers, of considerable size, had had no training in dermatology other than what they had obtained in the Army but had developed an interest in it during their service.

A precise appraisal in the Medical Consultants Division, OTSG, after the war in Europe had ended indicated that at least 275 qualified dermatologists were then needed to carry the dermatologic load in the various installations of the Army Service Forces in the Zone of Interior and overseas.

Despite all the problems of personnel assignment just outlined, it is gratifying to note that on V-E Day, 102 of the 107 medical officers certified in dermatology were in posts offering the opportunity to do professional work in dermatology, syphilology, or both. Furthermore, almost all the officers who were not certified but who had had sufficient formal training and experience to qualify as dermatologists also had relevant assignments. This favorable situation was finally brought about by the efforts of many medical officers in various headquarters with broad interest in providing adequate medical service for all patients. They had been impressed by the increasing evidence throughout the war that dermatologic disease was responsible for much disability and that lost manpower could be greatly curtailed if these patients with skin conditions were treated by qualified specialists early in their illness.

FACILITIES, EQUIPMENT, AND SUPPLIES

When the United States entered the war, in view of the status of dermatology in the Army, it was not surprising that no special provision had been made in most hospitals for dermatology or syphilology wards. When the need for these facilities arose, they had to be improvised, for both clinic and ward patients, from whatever space was available.

Early in the war, a great deal of equipment needed on these wards and clinics was on the critical list because of shortages and priorities, and treatment of patients was sometimes adversely affected. Even such items as tubs, basins, hotplates, bandages, dressings, instruments, and ordinary drugs could not be procured at all or were in continuously short supply. Vitamin B and zinc oxide, both badly needed, could be procured only in small amounts.

The medical supply officer at each station received from the medical depot certain items regularly used in dermatologic practice, such as ingredients for lotions, baths, ointments, and pastes (particularly zinc oxide) ; that is, starch, benzoic acid, salicylic acid, phenol, boric acid, potassium per-

manganate, sodium chloride, coal tar, ammoniated mercury, sulfur, alcohol, lanolin, and petrolatum. Local medical officers, depending upon their special needs and their own experience in dermatology, used these items as best they could, making up for shortages with substitutes among available pharmaceutical stocks. The usual situation developed: Each dermatologist desired the items he had been accustomed to use in private practice. The supply policy was somewhat flexible, and in late 1942, Col. Charles F. Shook, MC, then Assistant Chief, Finance and Supply Service, OTSG, recommended that dermatologists in the Zone of Interior be permitted to use local funds for pharmaceuticals they particularly desired, especially when only small quantities were needed. One reason for this recommendation was to avoid further changes in the master supply catalog, which by this time had been completed.

During the last year of the war, only a few dermatologic categories were in short supply, such as benzyl benzoate for scabies, tragacanth as an emulsifying agent, sulfurated potassium for lotio alba, and olive oil for lotions. In the summer of 1945, the Consultant in Dermatology, OTSG, recommended the addition of accepted dermatologic items to the standard supply tables. When the war ended in August of that year, most shortages had been overcome.

ARMY AIR FORCES

Administrative Considerations

In spite of the number of dermatologists on duty in the Army Air Forces (p. 560), no special professional attention was paid to dermatologic diseases in this service until August 1944. Then, in accordance with recommendations made to the Air Surgeon several weeks earlier, a dermatology branch was created in the Professional Division of his office, and Lt. Col. Jud R. Scholtz, MC, was appointed to direct it.[10]

In the recommendations made to the Air Surgeon in June 1944, it was pointed out that dermatologic diseases were an important cause of morbidity in military personnel. Separate statistics were not available for the Army Air Forces, but it was noted that collective figures for the Army in the continental United States revealed that time lost from duty from this cause each year approximated 3 million man-days, with an average loss of 11 days per patient. It was estimated that about 20 percent of all diseases in the Army required dermatologic management, and it was emphasized that hospital admissions did not give a true picture of the situation, since half or more of all cutaneous conditions did not require hospitalization.

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[10] The material for this section on the Army Air Forces was supplied by Dr. Jud R. Scholtz who, as Lieutenant Colonel, served as Chief of the Dermatology Branch, Office of the Air Surgeon, when the dermatology program was set up in that office.

It was therefore considered desirable to institute a dermatology program in the Army Air Forces; to establish dermatologic services in the regional hospitals of the service; to develop a consultation system in dermatology for station hospitals; to utilize to the maximum specialist personnel in the Army Air Forces; to set up a consultative and preventive program for civilian employees of the ATSC (Air Technical Service Command) ; and to develop a teaching program in dermatology for residents and general service medical officers.

Personnel.—When these recommendations were made in June 1944, there were in the Army Air Forces in the United States 31 medical officers classified as dermatologists; of these, 17 were board certified, and many of the others were well qualified, by training and experience, to be considered specialists. When the Dermatology Branch was created in the Office of the Air Surgeon in August 1944, 22 medical officers, 16 of whom were certified by the American Board of Dermatology and Syphilology, were available for assignment. Some of them were already working on dermatologic services in AAF hospitals. By March 1945, dermatologists had been assigned to 26 regional hospitals, and an additional 6 medical officers had been certified by the board.

Establishment of program.—The recommendations made in June 1944 were generally put into effect when the Dermatology Branch was established in the Office of the Air Surgeon in August 1944 in the following steps:

1. Regional AAF hospitals were staffed with qualified dermatologic personnel in relation to the availability of such personnel, the geographic location and bed capacity of the hospitals, and the prevalence of skin diseases in each area.

2. An official letter was issued announcing the creation of a dermatologic consultant service and listing the stations at which dermatologists would be available for consultation. Recommendations were also made concerning the area hospitals to be served by regional consultants; the routine treatment of common skin diseases; and the disposition of special categories of patients with skin conditions.

3. Consultant functions included initial visits to area hospitals to determine the scope and nature of the dermatologic problem; investigation of patients currently under treatment, to determine whether they should be transferred to the dermatologic service; the establishment of a basic routine of treatment; and the identification of qualified dermatologists who had not yet been classified as such.

4. After the initial visit to each hospital just described, provision was made for consultation service to area hospitals by telephone or by personal visits as indicated. It was part of the consultant function to recommend the transfer of patients from area to regional hospitals.

5. The dermatologic needs of the Air Technical Service Command in relation to its civilian employees were investigated and implemented.

6. Information was disseminated concerning treatment practices in both dermatology and venereal diseases.

7. An attempt was made to accumulate and analyze data on morbidity due to dermatologic diseases, the sick call load, and time lost from duty by hospitalization. An attempt was also made to institute clinical studies in skin diseases of particular significance in AAF personnel by virtue of type of duty or geographic location.

8. After the program was in full operation, return visits were made to AAF medical installations to evaluate the quality of dermatologic service in them.

Regional hospitals.—Each dermatologist assigned to a regional hospital developed a separate dermatologic service in it. A ward was set aside for the hospitalization of patients with severe, disabling dermatoses and for the definitive treatment of patients referred from satellite hospitals at which specialized medical care was not available. Clinics for outpatients who could be treated on an ambulatory basis were conducted several times a week, the number of clinics depending upon the caseload.

In his capacity as regional consultant, the dermatologist at each regional hospital visited each satellite station hospital once a month, to handle special problems and to evaluate the quality of dermatologic service provided.

Duty-assignment training.—In October 1944, a duty-assignment training program was set up in each major AAF command, intended to indoctrinate medical officers without training or experience in dermatology in the management and treatment of the common skin diseases encountered in military service. Each trainee was assigned for a 3-month period to a board-certified dermatologist who had been associated with a teaching institution in civilian life. The trainee assisted in the management of ward and clinic patients and, when it was practical, visited adjacent civilian teaching institutions.

The medical officers trained in this manner were assigned to station hospitals and proved of great assistance to the consultants in dermatology. It should be emphasized that the training program was set up only because of the shortages of qualified dermatologists in the Army Air Forces and the need for larger numbers of medical officers who could treat common skin diseases in installations to which no dermatologists were assigned. There was no idea that the training provided would qualify the trainees as dermatologists; in fact, it was specifically directed that officers thus trained would not be classified as dermatologists.

Manual.—The survey of dermatologic practices and patients in AAF hospitals and clinics undertaken when the new program was put into effect in August 1944 revealed that perhaps half of all admissions to the dermatology wards were the result of improper early treatment and overtreatment. It was also found that about 90 percent of all skin disorders encountered in the Army Air Forces were included in a small number of diagnoses. Similarly, large numbers of patients seen in outpatient clinics also presented conditions overtreated and aggravated by improper and irritating sensitizing therapy.

To remedy this situation, a manual was prepared particularly for AAF medical officers who had had no special training in dermatology. This manual, "Management of Common Cutaneous Diseases" (AAF Manual 25–1), which was the composite effort of several dermatologic officers, was dis-

tributed to all AAF installations in the continental United States for use
in dispensaries and station hospitals. The manual was not a directive and
did not restrict the exercise of clinical judgment by individual medical
officers.

The initial distribution of this manual was 1 copy each to stations
with strengths of 500 and under; 2 copies each to those with strengths
between 500 and 1,000; 3 copies each to those with strengths between 1,000
and 5,000; 5 copies each to those with strengths between 5,000 and 10,000;
and 9 copies each to those with strengths over 10,000.

Requests were subsequently received from several AAF commands for
individual copies of this manual for all medical officers within the com-
mands. Some 2,000 copies were distributed as the result of these requests,
including 800 copies to the Army Air Forces in the Mediterranean theater.
The manual was also reproduced in toto and used as a circular letter by the
Tenth Air Force in the China-Burma-India theater.

Categories of Disease

In the recommendations made to the Air Surgeon in June 1944 on
the establishment of a dermatologic program in the Army Air Forces, it
was pointed out that skin diseases in the age group in this service fell into
three categories:

1. Approximately 90 percent of all cutaneous morbidity were accounted
for by a group of conditions which were not in themselves disabling and
most of which, if properly treated initially, did not require hospitalization.
In this group were pyodermatoses, superficial fungal infections, parasitic
diseases, disturbances caused by excessive perspiration, and contact derma-
titis, including plant dermatitis.

2. Major dermatoses, which caused serious disability and required pro-
longed hospitalization, included erythema multiforme, drug reactions, gen-
eralized eczema, exfoliative dermatitis, dermatoses caused by photosensitiza-
tion, chronic granulomas, and lupus erythematosus.

3. Emergency situations were so uncommon in dermatologic practice
that they required no consideration in the routine of dermatologic care and
could be handled, usually by telephone consultation, when they arose.

Occupational dermatoses.—The Air Technical Service Command had
among its other duties the responsibility for maintenance and repair of
aircraft. For this purpose, it operated a number of large depots in the
United States, where several hundred thousand civilians were employed,
35 percent of whom, it was estimated, were exposed to occupational hazards
and chemical agents that could cause dermatitis. The annual report of this
command for 1943 revealed that the time lost from work for occupational
reasons was almost entirely the result of occupational dermatitis. This was
clearly an important condition, not only because of the time lost from work

but also because the treatment of occupational disease in civilian employees was an Air Forces responsibility. The depots at which it occurred were served by medical officers trained in industrial medicine, but with few exceptions, they were not trained in dermatology and experienced dermatologists were not available for consultation.

Another problem of considerable magnitude because of the large number of employees involved in these AAF projects was the cutaneous complications of sulfonamide prophylaxis, which was widely used for protection against bacterial disease. Reactions to this technique were fairly frequent, and cutaneous reactions were the most common of all. Qualified medical personnel had to be available to classify and treat these dermatoses and to advise, on an individual basis, concerning the propriety of continuing the medication.

As the result of these observations, a consultation service was set up by which AAF dermatologists in the general area of ATSC depots made regular visits to them, to assist in the diagnosis, classification, and management of skin diseases in civilian employees engaged in the care and repair of aircraft. This arrangement resulted almost immediately in more accurate classification of occupational dermatitis and in shorter periods of disability. It also laid the groundwork for the collection of valuable information concerning the cutaneous occupational hazards encountered in the maintenance and repair of aircraft.

In January 1945, a conference on occupational dermatoses was held in the Office of the Air Surgeon, the participants including Lt. Col. George Sladczyk, MC, Chief of the Industrial Medicine Branch, Headquarters, ATSC; Maj. (later Lt. Col.) Frank J. Lacksen, MC, Chief, Dermatology Section, Mitchel Field AAF Regional Station Hospital; Maj. (later Lt. Col.) Shepard Quinby, MC, dermatologic officer, Headquarters, Personnel Distribution Command; and Colonel Scholtz.

The agenda for this conference covered the following items:

1. The dermatologic consultation service in the Office of the Air Surgeon.

2. The scope of the problem of occupational dermatoses as indicated in reports available to Headquarters, Air Technical Service Command.

3. The desirability of preparing a manual on the prevention and management of occupational dermatoses for use by medical officers and contract physicians engaged in the industrial hygiene program.

4. The need for standardization of hand cleansers.

5. The need for increasing the number of medicaments available for treatment.

6. The need for further investigation of causes of dermatitis in ATSC depots and the development of engineering techniques for their elimination.

The conferees reached the following decisions:

1. The consultation service provided in the dermatologic program was by far the most important and most essential phase of the program. Headquarters, ATSC, agreed to institute a survey to evaluate its adequacy as it was presently operated.

2. Headquarters, ATSC, also agreed to make an additional effort to determine the

extent and nature of the problem of industrial dermatoses by compilation of reports to be secured from consultant dermatologists.

3. Any one of several hand cleansers was considered acceptable, and none of them could be regarded per se as the cause of dermatitis. Recommendations for standardization of these agents was not considered advisable.

Pressures engendered by the final campaigns of the war explained why these plans were not carried through to definitive conclusions.

DISTRIBUTION AND ADMINISTRATIVE MANAGEMENT OF SKIN DISEASES IN ZONE OF INTERIOR

Induction Centers

As might have been expected, diseases of the skin encountered in inductees occurred in about the same proportions and were of about the same character as in civilian practice. Some men who wished to avoid military service overemphasized their dermatoses. Others who wished to serve tried to underemphasize them and gave incomplete or misleading histories of past skin troubles.

There were few established policies for the acceptance or rejection of men with these diseases. Many physicians on examining boards, at least early in the war, tended to recommend for induction candidates with a variety of skin diseases, on the ground that a trial of military life was justifiable. As time passed, it became evident that a decidedly less liberal policy would have been wiser and would have eliminated a heavy burden on Army dispensary and hospital facilities. Experience showed that soldiers with extensive psoriasis, significant atopic dermatitis and related allergic diseases, extensive seborrheic dermatitis, severe acne involving the face and upper trunk, and chronic eczematous eruptions of the hands and feet were seldom able to do full duty. These men constituted problems in the Zone of Interior and constituted more difficult problems when they were sent overseas, especially to tropical areas. The burden on outpatient dispensaries and the long periods of hospitalization that many of them required far outweighed the military effort contributed by the small numbers able to do general or limited duty.

The literature before the United States entered World War II contained numerous studies of the incidence and age distribution of diseases of the skin but none of them dealt with diseases in the age group (18 to 45 years) encountered at induction stations. Lt. (later Maj.) Eugene S. Bereston, MC, and Lt. (later Capt.) Edward M. Ceccolini, MC, remedied the deficiency in 1943 by a study of the incidence of dermatoses in 20,000 men who passed through the U.S. Army Recruiting and Induction Station at Tacoma, Wash., in both the enlistment and selective service systems.[11]

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[11] Bereston, E. S., and Ceccolini, E. M.: Incidence of Dermatoses in 20,000 Army Induction Examinations, With Note on Syphilis With Negative Serologic Reactions. Arch. Dermat. & Syph. 47: 844–848, June 1943.

All the men were examined stripped, with at least ordinary care, but not by physicians with any special dermatologic training. One of the points made in the report of the investigation, in fact, is that a consultation dermatologic service that could have been called upon as needed would have been extremely helpful.

In these 20,000 candidates for induction into the Army, 733 (3.67 percent of the total number) were found to have diseases of the skin,[12] but of these, only 44 (6.00 percent of those with skin diseases and 0.22 percent of the total number of candidates) were rejected for diseases of the skin as compared with 4,650 (23.25 percent) of the total number rejected for all causes. Some candidates with skin diseases were, of course, rejected for other causes.

The 733 men with skin diseases presented 77 different clinical entities, the most common of which (except for dermatophytosis of the feet and small pigmented and nonpigmented nevi) are shown in table 101. Generalized psoriasis was the chief cause for rejection in the group of skin diseases, with disseminated neurodermatitis second and neurofibromatosis third. Other causes of rejection, in addition to those tabulated and discussed in footnote 11, were parapsoriasis (2 of 5 cases) ; epithelioma of the lip (4 of 4 cases) ; latent syphilis (3 of 3 cases) ; squamous cell epithelioma of the eyelid (1 case) ; epithelioma of the penis (1·case) ; generalized combined vascular and pigmented nevus (1 case) ; sarcoma (1 case) ; and epidermolysis bullosa (1 case).

Dispensaries

Most soldiers with dermatologic complaints were first seen at sick call. They were usually treated in company or training camp dispensaries that were staffed by one or more medical officers without any training in dermatology and with only limited facilities for treatment.

There was considerable variation in policy regarding the duration of dispensary treatment. In some camps, the patients were treated daily, often for several weeks, until they were cured (at least relatively) or were incapacitated from overtreatment. In others, patients with even simple and uncomplicated dermatoses, such as mild dermatophytosis, were promptly referred to the outpatient departments of station or regional hospitals. Their management depended to some degree on whether medical officers qualified in dermatology were on the staffs of the station or regional hospitals to which they would be sent. As in civilian practice, some medical officers without special training in it were interested in dermatology and some were not.

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[12] Included in this number are nine cases of central nervous system syphilis, one of which was an instance of dementia paralytica. These cases deserve special comment. All occurred in selectees who, before coming to this station, had had negative complement fixation or precipitation reaction tests reported by their local draft boards. It is not unusual, in central nervous system syphilis, to encounter positive clinical findings with negative serologic reactions.

TABLE 101.—*Rejections for skin diseases in 20,000 candidates for induction at U.S. Army Recruiting and Induction Station, Tacoma, Wash.*

Diseases in order of frequency	Number of cases	Number of rejections
Acne vulgaris	248	0
Psoriasis	55	11
Pyoderma	35	0
Tinea	27	0
Varicose eczema	20	0
Neurodermatitis disseminata	20	3
Lipoma	18	0
Sebaceous cyst	18	0
Seborrheic dermatitis	17	1
Naevus flammeus	17	1
Neurodermatitis, localized	15	0
Neurofibromatosis	14	2
Rosacea	14	0
Contact dermatitis	12	0
Giant pigmented nevus	12	0
Scabies	11	0
Pilonidal sinus	11	3
Vitiligo	10	0
Ichthyosis	9	0

Source: Bereston, E. S., and Ceccolini, E. M.: Incidence of Dermatoses in 20,000 Army Induction Examinations, With Note on Syphilis With Negative Serologic Reactions. Arch. Dermat. & Syph. 47: 844–848, June 1943.

It soon became evident, however, that most medical officers had no familiarity with even the most common forms of dermatitis. Overtreatment of minor dermatologic diseases at the dispensary level, particularly overtreatment of scabies, inflammatory eruptions of the feet, insect bites, and contact dermatitis, was therefore distressingly frequent and frequently produced major disabilities. The situation was not helped by the self-treatment practiced by the soldiers themselves. It should also be noted that if there was no qualified dermatologist at the station hospital to which the patient was referred, his referral to it did not insure him care superior to that he was receiving at the camp dispensary.

An analysis of the referral slips accompanying the patients sent to one station hospital, considered typical, showed that most dispensary medical officers were inclined to diagnose all eruptions of the hands and feet as fungal. Others made conscientious efforts to single out patients who could be treated in the camp dispensary on an ambulatory basis and referred others selectively to the dermatologic clinic of adjacent station hospitals. Frequently, an informal liaison was established between the dermatologist at the hospital, if there was one on the staff, and medical officers in the field, to the benefit of all concerned.

Station Hospitals

Although during the training period station hospitals were the most important units from the standpoint of dermatologic care, almost no provisions for it were originally made in them. Dermatologic care was entirely inadequate when it was most needed. As already mentioned, about 20 percent of all dermatologists who came into service expressed a preference for the Army Air Forces, and the majority of the remainder were assigned to general hospitals in the Zone of Interior or to units going overseas. Only a small number were left for duty in station hospitals, in most of which a medical officer became a dermatologist simply by order of the commanding officer.

From November 1940 to the middle of 1943, station hospitals supporting the various training camps in the Zone of Interior were much more important in meeting the problem of dermatologic disability than were general hospitals. Yet in late 1942, not a single qualified dermatologist was on the staffs of the hospitals caring for the large numbers of troops in training in Louisiana, and this situation was not unusual.

An occasional patient with severe, intractable, or obscure cutaneous disease was sent from the camp dispensary to a general hospital or, later in the war, to a regional hospital, but most patients with skin diseases were sent to station hospitals from dispensaries. The number referred to general hospitals from station hospitals was in inverse ratio to the skill and experience of the medical officers handling dermatologic conditions in the station hospitals. By this time, personnel in the Office of The Surgeon General, as well as surgeons of the service commands, fully recognized the importance of dermatologic care at station hospitals and tried to staff them accordingly, but their efforts, as already indicated, were seldom effective (p. 560).

One of the major responsibilities of station hospitals was the physical reclassification of inductees. Their staffs had the authority to recommend a man's change of status from full combat duty to limited service, as well as to recommend his discharge from service. After his induction, a soldier with a dermatosis first came to the attention of the medical officer in his unit either through his own professed inability to perform his duties or through detection of this inability by his superiors. When, usually after some treatment at the company dispensary, he was referred to a station hospital, he was either observed and treated tentatively on an ambulatory basis or was hospitalized at once for investigation. If it was determined, after careful examination, that his dermatologic condition warranted a change of status, he was recommended to the hospital disposition board, by the officers who had examined him, for reclassification for limited duty or for discharge from the Army. The procedure described was eventually streamlined, at least in comparison to the earlier routine, but it was always long, costly, and cumbersome, and as already pointed out, much time and

effort would have been saved if men with certain skin conditions had been rejected when they appeared at the induction station.

There were several reasons why it was difficult to determine whether a man with skin disease was able to perform full duty or limited duty or should be discharged from service. One was that if he wished to escape full combat duty or to be separated from service, he could achieve his desire simply by aggravating his objective findings by vigorous scratching or by the application of irritating local agents.

It became clear early in the training period that medical practice in the treatment of soldiers with skin diseases on a duty status was quite different in an army in active training and a peacetime army. A soldier with partly disabling dermatitis in a combat unit had to be fit for full duty or classified as not fit for duty at all. Early hospitalization was necessary for soldiers with dermatoses that were disabling, contagious, or so extensive as to make dispensary and self-treatment impractical. Once the situation was recognized, admissions for dermatologic disease constituted an increasing proportion (from 6 to 12 percent) of all admissions to station hospitals, depending upon the time of year and the part of the country in which the hospitals were located. Annual reports [13] from various station hospitals bear out these remarks. Many of them were located in areas in which climatic conditions were ideal for the development of a high incidence of disabling dermatoses.

Camp Polk, La.—Maneuvers were conducted in Louisiana during August and September 1941 for a total of 53 days. During this period, 4,391 patients were admitted to the station hospital at Camp Polk, which had a bed capacity of 600 and an expansion capacity of 804 beds. Gastroenteritis came first in the 10 leading causes of admission, but cutaneous diseases of various types came next, including dermatitis of various origins, dermatophytoses, pyogenic infections, insect bites with complications, eczematous dermatitides, scabies, pediculosis, and contact dermatitis of various types, including that caused by poison ivy. The dermatologic clinic set up to handle these patients registered 1,030 new patients in 1942 and 1,040 in 1943, when there were 31,553 hospital admissions. In the 1943 report, it was noted that delays of 4 to 8 weeks occurred before [dermatologic] patients could be transferred to general hospitals.

Camp Livingston, La.—At Camp Livingston, La., in 1942, 788 patients were hospitalized on the dermatologic section that had been set up in the station hospital, and 1,629 were hospitalized in 1943. The 858 hospitalized in 1944 constituted 9 percent of the total admissions. In 1943, 6,137 dermatologic patients were seen in consultation, and in 1944, there were 9,547 visits to the outpatient clinic. Many uncommon dermatoses were observed, including systemic lupus erythematosus, leprosy, hidradenitis suppurative,

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[13] When it is evident from the text that an annual report is the source for the material presented, no footnote reference is furnished for such source.

Fox-Fordyce disease, creeping eruption, epidermolysis bullosa, scleroderma, and prurigo nodularis. This was a burden far too heavy to be carried by a medical officer without special qualifications in dermatology.

Camp Shelby, Miss.—The station hospital at Camp Shelby, Miss., treated patients with skin diseases on a separate ward in the medical section in 1941 but did not establish a dermatology section until 1942. During the latter year, 453 patients were seen in the outpatient dermatology clinic. In 1943, 1,126 were seen in this clinic, about 19.7 percent of the total number of outpatients (5,699), and a figure second only to the neuropsychiatric visits.

Fort Bragg, N.C.—The station hospital at Fort Bragg, N.C., had 3,438 beds, which could be expanded to 4,469, and had other facilities for the care of about 75,000 troops in training. Diseases of the skin were first cared for entirely in the camp dispensary, but in 1942, three wards were established for the care of patients with these conditions, and a special clinic organization was also established. In 1943, a total of 1,721 patients were admitted to the dermatologic wards, 4,801 were seen in consultation, and 5,370 were treated in the outpatient clinic. This hospital had facilities for superficial X-ray therapy, and 851 treatments were given in 1942. A qualified dermatologist was assigned to the staff early in the training period, but most of his time had to be devoted to the diagnosis and treatment of syphilis and other venereal diseases.

Regional Hospitals

After regional hospitals were organized in the Zone of Interior, in the middle of 1944, an effort was made to assign qualified dermatologists to them, with priorities second only to certain named general hospitals and units going overseas. Excellent dermatologic services were eventually established in most of them.

The experience of the regional hospital at Camp Lee, Va., may be cited as typical. During 1945, when the average camp census was about 25,000 men, 2,884 dermatologic patients were seen, an average of about 9 new patients per day. The distribution of diseases appears in table 102. The unusually high incidence of scabies is explained by the fact that many of the patients had returned from Europe, where this condition was extremely frequent (p. 631). Before 1945, the incidence of scabies in station and regional hospitals was not more than 1 or 2 percent.

Staging Areas

Dermatologic conditions in station hospitals in staging areas presented rather special problems. The experience at Camp Kilmer, N.J., was typical:

Between its opening in June 1942 and 1 September 1945, this hospital admitted 52,788 patients, 38,209 to the medical service, and 2,968, about

TABLE 102.—*Proportionate distribution of skin diseases in Dermatology Clinic, ASF Regional Hospital, Camp Lee, Va., 1945*

Diseases	Number of cases	Percent
Scabies	283	9.3
Contact dermatitis	251	8.3
Dermatophytosis of hands and feet	213	7.3
Folliculitis of face, arms, and legs	163	5.4
Acne vulgaris	160	4.9
Eczematoid dermatitis	147	4.9
Tinea cruris	133	4.4
Verruca vulgaris	127	4.2
Seborrheic dermatitis	108	3.6
Pruritus ani	94	3.1
Psoriasis	90	3.0
Condyloma acuminatum	83	2.7
Miliaria rubra	79	2.6
Furunculosis	76	2.5
Impetigo	75	2.5
Tinea corporis	73	2.4
Tinea versicolor	70	2.4
Urticaria and angioneurotic edema	66	2.2
Verruca plantaris	61	2.0
Pityriasis rosea	59	1.9
Hyperhidrosis and bromidrosis of feet	56	1.8
Ecthyma	33	1.1
Neurodermatitis	28	.9
Ichthyosis	27	.9
Lichen simplex chronicus	25	.8
Herpes simplex	25	.8
Alopecia areata	22	.7
Onychomycosis	21	.7
Acne rosacea	20	.7
Erythema multiforme	18	.6
Sebaceous cysts on neck, ears, and back	18	.6
Herpes zoster	16	.5
Dermatitis papillaris capillitii	15	.5
Sycosis barbae	15	.5
Erythrasma	14	.5
Lichen planus	14	.5
Keratosis palmaris et plantaris	12	.4
Vesicular dermatitis of fingers and hands	12	.4
Herpes progenitalis	10	.3
Vitiligo	9	.3
Spider nevus	8	.3
Lupus erythematosus	8	.3
Dermatitis herpetiformis	7	.2
Dermatitis medicamentosa	6	.2
Basal cell epithelioma	4	.1
Keratosis pilaris	4	.1
Seborrheic eczema	3	.1
Cutis hyperelastica	3	.1
Hydroa aestivale	3	.1

6 percent of the total admissions, to the dermatology wards. In addition, 7,183 patients were observed in the dermatology outpatient clinic.

Every soldier who arrived at this camp was immediately examined by a medical officer and was reexamined 48 hours before he was scheduled for departure. The second inspection sometimes disclosed dermatoses that had originally been mild but that had recently become aggravated to such a degree that the soldier had to request treatment just as his unit was preparing to go overseas. At this point, the medical officer had to make an important and often difficult decision: It was his responsibility to send men forward with their units, but it was also his responsibility to hold back men who could not perform full duty. This was a decision that required wide experience and sound judgment and that involved more than strictly medical considerations. The individual's importance to his unit also had to be taken into account; it was much more difficult, for instance, to replace a trained technical sergeant than a private. It is worth noting that the majority of men in this group did not attempt to remain behind; most of them, even when their dermatoses were relatively severe, pleaded to be allowed to proceed with their units.

General Hospitals

The function of named general hospitals in the Zone of Interior was to provide definitive care for all types of patients. For this reason, patients with difficult diagnostic and therapeutic dermatologic problems were referred to them. Later in the war, when patients began to be evacuated from oversea theaters and were sent directly to general hospitals, Zone of Interior patients with special problems were sent to regional hospitals, leaving the bed space in general hospitals for patients from overseas.

In 1941, when Reserve officers who were qualified dermatologists began to come into service, general hospitals were given a high priority in their assignment, and the majority of these hospitals had excellent dermatology and syphilology sections during most of the war. In many instances, the dermatologist first assigned to a particular hospital remained in it until the end of the war; commanding officers were understandably reluctant to release qualified specialists for whom there were no suitable replacements.

In 1945, Moore General Hospital, Swannanoa, N.C., and Harmon General Hospital, Longview, Tex., were designated as tropical disease centers. Both had large, well-staffed dermatology sections, and it was planned that these general hospitals, as well as six others, should be designated as dermatology centers and that the best qualified dermatologists available should be assigned to them. The war ended before these plans could be implemented.

The dermatologic experiences of several general hosiptals in the Zone of Interior are worth relating in some detail.

LaGarde General Hospital.—The first dermatology section on the medical service of a general hospital in the Zone of Interior was set up in the summer of 1941 at LaGarde General Hospital, New Orleans, La., with Capt. (later Maj.) Robert Stolar, MC, as chief of the section. Captain Stolar remained in this assignment throughout the war. As in other hospitals, dermatology had originally been part of the urology service, but the chiefs of the medical and surgical services decided, wisely and promptly, that this was a totally illogical arrangement, and as just noted, a separate dermatology section was established without delay.

LaGarde General Hospital was located in a city that was a seaport as well as an important rail center. Many training areas were in Louisiana and other adjacent States, and during the training period and later, this hospital received large numbers of patients who required specialized dermatologic care. During the same period, it also received patients from the Caribbean Command and the Panama Canal Zone, and it therefore had a larger dermatologic section during the last half of 1941 and all of 1942 than other general hospitals. The annual report for 1942 records 10,800 visits to the dermatology outpatient clinic, and the 1943 report shows an average of 1,075 visits per month to this clinic.

By 1944, the routine of diagnosis and treatment was well established at this hospital, and the report for this year emphasizes several points:

1. All dermatologic conditions, as well as all primary and secondary syphilis, were treated on the dermatology and syphilology section. Darkfield apparatus was obtained for use on these wards, and examinations were made on them rather than in the laboratory. Patients with tertiary syphilis were admitted to other sections, depending upon the particular system involved.

2. Early in the year, a number of patients with neurosyphilis were treated with fever (malaria) therapy. This modality was discontinued with the establishment of neurosyphilis centers. The therapy of syphilis underwent a notable change with the introduction of penicillin.

3. The variety of skin diseases encountered was challenging and instructive. Biopsy was frequently necessary for diagnosis, and many pathologic examinations were made.

4. The number of fungal infections conformed to the general impression that cutaneous conditions of this origin were less frequent than had generally been supposed.

5. The incidence of psychosomatic manifestations in the form of skin disease was impressive.

6. Cold quartz ultraviolet light therapy, as well as other forms of therapy, produced good results, and most patients were returned to duty.

Brooke General Hospital.—At Brooke General Hospital, Fort Sam Houston, Tex., the dermatology section of the medical service in 1943 consisted of an 84-bed ward and an outpatient clinic, in which soldiers and their

civilian dependents were seen daily. As many dermatoses as possible were treated on an outpatient basis. The admission rate to the hospital varied with the season of the year but averaged 110 per month. During the spring and summer, when field units were maneuvering in the vicinity, the admission rate was high. Most admissions were for fungal infections, pyodermas, and contact dermatoses, chiefly caused by poison ivy *(Rhus toxicodendron)*.

In addition to standard equipment, the dermatology section had three large tubs available, in a separate room, for medicated baths. The equipment of the clinical laboratory, on the floor below, was used for fungal cultures and other diagnostic procedures. The radiology and physical therapy sections cooperated closely with the dermatology section. All X-ray therapy was administered by the radiology department, but the indications for it and the dosage were the province of the dermatologist.

Walter Reed General Hospital.—In 1943, patients with skin conditions were hospitalized at Walter Reed General Hospital, on the communicable disease section, under the supervision of Maj. (later Lt. Col.) Zeno N. Korth, MC, who also conducted the dermatology clinic. This clinic operated 4 mornings a week and had 3,341 new patients during the year. X-ray therapy was administered by the radiology department. In 1943, 2,550 patients received 5,025 treatments.

Foster General Hospital.—When Foster General Hospital, Jackson, Miss., began to receive patients in September 1943, a dermatology section was part of its original table of organization. The workload was always heavy. In 1944, 1,508 patients were hospitalized on this section, and 1,125 others were seen in consultation from surrounding posts and station hospitals. Microscopic studies and cultures for fungi were carried out, and biopsies and other standard diagnostic procedures were performed as indicated. The most frequent dermatologic conditions encountered were trichophytosis and acne vulgaris. The disease of greatest interest in 1944 was so-called New Guinea dermatitis, a then obscure and puzzling type of dermatitis apparently endemic in this part of the Pacific Ocean Areas and later diagnosed as atypical lichen planus (p. 638).

The chief of the dermatology section gave numerous demonstrations in the hospital and also provided instruction in dermatologic diseases here and elsewhere.

Harmon General Hospital.—Harmon General Hospital did not become operational until December 1942, and dermatology is not mentioned in its annual report for that year. In 1943, the report states that there were 400 admissions, with 366 dispositions, to its 66-bed dermatology section. Visits to the dermatology outpatient clinic averaged 100 per month. By 1944, the dermatology section had expanded to 8 wards, and there were 1,142 admissions with 908 dispositions. The highest daily census was 315. The 2 medical officers assigned to the section also saw 822 patients in consultation

on other services and supervised the X-ray treatments (422) of 182 patients. Many patients with resistant chronic dermatoses showed great improvement after superficial X-ray therapy.

In March 1945, Harmon General Hospital was designated a tropical disease center, with dermatology a subdivision. The report covering the period from 1 January to 1 November of that year showed 1,053 admissions to the dermatology section, with an average daily census in September of more than 500 patients. By this time, many patients were being received who did not need intensive dermatologic care; their original condition had improved with the elimination of the etiologic factors and predisposing causes of the diseases after the end of the war in the Pacific and their evacuation to the Zone of Interior. Their disposition, usually by furlough to convalescent hospitals, was rapidly accomplished.

Among the wide range of dermatoses seen at Harmon General Hospital were bacterial infections; cutaneous ulcers, some with *Corynebacterium diphtheriae* as the etiologic factor (p. 607) ; and the variety of dermatitis later traced to the use of Atabrine (p. 646).

The variety of dermatoses observed at this hospital and the concentration of patients there provided, theoretically, opportunities for close and prolonged study and created a field for many investigations. There were several reasons why the opportunities were not utilized. One was the small number of dermatologists on the section, whose professional duties kept them fully occupied. Another was the constantly high census, which generated an urgency for the rapid turnover of patients, to provide bed space for others. Still another was the pressure created by the end of the war, which required rapid demobilization of patients with the imminent closing of the hospital. It is unfortunate that a planned, well-controlled series of studies was not possible; such an investigation could have opened up avenues of further research that would have resulted in important advances in military dermatology.

Lovell General Hospital.—Little dermatology was done at Lovell General Hospital, Fort Devens, Mass., during 1941. During 1942, the section had 123 admissions for both skin diseases and syphilis. The skin conditions more frequently encountered were eczematoid dermatitis, dermatophytosis, disseminated neurodermatitis, and seborrheic eczema. In most instances, these conditions were difficult to handle because they were chronic and had been treated—and often overtreated—for many months in dispensaries and station hospitals.

In 1944, Lovell General Hospital became a 4,000-bed hospital, with an allotment of 500 beds for the dermatology section. It was one of the hospitals that was designated, the following year, as a dermatology center but did not become operational because of the end of the war.

During 1945, of the 22,923 admissions to the hospitals, 2,068 were to the dermatology section, and from 10 to 15 new patients were seen daily in

the outpatient clinic. This was another section that was constantly under pressure because of the heavy influx of patients. It was imperative to handle these incoming patients as promptly as possible, to clear the beds for other patients. The annual report for 1945 mentions with regret that, chiefly because of these pressures and because of understaffing, the wealth of dermatologic materials available could not be handled as scientifically as it should have been.

Fitzsimons General Hospital.—Between June 1943 and late in 1945, most of the patients on the dermatology service at Fitzsimons General Hospital, Denver, Colo., were evacuated directly to it from various oversea hospitals because of incapacitating disease. Between 1 July 1944 and 1 July 1945, there were 969 admissions to the dermatologic section and 5,652 consultations. The peak dermatologic load occurred in January and February 1945, when the ward census reached 154 and the average monthly admissions were 120.

The survey of the various diseases observed in this hospital made at the end of the war by Lt. Col. Arthur R. Woodburne, MC, Chief of the Dermatology Section, is discussed under appropriate sections elsewhere. Many of the patients flown directly to the hospital from overseas, especially from the Southwest Pacific Area and the China-Burma-India theater, could be held long enough for careful observation and definitive treatment. An interesting feature of this survey concerned the skin diseases common in civilian dermatologic practice but altered by military conditions.

DISTRIBUTION AND ADMINISTRATIVE MANAGEMENT OF SKIN DISEASES IN OVERSEA COMMANDS

Mediterranean Theater of Operations

With the notable exception of plant dermatitis, the major dermatologic problems in the North African (later Mediterranean) theater paralleled those encountered in troops under similar conditions of deployment in the Zone of Interior. In order of prevalence, they included bacterial infections; fungal infections; dermatitis of unknown etiology, including psoriasis, lichen planus, erythema multiforme, and the eczemas; dermatitis of known etiology, including dermatitis venenata, dermatitis medicamentosa, and infectious eczematoid dermatitis; and parasitic infections. The majority of these were bacterial infections, in which penicillin proved a valuable agent, fungal infections, and parasitic infections. A considerable number of cases of cutaneous diphtheria were observed in North Africa. Details of special diseases are commented on under appropriate headings.

Not very many trained troops were lost to duty in the Mediterranean theater because of skin diseases. A survey of 3,030 patients hospitalized for

these conditions in 4 general hospitals showed that 95.75 percent were returned to full duty after treatment.

European Theater of Operations

In the European theater, the proportion of admissions to hospitals for dermatologic conditions was at first similar to what it would be in civilian hospitals in peacetime except for the higher incidence of scabies (p. 631). When the care of battle casualties became of major importance, the number of dermatologic conditions increased in all categories because of the increased troop strength in the theater. Because of the pressing need for manpower, the pressure to return patients with medical diseases to duty was even greater than it had been before D-day.

The incidence of disability from skin diseases was significant in the European theater but not excessive as it was in the Pacific Ocean Areas and the China-Burma-India theater. Certain personally collected statistics will make this clear:

In the 21st Evacuation Hospital, from 26 December 1942 to 5 March 1943, 10 percent of all medical admissions were to the dermatology section and 30 percent of all dermatologic admissions were for scabies.

In the 5th General Hospital, during the latter part of 1942, 6.8 percent of 7,049 admissions were for the primary diagnosis of skin disease.

In all hospitals of the European theater, during November and December 1943, 7.2 percent (1,035) of 14,408 admissions were for skin disease.

Interviews with medical officers in the European theater revealed that the incidence of skin disease at sick call in both service and combat units ranged from 15 to 40 percent. Medical officers in the Mediterranean theater reported about the same proportions.

Syphilis.—Venereal diseases (fig. 64) are dealt with extensively in other volumes of this historical series,[14] but certain aspects of therapy in the European theater should also be mentioned here:

1. All patients with ulcerative venereal disease were admitted to the dermatosyphilology sections of hospitals, to insure more accurate diagnosis and adequate treatment. The responsibility for their care rested with the Professional Services Division, Office of the Chief Surgeon, but close liaison was maintained with the Preventive Medicine Division.

2. Individual treatment records were issued, which were carried on his person by the individual soldier. They served as guides to medical officers when, as often happened, syphilis registers were not transferred from unit to unit.

[14] (1) Medical Department, United States Army. Internal Medicine in World War II. Volume I. Activities of Medical Consultants. Washington: U.S. Government Printing Office, 1961, pp. 281–318. (2) Medical Department, United States Army. Internal Medicine in World War II. Volume II. Infectious Diseases. Washington: U.S. Government Printing Office, 1963, pp. 409–435.

FIGURE 64.—Syphilitic lesions. A. Typical penile chancre. B. Anal syphilitic condylomata. C. Acute florid secondary syphilis. D. Later recurrent secondary syphilis.

3. All syphilis registers of presumably cured patients were submitted to examination at the Medical Records Division, Office of the Chief Surgeon, by the Consultant in Dermatology and Syphilology before they were transferred from the theater to the Office of The Surgeon General. Deficiencies, which consisted of inadequate treatment or insufficient evidence of cure, could thus be detected and corrected at once.

4. Massive arsenotherapy was introduced into the theater early in 1943. Between April 1943 and July 1944, approximately 4,000 patients were treated by this technique; the absence of fatalities proved the value of careful supervision.[15] The technique was criticized later in some quarters

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[15] See footnote 14(1), p. 580.

because of presumed infectious relapses, but the experience was fairly comparable to the experience after penicillin therapy was introduced; biologic cure was frequently achieved, but reinfection on subsequent exposure was common.

5. Penicillin therapy for early syphilis was officially introduced into the theater on 26 June 1944, 20 days after D-day. In January 1944, it had been recommended that penicillin be used for the treatment of syphilis in operational Air Forces crews in the theater, but permission was refused by the Air Surgeon in Washington.

6. One of the most impressive figures to come out of the Army medical experience in World War II is the man-days lost because of venereal disease as compared with the figures for the American Expeditionary Forces in World War I.[16] For 1918, in World War I, the figure was 6,804,818 days, almost 19,000 men per day per year. For 1944, the comparable figure in the European theater was 221,184 days, a rate of 606 men per day per year. Over half of the World War II figures covered the period before the introduction of penicillin.

Southwest Pacific Area

Incidence.—Dr. Hopkins, in his report to General Denit after his survey of installations in the Southwest Pacific Area,[17] stated that time had not permitted extensive microscopic or cultural studies. It had also not been possible to obtain statistical data concerning the incidence of diseases observed in his survey because the number of troops from which the hospitalized patients were drawn could seldom be determined. His conclusions were therefore based on extensive discussions with medical officers who had studied these diseases; on clinical examination of numerous patients; and on mycologic examination of a few representative samples.

It was Dr. Hopkins' impression that the majority of patients who were hospitalized in the Southwest Pacific Area for severe skin conditions fell into two groups. The first, and larger, group of hospitalized patients had what was termed "symmetrical eczematoid dermatitis." The second group of hospitalized patients had what was termed "atypical lichen planus." Other men in the Southwest Pacific Area, who constituted an even larger group than those hospitalized, presented characteristic blue pigmentation of the nail beds. They had no symptoms, and they reported for treatment only when they became disturbed by the cosmetic appearance of their nails.

Although these three groups of skin conditions bore some resemblance to well-known dermatoses, none of them seemed precisely identifiable with

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[16] Medical Department of the United States Army in the World War. Communicable and Other Diseases. Washington: U.S. Government Printing Office, 1928, pp. 263–310.

[17] Unless otherwise indicated, the discussion of dermatologic diseases, presented for the Southwest Pacific Area throughout this chapter, is based on Dr. Hopkins' report to General Denit, submitted on 13 March 1945. See footnote 8, p. 557.

any disease which Dr. Hopkins, an experienced dermatologist and mycologist, had previously observed. It was his conclusion that they represented either three new clinical entities or three phases of a single new entity.

An analysis of all patients admitted to the dermatology wards of the 27th General Hospital, Hollandia, New Guinea, from 1 August 1944 to 7 July 1945 by Maj. (later Lt. Col.) Charles L. Schmitt, MC, Chief of the Dermatology Section, showed that 1,820 had been observed during this period. Of this number, 1,182, more than two-thirds, were returned to duty, and 636 were boarded to the Zone of Interior. There were two deaths, one from exfoliative dermatitis. The cause of the other death was not stated.

Investigation of these 1,820 cases showed that a considerable number previously diagnosed as dermatophytosis and dermatitis venenata were in reality early eczematoid dermatoses and were due, at least in part, to a drug intolerance. The investigation also showed that drug intolerance represented the principal cause for boarding patients to the Zone of Interior.

In this single hospital, for the 11-month period studied, 38,430 mandays were lost from duty because of skin diseases.

Recommendations.—At the conclusion of his survey of skin conditions in the Southwest Pacific Area, in his letter to General Denit, dated 13 March 1945, Dr. Hopkins made a number of suggestions, many of which were generally applicable, as follows:

1. Mycologic problems in the Southwest Pacific Area would not be solved until one or two mycologists competent in research were sent to the area. They must be provided with technical assistance, the necessary apparatus and media, and dustproof rooms for inoculation and preservation of cultures.

2. For accurate diagnosis of fungal infections (figs. 65, 66, 67, and 68), each medical laboratory sent to the Tropics should have on its staff an officer sufficiently trained to identify common pathogenic forms of fungi. Each hospital should have a technician competent to detect fungi by direct slide examination.

At the time Dr. Hopkins made his report, there seemed to be only a single officer in the whole Southwest Pacific Area with any training or experience in the identification of fungi. In only a single clinic, the 13th Medical Service Detachment, did Dr. Hopkins see practical use made of slide examinations for diagnosis; here, with the excellent cooperation of the 27th Medical Laboratory, examinations were made promptly and accurately. The same favorable situation might perhaps prevail in some of the installations that he had not visited, but in those that he had investigated, he did not encounter a single dermatologist who believed that he could obtain reliable examinations for fungi. Laboratory officers who were, reluctantly, making cultures for fungi stated that they were at a loss to identify any positive cultures that they might observe.
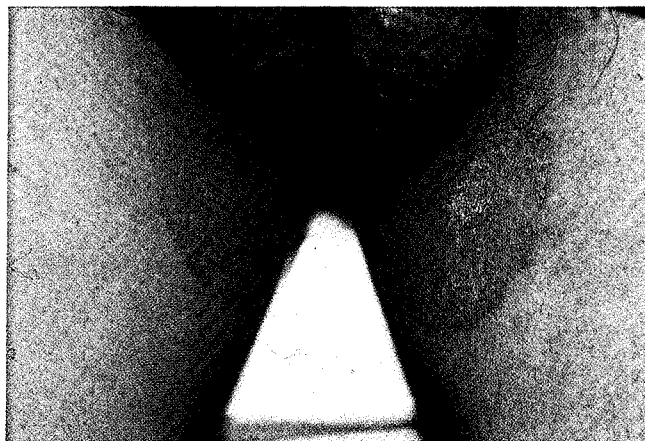
FIGURE 65.—Erythrasma or fungal infection of thighs.

FIGURE 66.—Acute tinea cruris.

In Dr. Hopkins' opinion, the situation could be corrected at once if a few laboratory officers were trained in mycology before they were sent to the Southwest Pacific Area and if short laboratory courses were substituted for the one or two lectures that now seemed to constitute the only mycologic training given to technicians.

The use of mycologic methods for diagnosis was more important than research in this field. Slide examinations would usually be sufficient, but cultures were necessary for the detection of *Monilia* and some of the more
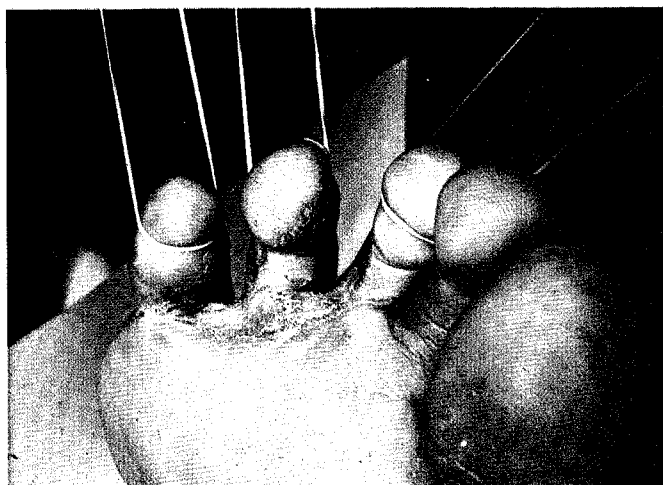
FIGURE 67.—Typical acute dermatophytosis caused by
Trichophyton mentagrophytes.
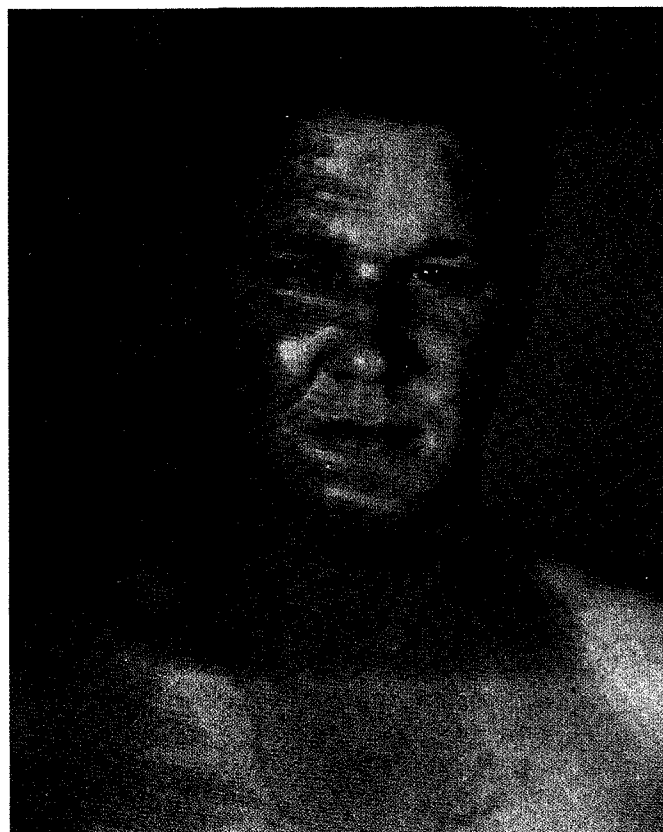
FIGURE 68.—Tinea corporis.

uncommon parasites. The routine use of such techniques would improve the accuracy of diagnosis and eventually result in therapeutic improvement.

3. As a therapeutic test, 1,000 tubes each of undecylenic acid and sodium propionate ointment should be issued to each of several infantry divisions, so that division surgeons could report on their effectiveness under field conditions. Liquid preparations of fatty acids might be similarly tested.

4. Sandals should be issued to infantrymen, for use as permitted by command after consultation with the medical officers concerned (p. 602). It was also recommended that troops be allowed to work during the day without shirts at such times and in such areas as were considered safe. External infection might sometimes be a causative factor in dermatophytoses of the groin and other parts of the body, but the prevalence of these eruptions in the Southwest Pacific Area, just as in the southern United States during the summer, could more reasonably be attributed to the wearing of impervious clothing that prevented the evaporation of sweat. Giving permission for troops to go naked during the sunny hours of the day would probably almost abolish extensive ringworm of the trunk without endangering the antimalarial program and would have an equally good effect on miliaria and the impetigoes. If this plan was considered undesirable, then it was recommended that the fabric used in Army shirts be changed. Closely woven, uncomfortable herringbone twill might be necessary under combat conditions, but in rear areas, a more loosely woven fabric, such as was used in the Australian Army, would be preferable.

5. To prevent ecthyma, which was prevalent among troops in combat areas, medical officers and company commanders should be instructed in the use of Freon-12 aerosol insecticide or DDT for the control of flies. Both were practical agents for forward use.

6: To prevent so-called tropical immersion foot (p. 600), mineral oil should be issued before landings on wet terrain, and the troops should be instructed to grease their feet before they went ashore and as often thereafter as possible. Careful check should be made of the condition of the feet and legs of the men thus treated as compared with a control group of similar size without treatment. ·

7. To prevent disability from acne, medical officers who examined troops before embarkation from the Zone of Interior should be informed of the bad prognosis for the cystic type of acne in the Tropics (p. 617) and should be advised against sending men with this disease to the Southwest Pacific Area.

8. One or more permanent hospitals should be designated for the treatment of warts by X-ray. A standard technique should be developed for their management in dispensaries. Formalin therapy [18] was considered well worth a trial.

[18] Thomson, S.: The Treatment of Plantar Warts by Formalin. Brit. J. Dermat. 55: 267–269, November 1943.

9. Every effort should be made to clarify the etiology of eczematoid dermatitis, which was the most serious dermatologic problem in the Southwest Pacific Area and the most frequent dermatologic cause for evacuation of personnel from this area to the Zone of Interior. It would be well if some of the men evacuated would volunteer to continue suppressive doses of Atabrine after their return to the United States.

10. The issue of multiple vitamin tablets should be increased, in the hope that their use might lower the incidence of dermatoses.

11. The following research studies were recommended:

    a. Determination of the presence of fungi in the lesions of lichen planus or in symmetrical eczematoid dermatitis, especially in the lesions of the nail so frequently seen in New Guinea (p. 643).

    b. The frequency of fungal infection as a cause of intertrigo of the toes and dermatitis of the feet.

    c. Identification of the species of fungi found in dermatomycoses on different parts of the body.

    d. The relation of *Monilia albicans* to miliaria.

    e. The relation of fungal infection to so-called tropical immersion foot.

    f. The possibility of sensitization to bacteria or fungi in lichen planus and eczematoid dermatitis with allergies.

China-Burma-India Theater

Venereal diseases.—The venereal disease rate in India among U.S. troops was one of the highest encountered in any theater or area in World War II. Maj. Harry M. Robinson, Jr., MC,[19] reported that one laundry battalion station in Calcutta had a rate of 1,500 per 1,000 per year. Although syphilis and gonorrhea were the major problems, chancroid and lymphogranuloma venereum were common. It was not unusual for a man to report for treatment with two, three, or even four separate venereal diseases at the same time, following several exposures over a short period.

Dermatologists of the 20th, 69th, and 142d General Hospitals played an important part in the management of these patients. During 1944 and early 1945, one of three wards in each of these hospitals was continuously filled with men with early syphilis, chancroid, lymphogranuloma venereum, or combinations of these diseases. Penicillin became available in the theater for the treatment of syphilis in September 1944, but supplies were limited.

Dermatologic diseases.—The major dermatologic problems in Burma and India were quite similar to those encountered in the Southwest Pacific Area. Many skin diseases with a high incidence in the United States were also common in the China-Burma-India theater. During the hot, humid monsoon season in particular, primary bacterial infections were widely

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[19] Robinson, H. M., Jr.: Personal communication.

prevalent, especially ecthyma and bullous impetigo. Secondary bacterial infections of eczematous eruptions, contact dermatitis, and tinea pedis were common, and their course was protracted. During the summer months, the incidence of miliaria rose to 75 percent in some units, and the condition was often incapacitating. Scabies was an important cause of disability in Chinese troops but was uncommon in U.S. Army personnel.

A unique form of contact dermatitis observed in the China-Burma-India theater was dhobie mark dermatitis (p. 626). Other cutaneous diseases of interest and importance in U.S. personnel included cutaneous diphtheria (p. 613) and the lichenoid and eczematoid dermatitis syndrome caused by Atabrine (p. 638). Among the unusual cutaneous diseases and systemic diseases with cutaneous manifestations seen in Chinese troops were leprosy, kala-azar, tuberculosis, syphilis of the bones and other deeper structures, and true tropical phagedenic ulcer associated with malnutrition. Superficial fungal infections were identical with those that occur in the United States, but they were more frequent, more extensive, and more difficult to control.

In summary, the effects of the hot, humid climate in India and Burma, plus the skin trauma incidental to active military campaigns and engineering activities in a jungle type of environment, led to a high incidence of incapacitating cutaneous bacterial infections, miliaria rubra, infected indolent insect bites, contact dermatitis, superficial fungal infections, eczematoid dermatitis, and cystic acne. In addition, the total disability caused by cutaneous diphtheria, dhobie mark dermatitis, and the lichenoid and eczematoid dermatitis syndrome was significant. Comment is made on certain of these conditions under appropriate headings.

Part II.   Clinical Considerations

FUNGAL INFECTIONS

General Considerations

Zone of Interior.—The popular impression that fungal infection was a serious condition in U.S. troops in World War II was universally disproved whenever adequate methods of diagnosis and evaluation were employed. At Fitzsimons General Hospital,[20] over a period of months, all patients hospitalized on the dermatology service were studied by direct examination of all lesions, fungal cultures, and the trichophytin test. The generally negative results of this careful study showed that superficial fungal infections were not a cause of significant disability among troops evacuated to the Zone of Interior because of skin diseases. Similar studies at other hospitals were to the same effect.

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[20] Woodburne, Lt. Col. Arthur R., MC: Dermatology at Fitzsimons General Hospital, n.d.

At Fitzsimons General Hospital, the incidence of onychomycosis of the nails was somewhat greater than in civilian practice. It was treated by removal of all infected material by nail clippers, files, curettes, and dental burs, after which the fingertips were soaked in soapsuds or in a 20-percent sodium hydroxide solution. Whitfield's ointment, full strength, was rubbed vigorously into the nails at night, and the affected parts were painted with a 3-percent iodine solution in the morning.

Mediterranean theater.—In the Mediterranean theater, mycotic infections accounted for about a fifth of all skin diseases, as the following personally collected figures show: [21]

1. These infections accounted for 16.7 percent of the admissions and dispositions for skin conditions and for the patients remaining in MTO hospitals in the week ending on 22 September 1944.

2. They accounted for 19.3 percent of all skin diseases in the Fifth U.S. Army for the same week.

3. They accounted for 21.9 percent of all skin diseases in the 34th, 85th, and 88th Infantry Divisions for the 3-week period ending on 22 September 1944.

4. They were less frequent in rear echelon troops. According to one survey, they accounted for only 13.3 percent of all the skin conditions treated in the outpatient dispensary of a large general hospital.

These figures, however, need some explanation before they are accepted absolutely. The Army figures were collected in September, when fungal infection was frequent. The outpatient dispensary figures just cited were collected over a period of several months. Furthermore, a higher incidence of fungal infections would be expected in combat troops because of long marches and their frequent inability to bathe, remove their shoes, change their socks, and use foot powder. Nonetheless, the fact that fungal infections accounted for 13.3 percent of all skin conditions in an outpatient dispensary in a base section, where living conditions were at least fair and where reasonable personal hygiene was possible, indicated that they were rather prevalent. When field and combat conditions are taken into account, it is small wonder that these conditions were recorded so frequently and meant the loss of so many man-days. One reason for the amount of disability they produced lies in the fact that most mycotic infections involved the feet or the genitocrural region.

Two conditions secondary to primary fungal infection in the Mediterranean theater require special comment:

1. In many instances of cellulitis (figs. 69, 70, 71, and 72), the portal of entry of the invading organism was a fissure or ruptured vesicle in which dermatophytosis was the original lesion. The primary disease was not in

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[21] All data for the Mediterranean theater were provided by Dr. R. N. Buchanan, Jr. (formerly Lieutenant Colonel, MC), Dr. R. E. Imhoff (formerly Major, MC), Dr. C. Barrett Kennedy (formerly Major, MC), and Dr. Richard C. Manson (formerly Major, MC).
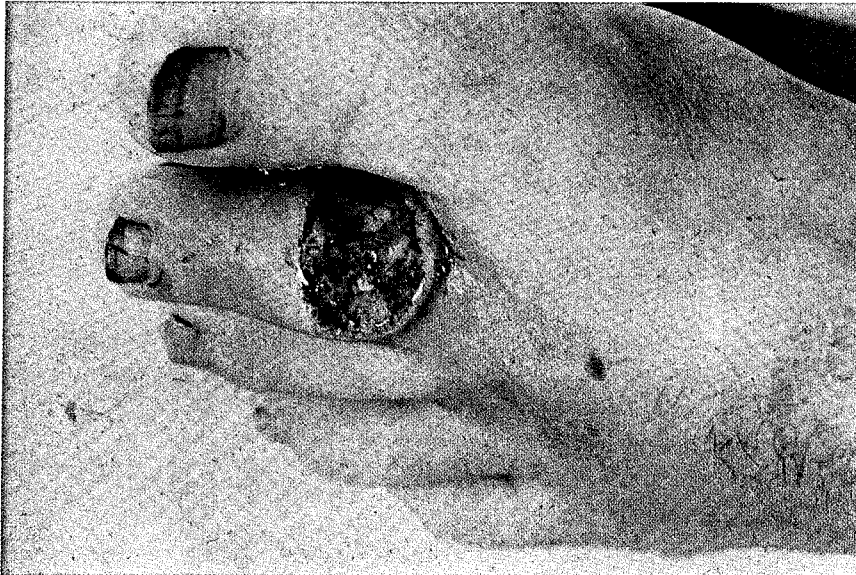
FIGURE 69.—Proved leishmaniasis of toe, with numerous Vincent's spirochetes.

FIGURE 70.—Cutaneous leishmaniasis.

itself disabling, with the secondary condition was potentially serious, likely to be disabling, and very often entirely preventable.

2. Dermatophytids developed in a great many instances of fungal infection. Many patients were sensitized to the products of infection because

FIGURE 71.—Diphtheria of skin of foot.

the fungal infection had been allowed to persist; to go through phases of more or less activity; to become acute, with fissuring and oozing; then to improve but never to heal completely. Often, patients of this type, when they were received in the Zone of Interior, had not only primary mycotic infections but also eczematous vesicular dermatitis, usually on the palmar and plantar surfaces, which was quite resistant to treatment. It was repeatedly stressed to medical officers that early, appropriate treatment of primary fungal and other infections would result in their control and would prevent complications. Many of these conditions, unfortunately, resulted from sensitization by the use of strong fungicidal preparations, particularly ointments issued for use on a duty status.

When soldiers with fungal infections presented themselves on sick call, it was often because of secondary infection, to which primary thera-

FIGURE 72.—Scrub typhus with eschar.

peutic attention had to be directed. Measures most frequently used included compresses and soaks of boric acid solution, dilute potassium permanganate solution, aluminum acetate solution, or a saturated solution of magnesium sulfate. After secondary infection had been controlled, therapeutic measures included Lassar's paste; Whitfield's ointment, half strength; keratolytics; a 3-percent sulfur and salicylic acid ointment; 4 percent salicylic acid; 2 percent thymol in tincture of benzoin compound; and a 5-percent crude tar ointment. Some patients with chronic fungal infections were benefited by superficial X-ray therapy. When treatment was concluded, the patient was given a can of GI (Government-issue) foot powder and urged to use it.

Most men with fungal infection seen in the Mediterranean theater were returned to duty, but occasional patients with chronic diseases and dermatophytid reactions were resistant to all types of therapy. They were usually evacuated to the Zone of Interior, but only after they had been hospitalized for long periods of time and spent many days away from their units.

Southwest Pacific Area.—Fungal infections in the Southwest Pacific Area have been discussed in detail elsewhere (p. 582) and will be discussed further under appropriate headings.

Inflammatory Conditions of the Feet

Zone of Interior.—The extremely unsatisfactory terminology of athlete's foot was used by many medical officers to cover a wide variety of disturbances of the feet (figs. 73, 74, 75, and 76). The nomenclature was not scientific. It had no etiologic significance, and it was even more unreliable as a basis of treatment.

At Fitzsimons General Hospital, after classification and appropriate studies, patients referred with this diagnosis were divided into the following categories and proportions:[22]

1. The hyperhidrosis (dyshidrosis) syndrome, 51 percent.

2. Pyoderma secondary to trauma, maceration, or the hyperhidrosis (dyshidrosis) syndrome, 14 percent.

3. Dermatophytosis, 20 percent.

4. Dermatitis venenata produced by medication (which had usually been prescribed for the treatment of the presumed fungal infections), 11 percent.

5. Other dermatitis venenata, 2 percent.

6. Resistant pustular eruptions (the so-called bacterid of Andrews), 1 percent.

7. Pustular psoriasis, 0.5 percent.

8. Acrodermatitis continua of Hallopeau, 0.5 percent.

Hyperhidrosis (fig. 77) was the most frequently observed entity at this hospital. It was psychogenic in origin, and it was seen not only on the dermatology wards but also in consultation on neuropsychiatric wards and on other services. It was readily explained by removal of men from their normal environment, disciplinary restrictions, their often hazardous living conditions, and similar precipitating causes. The correctness of these theories of etiology was proved by the fact that a quiet, restful environment, without other treatment, was frequently sufficient for a cure.

Hyperhidrosis in the Zone of Interior and elsewhere was an annoying and uncomfortable condition, but one that was seldom disabling per se. What made it important was that it was widely prevalent and that the lesions that developed in it constituted portals of entry for secondary bacterial invasion, with resulting and disabling pyoderma, cellulitis, lymphangitis, and lymphadenitis. Another consideration was that the diagnosis of fungal infection as the cause of the hyperhidrosis was often made incorrectly, and the strong and irritating fungicidal agents used unnecessarily often resulted in severe and disabling dermatitis.

Local therapeutic measures included 20 percent benzoic acid in Lassar's paste; 1 : 500 solution of formalin used as a soak for a brief period once daily; compresses of Burow's solution; and foot powder. The inclusion

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[22] See footnote 20, p. 588.

FIGURE 73.—Allergic dermatitis.

FIGURE 74.—Allergic dermatitis.

FIGURE 75.—Severe fissuring bilateral keratosis of heels. The
patient was completely disabled.

FIGURE 76.—Epidermolysis bullosa.

in the supply tables of one or more soluble aluminum salts, such as alumi-
num chloride or aluminum sulfate, would have provided additional agents
for the treatment of ambulatory patients and would have been useful in
preventing recurrences.

It was the opinion at Fitzsimons General Hospital that elimination of
the so-called fungicidal prophylactic footbath and the substitution of indi-

FIGURE 77.—Hyperhidrosis of hands.

vidual prophylaxis, including thorough drying of the feet and the liberal use of foot powder, would have materially decreased the incidence of fungal infections of the feet.

Mediterranean theater.—Hyperhidrosis of the feet was extremely common in the Mediterranean theater where, as elsewhere, it was associated with emotional stress and strain. It was also secondary to vascular changes, particularly those associated with trenchfoot.[23] It was frequently antecedent to that condition. It was difficult to handle and extremely resistant to treatment. Indeed, it often required reclassification of the soldier.

Among the multiple treatments used were painting the area with straight formalin once daily for 3 days; 1-percent formalin soaks; potassium permanganate soaks; and foot powders, such as tannic acid powder or the regular-issue foot powder. Lumbar sympathetic ganglionectomy was occasionally necessary to convert disabling hyperhidrotic feet to dry and serviceable members.

European theater.—In the European theater, inflammation of the feet, whether from fungal infection (figs. 78, 79, 80, and 81), mechanical irritation, sensitivity to footgear, or hyperhidrosis, particularly after mild trenchfoot,[24] represented an important aspect of dermatology, because soldiers with any degree of inflammation of the feet were frequently unable to do full duty either in the rear or in the field.

An epidemic of what was diagnosed as fungal infection occurred in July 1943 and well illustrated the factors that can contribute to such a condition. Word of the incidence of the infection reached the ears of the Commanding General, SOS, who had had difficulties with a presumed fungal in-

[23] Medical Department, United States Army. Cold Injury, Ground Type. Washington: U.S. Government Printing Office, 1958.
[24] See footnote 23.

FIGURE 78.—Typical dry tinea pedis caused by
Trichophyton rubrun.

FIGURE 79.—Typical dry tinea pedis caused by
Trichophyton rubrun.

fection himself and who was correspondingly preoccupied with the problem.
The Senior Consultant in Dermatology was directed to investigate the situa-
tion and correct it immediately. The circumstances were as follows:

A large detachment of men at Depot G-25 were doing heavy work in
the machine shops or elsewhere that often involved long periods of standing

FIGURE 80.—Secondarily infected interdigital fungal infection.

FIGURE 81.—Symmetrical lividity of soles.

on cold, damp concrete floors. When the depot was visited by Mrs. Eleanor Roosevelt in 1942, she apparently heard a number of complaints of cold feet from the men with whom she talked, and with her usual sympathetic understanding, she arranged for heavy British-issue socks to be supplied to them. These socks were much heavier than any regular U.S.-issue socks, and they proved very satisfactory during the winter of 1942-43. Over the same period, there was a steady increase in the issue of GI shoes with rubber soles.

In late May and early June 1943, the weather in England turned unseasonably warm, and with the change came a precipitous rise in the incidence of inflammatory conditions of the feet at this particular depot. Medical officers reported that between 50 and 75 percent of the soldiers serving there were examined at the post dispensary and showed some changes, ranging from mild scaling between the toes to more severe involvement, with blisters and fissures. It was estimated, without benefit of microscopic examinations and cultures, that about two-thirds of these men were suffering from true ringworm infections, a percentage that, at a distance of years, now seems somewhat excessive.

In any event, the epidemic was promptly brought under control by the institution of foot inspections, issue of lighter footgear, particularly socks, and emphasis upon the importance of foot hygiene, including regular washing and careful drying of the feet and the application of foot powder.

This minor episode was instructive. It emphasized the relation between proper footgear and climatic and industrial conditions, as well as the great importance of individual foot hygiene, with special relation to thorough drying of the feet, particularly the intertriginous areas, and the regular use of foot powder to promote dryness and prevent friction.

A survey of showers, sterilization of duckboards, and similar matters showed that they played no part in the increased incidence of infection at this depot or elsewhere. The provision of chemically treated footbaths served no useful purpose. In fact, there was some evidence that, if the solution in them was not changed regularly, they might serve as a means of transmitting infection rather than of preventing it. During 1942-43, when shipping space to the European theater was desperately short, tubs for these footbaths were received on a regular schedule. The Consultant in Dermatology, ETOUSA, could not understand why they were ever introduced into Army dermatologic practice.

Southwest Pacific Area.—In base and station hospitals in the Southwest Pacific Area, well removed from the front, interdigital infection of the feet accounted for only a small number of cases, fewer, indeed, than might be found in a group of healthy soldiers on active duty. All these patients had been hospitalized for varying periods, and their infections had cleared, with or without treatment. In many cases in which the diagnosis of epidermophytosis had been recorded, Dr. Hopkins found no fungi on

examination. He could not, it is true, exclude the possibility that the eruptions observed were primary fungal infections secondarily infected with pyogenic bacteria, but he found very few cases in which there seemed a sound basis for this assumption.

In base dispensaries, fungal infections of the feet were far more frequent than in hospitals, but the incidence was apparently no higher than in military dispensaries in the Zone of Interior. In regimental aid stations, however, and in clearing companies directly to the rear, fungal infections of interdigital areas and of the soles of the feet among troops in combat were far more numerous and were often severe.

After the Leyte landings, men stood, marched, and even slept for long periods in flooded rice paddies. There was a significant amount of disability from the resulting dermatoses. Patients were sent back to rear hospitals with the diagnosis of immersion foot (tropical cold injury),[25] though no evidence of peripheral vascular damage was ever obtained. Dr. Hopkins, who obtained his information about the condition from Maj. James R. Webster, MC, at the 54th General Hospital, considered the term unfortunate. No fungi were identified in the lesions during the acute phase, which suggested that they were essentially bacterial, but in many instances, fungi were found after acute symptoms had subsided, which suggested that bacterial infection was secondary to fungal infection. Whatever the chronology, the essential etiologic factor was maceration of the stratum corneum by prolonged immersion.

Etiology.—Available evidence in both the Zone of Interior and the Southwest Pacific Area indicated that attacks of dermatophytosis were almost never caused by external infection or by reinfection from shoes or clothing. Probably few men contracted the infection in the Southwest Pacific Area. More likely, most of them brought it with them, in latent form, and it simply flared up under climatic conditions. Acute outbreaks were usually caused by sudden lowering of the natural resistance of the skin, which permitted fungi already present on the surface to multiply. The essential factor was lowering of resistance by maceration of the skin by sweat or water. It was a common observation, as already mentioned, that when patients were confined to bed for some reason, their dermatophytoses healed without treatment.

Apparently some individual immunity existed to dermatophytosis of the feet because, in any platoon or company, a certain number of men, constituting not more than 10 percent of the total number, would never develop the condition though they mingled freely with infected men and for the most part used no special prophylactic measures. The basis of their immunity was unknown, and Dr. Hopkins considered that a study of it might be rewarding.

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[25] See footnote 23, p. 596.

Therapy.—The treatment of dermatophytosis in men on active duty was frequently ineffective. The tendency was to use irritating fungicides, such as salicylic acid in alcohol, full-strength Whitfield's ointment, and Frazer's solution. These agents were frequently curative, but they sometimes produced severe irritation and led to the development of the acute dermatitis seen later in many hospitals.

In a study conducted at Fort Benning, Ga.,[26] it was found that water-soluble ointments prepared from undecylenic acid or sodium propionate could be used in dermatophytoses without the risk of irritation inherent in the agents just listed. When these ointments were tested at base and station hospitals, the results were fairly satisfactory but not striking. When, however, they were issued to groups of infantry in combat, results were highly favorable. Capt. William B. Guy, MC, for instance, who served as battalion surgeon with the 136th Infantry, reported, after he had used them for several weeks, that these ointments had given more prompt relief than any preparations he had previously used and that they caused no irritation. He thought solutions somewhat more satisfactory than ointments but was unwilling, because of the brief period of observation, to commit himself definitely on this point.

In some instances, an ointment containing 5 percent undecylenic acid and 10 percent peroxide was used for testing purposes, but as a rule, fatty acid preparations of the following composition were employed:

Sodium propionate ointment: Sodium propionate, 16.4 percent; propionic acid, 3.6 percent; n, propyl alcohol, 10.0 percent; zinc stearate, 5.0 percent; and Carbowax base, 65.0 percent.

Undecylenic ointment: Undecylenic acid, 5.0 gm.; triethanolamine, 3.0 gm.; methocel 15 CP, 2.0 gm.; propylene glycol, 22.0 cc.; zinc stearate, 13.0 gm.; and Carbowax 1500, 55.0 grams.

Undecylenic solution: Undecylenic acid, 5.0 gm.; triethanolamine, 3.0 gm.; ethyl alcohol, 30.0 cc.; and propylene glycol, 62.0 cubic centimeters.

Prophylaxis.—Dermatophytosis of the feet, as already indicated, was seldom disabling in itself in rear areas. Practically all the patients hospitalized with it either had secondary infections or had been so overtreated that their lesions had become eczematized. The number of such cases was, unfortunately, quite large. Under combat conditions, in which men had little opportunity to care for their feet and could not remove their shoes for days at a time, a significant amount of complete disability apparently occurred, though Dr. Hopkins did not consider his investigation of troops in combat sufficient to warrant generalizations.

Tests of prophylactic measures were also not conclusive:

1. Nothing at all was achieved by measures aimed at preventing con-

[26] Grauer, Franklin H., Helms, Samuel T., and Ingalls, Theodore H.: Skin Infections. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume V. Communicable Diseases. Washington: U.S. Government Printing Office, 1960, pp. 83–125.

tagion, such as the use of hypochlorite footbaths or disinfection of shoes, socks, and shower room floors.[27]

2. At Fort Benning, systematic attempts were made to prevent recurrences of dermatophytosis by prolonged treatment after manifestations had subsided. They failed utterly, as might have been expected. Experiences with attempted surgical disinfection of the hands have always shown that it is impossible to rid the skin of *Staphylococcus;* the application of antiseptics simply reduces the number of organisms present. It was found equally impossible to rid the skin of fungi; once the infection had occurred, it was unlikely that the application of any fungicide would destroy all the spores present.

3. Even under combat conditions, if the terrain was dry and the dermatophytosis was latent or very slight, the use of a mild fungicide, such as regular-issue foot powder, seemed reasonably effective in preventing severe outbreaks. It was also more comfortable and convenient to use routinely than were ointments. Whatever the explanation, the use of this powder seemed to prevent fungi from multiplying to the point at which they would become troublesome.

Civilian experience had showed that painting the toes once weekly with Frazer's solution was even more effective than the use of fungicidal powder in preventing recurrent attacks of dermatophytosis, but this measure was aimed at the suppression of latent infection, not at cure. Reports from dispensaries and hospitals indicated that it was effective in chronic cases. It was often irritating in active infections and therefore was not suitable for the emergency relief of acute conditions, though it was included in jungle kits for this purpose.

4. All the evidence indicated that the most effective prophylaxis in dermatophytosis of the feet was strict skin hygiene, which meant keeping the skin as dry as possible, provision of ways for evaporation of sweat, and direct exposure to sunlight for its tonic and sterilizing effects.

A convincing controlled study along these lines was conducted by Maj. (later Lt. Col.) Laurence Irving, Chief, Physiology Section, Headquarters, Eglin Field, Fla.[28] Sandals were issued to approximately 1,000 men, who were permitted to wear them on the post as much as they wished; most of them practically gave up wearing shoes. A similar number of men wore shoes as usual. Within a month, the proportion of severe dermatophytoses in men wearing sandals fell from 30 to 3 percent, while in the control group, the disease remained as troublesome as usual.

A similar study was conducted in New Guinea, while the 43d Infantry Division was in a rest area. Some 300 men with unclassified skin diseases, many of whom undoubtedly had dermatophytosis of the feet, were kept on the beach for 4 hours daily, without clothing or shoes. They bathed, exer-

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[27] See footnote 26, p. 601.
[28] See footnote 26, p. 601.

cised, or just lay in the sun as they wished. Within a month, the majority of infections had cleared without any other treatment.

Any measures adopted in the Southwest Pacific Area for prophylaxis of skin conditions had to avoid serious interference with the antimalarial program or with the protection against hookworm and other parasites. These considerations made the wearing of sandals impractical in many areas, though it was entirely practical in New Guinea for men on ground duty on airstrips and in headquarters. In the Philippines, the plan was considered practical during the dry season except for troops in combat or training for combat. In most areas, it seemed safe to expose the feet during the middle of the day; they would never be more exposed to mosquito bites than the face, neck, and hands were exposed at all times. The use of thick-soled sandals, with some sort of guard in the toe to prevent scuffing up of dirt, would afford reasonable protection against hookworm. The plan seemed worth a trial to Dr. Hopkins. He believed that the issuance of sandals to the majority of troops, with permission to wear them in areas and during hours defined by the surgeon in charge, would be the most effective measure that could be adopted for the prevention of dermatophytosis of the feet. When the ground was extremely muddy, this plan, of course, was impractical from any point of view.

5. Comparative tests of undecylenic acid ointment, sodium propionate ointment, and regular-issue foot powder during the landings at Lingayen in the Philippines were too fragmentary to permit conclusions, but Dr. Hopkins believed that a full field test with them was warranted. In all such tests, it had to be remembered that any study that involved self-treatment was subject to error, beginning with doubt as to whether the agents issued were used at all.

Other Dermatophytoses

Dermatophytosis of the hands.—Dermatophytic infection of the skin of the hands was extremely infrequent. Dr. Hopkins saw only 1 proved instance in his survey of SWPA installations, and in a study that he had directed at Fort Benning, of 1,472 cases in which dermatophytes were isolated, the hands were involved only twice.

Eczematous eruptions frequently seen on the hands in the Southwest Pacific Area and frequently diagnosed as dermatophytids were not so regarded by Dr. Hopkins because they were far more exudative and far more inflammatory than true dermatophytids and also because they occurred in many soldiers with no visible mycotic lesions of the feet. He did not exclude the possibility of a mycotic origin, but he considered it highly improbable.

Even in the Southwest Pacific Area, dermatophytosis of the hands was not of military significance.

Dermatophytosis of the groin.—Dermatophytosis of the groin (tinea cruris) had a high incidence in the Southwest Pacific Area, especially among troops in combat or in active training. While it was seldom the cause of complete disability or an indication for hospitalization, it was a frequent source of great discomfort, and it handicapped many men in the performance of their duties.

No extensive trials of therapy were made in the Southwest Pacific Area, but in the cases of tinea cruris treated under Dr. Hopkins' direction at Fort Benning, undecylenic acid and sodium propionate proved as satisfactory for the treatment of lesions in this location as it had proved for similar lesions on the feet.

Dermatophytosis of the trunk and extremities.—Widespread involvement of the skin of the trunk, arms, and legs (tinea corporis) was frequently encountered in the Southwest Pacific Area and was sometimes severe enough to require hospitalization. In almost every dermatologic ward that Dr. Hopkins visited, he found 3 or 4 patients with generalized ringworm in each 100 to 200 patients. The condition was no more severe, however, and the incidence was probably no higher, than at Fort Benning during August and September. The condition was of military significance in the Southwest Pacific Area chiefly because it was perennial.

The growth of fungi on the skin of the trunk and limbs seemed to depend upon the presence of unevaporated sweat, which was related, in turn, to the wearing of clothing in hot, humid weather. The effect of clothing on the distribution of these infections was strikingly illustrated in a group of some 700 prisoners of war, among whom there were almost 100 cases of extensive tinea corporis. Most of the prisoners had confluent lesions extending from the ankle to the knee, a distribution seldom observed in U.S. troops. Questioning revealed that these men had worn spiral cloth puttees, which most certainly increased sweating and prevented evaporation of sweat on the lower legs. In U.S. soldiers, the eruption was often concentrated in a band about the belt and over the buttocks, where there were several layers of clothing.

Dr. Hopkins had little success in identifying the species of fungi responsible for tinea corporis in the Southwest Pacific Area. His visits to hospitals were brief, and cultures had to be made and studied in laboratories housed in temporary buildings or tents, without assistants trained in mycology. Reliable mycologic work was impossible under such conditions. In a total group of 13 positive cultures, 2 of which were isolated by Lt. Walter L. Barksdale, SnC, 10 were *Trichophyton gypseum,* 2 *Trichophyton purpureum,* and 1 *Epidermophyton floccosum (inguinale).* These findings were in sharp contrast to those obtained in a study at Fort Benning: In 62 cultures of tinea corporis, 68 percent were *T. purpureum* and 32 percent *E. floccosum; T. gypseum* was not represented. In 198 positive

cultures in dermatophytosis of the groin, 36 percent were *T. purpureum,* 62 percent *E. floccosum,* and only 2 percent *T. gypseum.*

These differences, of course, are not statistically significant. It was also noted in the Southwest Pacific Area, however, that, in dermatophytosis of the body, a pattern was frequently observed of small, well-defined annular lesions. Less often, there were large areas of involvement, with serpiginous borders, corresponding to the type frequently observed in Georgia. It was thought that these differences might be corrected with the species of causative fungus present. The observations in the Southwest Pacific Area, though few, confirmed the opinions expressed by Lieutenant Barksdale and a Navy colleague that dermatophytoses seen in the Pacific were caused by the same fungi that caused similar lesions in temperate climates.

The best therapy of tinea corporis was the application of gentian violet, wet boric acid solutions, or undecylenic acid or sodium propionate ointment until the acute inflammation had subsided. Then Frazer's solution was applied, or tincture of iodine, or a solution of 3 percent salicylic acid in Mercresin (mercocresols).

Dermatophytosis of the beard.—Dr. Hopkins saw only one instance of tinea barbae in a U.S. hospital in the Southwest Pacific Area. The culture was positive for *T. purpureum.* He observed two additional cases in an Australian hospital.

Tinea versicolor.—Tinea versicolor was frequently observed at Fitzsimons General Hospital in troops received from tropical oversea theaters.[29] The eruption usually disappeared promptly after the application of an ointment consisting of 3 percent salicylic acid and from 6 to 8 percent ammoniated mercury in a standard emulsion base. Treatment was continued for several weeks, until all evidence of infection had disappeared.

Tinea versicolor was also extremely prevalent in the Southwest Pacific Area. It presented no military problem, since it seldom caused symptoms, and most men complained only of the discoloration of the skin. If the body had been exposed to sun, the usual coloration was reversed; the involved areas appeared white against the tanned areas of normal skin. Some native physicians, for obvious reasons, called the condition tinea alba. Some explained it by the growth of saprophytic molds on the skin, with consequent protection of it from ultraviolet rays.

Tinea versicolor in the Tropics was undoubtedly the same disease that was observed in temperate climates, but in the Tropics, it was more frequent as an acute eruption of small, round macules.

Scrapings from representative cases showed a fungus indistinguishable from the *Malassezia furfur* found in temperate climates. Dr. Hopkins observed a typical case of achromia parasitica in a Philippine child, whose

[29] See footnote 20, p. 588.

lesions resembled tinea versicolor, though they were less scaly. *Malassezia* could not be demonstrated.

Applications of saturated solution of sodium thiosulfate, followed by a 3-percent aqueous solution of tartaric acid, were often effective. Lesions refractory to this method were painted with 3 percent iodine in spirits of camphor. The disease was more resistant to treatment in the Southwest Pacific Area than it was in temperate climates.

Tinea imbricata.— Tinea imbricata was extremely common in natives of New Guinea but does not seem to have been reported in either United States or Australian troops. The disease was readily identified by the beautiful, scroll-like patterns that often covered the trunk and extremities. If it was of long standing, this pattern changed to sheets of large rhomboidal scales, firmly adherent at the center but free at the border.

On slide examination, an astonishing amount of delicate branching mycelium was found in these scales. Cultivation of the causative organism, *Endodermophyton tropicale,* was difficult because it is slow growing and flora of the Papuan epidermis proved extremely luxuriant. The few cultures resembling this parasite that were isolated were sent to the United States for identification.

Australian physicians reported that tinea imbricata had disappeared in natives employed to spray pools with Diesel oil, an observation that was confirmed by several U.S. medical officers. Dr. Hopkins suggested further investigation of the possible fungicidal properties of Diesel oil.

Otomycosis

Otomycosis (otitis externa) was a frequent diagnosis in patients received from tropical oversea theaters, but hospitals such as Fitzsimons General Hospital reported that the diagnosis could seldom if ever be confirmed by culture of pathogenic fungi.[30] The opinion of dermatologists in the Zone of Interior was that none of these patients had fungal infections of the external auditory canal but that, instead, they could be divided into two groups, a larger group composed of those with seborrheic dermatitis and another composed of those with eczematous dermatitis caused by maceration of the skin, collections of cutaneous debris, and secondary pyogenic infections.

Otitis externa was reported to be prevalent in the Pacific Ocean Areas [31] but was seldom observed on dermatologic wards. Dr. Hopkins had the opportunity to study a small number of patients with this condition at the 37th General Hospital, where Capt. A. Reas Anneberg, MC, had separated them into two groups. In the first group, the clinical diagnosis of otomycosis was made because a fluffy mycelium was visible on the surface of the aural

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[30] See footnote 20, p. 588.

[31] Medical Department, United States Army. Surgery In World War II. Ophthalmology and Otolaryngology. Washington: U.S. Government Printing Office, 1957, pp. 417–426.

canal. *Aspergillus* (species not identified) was demonstrated on slide examination, and the response to undecylenic ointment was good and was even better when peroxide of hydrogen was added to it. The second group of cases was characterized by fissures, exudation, and crusting, and fungi were not found on slide examination. These patients, whose disease was assumed to be of bacterial origin, reponded well to penicillin ointment.

Dr. Hopkins' opinion, which was concurred in by many otolaryngologists in the area,[32] was that most of the reported cases diagnosed as otomycosis were not fungal infections, though a sizable number were. He believed that fatty acids offered a more satisfactory treatment for them than any method previously used and recommended a systematic trial of these agents.

BACTERIAL DISEASES

General Considerations

Bacterial infections of the skin (figs. 82, 83, and 84) were present in all theaters, and the experience of the Mediterranean theater may be described as typical. In this theater, the principal etiologic agent in the largest number of such cases was *Staphylococcus* or *Streptococcus*. Bacterial infections were consistently responsible for the highest morbidity rates in statistics collected from representative hospitals, and in a spot check of three divisions for the 3-week period ending on 22 September 1944, they were found responsible for 69.6 percent of lost man-days. A considerable number were also caused by *Corynebacterium diphtheriae* (p. 614).

The high incidence of bacterial infections is easy to explain—irregular bathing habits; the difficulties of access to, or lack of access to, facilities for personal hygiene; irritation of the skin by rough clothing; exposure to oils and greases; minor traumatic abrasions incidental to combat; insects bites, which were frequent; patronizing civilian barber shops; and mingling with the native population.

Bacterial infections in the Mediterranean theater fell into two chief groups:

1. Cellulitis, which had its highest incidence in field troops because of lack of facilities for personal hygiene; antecedent trichophytosis, whether treated or untreated; and antecedent insect bites and trauma, including trauma from ill-fitting shoes.

2. Furunculosis, which was extremely frequent, again because of lack of facilities for personal hygiene; the high incidence of scabies reported from all dispensaries and other installations; and repeated chronic reinfections from equipment and clothing.

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[32] See footnote 31, p. 606.

FIGURE 82.—Epidermophytosis with eczematoid dermatitis.

FIGURE 83.—Phagendenic ulcer of lower leg in North African native. Destructive lesions of this degree of severity sometimes developed within 2 to 4 weeks after the initial infection.
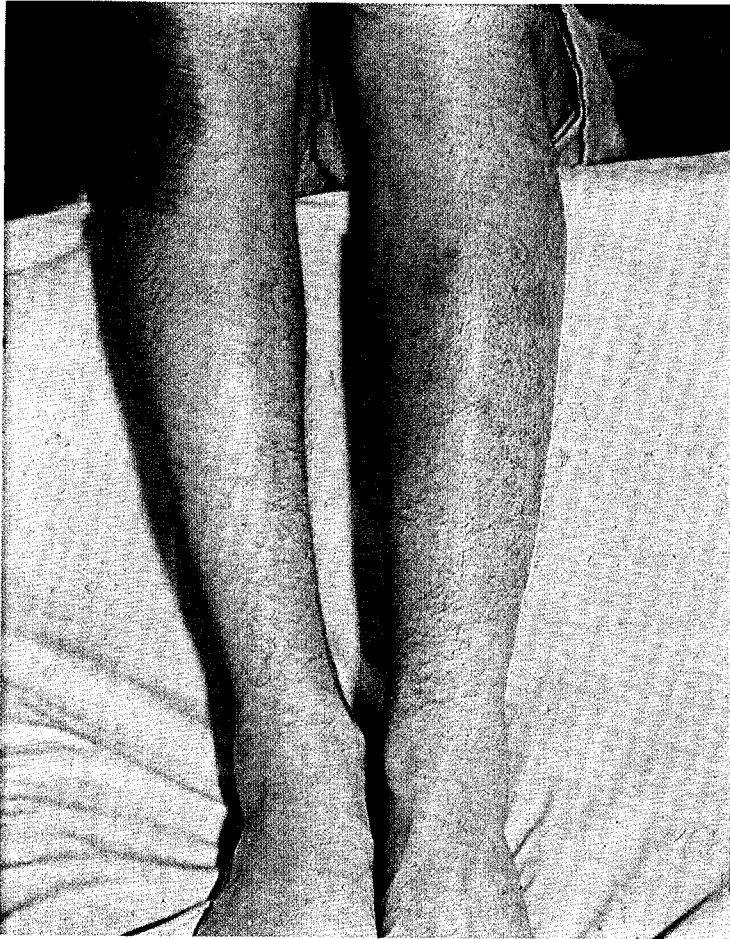
FIGURE 84.—Recurrent erysipeloid infection of lower leg.

Diagnosis of bacterial infections was made by clinical observation, supplemented by laboratory studies (smears and cultures), which were carried out whenever practical before therapy of any kind was instituted. A survey of 50 bacterial infections at one general hospital revealed that 6 distinct groups of diseases were present, including sycosis vulgaris, impetigo contagiosa, impetiginous dermatitis, secondarily infected trichophytosis pedis, generalized furunculosis, in addition to a small group of miscellaneous conditions. In 48 of the 50 cases, the predominant organism cultured was *Staphylococcus aureus haemolyticus. Streptococcus haemolyticus,* which was the sole organism cultured in 2 cases, was also present in 11 of these 48 cases.

Penicillin, which became available in the spring of 1944, proved remarkably effective in the treatment of carbuncles and miscellaneous staph-

ylococcic and streptococcic infections of the skin and subcutaneous tissues. The usual effective dose was 1 million units given in 25,000-unit doses every 3 hours intramuscularly for 5 days or until obvious regression of the lesions. In the 50 cases just described culturally, cure was achieved in 43, and only 4 were entirely unimproved. In 90 cases treated by penicillin in another general hospital, the period of hospitalization was shortened on an average of 12 days per case as compared with 124 cases in which penicillin was not employed. Hot compresses, local antiseptics, and topical sulfonamide therapy were used in conjunction with penicillin therapy, and when necessary, accumulations of pus were incised and drained.

Ecthyma

Zone of Interior.—Ecthyma was one of the most frequent causes of disability in men evacuated from overseas to Fitzsimons General Hospital.[33] The lesions were chiefly on the legs, ankles, and feet, though they also appeared on other portions of the body. Questioning revealed that important antecedent causes were insect bites, small scratches, abrasions, and cuts, particularly cuts caused by coral in the Southwest Pacific Area. Apparently any small abrasion, when constantly macerated by perspiration and infected with surface organisms, could produce ecthymatous ulcers. *C. diphtheriae* was cultured from the lesions of some patients evacuated from the Mediterranean theater, the China-Burma-India theater, and the Pacific Ocean Areas.

Most ecthymas cleared up promptly in the cool, dry climate of Denver. Local treatment consisted of cleansing with soap and water, simple boric acid dressings, and the application of 3-percent ammoniated mercury ointment. Specific medications were unnecessary in most cases, but penicillin parenterally, sulfadiazine orally, or both agents in combination were useful in lesions surrounded by a considerable inflammatory response. Ulcerated areas that were clean but were slow in healing were sometimes managed by the application of Unna's gelatin boot.

Southwest Pacific Area.—Dr. Hopkins, who discussed ecthyma and tropical ulcer under the same heading, noted that ecthyma was usually a mixed infection caused by hemolytic streptococci and hemolytic staphylococci. Unlike impetigo, which was confined to the stratum corneum, ecthyma invaded the deeper epidermis and, at times, the cutis. It usually took the form of discrete lesions covered with a thick crust and somewhat undermined at the border. The location of the lesions on the lower legs and the dorsum of the feet suggested that venous stasis might be a possible factor, though similar lesions were frequently observed on the dorsum of the hands, on the arms, and, occasionally, on the trunk.

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[33] See footnote 20, p. 588.

Deeper ecthymatous lesions often became persistent ulcers. All lesions diagnosed as tropical ulcer that Dr. Hopkins observed in U.S. troops he regarded as deep ecthyma and unrelated to the destructive ulcers seen in the native population.

Ecthyma usually resulted from infection of an insignificant scratch or insect bite. It was extraordinarily prevalent among U.S. troops on the Rosario Front in the Philippines; Dr. Hopkins was informed by battalion officers that, exclusive of battle wounds, 70 to 80 percent of the men who attended sick call complained of these lesions. At the time of his survey, flies were an uncontrollable plague and were probably the chief factor in spreading the infection, for they promptly attacked any exposed bleeding or exuding surface. Two situations explained the presence of flies in such numbers—there had been no time to construct latrines, and enemy dead and dead animals were often inadequately buried because of shellfire.

Bed rest was apparently the most important component of treatment. Healing was usually satisfactory if the part were kept elevated and covered with boric acid dressings. Ambulant patients treated with mercurial antiseptics and sulfonamides improved only moderately. The application of iodine and other irritating solutions caused dermatitis.

Penicillin, however, produced spectacularly good results. Hospitalized patients were treated with penicillin solutions applied as wet dressings. This technique was less practical for ambulant patients, but equally good results were obtained by another method: Crusts were removed as thoroughly (and as atraumatically) as possible, by cutting them off or by wiping them off after they had been moistened with water or peroxide of hydrogen. Penicillin incorporated in a water-miscible base was then applied in a thick layer, which was covered by a gauze dressing. The patient was instructed to keep the dressing moist with water from his canteen. The effect of a wet dressing was thus obtained with the expenditure of only a small amount of penicillin, which was usually in short supply. As soon as exudation was ended, ointment was applied until healing was complete. Exposure to sunlight was helpful during the later stages of healing if covering was not necessary for protection from flies. Whenever practical, the dressing was changed at least once daily, and more often if practical. Every medical officer interviewed by Dr. Hopkins regarded this technique with great favor.

Good results were also reported from the use of penicillin in lanolin or in combinations of lanolin and petrolatum. In general, however, ointments with these bases were not well tolerated in the climate of the Southwest Pacific Area. Droplets of penicillin emulsified in a continuous phase of oil seemed to reach the skin less effectively than in an emulsion in which the continuous phase was aqueous.

The prophylaxis of ecthyma was based on cleaning any visible scratch or traumatic lesion with soap and water. An antiseptic was sometimes added. The use of iodine was not recommended, as it destroyed tissue and

created foci of lowered resistance. Tincture of Merthiolate (thimerosal), Mercresin, and tincture of Zephiran (bensalkonium chloride) were preferable. In the special circumstances that prevailed on the Rosario Front, control of flies was extremely important. Fairly effective protection against them could be obtained, as well as protection against mosquitoes, if the foxhole was covered with a shelter half or a bit of thatch and if a Freon-12 aerosol "bomb" was used. It was found at aid stations that if a bandage was sprayed with Freon-12 aerosol insecticide (the so-called "mosquito bomb") before it was removed and the wound or inflamed area was sprayed as soon as it was exposed, flies could usually be kept from contact with the lesion. DDT was not available until later, but it was thought that it would be even more effective. Under battle conditions, men were prone to neglect anything they considered unessential to their safety, but if they were properly instructed and were provided with the mosquito bomb, it was found that they were likely to use it.

Impetigo

Ordinary impetigo of the face was frequently encountered in the Southwest Pacific Area under battle conditions. Numerous lesions of the toes and feet that were essentially impetiginous were also encountered. These lesions occurred on the face in the form of large, discrete pustules, which ruptured quickly, in contrast to lesions on the feet, which tended to remain intact and to penetrate the underlying soft tissues. A survey of dermatoses in the 43d Infantry Division by Capt. Charles S. D'Avanzo, MC, showed that they tended to occur most frequently in men who sweated excessively. It was generally observed that inadequately treated impetigo tended to persist longer in the Tropics than in temperate climates.

Another eruption, variously called tropical impetigo, pyosis Mansoni, or bullous impetigo, was widely prevalent. The characteristic lesion was a flaccid bulla, from 5 to 8 millimeters in diameter, filled with thick, purulent fluid, often without surrounding erythema. These lesions occurred in groups, especially just below the axillary fold and in and below the groin. They appeared only on the parts of the body covered by clothing. Cultures were reported to show Staphylococcus aureus, and clinically the lesions resembled the type of staphylococcic impetigo observed in troublesome epidemics in the newborn. It was Dr. Hopkins' opinion that so-called tropical impetigo resulted from excessive sweating and was closely related to skin conditions of miliarian etiology. He did not consider contagion important. He observed a number of extremely interesting generalized eruptions on the trunk that appeared to be circinate impetigo. They simulated dermatophytosis of the trunk so closely that differential diagnosis was difficult. No fungi could be found after repeated search.

Treatment directed toward aeration of the skin and prevention of sweating was apparently much more important in the management of these

cases than the application of antiseptics. When circumstances permitted, patients were allowed to remove their shirts and take short sunbaths. Bathing the skin with a mild antiseptic or antipruritic lotion was useful, as was the use of talc or foot powder. In obstinate cases, rupture of the bullae and painting of their bases with 10 percent silver nitrate usually effected a cure.

Pyogenic Intertrigo of the Feet and Groin

Many of the intertrigos of the feet in the Southwest Pacific Area that were inflamed and troublesome were apparently pyogenic in origin, though the general assumption was that the infection was secondary to an original fungal infection. Dr. Hopkins thought there was little reason for this assumption, since fungi could seldom be demonstrated.

Reliable differentiation of these lesions from dermatophytosis was impossible without laboratory study, which was frequently not practical (p. 604). Certain clinical criteria, however, were useful: The lesions were more likely to be pyogenic than mycotic if (1) the patient suffered from hyperhidrosis; (2) the inflammation was more pronounced on the dorsal than on the plantar aspect of the feet; (3) there was about equal involvement of all the toes; (4) the skin was red and edematous and there was weeping from pinpoint vesicles; (5) the patient complained of pain rather than itching; and (6) pustules were present on the dorsum or the sole.

Without facilities for laboratory diagnosis, the best plan was to treat these very common dermatoses of the feet with penicillin ointment or wet dressings and to resort to fungicides only if there was no improvement or only slight improvement. Instances were observed in which a change of therapy from penicillin to fungicides resulted in prompt cures of hitherto refractory lesions. Since the causes of intertrigo of the feet were probably the same as those of dermatophytosis, the same methods of prophylaxis were employed.

Intertrigos of the groin of pyogenic and seborrheic origin rather than mycotic origin were rather frequently encountered.

Diphtheria[34]

Zone of Interior.—In the detailed study of skin conditions made at Foster General Hospital, it was found that in indolent cutaneous ulcers organisms of the diphtheria group, which in most instances were biologically avirulent, could often be recovered. In August 1945, a special investigation of cutaneous diphtheria and tropical ulcers included a survey of all incoming patients with medical and dermatologic conditions. These patients were studied bacteriologically and by the Schick test, and special attention was

[34] McGuinness, Aims C.: Diphtheria. *In* Medical Department, United States Army. Preventive Medicine in World War II. Volume IV. Communicable Diseases. Washington: U.S. Government Printing Office, 1958, pp. 167–189.

paid to those received from tropical theaters. All hospital personnel were also Schick tested.

Of 70 patients admitted to isolation wards because of the proved or suspected presence of diphtheria bacilli, 56 had ulcerative lesions. Two patients with faucial diphtheria were identified in this group, and 12 suspected or proved faucial carriers were found.

Therapy of the ulcerative lesions consisted of dressings of physiologic salt solution; local or parenteral penicillin therapy; or combined local and parenteral penicillin therapy. Local application of penicillin was generally the preferable treatment.

Mediterranean theater.—In a survey of bacterial lesions in 6 hospitals in the Mediterranean theater, 32 cases were found in which the diagnosis of cutaneous diphtheria had been made. Although this was a rather large number of cases in itself, it was thought that the condition was even more frequent than the figures suggested and that additional instances would be found if there were a more diligent effort to culture the organisms, especially when faucial diphtheria was present in the local area. Of the 32 patients, 2 died, both of myocarditis, and 2 others survived serious complications (myocarditis with cardiac failure, peripheral neuritis).

Nothing in the clinical appearance of a diphtheritic ulcer distinguished it from other ulcers. Diagnosis was possible only by culture, but certain suggestive observations were made:

1. The lesions were painful when they were exposed to air.
2. The lymphatics draining the ulcers showed noninflammatory hypertrophy in the form of thickened vocal cords.
3. The regional lymph nodes were enlarged.
4. All forms of therapy failed except penicillin.

Most instances of diphtheria in the Mediterranean theater occurred before penicillin became generally available. It was important to remember that this agent so altered the bacterial flora of cutaneous ulcers that cultures positive for *C. diphtheriae* could not be obtained. In other words, a man might have cutaneous diphtheria and might be improving under penicillin therapy but at the same time be harboring toxins from which polyneuritis, myocarditis, and other serious complications might develop.

Once the diagnosis of diphtheria was established, 100,000 units of diphtheria antitoxin were given. If the patient demonstrated any of the clinical features typical of absorption of diphtheria toxins, and if he had a cutaneous lesion possibly caused by *C. diphtheriae,* the antitoxin was given without waiting for the results of cultures.

European theater.—Diphtheria cutis occurred in the European theater but was uncommon as compared with its incidence in the Pacific Ocean Areas and the China-Burma-India theater. The small number of cases, however, engendered lack of suspicion, and there were sometimes dangerous delays in diagnosis. In one of the first cases observed in the theater, for

instance, myocarditis appeared before it was realized that an ulcer on the genitalia was diphtheritic and not an unusual type of venereal disease.

Southwest Pacific Area.—In his survey of dermatologic disease in the Southwest Pacific Area, Dr. Hopkins observed that at several bases virulent diphtheria bacilli had been recovered from chronic ulcers resembling those usually described as ecthyma (p. 610). He believed that several other exceptionally deep and necrotic ulcers that he observed might also be of the same origin. There was little doubt that the paralyses reported in these cases were diphtheritic. Major Webster, at the 13th General Hospital, was able to recover diphtheria bacilli from eczematous lesions of the eyebrow, paronychia of the toe, suppurating keratosis of the heel, and otitis externa. Brigadier Robert M. B. MacKenna, RAMC, Consulting Dermatologist to the British Army, made a study of diphtheria of the skin in Iraq in 1944.[35] He reported acute bullous diphtheria on the basis of previous erythema; diphtheritic cellulitis that often went on to ulceration; and a chronic type of cutaneous diphtheria that simulated infectious eczematoid dermatitis.

Diphtheria bacilli were seldom isolated from cutaneous lesions in the Southwest Pacific Area, except in patients known to have been exposed to pharyngeal diphtheria. Mixed streptococcic-staphylococcic infections could produce ulcers clinically indistinguishable from most of those from which the Klebs-Löffler bacillus was recovered. It was Dr. Hopkins' opinion that the bacilli found in most cutaneous lesions in the Southwest Pacific Area were secondary invaders and that, if there was sufficient exposure, they could infect any severely damaged area of skin. He doubted that they could invade normal skin. Their presence sometimes seemed to have no effect on the clinical picture, but they sometimes increased the severity and chronicity of the lesions, and in a few instances, they seemed responsible for regional or distant paralyses.

Most diphtheritic infections of the skin responded well to dressings wet with penicillin solution. Some healed only after antitoxin was given. Brigadier MacKenna recommended the use of antitoxin in all cases, but Dr. Hopkins did not consider the information then available (1944–45) sufficiently conclusive to warrant the recommendation of definitive policies. He emphasized the risk of contagion, considering skin lesions at least as dangerous as pharyngeal diphtheria as a source of infection, and perhaps more dangerous.

China-Burma-India theater.—The whole group of tropical dermatoses was of little significance in China-Burma-India as regards total disability except for cutaneous diphtheria, which can properly be classified as a tropical disease since it is very much more common in hot, humid climates than in temperate climates. In this theater in the summer of 1944, during and after the Myitkyina campaign, its incidence reached epidemic proportions. Capt. (later Maj.) Harvey Blank, MC, Chief of Dermatology and

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[35] MacKenna, R. M. B.: Notes on Military Dermatology. Brit. J. Dermat. 56: 1–11, January 1944.

Syphilology at the 69th General Hospital, reported 70 cases, and Major Livingood and his associates observed 140 at the 20th General Hospital.[36] In most instances, the disease was contracted initially in Burma, but later cases were contracted in Assam, and some occurred in hospital personnel who were attending infected patients.

Cutaneous diphtheria occurs in epidemic form under the following circumstances:

1. A significant percentage of exposed individuals must be susceptible to the infection.

2. There must be a source of diphtheritic infection. Among military personnel, the source was either the native population or a high carrier rate in their group.

3. Factors must exist which make for multiple superficial traumata to the skin. Poor personal hygiene and close personal contact must prevail.

All these circumstances were present in the Mitykyina combat area during the campaign which began in the latter part of May 1944 and ended the first week of August 1944. The high incidence of leech and other insect bites and the constant maceration of the skin, combined with lack of bathing and laundry facilities, predisposed to superficial abrasions and cutaneous infections of all types. The epidemic of cutaneous diphtheria that ensued reached its height during combat activities and the hot, humid monsoon (rainy) season, and decreased after the cessation of fighting, the advent of cooler weather, and improved facilities for personal hygiene.

According to Captain Blank, neurologic complications occurred in about 40 percent of all cases of cutaneous diphtheria, and cardiac complications occurred in about 5 percent. Other studies bore out these figures.[37] There were two deaths, both caused by myocarditis.

Almost all patients with cutaneous diphtheria required at least 4 months of hospitalization before their return to duty. The slow healing of the lesions was characteristic. On the average, skin ulcers persisted for about 3 months. In 6 of the 140 patients observed at the 20th General Hospital, the lesions were still unhealed at the end of 6 months.

It should be emphasized that almost all the patients who contracted diphtheria in the China-Burma-India theater had secondary diphtheritic infection of skin lesions, such as insect bites. None of them had faucial diphtheria, and diphtheritic infection of surgical wounds was extremely uncommon.

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[36] Livingood, C. S., Perry, D. J., and Forrester, J. S.: Cutaneous Diphtheria: A Report of 140 Cases. J. Invest. Dermat. 7: 341–364, December 1946.

[37] (1) Gaskill, H. S., and Korb, M.: Occurrence of Multiple Neuritis in Cases of Cutaneous Diphtheria. Arch. Neurol. & Psychiat. 55: 559–572, June 1946. (2) Kay, C. F., and Livingood, C. S.: Myocardial Complications of Cutaneous Diphtheria. Am. Heart J. 31: 744–756, June 1946.

Acne

Zone of Interior.—The survey of skin conditions (fig. 85) at Fitzsimons General Hospital [38] showed oily skins and seborrheic dermatitis to be less frequent there than in similar civilian groups, probably because of the vigorous outdoor activity that was a part of military life in the United States. Acne vulgaris (often called tropical acne) was, however, definitely activated by military service in the Tropics, particularly in older men, many of whom were returned from overseas to this hospital.

A typical history revealed that the patient had had some trouble with blackheads and acneiform lesions when he was 15 to 18 years of age, but none since, including his period of training in the Zone of Interior. Trouble began, however, some 6 months after his arrival in the Southwest Pacific Area or some other tropical area. The first manifestation was the development of large, tender, inflammatory cystic lesions on the shoulder and back, which made it impossible to carry a pack. After he was treated for a considerable time by the battalion surgeon, sometimes in a forward hospital and occasionally in a general hospital, the patient was evacuated to the Zone of Interior.

Such patients, on their arrival, presented the usual combination of comedones, papulopustular lesions, and numerous deep, inflammatory, tender cystic lesions from which oily, purulent material could be expressed. Many lesions, particularly on the dorsal surface of the neck, shoulders, hips, and thighs, had become confluent. Extension over the buttocks and over the dorsal and lateral surfaces of the thighs was not uncommon in these patients, though such an extension is seldom observed in acne vulgaris seen in civilian practice.

Most acne vulgaris observed at Fitzsimons General Hospital originated in tropical theaters, in combat troops who had been deprived of proper bathing facilities and who had been in an environment characterized by extreme heat and poor hygienic conditions for long periods of time. This disease was not observed in supply or garrison troops evacuated from tropical theaters or in men evacuated from the European theater. In that theater, it was a condition of no consequence.

Southwest Pacific Area.—In his survey of skin conditions in the Southwest Pacific Area in 1944–45, Dr. Hopkins was impressed with the complications that could arise from the type of acne characterized by double comedones and cysts, even in men who had had little trouble with acne in civilian life. The original lesions became very large, exquisitely tender, and suppurative. If packs were carried, the infected cysts often ruptured, and rupture was followed by painful ulceration.

Treatment was not satisfactory. The care required to evacuate and dress multiple individual lesions was more than could be afforded in a mili-

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[38] See footnote 20, p. 588.
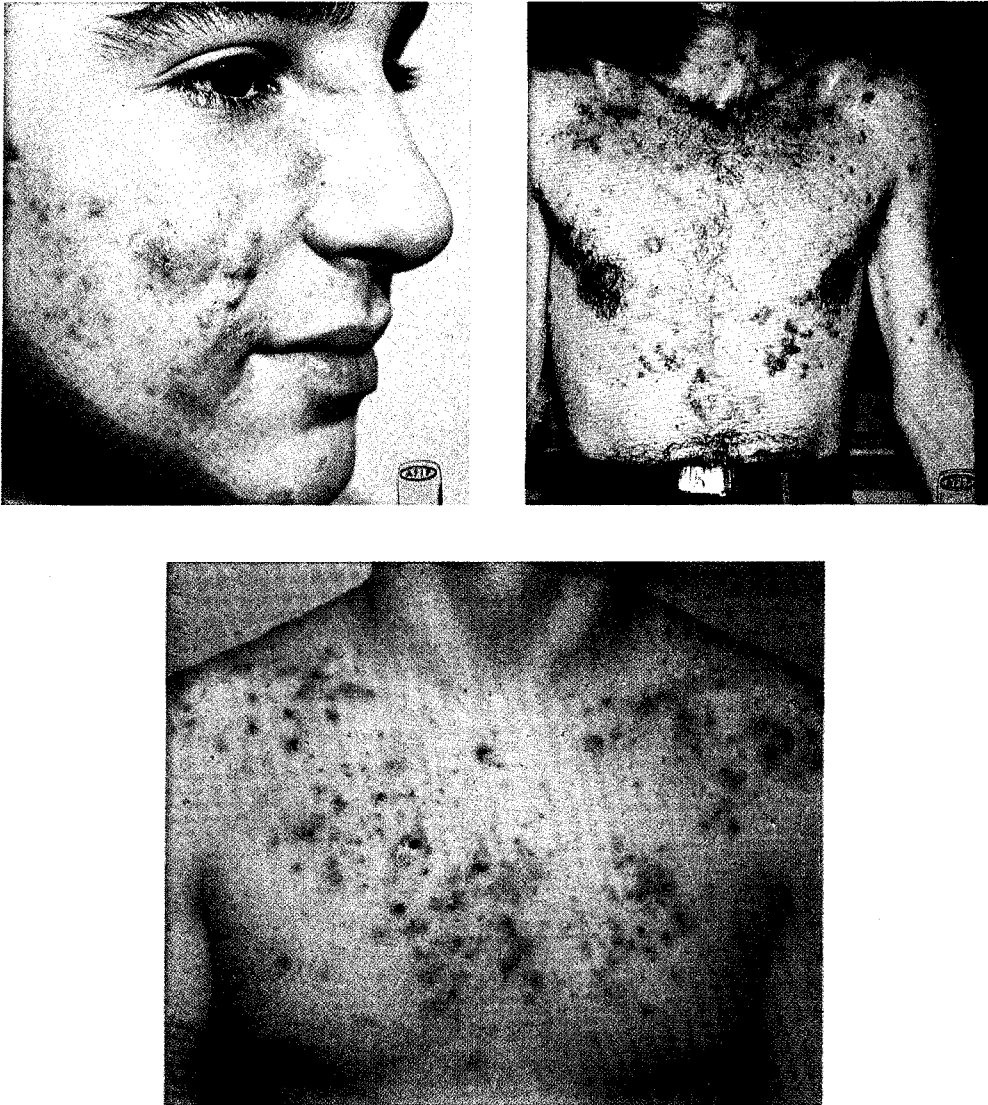
FIGURE 85.—Acne vulgaris. A. Cystic acne of face. B. Subsiding tropical acne of trunk. C. Extensive acne of chest and shoulders.

tary hospital. Some men were returned to duty after drainage of the suppurative lesions and treatment with sunbaths, hotpacks, and drying lotions, but relapses were prompt. In Dr. Hopkins' opinion, the SWPA policy of hospitalization of men with relatively mild acne was unwise. He believed that they should be kept on duty as long as possible and that, if the lesions became severe enough to require hospitalization, immediate return to the Zone of Interior was preferable, because of the risk of relapse after any treatment.

China-Burma-India theater.—The experiences in Burma and India with acne was much the same as in the Southwest Pacific Area. There was a notable tendency for the condition, particularly the cystic type (acne conglobata), to increase in severity after affected individuals had been overseas for a short time. The development of large, painful cystic lesions on the shoulders, back, neck, and face resulted in varying degrees of disability. It was necessary to hospitalize many of these patients for prolonged periods. Exacerbations were common after they had been returned to duty, and it soon became obvious that the best course to follow was the evacuation of men with severe cystic acne to the Zone of Interior.

Miliaria

The condition loosely known as prickly heat (fig. 86) was one of the three dermatologic diseases most frequently encountered in the Tropics, and all Army and Navy dermatologic statistics placed it near the top of the list.[39] It was also something of a problem in the Zone of Interior.

Zone of Interior.—The clinical picture of miliaria in the Zone of Interior was usually typical. The eruption, which was originally confined to the flexural and intertriginous areas of the body, was a brightly erythematous, follicular, vesicopapular dermatitis. It tended to flare up during the heat of the day and subside at night. Pruritus was usually intense, and many patients also complained of severe burning. As time passed without treatment, the eruptions became more and more extensive and, after varying periods, failed to involute during the night. Its character also changed; it became more inflammatory and more fixed, and individual lesions appeared as single hypertrophic sweat glands. When perspiration was excessive, the papules were capped with small, hard vesicles.

Miliaria was one of the conditions associated with dysfunction of the sweat apparatus that were not incapacitating in themselves but that had a propensity for damaging the protective barriers of the skin and thus increasing the tendency to both mycotic and pyogenic infection. Impetigo contagiosa and bullous impetigo were frequent complications.

Southwest Pacific Area.—Miliaria was widely prevalent and extremely troublesome in the Southwest Pacific Area. British observers, according to Dr. Hopkins, considered it to be a *Monilia* infection, and it was generally believed to be caused by sodium depletion. He considered both theories worth further investigation.

The usual routine of management was exposure to air and sun and application of drying and cooling lotions. No form of therapy was really satisfactory.

According to Dr. Hopkins, a condition generally known as heat rash was even more common in the Southwest Pacific Area than true vesicular

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[39] The others were Atabrine dermatitis and bacterial infections.

FIGURE 86.—Miliaria rubra.

miliaria. It took the form of blotchy, red, wheal-like eruptions that appeared suddenly on the trunk after exposure to heat. The condition was not described in texts, and he thought that both etiology and therapy should be investigated.

DERMATITIS VENENATA

Zone of Interior.—Contact dermatitis (figs. 87, 88, 89, and 90) was a rather frequent form of disability in soldiers observed in outpatient clinics and on dermatologic sections in Zone of Interior hospitals. As a rule, a single agent was responsible for only small numbers of cases and was therefore of no particular military importance, though this was not always true. The so-called rubber dermatitis seen early in the war is an illustration. The etiologic agent was the rubber used in gas masks, and the dermatitis characteristically appeared on the forehead, the chin, and the lateral aspects of the cheeks. The responsible agents were probably the antioxidants and accelerators used in the manufacture of the rubber. Men who were sensitive to them were provided with gas masks of different manufacture, such as the older black rubber type or the cloth-impregnated type.

Rhus toxicodendron (poison ivy) was the most frequent cause of plant dermatitis (figs. 87 and 88), but dermatitis caused by ragweed and marsh elder was also relatively frequent.
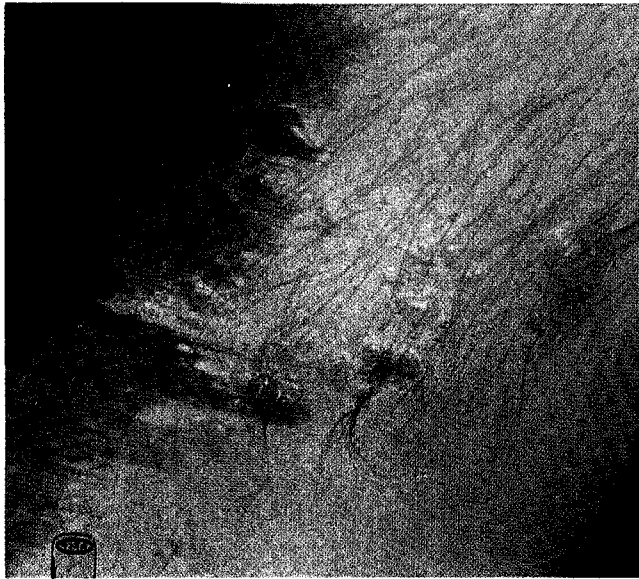
FIGURE 87.—Reaction to poison ivy.
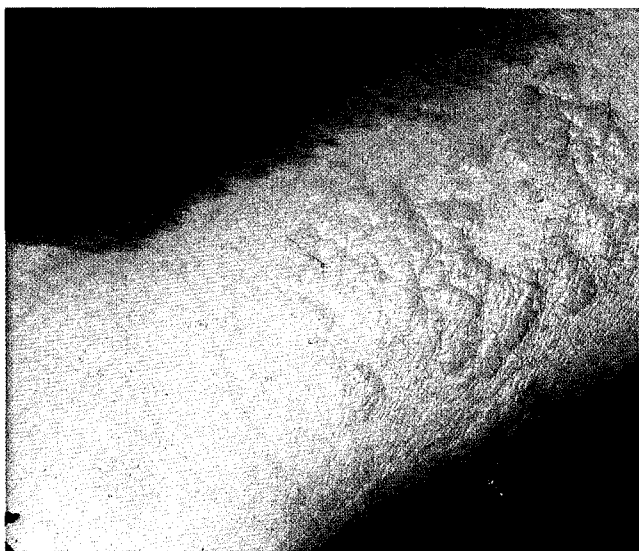
FIGURE 88.—Reaction to poison ivy.
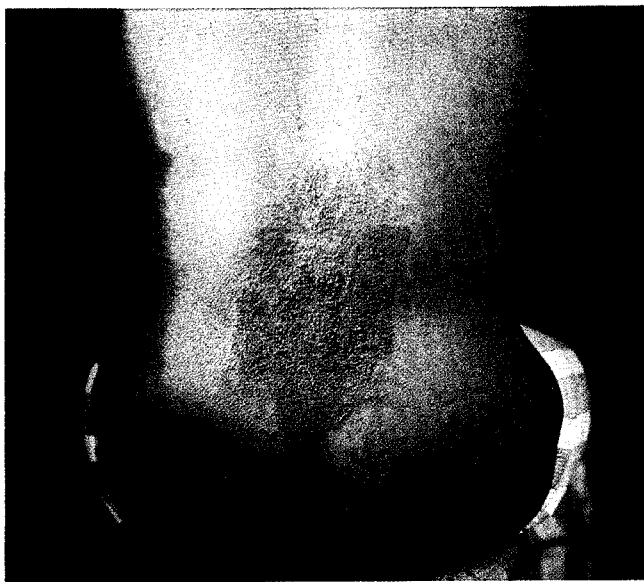
FIGURE 89.—Reaction to Merthiolate (thimerosal) applied
before spinal puncture.

FIGURE 90.—Reaction to elastic in shorts.

The experience at Fitzsimons General Hospital [40] and other hospitals in the United States indicated that sensitization and primary irritant reactions caused by topical medication were more significant and more frequent causes of disability than other types of contact dermatitis. Dermatologists in the Zone of Interior, observing the cases of contact dermatitis due to the unwise use of Whitfield's ointment in the treatment of acute and subacute dermatitis, took the position that correct training of battalion surgeons and other medical officers doing dispensary practice would have resulted in a considerable decrease in the incidence of the so-called overtreatment syndrome. Their reasoning seems particularly sound when one recalls that in some oversea theaters, dermatologic diseases accounted for as much as 75 percent of dispensary practice.

Sulfonamides were also responsible for a high incidence of dermatitis medicamentosa in Zone of Interior hospitals. As time passed, the original routines were modified in the light of experience, but many medical officers failed to learn the lesson and continued to use sulfonamide ointments in the treatment of pyogenic infections as well as for other cutaneous diseases. Some of the most serious drug reactions encountered were the generalized id type of sulfonamide dermatitis first reported by Major Livingood and Colonel Pillsbury.[41] Several patients in this group were seriously ill for as long as 4 to 6 weeks. Other sulfonamide reactions were reported by Peterkin,[42] Weiner,[43] and Cohen and his associates.[44]

Mediterranean theater.—In the Mediterranean theater, true dermatitis medicamentosa (fig. 91) was infrequent, which is remarkable, considering the widespread administration of drugs capable of producing rashes, particularly the sulfonamides and barbiturates. Reactions to the sulfonamides most often followed their topical use on moist, eczematized lesions. Subsequent exposure to sunlight precipitated the appearance of eruptions on exposed parts, and oral medication after local sensitization sometimes precipitated exfoliative dermatitis.

Dermatitis venenata, especially of the face, ears, and eyelids, was frequently reported in men preparing penicillin solutions for injection. Once the danger was realized, enlightened techniques usually permitted individuals who had been sensitized to penicillin to work safely with it.

Contact dermatitis ordinarily responded promptly to avoidance of the offending contact and the use of soothing and drying topical agents. Local therapy with sulfonamides was discouraged because sensitization to it after

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[40] See footnote 20, p. 588.

[41] Livingood, C. S., and Pillsbury, D. M.: Sulfathiazole in Eczematoid Pyoderma; Sensitization Reaction in Successive Local and Oral Therapy; Report of 12 Cases. J.A.M.A. 121: 406–408, 6 Feb. 1943.

[42] Peterkin, G. A. G.: Skin Eruptions Due to the Local Application of Sulphonamides. Brit. J. Dermat. 57: 1–9, January–February 1945.

[43] (1) Weiner, A. L.: Cutaneous Hypersensitivity to Topical Application of Sulfathiazole. J.A.M.A. 121: 411–413, 6 Feb. 1943. (2) Weiner, A. L.: Cutaneous Eruptions Following Topical and Oral Sulfathiazole (Correspondence). J.A.M.A. 123: 436, 16 Oct. 1943.

[44] Cohen, M. H., Thomas, H. B., and Kalisch, A. C.: Hypersensitivity Produced by the Topical Application of Sulfathiazole. J.A.M.A. 121: 408–410, 6 Feb. 1943.
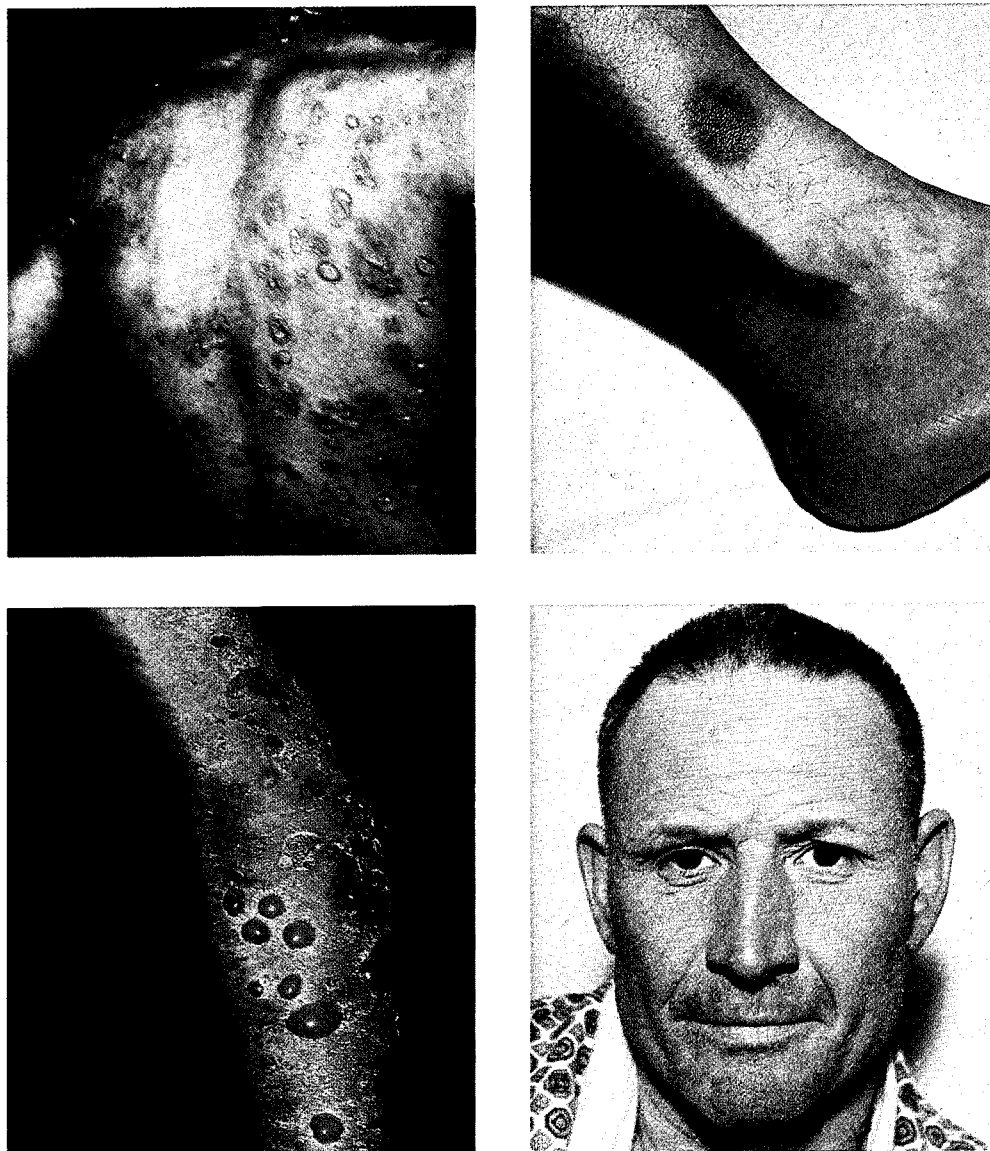
FIGURE 91.—Drug eruptions. A. Bullous dermatitis medicamentosa caused by sulfa-thiazole. B. Fixed drug eruption caused by phenolphthalein. C. Bullous erythema multi-forme. D. Diffuse photosensitivity reaction.

its topical use prevented its later administration in infections in which such therapy might be lifesaving.

Plant dermatitis was conspicuously absent in the Mediterranean the-ater, because of the absence of common plant offenders. Contact with gaso-lines and oils, however, was often the cause of a refractory dermatitis and folliculitis, which sometimes required change in duty assignments. Deter-

gents used for dishwashing sometimes produced a severe dermatitis, which was responsible for a large loss of man-days among Italian civilians working in Army kitchens.

European theater.—Contact dermatitis was extensively prevalent in the European theater, but since poison ivy is not indigenous to the British Isles or continental Europe, there were no cases of that origin.

The topical application of sulfonamide ointments was responsible for many cases of contact dermatitis, sometimes with associated photosensitivity. After penicillin became available, dermatitis caused by it became increasingly frequent, and as in the Mediterranean theater, it occurred in hospital teams engaged solely in the preparation and administration of penicillin solutions.

In retrospect, many dermatologists who had served in the European theater expressed the opinion that, in spite of their immediate value, it might have been better if topical sulfonamide and penicillin preparations had not become available, for individuals who became sensitized to them from their local use frequently had systemic reactions when either agent was used, either orally or parenterally, for more serious conditions.

Southwest Pacific Area.—There were some reports of acute but short-lived eruptions from contact with unidentified plant or animal life encountered in sea bathing in New Guinea, but as a rule, dermatitis from contact with plants was a problem of minor importance in that area.

Dermatitis venenata in New Guinea was also reported as caused by the sap of palms used in building bridges and other structures. It began on exposed areas but often became generalized. The eruption was sometimes severe but did not last very long. Dr. Hopkins did not observe any instances of this type of dermatitis himself, but obtained his information about it from Maj. Delmar R. Gillespie, MC, at the 233d Station Hospital, who had studied it carefully.

China-Burma-India theater.—A number of special forms of contact dermatitis were observed in military personnel stationed in China-Burma-India:

1. Tree sap dermatitis was caused by contact with the foliage and sap of certain indigenous trees encountered by the Corps of Engineers when they were clearing the forest in the early stages of construction of the Ledo (Burma) Road in Assam and Burma. Contact caused considerable disability in susceptible personnel, who amounted to some 15 to 20 percent of those exposed and represented the manpower loss of several hundred badly needed workers. The sap of these trees (family Anacardiaceae) was originally milky-white, but on contact with air it turned black or dark red.

2. In some areas of India and Burma, a lacquer prepared from another tree of the Anacardiaceae family and used to paint toilet seats gave rise to dermatitis of the anogenital area in susceptible individuals.

3. The most interesting type of contact dermatitis encountered in China-Burma-India was the result of sensitivity to the substance used by native washermen (dhobies) for marking clothes to be laundered.[45] Soon after the 20th General Hospital arrived in the theater and its personnel sent their clothes to be laundered by dhobies, a small epidemic of patchy dermatitis made its appearance. The eruption always involved, singly or in several areas, the nape of the neck, the upper back, the waistline (anterior, posterior, or unilateral), the lateral aspects of the ankles, the dorsal surface and sides of the feet, and the lower third of the legs. It soon became apparent that these circumscribed patches of dermatitis exactly corresponded with the parts of the body in contact with the laundry mark used by the dhobies. They marked shirts on the collar, which accounted for the localization of the dermatitis on the dorsal surface of the neck. Shorts were marked on the waistband, socks at various places, and nurses' brassieres at the point at which the strap was attached to the cup (fig. 92).

Dhobie mark dermatitis was characterized by intense pruritus, vesiculation, oozing, and, in some instances, a more or less chronic eczematoid
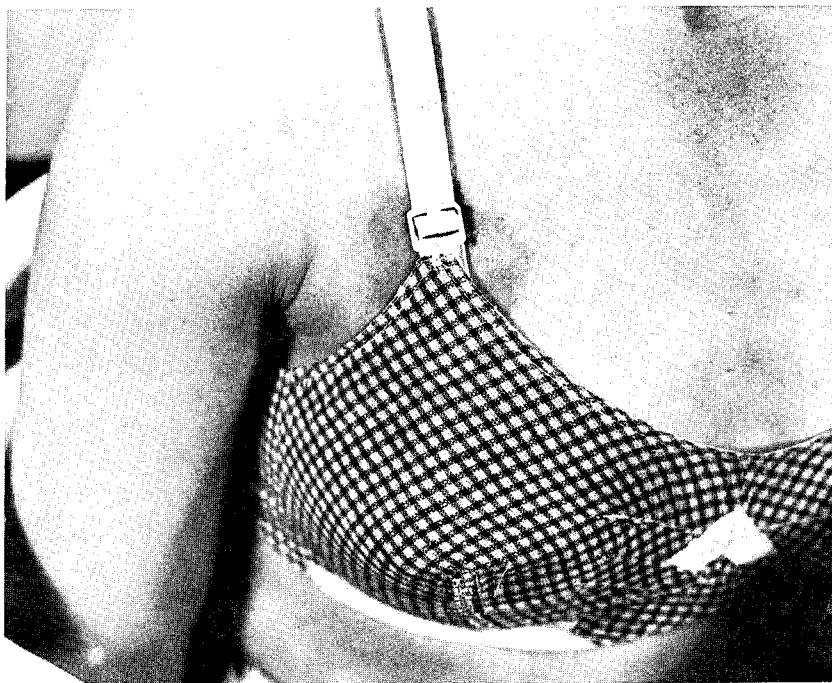
FIGURE 92.—Dhobie mark dermatitis. The skin involvement corresponds exactly with the dhobie laundry mark which is just under the buckle of the brassiere strap at its attachment to the cup.

[45] Livingood, C. S., Rogers, A. M., and FitzHugh, T.: Dhobie Mark Dermatitis. J.A.M.A. 123: 23–26, 4 Sept. 1943.

reaction. The intensity of the process depended upon the sensitivity of the individual. The incidence of the condition was some 15 to 20 percent of those exposed.

Investigation of the condition at the 20th General Hospital in Assam in collaboration with the Forest Research Institute in Derha Dun, India, and the Indian Botanical Institute in Calcutta resulted in the identification of the offending trees as members of the Anacardiaceae family. This family includes poison ivy, poison oak, sumac, the cashew nut tree, the Bhilawanut tree, and the Japanese lacquer tree. Persons sensitive to poison ivy will almost always be sensitive to the nut of the Bella gutti tree, the sap of which the dhobies were using for laundry marks, as well as to other plants and trees of this family.

When the native washermen were questioned, it was found that the marking fluid they were using was obtained from the nut of the Ral or Bella gutti (Bhilawanut) tree, which grows all over India. A straight pin was pushed through the hard capsule of the nut, and enough brown or black fluid adhered to it for the marking of garments with small crosses, dots, or lines in varying identifying combinations. The marks were fairly permanent and withstood repeated washings.

The term "dhobie itch" had been in use in dermatology for some time. Sutton and Sutton,[46] in the 1935 edition of their textbook on diseases of the skin, defined it, with washerman's itch as a synonym, as tropical epidermatophytosis, corresponding to eczema marginatum observed in other climates. They pointed out that symptoms were greatly exacerbated by warmth and perspiration and that violent scratching and secondary pyogenic infections often rendered the parts raw and inflamed, so that impetigo, infectious eczematoid dermatitis, and even furunculosis might result.

In India and other countries, the terms "dhobie itch" and "tinea cruris" seem to have been used more or less interchangeably for many years. The explanation was that the nomenclature was associated with the premise that clothing was infected by the dhobies when it was washed. The concept was entirely erroneous. It was never demonstrated that cutaneous fungal infections were transmitted via clothing washed by dhobies. On the contrary, the World War II experience showed that dhobie-mark dermatitis was exactly what the term implies, a contact dermatitis caused by an allergen, the marking fluid, which is not unlike the allergen that causes *Rhus* dermatitis.

PSORIASIS

Mediterranean theater.—Psoriasis was not a problem in the Mediterranean theater because of its frequency. The difficulties connected with it,

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[46] Sutton, Richard L., and Sutton, Richard L., Jr.: Diseases of the Skin. 9th ed. St. Louis: C. V. Mosby Co., 1935.

like those connected with seborrheic dermatitis (figs. 93 and 94), arose from the chronicity of these diseases, their resistance to treatment, and their tendency to recurrence. The causes of both were unknown, but it was recognized that good personal hygiene, if it did not prevent them entirely, at least maintained the underlying dermatitis at a subclinical level. Exposure to direct sunshine was of prophylactic as well as therapeutic value. Cold, wet weather had a particularly adverse influence on psoriasis, and patients seeking treatment for it increased sharply in numbers as winter came on.

In addition to sunlight, certain other measures were at least temporarily successful, including local applications of tar, resorcin (resorcinol), and chrysarobin (Goa powder). With the use of these agents, it was possible to discharge the majority of patients to duty, but relapses were frequent and repeated hospitalization was necessary. When the condition developed or became apparent overseas, relapses could be reduced by assigning the men to duty in base sections or other areas where good personal hygiene was possible and specialized medical care was available. This was not a desirable expedient, however, and it was the conclusion of dermatologists in the Mediterranean theater that it was highly questionable whether men with significant psoriasis and seborrheic dermatitis should ever be sent overseas. There was no doubt at all that only in the most unusual circumstances should they be assigned to combat units.

There was also an important psychic factor in psoriasis. Men with this disease, who understood their problems and adjusted to them, could be given what medicine had to offer and returned to their units, occasionally even to combat units. Often they became sterling soldiers. Others, however, when the going became hard, were willing to use their disease as a means of getting into the hospital or being sent home. It is fair to assume that perhaps 20 percent of all patients with seborrheic dermatitis and psoriasis became liabilities rather than assets to the troops in the Mediterranean theater and had to be evacuated to the Zone of Interior.

Observations at Fitzsimons General Hospital [47] bore out these conclusions. The histories showed that good soldiers had ignored their disease and continued on duty until they were incapacitated, while others who were indifferent to their responsibilities continued to report at sick call until they were hospitalized and returned to the United States.

Southwest Pacific Area.—Dr. Hopkins' 1944–45 survey of dermatologic conditions in the Southwest Pacific Area revealed only a few instances of severe psoriasis.

PARASITIC INFECTIONS

Parasitic infestations (scabies and pediculosis) were among the major sources of disability in the American and British Expeditionary Forces in

[47] See footnote 20, p. 588.
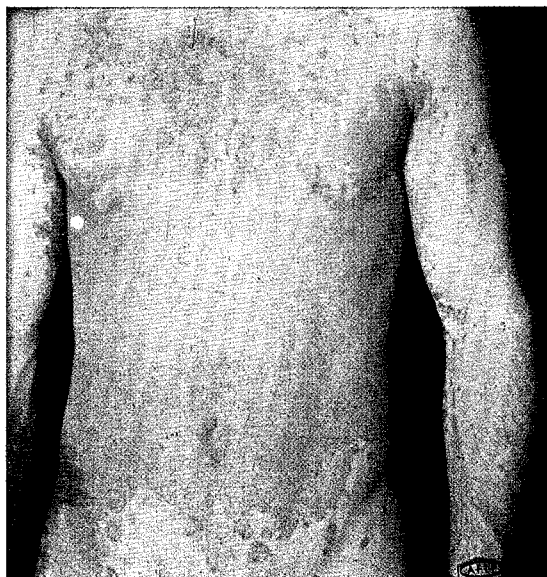
FIGURE 93.—Extensive acute psoriasis of trunk.
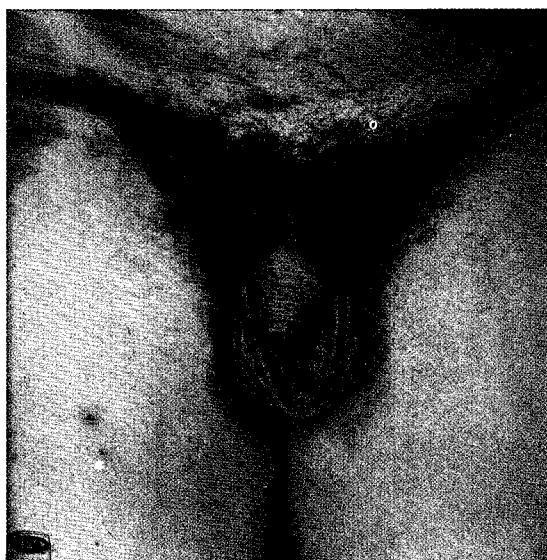
FIGURE 94.—Acute seborrheic dermatitis of supra-
pubic and crural region.

World War I. The principal reasons were not the primary infestation but the sequelae of secondary bacterial infection and chronic dermatitis from excoriation and overtreatment.

In World War II, scabies was very common in some theaters, but pediculosis was a most infrequent reason for seeking medical attention.

Mediterranean theater.—Parasitic infestations of the skin accounted for 4 to 18.5 percent of the admissions to dermatologic services in six hospitals in the Mediterranean theater surveyed in 1943, with the great majority of cases scabies. These percentages cover only primary diagnoses and require some explanation: It was repeatedly noted in this theater that patients who presented themselves for treatment for furunculosis, pyoderma, cellulitis, impetigo, and similar conditions were referred with those diagnoses, while the coexisting parasitic infestation, which frequently was the underlying cause of these infections, was either reported as a secondary diagnosis or was not reported at all. It is therefore fair to conclude that the actual prevalence of parasitic diseases in this theater was higher than collected statistics indicate. This consideration is of special importance in the evaluation of figures collected from forward hospitals, where opportunities for examination with the patient stripped, in a good light, and for detailed history taking were frequently lacking.

Pediculosis, sample checks showed, was not frequent in the Mediterranean theater. Over a 3-week period in 1944, no cases were reported from the 34th, 85th, and 88th Infantry Divisions; none were reported from 10 hospitals surveyed in the spring of 1944, and none from the Fifth U.S. Army for the week of 15–22 September 1944. For the entire year, only 2 cases were reported from the 64th General Hospital and only 11, from the 8th Evacuation Hospital.

Soldiers with pediculosis pubis frequently treated the condition themselves with aerosol bomb sprays or blue ointment, and an occasional patient presented himself with dermatitis caused by such self-treatment. There was no doubt that aerosol sprays would kill the irritating parasite and that repeated applications of blue ointment to infested areas would kill both adults and eggs, but less irritating methods were more desirable. Pubic lice were readily eliminated by the application of calomel ointment on 2 successive days. For head lice, the hair was cut short and the head was shampooed for 3 successive nights with a mixture of 1 part kerosene to 3 parts of hot, soapy water. Both patient and clothing were sprayed with Army louse powder, which was extremely efficient.

The most frequent parasitic infection in the Mediterranean theater was scabies, caused by the itch mite *Acarus scabiei hominis*. The condition was acquired, as in civilian life, by contact with the person, personal clothing, or, less often, bedding of an infected individual. In this theater, the great reservoir for the spread of infection was the native population, in whom the incidence was very high and by whom it was regarded with amazing in-

difference. The incidence in U.S. troops reflected the extent of their co-mingling with the natives.

Uncomplicated scabies could be treated effectively with sulfur ointment or benzyl benzoate by the unit surgeon. Both produced good results, but sulfur was preferable in cases complicated by scratching, secondary infection, or dermatitis. Clothing and bedding were disinfested by laundering, dry heat, live steam, louse powder, or the use of a methyl bromide bag. The reward of early diagnosis and treatment was a lower incidence of contact cases, less discomfort for the patient, shorter duration of treatment, and fewer days lost from duty.

Men with complications of scabies were usually hospitalized, for soap and water baths, moist compresses as indicated, and treatment for 3 or 4 days, preferably with the active assistance of a medical aidman, by the application of sulfur ointment from chin to toes. The application was followed by a warm soap and water bath and the use of an antipruritic lotion.

If a second course of treatment was necessary, modified sulfur ointment was used, containing 2 to 5 percent of balsam of Peru. If dermatitis was only slight, benzyl benzoate ointment could be used instead of sulfur ointment. Benzyl benzoate, however, was extremely irritating and had to be used with caution if there were many breaks in the skin and in fair-haired, blue-eyed blonds.

The average stay for patients with scabies in station and general hospitals in the Mediterranean theater was 14 days, because of the high proportion admitted with either secondary infection or complications of earlier treatment. Return to duty was practically total.

Experience showed, however, that it was not sufficient to supply these patients with antiscabitic ointment and oral instructions. It was necessary to give them printed sheets, setting forth the routine in simple, detailed fashion and stressing also the absolute necessity for 100-percent compliance with it. The difficulties of managing scabies could be considerable, and complications could be alarmingly frequent, but both were overcome by complete adherence to the routine of treatment prescribed.

European theater.—In 1942, scabies was rife in the British civilian population, in which it constituted such a problem that the Emergency Medical Service was forced to set up numerous units devoted entirely to its treatment. The high incidence was clearly related to the severe dislocation of civilians, to overcrowding, and to the disruption of hygienic facilities caused by German bombing raids.

The increased incidence of scabies in the British civilian population was soon reflected in the British Armed Forces. The incidence in the U.S. Army in the United Kingdom never reached particularly high levels, but the number of cases, from 3.8 to 8.35 per 1,000 per year for the period 1942–45, was accompanied in the early years by delays in diagnosis and by therapeutic mismanagement that led to complications and required unnecessary

FIGURE 95.—Scabies.

hospitalization for many patients. In 1943, ward rounds in station and general hospitals invariably revealed that from 20 to 30 percent of all admissions on dermatology services were for scabies and for complications of it that were entirely preventable and that would not have developed if the diagnosis had been made promptly and if adequate treatment had been instituted.

An intensive campaign was undertaken to remedy the situation. Brigadier MacKenna was extremely helpful, as was Dr. Kenneth Mellanby, whose studies, which were of great value, had been carried out with the support of the British Medical Research Council.[48] It was not only important to train medical officers in the early recognition of scabies (figs. 95, 96, and 97), which many of them had seldom observed in their civilian careers, but it was also necessary to discontinue useless and outmoded methods of disinfestation of clothing and gear, frequently by techniques that were destructive to both. Treatment in 1943 also differed sharply from methods recommended in most standard texts.

The regulation methods of diagnosis and treatment were outlined in Circular Letter No. 77, Office of the Chief Surgeon, Headquarters, ETOUSA,

48 Mellanby, K.: The Transmission of Scabies. Brit. M.J. 2: 405–406, 20 Sept. 1941.

FIGURE 96.—Scabies, with louse infestation and malnutrition.

8 May 1943. The basis of treatment was the use of benzyl benzoate, but the shortages of shipping delayed the receipt of the emulsion in which it was used, and sulfur ointment had to be substituted. Sulfur therapy was entirely satisfactory if a strength of 10 percent rather than USP 15 percent was used and if the specified details of application were scrupulously adhered to. The film on scabies, prepared under the auspices of the British Medical Research Council, was widely used in the instruction of medical officers.

Once the correct principles and practices were put into operation, disability from the complications of scabies decreased sharply and hospital admissions for this condition became uncommon.

Southwest Pacific Area.—Most of the scabies seen in U.S. troops in New Guinea occurred in men returning from leave in Australia. The incidence was high in Japanese prisoners of war; one group showed a 25-per-

FIGURE 97.—Scabies, with secondary infection, malnutrition, and edema.

cent infestation. Dr. Hopkins pointed out in his March 1945 report to General Denit that scabies was likely to be a more serious problem in the Philippines and in other populated areas. He believed, however, that the successful results obtained with benzyl benzoate in the European theater could be duplicated in the Southwest Pacific Area.

OTHER DERMATOSES

Zone of Interior.—Experiences with miscellaneous dermatoses in the Zone of Interior did not differ materially from experiences in civilian practice (figs. 98, 99, 100, and 101). At Fitzsimons General Hospital, for instance, six patients were encountered with chronic discoid lupus erythematosus, together with two with acute disseminated lupus erythematosus and one with subacute disease.[49] The incidence was considered somewhat

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[49] See footnote 20, p. 588.
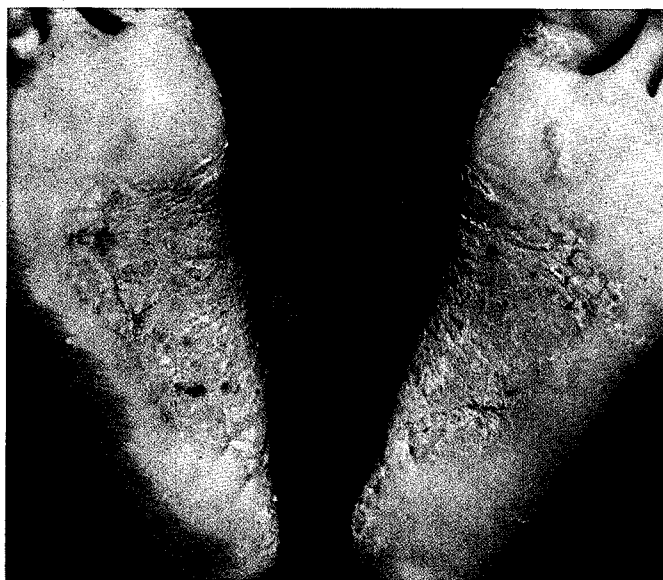
FIGURE 98.—Psoriasis of soles.
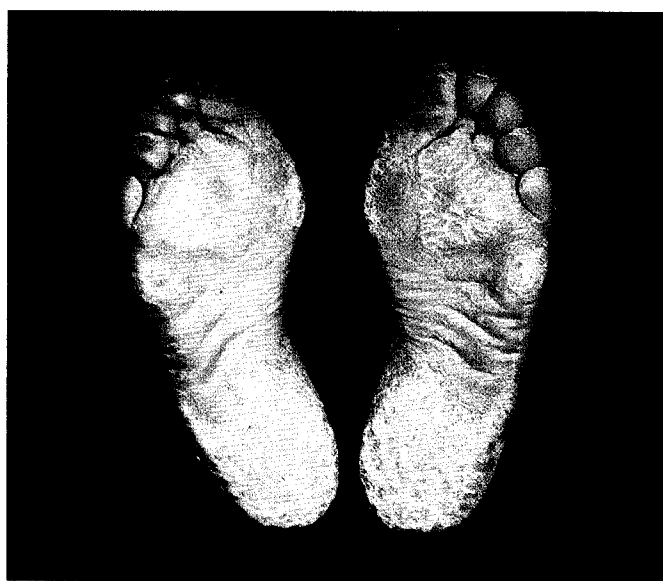
FIGURE 99.—Congenital keratosis plantaris occurring at site
of pressure.

FIGURE 100.—Psoriasis of palms.
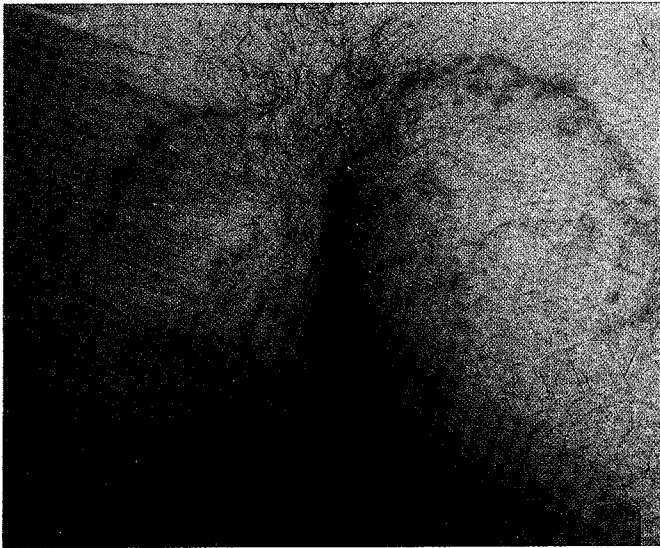
FIGURE 101.—Circinate tinea of buttocks.

lower than would be encountered in civilian life, probably because, as Dr. Hopkins pointed out in commenting on the few cases he had observed in the Southwest Pacific Area, medical officers were dealing with a selected population of healthy young men. He had seen no instances of granuloma fungoides or of pemphigus and had seen only a very few cases of severe psoriasis and chronic urticaria, probably for the same reason.

Dermatophytid was a fairly frequent admission diagnosis at Fitzsimons General Hospital, but it was seldom supported by clinical and laboratory findings. At this hospital, the minimum criteria for diagnosis were:

1. A proved fungal infection, almost always inflammatory and acute.

2. A positive trichophytin test.

3. A symmetrical, erythematous, maculopapular or vesicular eruption compatible with the diagnosis.

4. Disappearance of the id eruption on elimination of the primary focus of infection.

Tuberculosis of the skin was important on the dermatology service at Fitzsimons General Hospital, as well as interesting, because this hospital served as a tuberculosis center. All patients on the tuberculosis wards who presented any type of skin disease were seen routinely in consultation with the dermatology service. It was considered significant that tuberculous adenopathy was observed in only three patients, all from racial groups (Negro, American Indian) peculiarly susceptible to tuberculosis, and that the only three cases of lichen scrofulosus observed at this hospital all occurred in Negro patients with pulmonary tuberculosis. Tuberculosis verrucosa cutis, the rosacea-like tuberculid of Levandowski, and lupus miliaris disseminatus fasceii were seen in one case each. Papulonecrotic tuberculids were infrequent, and no instance of lupus vulgaris was observed.

Mediterranean theater.—Atopic dermatitis (neurodermatitis disseminata), along with allergic dermatitis, was not frequent in the Mediterranean theater but was a cause for prolonged and repeated hospitalization when it was encountered. The final disposition of most patients was reclassification or return to the Zone of Interior. Dermatologists in this theater shared the opinion of many dermatologists in the Zone of Interior as to the unwisdom of sending overseas any men with a background of allergic skin disease and eczema. Inability to control such causative factors as diet, inhaled and contact allergens, and emotional stress made it impossible for most of them to be useful soldiers.

In the Mediterranean theater, a large proportion of the patients admitted to dermatology services had eczematoid dermatitis. Their lesions were either localized or diffuse. They might have been produced by scabicides, fungicides, or sulfonamides, though most of the time the exact cause was not apparent. Psychic tension often predisposed to, or resulted from, dermatitis in this category.

Therapy consisted of simple, soothing remedies, such as compresses, calamine lotion, crude coal tar, and Lassar's paste, plus protection of the lesions. Superficial X-ray was often useful, but it had to be employed judiciously and administered only by qualified personnel.

Infectious eczematoid dermatitis, which was rebellious to treatment and accounted for many hospital admissions, was secondary to infected wounds, draining sinuses, chronic otitis media, otitis externa, and other septic foci. It responded to elimination of the local focus, penicillin parenterally, and local compresses of penicillin solution in concentrations of 250 to 2,500 units per cubic centimeter.

Southwest Pacific Area.—Warts (figs. 102, 103, 104, and 105) were surprisingly frequent on the hands in the Southwest Pacific Area. They were less frequent on the feet, but there they could be extremely painful and practically disabling. They responded well to X-ray therapy, but it had to be given with great caution to prevent damage.

Exfoliative dermatitis was infrequent in the Southwest Pacific Area, but a sufficient number of severe cases occurred to make it of medical importance. Fatal sepsis or aplastic anemia developed in a number of patients. The use of plasma to combat hypoproteinemia that often resulted from voluminous exudation was strikingly successful, as was the use of penicillin parenterally to combat secondary infection. The absence of fatalities in uncomplicated cases was, in Dr. Hopkins' opinion, "a striking tribute to the therapy employed."

LICHENOID AND ECZEMATOID DERMATITIS (ATABRINE DERMATITIS, ATYPICAL LICHEN PLANUS)

In the latter part of 1943, medical officers in the Southwest Pacific Area began to call attention to a characteristic cutaneous syndrome beginning to be observed in men who were serving in New Guinea and adjacent islands or who had been evacuated from these areas.[50] The condition was termed, provisionally, "atypical lichen planus," because of resemblances of the lesions to those of lichen planus or lichen planus hyptertrophicus. Most of these patients, however, also had skin lesions with other morphologic characteristics, particularly certain eczematoid characteristics, while some patients with these eczematoid lesions did not have any lichenoid lesions (figs. 106, 107, 108, and 109).

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[50] As a convenience for the reader, references to the periodical literature are listed whenever official reports of observations or investigations are known to have been published. In addition, the following are presented as a matter of interest: (1) Agress, C. M.: Atabrine as a Cause of Fatal Exfoliative Dermatitis and Hepatitis. J.A.M.A. 131: 14–21, 4 May 1946; (2) Bereston, E. S., and Saslaw, M. S.: Complications of Lichenoid Dermatitis: Glomerulonephritis and Severe Pigmentary Changes in Exfoliative Stage of Lichenoid Dermatitis. Arch. Dermat. & Syph. 54: 325–329, September 1946; (3) Ginsberg, J. E., and Shallenberger, P. L.: Wood's Fluorescence Phenomenon in Quinacrine Medication. J.A.M.A. 131: 808–809, 6 July 1946; (4) Livingood, C. S., and Dieuaide, F. R.: Untoward Reactions Attributable to Atabrine. J.A.M.A. 129: 1091–1093, 15 Dec. 1945; (5) Rosenthal, J.: Atypical Lichen Planus. Am. J. Path. 22: 473–491, May 1946; (6) Sugar, H. S., and Waddell, W. W.: Ochronosis-Like Pigmentation Associated With the Use of Atabrine. Illinois M. J. 89: 234–239, May 1946.

FIGURE 102.—Warts on fingers.
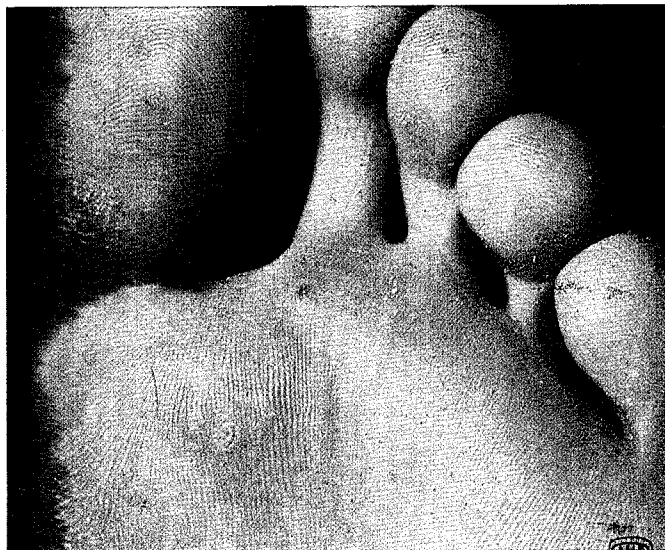
FIGURE 103.—Wart on plantar surface of great toe.

FIGURE 104.—Condyloma acuminatum of penis.
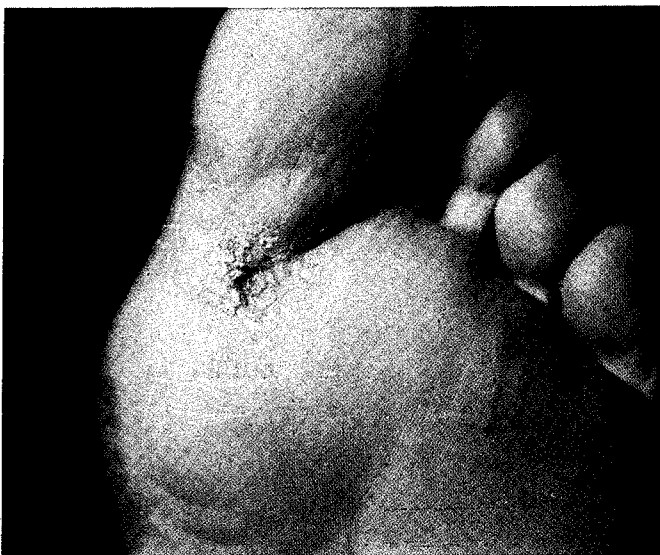
FIGURE 105.—Painful X-ray atrophy and ulceration following
excessive radiation for plantar wart.

FIGURE 106.—Lichenoid dermatitis with secondary infection.
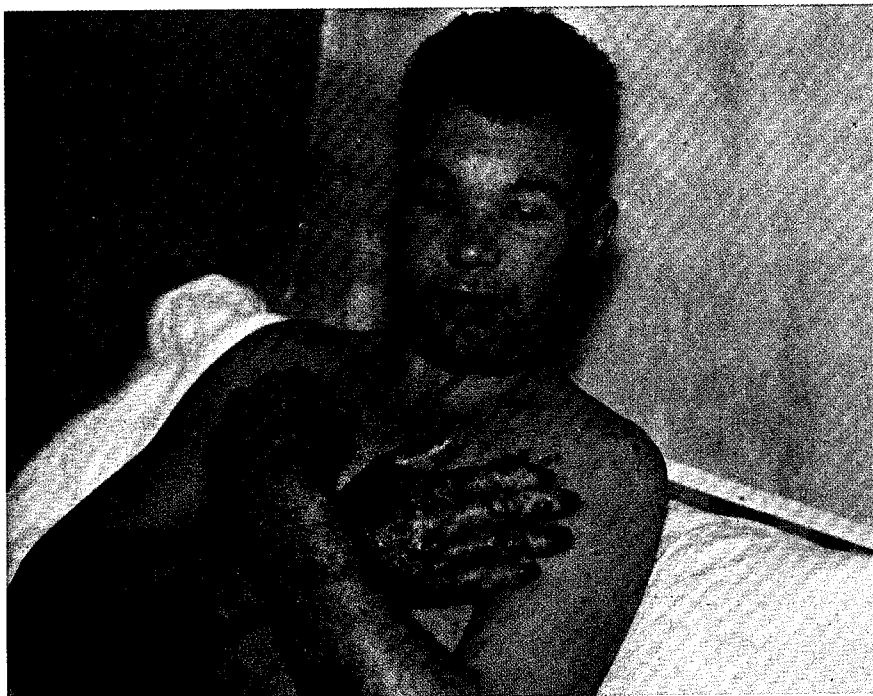
FIGURE 107.—Lichenoid dermatitis with secondary infection.
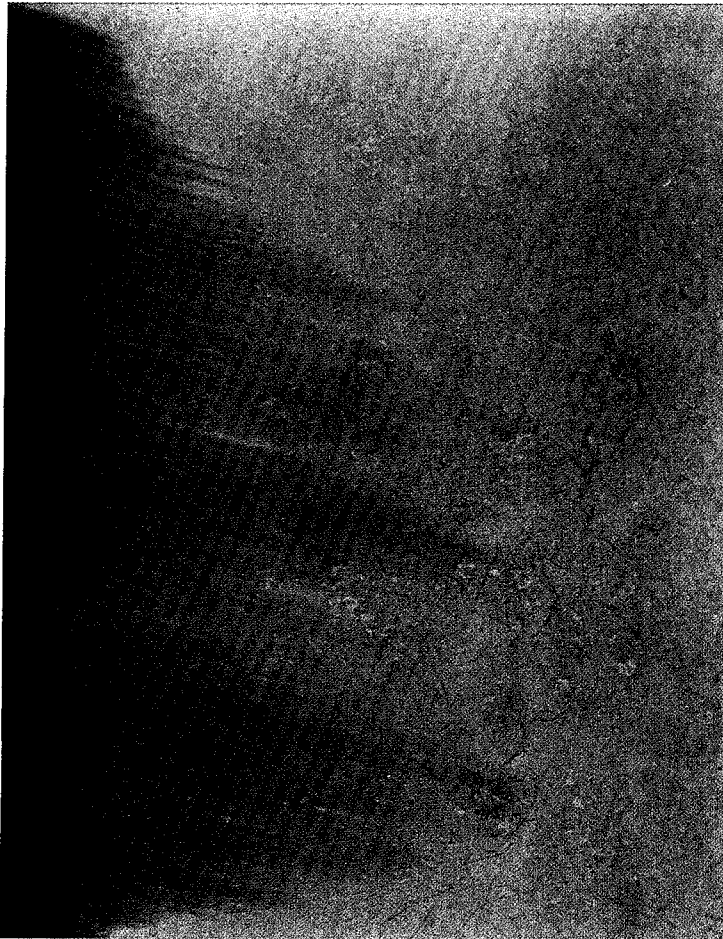
FIGURE 108.—Lichen planus.

It seemed reasonable at this time to conclude that the lichenoid lesions were only part of a multiforme complex and also to assume that certain cases of eczematoid dermatitis in which no lichenoid lesions were present probably fell into the same etiologic group.

Realization that this group of dermatoses represented a new and hitherto unknown disease developed only gradually, as did the realization that the frequency of the condition might make it a significant military problem, not only in itself but because of its relation to Atabrine, the drug by which the devastating effects of malaria were being held in check.[51] Once the existence of the new syndrome was recognized, it became the subject of

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[51] Medical Department, United States Army. Preventive Medicine in World War II. Volume VI. Communicable Diseases: Malaria. Washington: U.S. Government Printing Office, 1963.

FIGURE 109.—Lichen planus affecting lip.

more reports and publications than any other cutaneous disease encountered in World War II.

Evolution of the Concept

The account of this new syndrome might profitably begin with the over-all report made to General Denit in March 1945 by Dr. Hopkins after his survey of dermatologic conditions in the Southwest Pacific Area. He found that three groups of cases, symmetrical eczematoid dermatitis, atypical lichen planus, and blue nails, constituted, numerically, the major dermatologic conditions encountered in this area. Blue nails had no clinical significance (p. 582), but the other two conditions constituted major military problems. Dr. Hopkins had not observed any of these dermatoses in his previous (very wide) experience, and he regarded them either as three new entities or as three separate phases of a new entity.

The eczematoid eruption, as he observed it in his movements about the Southwest Pacific Area, usually began on the hands (fig. 110) but frequently involved the arms, feet, legs, and sometimes the entire body. The most striking features of the disease, to him, were the remarkable bilateral symmetry of the lesions; the frequent involvement of the nail bed and the
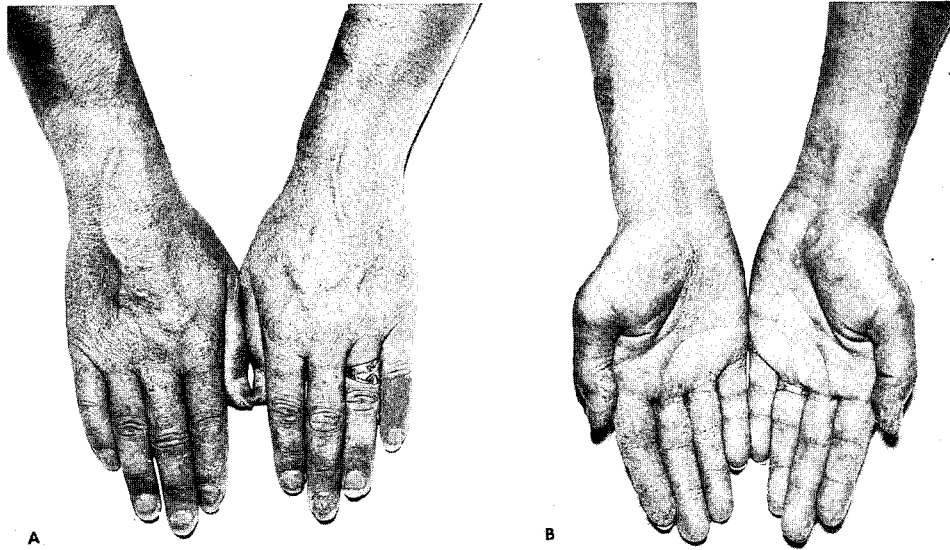
FIGURE 110.—Eczematoid Atabrine dermatitis. A and B. Bilateral symmetrical involvement of hands.

skin of the nail fold; and the frequent exfoliation of the nails in the absence of true suppurative paronychia. The involved areas, particularly those in which dry involuting lesions were present after acute vesiculation had subsided, often presented the bluish tinge common in many skin lesions in the theater (p. 661). Another striking feature was the appearance of dermatitis in a band extending along the radial side of the index finger and the ulnar aspect of the thumb; the first lesions were often observed in these locations. The vesicles on the fingers seemed larger, deeper, and less fragile than those typical of contact dermatitis or dermatophytids.

The involvement of the hands, in itself, made this disease of military importance, for even relatively slight eruptions disqualified men for full military duty. Moreover, Dr. Hopkins found that no curative treatment had been devised, relapse was almost certain after return to duty, and it had already become clear that prompt evacuation to the Zone of Interior was the best therapeutic policy.

At the time he made his survey, Dr. Hopkins considered the etiology of symmetrical eczematoid dermatitis entirely obscure. Fungi were demonstrable in the cases he examined in only a single instance: Capt. P. A. Beal, MC, at the 27th Medical Laboratory, had isolated a *Monilia*, apparently *M. albicans*, from the nail of this patient. The finding was probably coincidental, but in view of the paucity of other leads, it seemed worth following up. A small series of patients had been tested for hypersensitivity to *Monilia*, *Staphylococcus*, and trichophyton, but the uniformly negative results were
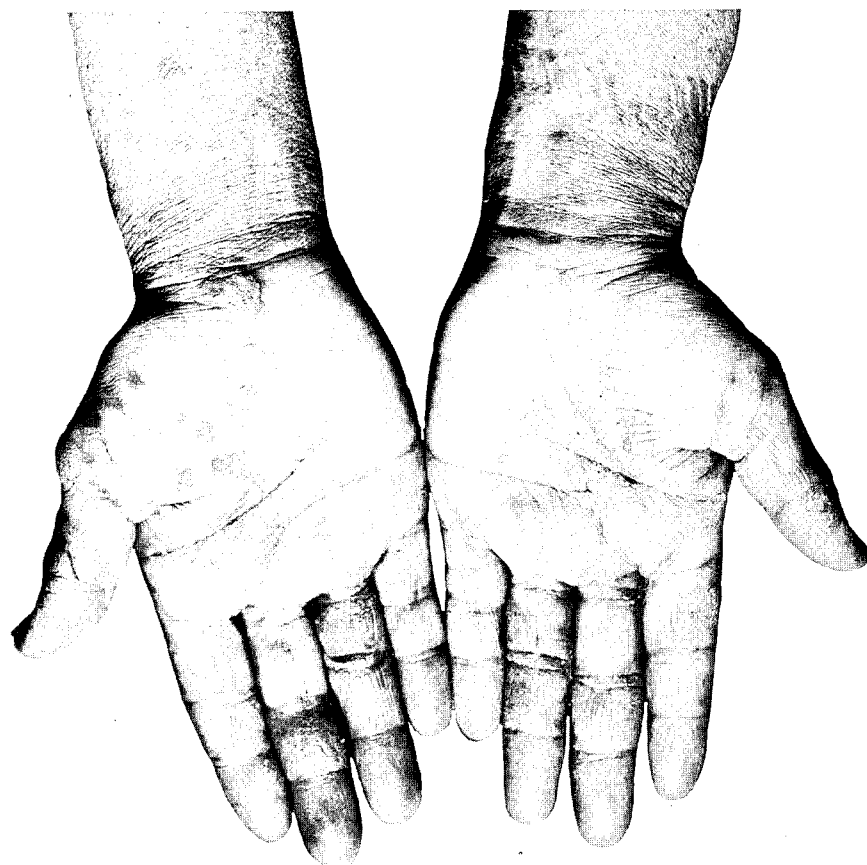
C

FIGURE 110.—Continued. C. Eczematous lesions on palmar surfaces of fingers, combined
with verrucous, somewhat inflammatory, lichenoid papules and plaques on palms.

regarded as unreliable because the extracts used in the test had been ex-
posed for a long period to room temperatures. Much more careful and more
systematic work would be necessary before it could be said with certainty
that these lesions were not the result of sensitivity to bacteria or fungi,
though no evidence existed that they were.

The absence of interdigital lesions on the feet in many patients was
strongly against the then prevalent assumption that these lesions were
dermatophytids. In most instances, no history of an external irritant or
allergen could be obtained, and while the theory that this was a contact
dermatitis could not be excluded, it was a remote possibility, if only because
of the sharp circumscription and striking symmetry of the lesions.

Both of these latter features pointed to some internal cause. The single
clue to this assumption was the fact that the lesions Dr. Hopkins observed
were frequently seen in patients with atypical lichen planus and that many
patients with atypical lichen planus described inflammatory lesions on the

dorsum of the hand or on the fingers as the first manifestation of their disease. Although it might be that the etiology of atypical lichen planus and symmetrical eczematoid dermatitis was the same, the fact that patients with eczematoid dermatitis seemed to recover more promptly than patients with atypical lichen planus was against the supposition that Atabrine was the causative factor. It would be profitable, Dr. Hopkins thought, to run control studies, continuing Atabrine in one group of patients but keeping the other group off it long enough to permit its complete elimination from the body. Results would determine whether the withdrawal of Atabrine was essential for cure.

As time passed, it became quite clear that Atabrine was the responsible factor in both symmetrical eczematoid dermatitis and atypical lichen planus, and it did not seem advisable to make a sharp distinction between them, for many of the same patients exhibited lesions of both types. In the 118 cases, for instance, observed by Maj. (later Lt. Col.) Charles L. Schmitt, MC, at the 27th General Hospital (table 103), a small number of patients had only lichenoid lesions, a larger group had both lichenoid and eczematoid lesions, and a still larger group had only eczematoid lesions. Exfoliative dermatitis could occur in any of these groups.

TABLE 103.—*Anatomic distribution of lichenoid papules and nodules in 118 patients with so-called atypical lichenoid planus*

Site	Number of cases	Percent
Thighs and legs	31	26
Hands and fingers	31	26
Arms	25	21
Torso	24	20
Buttocks	20	17
Eyelids	17	14
Feet	17	14
Penis	13	11
Neck	11	9
Ears	10	8
Waistline	10	8
Scalp	7	6
Groins	7	6
Scrotum	6	5
Face	6	5
Listed as generalized	37	31

Source: Collected in the Southwest Pacific Area by Maj. Charles L. Schmitt, MC, 27th General Hospital.

Incidence and Etiology

Southwest Pacific Area

No doubt many of the earliest cases of atypical lichen planus were overlooked because they were classified under such diagnoses as dermatitis,

unclassified, or trichophytosis corporis. While it is impossible to state positively when the first case occurred, in retrospect it seems likely that two patients evacuated from New Guinea to the Zone of Interior in March 1943, with the diagnosis of dermatitis, chronic, lichenoid, might have had atypical lichen planus. In July 1943, two patients who were later found to have had atypical lichen planus (though it was not then diagnosed under that terminology) were evacuated from the same area, one from the 4th and the other from the 118th General Hospital. At least nine additional patients were evacuated during the remainder of this year with the same condition.

Meantime, reports were being received concerning the increasing frequency of this new disease. In November 1943, Maj. (later Lt. Col.) Robert B. Palmer, MC, reported (verbally) that he had seen a remarkable number of patients with hypertrophic lichen planus. The station hospital at Port Moresby received 14 patients with severe lichenoid disease between September 1943 and February 1944. In January 1944, Major Ambler observed 16 cases in his tours of various hospitals in the Southwest Pacific Area. In April 1944, he reported on 28 cases he had observed in forward areas. By July of this year, he had personally observed 130 cases, and by December, the number had risen to 200.[52]

Several comprehensive reports on the condition were prepared for The Surgeon General through the Surgeon, SWPA, by Maj. Thomas W. Nisbet, MC, in June and again in August 1944, covering the cases observed at Milne Bay, New Guinea;[53] by Major Schmitt, in collaboration with Capt. George Chambers, MC, and Maj. O. Alpins, MC, of the Australian Army;[54] and by Major Ambler, Dr. Hopkins, and Col. Maurice C. Pincoffs, MC.[55] Numerous other reports covered smaller numbers of cases and less extensive observations.

The possible relation of Atabrine to this new syndrome, in which both eczematoid and lichenoid manifestations were often present in combination, seems to have been mentioned for the first time in the Southwest Pacific Area in November 1943, when the Consultant in Dermatology for the Australian Army, at a meeting of the Sydney Medical Society, presented a patient with severe lichen planus, which he attributed to this drug. Major Nisbet and Major Schmitt were the first U.S. Army Medical Corps officers to point out, in separate official reports to The Surgeon General, that Atabrine was probably the essential etiologic factor in this new type of dermatitis.

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[52] Report, Maj. John V. Ambler, MC, to the Theater Surgeon, Southwest Pacific Area, 15 Dec. 1944, subject: Statistical Survey of 200 Cases of Atypical Lichen Planus.

[53] Nisbet, T. W.: A New Cutaneous Syndrome Occurring in New Guinea and Adjacent Islands: Prelimnary Report. Arch. Dermat. & Syph. 52: 221–225, October 1945.

[54] Schmitt, C. L., Alpins, O., and Chambers, G.: Clinical Investigation of a New Cutaneous Entity. Arch. Dermat. & Syph. 52: 226–238, October 1945.

[55] Minutes of the Conference on Atypical Lichen Planus, Board for the Coordination of Malarial Studies, 6 June 1945, exhibit V thereto, "Atypical Lichen Planus: Present Status of the Problem."

These officers based their conclusions on the observations (1) that all patients with this new skin disease had taken suppressive Atabrine; (2) that their skin lesions had progressed as long as they were on the drug; (3) that improvement or complete healing had followed its withdrawal; and (4) that in some instances new lesions appeared when the medication was resumed. Major Nisbet also called attention to the occurrence of fixed eruptions of exfoliative dermatitis and the occasional development of aplastic anemia in these patients; both of these manifestations were suggestive of a drug etiology. He also stated that until Atabrine was introduced into the Southwest Pacific Area, he could find no record of any such cases at Milne Bay or elsewhere in New Guinea.

When the mounting number of cases of atypical lichen planus indicated that the disease might become a serious military problem in relation to suppressive Atabrine, the use of which was considered essential,[56] 26 patients with the disease were assembled, in July 1944, for study by a group of officers of the Malarial Research Unit attached to the 3d Medical Laboratory at Base B (Oro Bay, New Guinea). The group consisted of Maj. (later Lt. Col.) Abner M. Harvey, MC, Capt. (later Maj.) Frederik B. Bang, MC, Lt. (later Maj.) John M. Myer, MC, and Lt. Nelson G. Hairston, SnC.[57] Maj. A. M. Pappenheimer, SnC, was later assigned to the project, to conduct nutritional studies. These 26 patients, who had both lichenoid and eczematoid manifestations, were kept under constant observation for a 5-month period. In addition to studies of the skin lesions in relation to the administration and withdrawal of Atabrine, laboratory studies were carried out to determine the levels of the drug in skin and plasma. Vitamin saturation tests were also carried out.

These studies showed that in 18 of 22 patients kept on Atabrine after hospitalization, the original lesions continued to progress and new ones appeared. The condition of three other patients in this group remained unchanged. The remaining patient showed some improvement.

In another test, Atabrine was discontinued in 19 patients, 15 of whom then showed improvement. Two showed no improvement, and the other two, both of whom had had bismuth injections, had progressive lesions.

When Atabrine was readministered to nine patients whose lesions had begun to heal after it was discontinued, seven had acute exacerbations of the disease within 24 to 72 hours.

A significant finding in this study was the appreciable amounts of Atabrine found in the skin of the patients, from 7 to 9 weeks after the drug had been discontinued, although at these times there were no detectable amounts in either urine or blood.

[56] See footnote 51, p. 642.

[57] Minutes of the Conference on Atypical Lichen Planus, Board for the Coordination of Malarial Studies, 6 June 1945, exhibit IV thereto, "Clinical and Laboratory Studies on Atypical Lichen Planus With Particular Reference to the Role of Atabrine."

Mediterranean Theater of Operations

All of the data presented up to this point concern the Southwest Pacific Area. Informal communications from medical officers in the South Pacific Base Command also described patients with atypical lichen planus but commented on its infrequency.

Meantime, cases were being reported from both the Mediterranean and the China-Burma-India theaters. In July 1944, Capt. (later Maj.) Lawrence M. Nelson, MC, reported from the Mediterranean theater two cases of a characteristic type of eczematoid dermatitis without lichenoid lesions.[58] He attributed the eruption to Atabrine.

In January 1945, Maj. (later Lt. Col.) R. N. Buchanan, Jr., MC, reported from the same theater five cases of symmetrical, generalized eczematoid dermatitis that subsided when Atabrine was discontinued and recurred when its administration was resumed.[59] In July of this year, Major Nelson reported six cases of atypical lichen planus apparently caused by Atabrine; all the patients had acquired the disease late in 1944.[60] For the last several months, evacuees with this condition had been reaching the Zone of Interior from the Mediterranean Theater of Operations. Available evidence indicates, however, that the incidence of both the lichenoid and the eczematoid syndrome was much less in the Mediterranean theater than in either the Southwest Pacific Area or the China-Burma-India theater.

China-Burma-India theater

The first three cases of atypical lichen planus in the China-Burma-India theater were recognized and reported to The Surgeon General through the theater surgeon by Major Livingood in November 1944.[61] Later reports indicated that the incidence of this condition in this theater was perhaps as high as it was in the Southwest Pacific Area.

In March 1945, in view of the data that he had accumulated since this condition was first recognized, Major Livingood recommended that suppressive Atabrine be discontinued not only in men with lichenoid dermatitis but also in those with characteristic prodromal eczematoid lesions. He made the same recommendation for sulfathiazole, the arsenicals, and other potentially sensitizing drugs.[62]

[58] Report, Capt. Lawrence M. Nelson, MC, to The Surgeon General, through the Surgeon, Mediterranean Theater of Operations, U.S. Army, 3 July 1944, subject: Eczematoid Dermatitis Due to Atabrine.

[59] Report, Maj. R. N. Buchanan, Jr., MC, to The Surgeon General, through the Surgeon, Mediterranean Theater of Operations, U.S. Army, January 1945, subject: Dermatology in an Army General Hospital Located in a Theater of Operations.

[60] Report, Maj. Lawrence M. Nelson, MC, to The Surgeon General, through the Surgeon, Mediterranean Theater of Operations, 20 July 1945, subject: An Unusual Dermatitis Simulating Lichen Planus and Lichen Corneus Hypertrophicus.

[61] Letter, Maj. C. S. Livingood, MC, to The Surgeon General, November 1944, subject: Report of the Occurrence of an Unusual Skin Disease.

[62] Report, Dr. Clarence S. Livingood, 14 Feb. 1951, subject: Lichenoid and Eczematous Dermatitis Syndrome Due to Atabrine.

In July 1945, Maj. James M. Flood, MC, reported his observations on the relation between atypical lichen planus and Atabrine in the 20th General Hospital.[63] They covered not only patients but the 800 officers, nurses, and enlisted men on the staff and in the personnel. He considered the evidence for the relationship convincing for several reasons:

1. There was a large number of troops in the theater between March 1943 and November 1945.

2. No cases of this syndrome were observed between March 1943 and March 1944. Suppressive Atabrine was not used during this period.

3. After March 1944, Atabrine therapy was used in two distinct programs. Between March 1944 and 15 February 1945, it was used in selected troops in the forward area, and so-called Atabrine discipline was poor. Scattered cases of atypical lichen planus began to occur about 6 weeks after the program was instituted. Between 15 February 1945 and 1 November of that year, all troops in Assam and north Burma received Atabrine, and discipline in respect to its use was reported excellent. By April 1945, the number of cases of atypical lichen planus had begun to increase sharply.

4. Patients with this syndrome were observed only in Assam and north Burma, the only sections of the theater in which suppressive Atabrine medication was used.

5. All other factors in the theater, including climate, working conditions, and diet were approximately the same during the entire time except for a considerable improvement in diet later in the period.

Major Flood's and Major Livingood's studies, as already indicated, covered the 800-member personnel of the 20th General Hospital. Most of them had been in the same area and worked under the same conditions for about 20 months before suppressive Atabrine therapy was instituted. During this period, not a single individual acquired cutaneous lesion in any way suggestive of either atypical lichen planus or eczematoid dermatitis. Within 5 months after the regimen had been instituted, seven persons had acquired the complex. Most of the lesions improved when Atabrine was discontinued, but new lesions appeared in some cases when it was reinstituted.

Investigations in the Zone of Interior

The study of atypical lichen planus in the Zone of Interior was facilitated by concentrating the patients with this syndrome first at hospitals designated as tropical disease centers and later at Moore General Hospital and Harmon General Hospital, which were designated as dermatology centers. Here they were studied by a routine devised by the Medical Consultants Division, OTSG, with the cooperation of the civilian consultants and the Board for the Coordination of Malarial Studies.

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[63] Letter, Maj. James M. Flood, MC, to Commanding General, 20th General Hospital, APO 689, 27 July 1945, subject: Atypical Lichen Planus.

At Moore General Hospital, Maj. James M. Bazemore, MC, and his associates studied intensively 51 patients who were selected because their lesions were predominantly lichenoid and had involuted after withdrawal of Atabrine for varying periods.[64] When suppressive therapy was reinstituted, two distinct reactions were observed:

1. Five patients developed an eczematoid type of eruption that began characteristically as a generalized pruritus and was followed by erythema of the skin, most marked in the antecubital and popliteal spaces, the anterior aspect of the neck, and friction points. In the most severe cases, the eruption became red and generalized and went on to scaling. The time of development after the first dose of Atabrine given after the period of withdrawal varied from 4 hours to 7 days. All five patients, all of whom had to be dropped from the study group, had positive patch tests to Atabrine.[65]

2. The second type of reaction observed at Moore General Hospital was a clear-cut exacerbation of the lichenoid lesions, manifested by recurrences at the sites of previous lesions and development of new lesions. The earliest recurrences were observed 23 days after the reinstitution of Atabrine therapy; the majority occurred between 40 and 63 days afterward. Only two of the nine patients who manifested this second type of reaction had positive patch tests.

The proportion of patients in the experimental group who developed exacerbations of their lesions within 3 months after the reinstitution of Atabrine therapy was practically identical with the proportion who had developed the syndrome within a similar period after beginning suppressive Atabrine. This particular phase of the investigation at Moore General Hospital explains why some observers reported no exacerbations of the original lesions when Atabrine was readministered for short periods of time. On the other hand, all investigators in oversea theaters who had the opportunity to readminister the drug to patients with atypical lichen planus or eczematoid dermatitis reported a higher incidence of exacerbations than were observed when experimental readministration was carried out in patients who had been evacuated to the Zone of Interior.

Geographic Distribution and Incidence

The more careful investigation that was possible after the war left no doubt that atypical lichen planus and eczematoid dermatitis occurred in all areas and commands in which suppressive Atabrine was in general use. It was recorded in New Guinea and neighboring islands on the north coast;

[64] Bazemore, J. M., Johnson, H. H., Swanson, E. R., and Hayman, J. M., Jr.: Relation of Quinacrine Hydrochloride to Lichenoid Dermatitis (Atypical Lichen Planus). Arch. Dermat. & Syph. 54: 308–324, September 1946.

[65] Capt. Harvey Blank, MC, Chief of Dermatology and Syphilology, 69th General Hospital, informed the writers of this chapter that in the 33 cases he personally observed, patients with typical lichenoid lesions were generally patch-test negative to Atabrine while those with the eczematous and exfoliative types were likely to be patch-test positive.

Bougainville; Guadalcanal; Green Island; the Carolines; New Britain; Morotai Island; the Solomon Islands; the Admiralty Islands; the Trobriand Islands; Okinawa; Assam; north Burma; the Philippine Islands; parts of Australia; and Italy.

No data are available on the incidence of atypical lichen planus and eczematoid dermatitis in relation to troop strengths in the various areas in which these diseases were encountered. The largest numbers of cases are known to have occurred in New Guinea and adjacent islands and in the Assam-Burma area. Major Ambler estimated the incidence in the Southwest Pacific Area at 2 or 3 per 1,000 per year, which most observers considered too low. Colonel Schmitt, basing his estimates on his experience in a general hospital in New Guinea, estimated the incidence at 11–14 per 1,000 per year, and Major Flood, using his experience in a general hospital in Assam, estimated the incidence at 10 per 1,000 per year.

Contributory Factors

The fact that the incidence of this syndrome was so much higher in New Guinea and adjacent islands, and in Assam and north Burma, than in other areas suggests that factors other than Atabrine might also play contributory roles in its causation. Some investigations substantiated this theory, at least to a limited degree.

Major Ambler and his associates,[66] Major Livingood,[67] Lt. Col. Donald J. Wilson, MC,[68] and others presented evidence that indicated that various forms of cutaneous trauma contributed to the onset and localization of the lesions, particularly during the eczematoid phase of the eruption. The assumption was that something happened to the skin of a certain proportion of men who were taking Atabrine regularly that made them particularly vulnerable to irritation and infection. As a result, they developed an increased tendency to acquire chronic eczematoid dermatitis on contact with external allergens. It naturally followed that a larger proportion of men on suppressive Atabrine would develop cutaneous eruptions in hot, humid climates such as New Guinea, Assam, and north Burma, than in other parts of the world, where the skin was less subject to trauma, infection, and inflammation.

Dietary deficiencies and psychosomatic factors were also investigated as possible principal contributory causes of this syndrome. Major Harvey and his group found a slightly lower nutritional status in patients with this disease than in a control group, but they did not implicate dietary deficiency as a cause. It was emphasized by Col. Benjamin M. Baker, MC, Consultant in

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[66] See footnote 55, p. 647.

[67] See footnote 62, p. 649.

[68] Wilson, D. J.: Eczematous and Pigmentary Lichenoid Dermatitis: Atypical Lichen Planus. Arch. Dermat. & Syph. 54: 377–396, October 1946.

Medicine, in the South Pacific Area,[69] that a greater variety of fresh vegetables and fruits, as well as larger quantities of milk and eggs, was available in that area than in the Southwest Pacific Area. These facts might explain the much lower incidence of the syndrome in the Solomon Islands than in New Guinea and its adjacent islands, although the use of suppressive Atabrine was approximately the same in both regions.

A number of observers analyzed the available data in reference to race, sex, age, and complexion. The only finding of any possible statistical significance was that patients with the lichenoid and eczematoid dermatitis syndromes were in a somewhat higher age group than the average military population.

Virus studies carried out at Moore General Hospital,[70] as well as cultural studies for fungi and bacteria carried out here and elsewhere, produced no significant data.

Clinical Considerations

It was the combination of various types of lesions in a characteristic fashion, plus their occurrence in large groups of individuals under similar circumstances, that made this syndrome a new entity. All observers agreed that the lesions were polymorphous and that they appeared in many different combinations. At the same time, they emphasized also that these patients reacted dermatologically in a highly characteristic fashion and that the clinical picture soon became unmistakable, even to medical officers with little or no experience in dermatology.

Initial manifestations.—The disease almost invariably began with a prodromal inflammatory cutaneous eruption that varied in character and distribution. The most typical initial manifestation was a rather sharply marginated, patchy, eczematoid eruption, either exudative or nonexudative, most frequently on the dorsal surfaces of the hands, feet and legs, and in the crural region. The wrists, eyelids, ears, and neck were other sites of predilection.

Other clinical manifestations seen early in the illness included an eruption resembling seborrheic dermatitis in the scalp, eyebrows, bearded region, axilla, and suprapubic region; discrete and confluent erythematous, pinhead-size vesicles and papules that resembled miliaria; and flat, erythematous patches that soon became scaly and sometimes exfoliative. Often, the eczematoid and intertriginous lesions became impetiginized; in such instances, they were apt to extend more rapidly.

As this description indicates, these early eruptions often so closely resembled other forms of eczematoid dermatitis that an exact clinical diag-

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[69] Baker, Benjamin M.: South Pacific Area. *In* Medical Department, United States Army. Internal Medicine in World War II. Volume I. Activities of Medical Consultants. Washington: U. S. Government Printing Office, 1961, pp. 569–623.

[70] See footnote 64, p. 651.

nosis was difficult. So-called nummular eczema, contact dermatitis, seborrheic dermatitis, pyoderma, tineal infections, miliaria, and dermatophytids all had to be excluded. It was sometimes necessary to follow the eruption from day to day in order to detect the lichenoid lesions upon which the diagnosis of atypical lichen planus was based. In other cases, the symmetry, distribution, and violaceous color of the initial lesions were sufficiently characteristic for an experienced dermatologist to make the diagnosis very early in the course of the disease.

The personally collected data of Major Ambler on 200 cases in the Southwest Pacific Area [71] (table 104) and of Major Schmitt and his group on 118 cases in the same area [72] (table 103) closely parallel the observations of Major Bazemore and his associates on 302 cases at Moore General Hospital in respect to the initial sites of cutaneous involvement.[73] Opinions differed, however, as to the significance of these early, antecedent eruptions. Some dermatologists regarded them as unrelated dermatoses that predisposed to lichenoid lesions. There was some evidence to support this opinion; trauma of various types, sunlight, and mechanical and chemical agents unquestionably predisposed to the development of lichenoid lesions. Other observers pointed out that eczematoid patches, crusted plaques, and

TABLE 104.—*Anatomic distribution of lesions of fully developed lichenoid and eczematoid dermatitis complex in 200 patients*

Sites	Number of cases	Percent
Dorsum of hands	152	76
Lower legs	137	69
Lips	127	64
Eyelids [1]	114	57
Dorsum of feet	102	51
Forearms	99	50
Ears [1]	86	43
Buccal mucosa	70	35
Palms	70	35
Penis	63	32
Manubrial region	56	28
Scalp	51	26
Soles	49	25
Buttocks	49	25
Face	39	20

[1] Originally, only 1.5 percent of these patients had lesions of the eyelids and only 3 percent lesions of the ears. The percentages shown in this table were a later development in each instance.

Source: Report, Maj. John V. Ambler, MC, to the Theater Surgeon, Southwest Pacific Area, 15 Dec. 1944, subject: Statistical Survey of 200 Cases of Atypical Lichen Planus.

[71] See footnote 52, p. 647.
[72] See footnote 54, p. 647.
[73] See footnote 64, p. 651.

severe intertriginous dermatitis frequently developed in the presence of lichenoid lesions. Whatever the causation, it seems probable that the initial lesions, even though they occurred independently and in advance of the lichenoid eruption, were still part of the lichenoid complex.

Later manifestations.—The lichenoid lesions characteristic of atypical lichen planus assumed a variety of forms, as follows:

1. Annular, scaling violaceous lichenoid papules occurred singly or in sharply outlined patches of varying sizes. Pigmentation (melanin) that became deeper as time passed regularly accompanied some of these lesions [74] (figs. 111 and 112). The papules resembled those seen in lichen planus ruber but were not angular and their surfaces were not ordinarily shiny. Wickham's striae seen in true lichen planus were only occasionally observed.

2. Hypertrophic and hyperkeratotic lichenoid plaques represented another secondary manifestation of the syndrome (fig. 113). Large, elevated plaques and nodules began as such; they were not the result of coalescence of small papules. These plaques, which were either annular or linear, ranged in diameter from 0.5 to 5.0 centimeters. They were often elevated 0.5 cm. or more above the surface of the skin, but they did not usually infiltrate it deeply. Initially, their coloration varied from erythematous to a deep violaceous hue. Later, they assumed a dark brown or slate-gray color. Extremely dense, grayish scales were seen in lesions that became verrucous. This variety, as well as lichenoid papules, usually developed at the sites of healing eczematoid lesions. While they might occur almost anywhere on the face, trunk, or extremities, they were most often localized on the dorsal surface of the hands, the extensor surface of the forearms and legs, and the dorsal surface of the feet. These lesions, in general, resembled those seen in lichen planus hypertrophicus.

3. Lichenoid lesions of the mouth (fig. 114) involved the vermilion borders of the lips, the buccal surface of the cheeks, and the dorsal surface of the tongue. They took the form of whitish or violaceous-tinged, slightly elevated, reticular leukokeratoses that resembled true lichen planus except that the involvement was usually more extensive. Erythema and some degree of erosion were quite common. Major Nisbet described several instances of severe stomatitis, with bullous lesions.[75]

Concomitant lesions.—In addition to the lichenoid lesions just described, the fully developed syndrome included a wide variety of other lesions, not all of which were observed in all patients, though the lesions were always polymorphous. Among these lesions were the following:

1. Pigmented patches, which were frequently at sites other than those of the earlier lichenoid or eczematoid lesions (figs. 115 and 116). The coloration varied from violaceous to slate-gray, dark brown, or almost coal-black.

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[74] Lutterloch, C. H., and Shallenberger, P. L.: Unusual Pigmentation Developing After Prolonged Suppressive Therapy With Quinacrine Hydrochloride. Arch. Dermat. & Syph. 53: 349–354, April 1946.

[75] Nisbet, T. W.: Dermatitis Due to Quinacrine Hydrochloride ("Atabrine"). J.A.M.A. 134: 446–450, 31 May 1947.

FIGURE 111.—Lichenoid Atabrine dermatitis. A. Lichenoid lesions of hands
with hyperpigmentation and some tendency to superficial scarring.

These patches resembled, in some respects, the fixed drug eruptions caused
by phenolphthalein and other compounds.

2. Faintly erythematous, scaling, papulosquamous lesions with an
axial distribution not unlike that of pityriasis rosea (figs. 117 and 118).

3. Flat, squamous, well-demarcated geographic plaques on the trunk,
axilla, and groin, which resembled fungal lesions.

4. A diffuse, exfoliative type of generalized eczematoid dermatitis
(fig. 119), with increased involvement and marked weeping of the inter-
triginous sites, the flexors of the knees and elbows, the inner surfaces of
the thighs, and the neck.
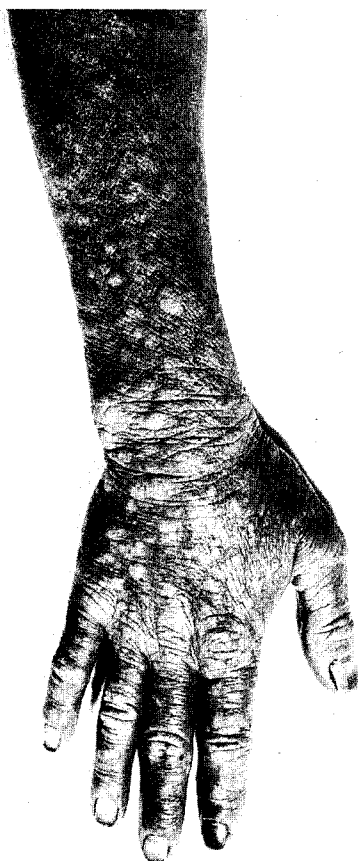
B

FIGURE 111.—Continued. B. Lichenoid lesions
of hand and forearm (this same patient is
shown in figures 111C and 112). Note the some-
what verrucous character of the lesions.

5. Follicular involvement, which took the form of either (1) a patchy
or a diffuse keratosis pilaris or (2) papular lesions in the hair follicles.
These lesions were most frequent on the buttocks, shoulders, back, arms,
and legs.

6. A scaling, erythematous, eczematoid dermatitis of the eyelids (fig.
120). This was a very common finding.

7. Hyperkeratosis, superficial fissuring, and pigmentation of the ver-
milion border of the lips (fig. 121) ; fissures at the angles of the lips; and,
occasionally eczematous cheilitis with edema, fissuring, and oozing.

8. Erythematous and violaceous-tinged, oozing, scaling, eczematoid
plaques, well demarcated in some instances and ill defined in others.

FIGURE 111.—Continued. C. Lichenoid, verrucous-like lesions on anterolateral
surface of foot.

9. Oozing intertriginous dermatitis of the groins, axillas, and inter-
gluteal surfaces.

10. Scaling, hyperkeratotic papules of the palms and soles. The entire
area was occasionally so greatly thickened, fissured, and glazed as to sug-
gest a hyperkeratotic eczema.

FIGURE 112.—Lichenoid Atabrine dermatitis. Closeup of elevated, shiny, violaceous papules and plaques on lateral surface of neck and preauricular region, 2½ months after onset.

11. Scaling, bilateral, dry dermatitis of the ears, especially the tips of the auricles, or a weeping dermatitis involving the entire auricle and the retro-aural folds. The lesions observed in these cases resembled seborrheic dermatitis with secondary streptoderma.

12. Diffuse, adherent, thick scaling of the scalp, with or without hyperkeratotic plaques, usually accompanied by diffuse or patchy alopecia. Alopecia occurred in some instances, however, without lesions of the scalp.

13. Crusted pyogenic lesions, which in some instances went on to generalized pyoderma and septicemia. These were extremely serious complications.

14. Ecthymatous ulcerations, which were in part the result of excoriation of the hypertrophic nodules and plaques just described. In the strictly
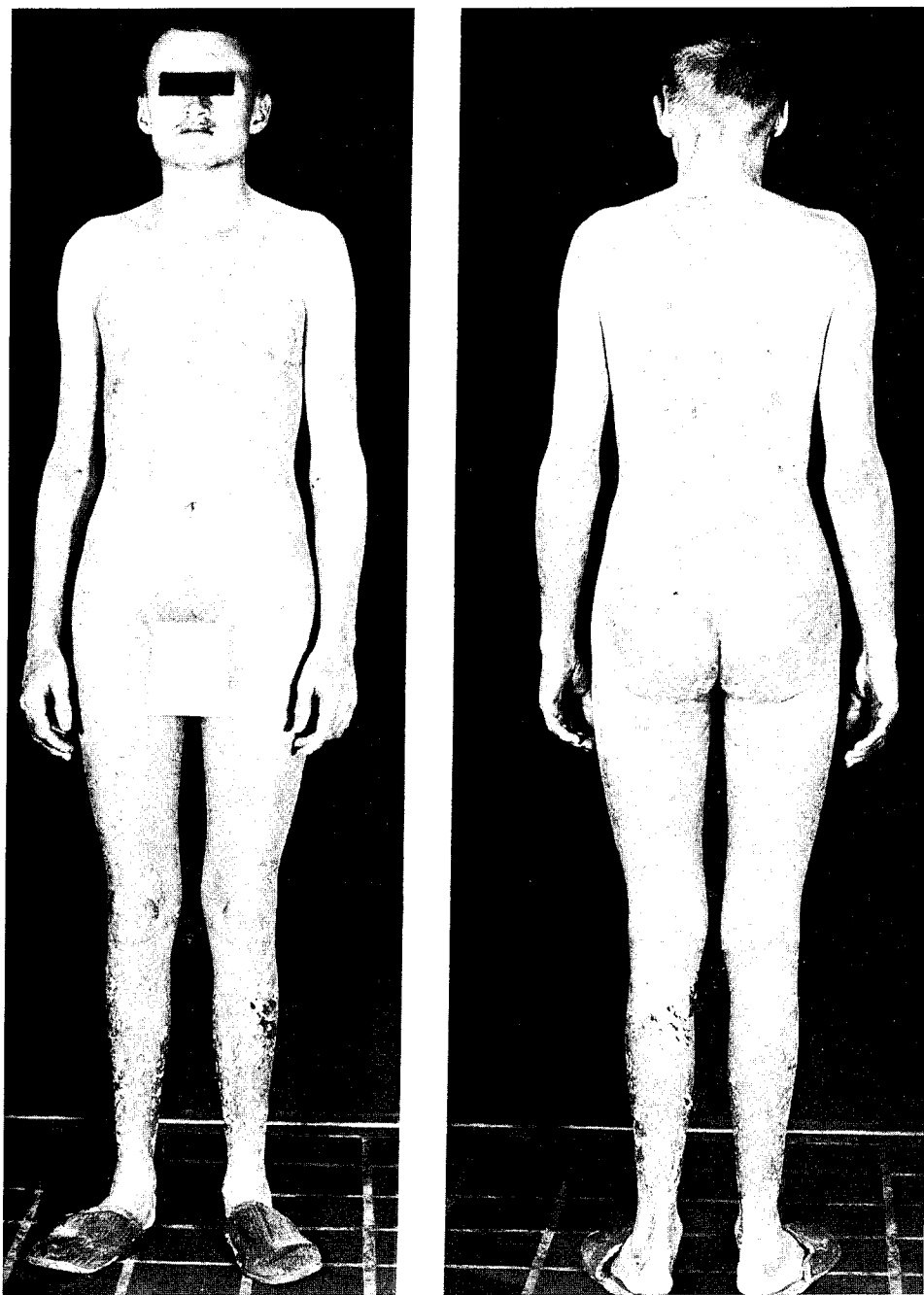
FIGURE 113.—Lichenoid Atabrine dermatitis. Note symmetry and extensive involvement. Superficially, these lesions resembled psoriasis.
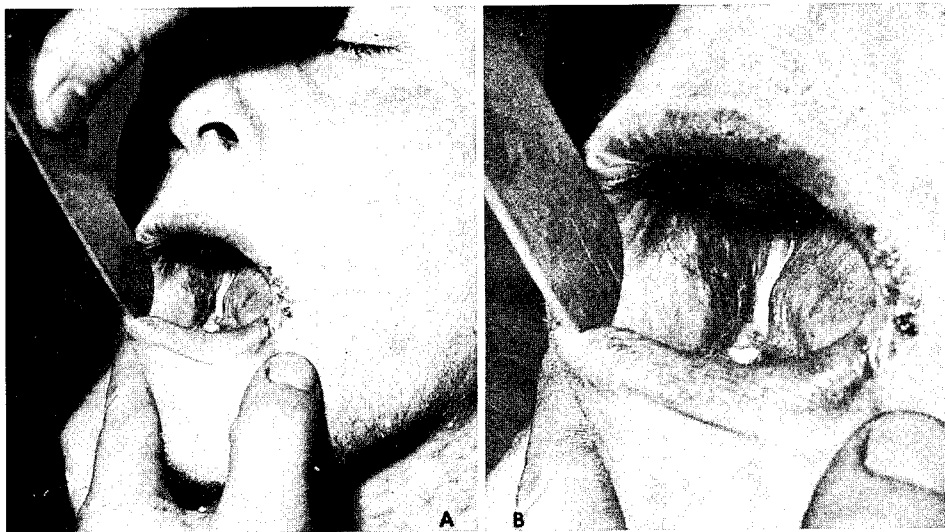
FIGURE 114.—Lichenoid lesions of mouth in Atabrine dermatitis. A. Cheilitis limited to commissures. B. Lesions of oral mucous membrane characterized by whitish, lacy plaques with a predilection for the buccal mucosa. Note the superficial fissuring and inflammatory response at the oral commissure.

accurate sense of the word, it seems more logical to classify the various types of pyoderma observed not as an integral component of atypical lichen planus but rather as secondary complications.

15. Abnormalities of the nails, which took various forms (fig. 122), including separation of the distal margin with accumulations of whitish, cellular debris under it; roughening or destruction of the nail near the matrix; linear striation and transverse depression; brittleness; pitting and lack of luster; and, in some cases, subacute paronychial infections. All of these varieties of nail involvement occurred more frequently when the hands, feet, or both had been involved in the process for some time.

In his trips about the Southwest Pacific Area, as already mentioned, Dr. Hopkins was greatly impressed by the frequency of a blue discoloration of the nail beds in men in the area. The first such cases he observed were in patients with atypical lichen planus, who frequently had pigmented plaques elsewhere in the body which resembled the fixed eruption caused by phenolphthalein. The nail anomaly appeared as a wide, transverse band, ranging from slate-colored to violet. The band, which was usually located in the mid zone of one (or more) of the nails on the fingers or the toes did not shift as the nail grew. Small macules of the same color were sometimes seen beneath the nails. It was reported to Dr. Hopkins, though it was no more than a rumor, that some men with blue nails had similar pigmented areas elsewhere on the body. Some lesions were said to resemble argyria,
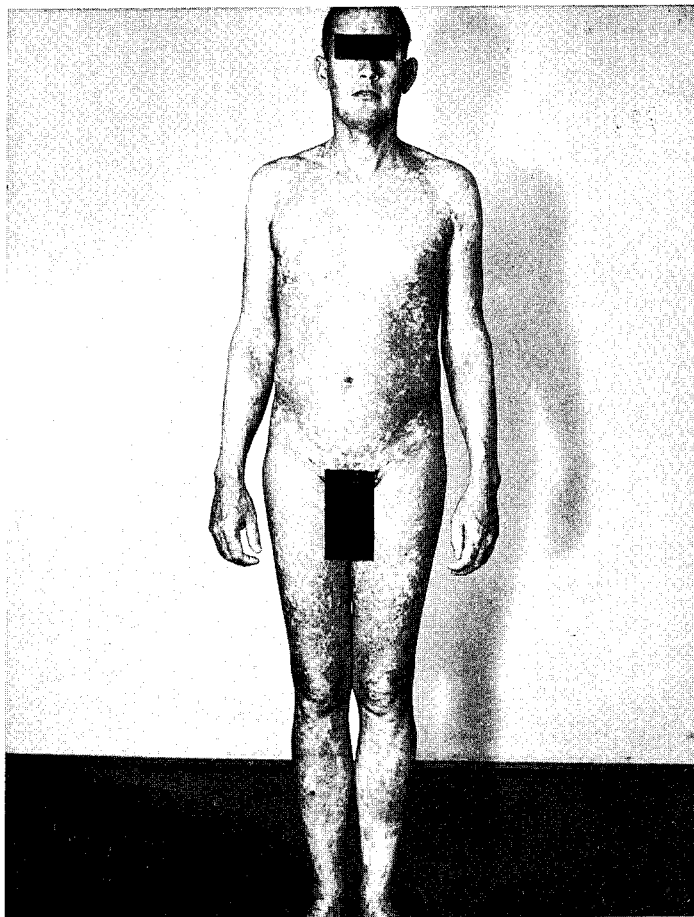
FIGURE 115.—Atabrine dermatitis. Marked, very extensive hyperpigmentation, 6 months after onset of eruption, which was mixture of lichenoid and eczematoid lesions.

but he himself saw no such cases, and he doubted the accuracy of the description. The discoloration of the nails gave rise to no symptoms, and soldiers seldom sought medical attention except to satisfy their curiosity.

One patient observed by Capt. William D. Wolfe, MC, at the 35th General Hospital, presented a wide zone of deep violet pigmentation across the anterior aspect of the neck and extending onto the upper chest, where it ended sharply. Except for its extent, it suggested (as did the first cases observed by Dr. Hopkins) a phenolphthalein reaction. Biopsy revealed a strip of lymphocytic infiltration in the papillary zone of the cutis. The violet color was explained by the presence of numerous chromatophores stuffed with melanin.

FIGURE 116.—Pigmented patches in Atabrine dermatitis.

Dr. Hopkins conceded that the occurrence of blue nails with lichen planus might be no more than a coincidence. Many other skin lesions in the Southwest Pacific Area, especially ecthyma, showed puzzling blue to violet tinges and scars, sometimes when there was no other evidence of skin disease. He believed that the problem should be investigated but confessed that he could see no approach that offered any promise.

16. Cutaneous sequelae, including the pigmentation already described; atrophy of the skin, varying from slight to marked and occurring after involution of some of the lichenoid nodules and plaques; the development, in some cases, of paper-thin skin, mottled with areas of pigmentation and depigmentation and usually occurring on the dorsal surfaces of the feet and hands; alopecia; exfoliation of the nails; and, in severe cases, generalized and localized anhidrosis that exempted the forehead and axillas.

Figures collected by Major Schmitt and Major Ambler (tables 103 and 104) show the respective anatomic distribution of lesions in the fully developed lichenoid and eczematous complex and of lichenoid papules and nodules. It is notable that the distribution of the lichenoid papules differs from that of combined lichenoid and eczematoid lesions.

Symptoms.—Pruritus was present in all cases, but varied greatly in severity. As a rule, it was severe initially and then moderated. Acute inter-

FIGURE 117.—Atabrine dermatitis, with papulosquamous lesions resembling pityriasis rosea.

triginous lesions caused pain on movement, and lesions on the hands interfered with useful work.

Constitutional manifestations.—The majority of patients with uncomplicated diseases had little evidence of systemic involvement, and many with serious lichenoid lesions appeared well nourished and in excellent general health. Major Ambler, however, and a number of other observers noted significant losses of weight in about half of their cases. Patients with extensive exfoliative dermatitic complications usually suffered from malaise, asthenia, fever, and lymphadenopathy, though the proportion of such manifestations was no greater in this syndrome than in generalized cutaneous eczematoid eruptions from other causes.

In very occasional cases, aplastic anemia, other severe blood dyscrasia such as agranulocytosis, and severe acute hepatitis occurred in association with the lichenoid-eczematoid syndrome. Similar complications, however, were occasionally observed in men taking Atabrine who did not develop skin lesions. The case fatality rate of hematopoietic complications was very high. The relation between them and the skin disease was not clear, but the association was striking.

Chronology and course.—The sequence of events in atypical lichen planus and eczematoid dermatitis, as well as the types and combinations

FIGURE 118.—Atabrine dermatitis, showing closeup of lesions which resemble pity-
riasis rosea.

of lesions, varied from patient to patient, though many reports emphasized
that most men who developed the syndrome had been on suppressive Ata-
brine therapy for relatively long periods before the disease appeared.
Lesions sometimes occurred abruptly, in the form of a widespread eruption,
and attained a lichenoid appearance within a week. In many other cases, the
prodromal lesions were present for weeks and the lichenoid lesions de-
veloped insidiously.

In the cases analyzed at Moore General Hospital,[76] only 20 percent of
the patients developed the disease within 3 months after institution of
Atabrine therapy, as compared with 70 percent within 6 months and 90
percent within 10 months. In the 200 cases analyzed by Major Ambler
(table 104), the onset of the lichenoid lesions was sudden (within 2 weeks)
in 126 cases and gradual in the remainder. In the 118 cases studied by
Major Schmitt (table 103), the initial eruption appeared within 1 and 3
months after suppressive Atabrine therapy was begun. The largest number
of cases developed in the fourth and fifth months; 85.3 percent of the

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[76] See footnote 64, p. 651.

FIGURE 119.—Chinese patient with severe generalized exfo-
liative dermatitis complicated by severe hepatitis and aplastic
anemia. This patient died.

eruptions became evident within the first 8 months, and only 3 percent ap-
peared after a year.

Major Harvey's group,[77] as well as other observers, thought that, when
daily doses of Atabrine were larger than the routine prescribed dosage
(0.1 gm.), the percentage of cutaneous reactions was unusually high. Nu-
merous patients were observed who tolerated routine suppressive therapy
for long periods and who acquired the lichenoid and eczematoid syndrome
only when the suppressive dosage was increased or when malarial symptoms
required therapeutic dosages.

In many instances the general course of the disease was slowly pro-
gressive, with enlargement of old lesions and the appearance of new lesions

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[77] See footnote 57, p. 648.

FIGURE 120.—Atabrine dermatitis of eyelids. Note scaling, ecze-
matous character of lesions. The eyelids were a frequent early site
of involvement. This patient also had mucous membrane lesions
similar to those observed in lichen planus; scattered inflammatory,
violaceous plaques; and oozing intertriginous dermatitis of the
groins, axillas, and perianal region.

in other locations. It was often many weeks before the comfort and ef-
ficiency of the patient were seriously affected. In other cases, however, there
was rapid, generalized development of eczematoid lesions, and the clinical
picture was almost identical with that of exfoliative dermatitis except that
the skin was less uniformly involved and there was less infiltration. These
generalized exacerbations, which could occur at any time during the course
of the disease but which were likely to occur early, were always serious and
were potentially fatal. When the lesions involuted, the eruption became
dry and scaly and often progressed to the development of pigmented flat or
hyperkeratotic lichenoid lesions on the sites of former eczematoid plaques.

In some instances, there was definite evidence of photosensitivity, with
lesions on the face, the anterior surface of the neck, and the dorsal surface
of the hands. In other instances, no reactions of this kind were seen, even
after prolonged exposure to sunlight.

In general, the lesions persisted for weeks and months, depending upon
a number of factors, some of which were poorly understood.

To summarize the clinical course: A few patients had a gradual or
rapid onset of lichenoid lesions, either preceded or accompanied by eczema-
toid lesions. A large group presented prodromal eczematoid or inflammatory
lesions of one type or another, followed by gradual or rapid onset of
lichenoid lesions that developed primarily or at the sites of the eczematoid
lesions. In these cases, the eruptions were a mixture of lichenoid and ecze-
matoid lesions, with one type or the other predominating. Still another
group of patients had an almost concomitant onset and development of
lichenoid and eczematoid lesions. Some patients had eczematoid lesions fol-
lowed in a short time by explosive generalized exacerbations suggestive of
exfoliative dermatitis; when the eczematoid-exfoliative reaction subsided,

FIGURE 121.—Atabrine dermatitis. Note the
cheilitis characterized by superficial fissuring. Note
also the diffuse violaceous hyperpigmentation of the
face and neck. This picture was taken 2½ months
after an acute exacerbation, characterized by oozing
dermatitis of the face and neck.

there was an onset of lichenoid papules and plaques. Finally, some patients
had lesions that remained primarily eczematoid throughout the course of
the eruption, with the lichenoid phase limited to relatively transitory lesions
of the mucous membranes.

The degree and rate of improvement also varied. In the majority of
the cases studied at Moore General Hospital,[78] improvement progressed to
a point at which the lesions became flat, erythema subsided, and, at the end
of 6 to 9 months, pigmentation was the only evidence of the disease.

Although precise data on comparable groups of cases are not avail-
able, it seems clear that improvement was much more rapid when patients
were removed to a temperate climate from the hot, humid climate in which
their disease had developed. On the other hand, their lesions sometimes
cleared up completely even when they were hospitalized in the Tropics.

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[81] See footnote 64, p. 651.

FIGURE 122.—Nail changes in Atabrine dermatitis, 3 months after onset. Note linear striation and thickening of distal part of nails. In this case, all the toenails and all the fingernails were involved.

Laboratory Investigations

The reports of the laboratory studies on this syndrome carried out by various observers and groups in the Southwest Pacific Area were collected and analyzed by Major Ambler and his associates.[79] They included urinalysis, blood counts, blood sedimentation rates, serum protein determinations, serologic tests, and examinations for fungi. All results were negative except for (1) leukocytosis and increased sedimentation rates, both of which, when they occurred, could be attributed to secondary pyogenic infection, and (2) low serum protein levels in patients with exfoliative dermatitis and extensive exudation.

The (summarized) report that follows concerns the results of multiple tests of hepatic function carried out on 24 patients who had contracted the disease in Assam and north Burma by Maj. Thomas E. Machella, MC.[80]

1. Definite evidence of abnormalities in the role of the liver in carbohydrate metabolism was found in patients with active skin lesions of atypical lichen planus. There was evidence of impairment of glycogenolysis in all cases; increased tolerance to glucose in 11; and decreased tolerance to it in 2.

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[79] See footnote 55, p. 647.

[80] Letter, Maj. Thomas E. Machella, MC, 20th General Hospital, to The Surgeon General, War Department, Washington, D.C., through the Commanding General, 20th General Hospital, Advance Section, U.S. Forces in IBT, APO 689, 6 Aug. 1945, subject: Atypical Lichen Planus.

2. Impairment of the ability of the liver to remove bromsulphthalein from the bloodstream was found in 16 of the more severe cases of atypical lichen planus and in 3 of those with mild lesions or lesions that had involuted.

3. The mean total serum proteins were low normal or actually low, with the albumin fraction decreased. The lowest values occurred in those patients with the more severe skin lesions who also had disturbances in carbohydrate metabolism and excretory function.

4. No significant disturbances were found in cholesterol or the cholesterol esters, the plasma fibrinogen, or the detoxifying function of the liver.

5. The disturbances observed in these cases in carbohydrate metabolism, serum protein levels, and excretory hepatic function were comparable with the abnormalities that may occur when a liver is low in glycogen and high in fat. They were such as might occur when the sympathetic nervous system is not functioning properly.

The liver function tests performed on 35 patients at Moore General Hospital [81] included hippuric acid synthesis, bromsulphthalein retention, cephalin-cholesterol flocculation, icterus index, and prothrombin time. Three of these tests were abnormal in 1 patient, 2 were abnormal in 7, and 1 was abnormal in 6. It should be emphasized that these studies were made in a hospital in the Zone of Interior weeks and months after the onset of the disease, in contrast to Major Machella's studies, which were carried out in an oversea theater a few weeks after the onset.

Therapy

Recognition of the fact that Atabrine was the basic etiologic factor in eczematoid dermatitis and atypical lichen planus pointed to the basic therapeutic measure, withdrawal of the causative drug. Majors Schmitt, Ambler, Nisbet, and Harvey promptly arrived at this conclusion in the Southwest Pacific Area, as did Major Livingood and others in China-Burma-India. It was also soon learned, as already mentioned, that these patients were likely to clear more rapidly if they were removed to a cooler climate and that relapse was likely to occur if they were returned to the Tropics.

Time-honored textbook remedies for lichen planus, such as bismuth and arsenic, had no effect on the course of this new syndrome, and on theoretical grounds, these drugs were strictly contraindicated. These patients would not tolerate irritating local treatment, such as salicylic acid and tincture of iodine. In fact, the commonest mistake in the treatment of the eczematoid phase of the eruption was the use of strong fungicidal measures.

Penicillin, used parenterally and locally, was beneficial, and was sometimes lifesaving, in the treatment of secondary pyogenic infection, particularly of exacerbations in the form of generalized exfoliative dermatitis.

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[81] See footnote 64, p. 651.

Other useful measures in generalized involvement were plasma and glucose infusions, vitamin therapy, and liver extract.

Major Machella pointed out, in view of the abnormalities found in the liver function studies made, that correction of these dysfunctions should be an integral part of the therapeutic regimen.[82] An important component of treatment was a diet high in protein and carbohydrate but low in fat. A vitamin supplement was also recommended.

In the 118 cases studied by Major Schmitt and his Australian associates,[83] well over half of the patients experienced improvement within a month after Atabrine was discontinued, but 20 percent noted no improvement for 2 to 3 months. About 10 percent began to improve while they were still in New Guinea and still taking Atabrine. Of the patients not taking Atabrine when improvement began, 57 were in the United States, 20 were en route there, and 7 were still in New Guinea.

Administrative Action

Administrative action in this matter had to be undertaken carefully. Widespread dissemination of information concerning the relation between Atabrine and lichenoid and eczematoid dermatitis would have resulted in a sharp decrease in the use of suppressive malaria therapy. The increased malaria rate that would inevitably have resulted might have seriously impaired the military effort in both the Southwest Pacific Area and the China-Burma-India theater. For these reasons, as soon as the causal relation was recognized, every effort was made to avoid open discussion of the subject, and The Surgeon General placed a RESTRICTED classification on all oral and written communications concerning it. On the other hand, it was essential that medical officers in the theaters and areas affected should have the information. It was widely disseminated by appropriate consultants, but the restriction was so effective that many medical officers did not learn of the relation of Atabrine to the lichenoid-eczematoid syndrome until after the war.

The increasing proof that Atabrine was the basic etiologic factor in this new syndrome, the evident magnitude of the problem, and the realization that many medical officers were aware of the data that had been accumulated prompted the Medical Consultants Division, OTSG, to issue a RESTRICTED letter on the subject which was eventually disseminated to all theaters and commands.[84] In substance, this letter contained the following information:

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[82] See footnote 80, p. 669.

[83] See footnote 54, p. 647.

[84] Restricted Letter, Office of The Surgeon General, U. S. Army, to Surgeons, all major oversea theaters, all Army Service Forces service commands, and the Military District of Washington, 14 Aug. 1945, subject: Reactions Attributed to Atabrine.

1. The military value of Atabrine in suppressing vivax malaria and in attacks of falciparum malaria far outweighs the untoward effects that have been attributed, with reason, to the use of this drug.

2. Suppressive doses greater than 0.7 gm. per week should not be employed routinely. This amount has been shown to provide adequate protection against clinical attacks of malaria if Atabrine discipline is strictly enforced. In the clinical treatment of malarial attacks, the routine dosage of Atabrine should not exceed 2.8 gm. over a 7-day period.

3. Suppressive Atabrine medication should be discontinued promptly, and Atabrine should not be used therapeutically, if troops develop any of the following conditions: Atypical lichen planus; unexplained chronic eczematoid dermatoses; unexplained toxic erythematous eruptions; exfoliative dermatitis; severe leukopenia, agranulocytosis, and aplastic anemia; acute hepatitis (not including disturbances believed to be caused by malaria); and any toxic psychoses that, after careful clinical study, can be reasonably attributed to Atabrine.

4. Quinine is available for the treatment of individuals who are known to be sensitive to Atabrine or to be seriously intolerant of it. Quinine should not be used, however, for units or organizations as a whole.

5. When, after thorough study, it is concluded that an individual is definitely sensitive to Atabrine (or quinine), an appropriate entry should be made, as in the case of other drugs, on WD AGO Form 8-117 (Immunization Register).

6. Caution should be exercised in attributing disease conditions to Atabrine until careful and complete studies over a period of time have established the relation. Because of the widespread use of this agent, its administration inevitably coincides with the existence of many diseases with which it has no connection. Even if a connection is established between Atabrine and any given untoward effect, the connection must be evaluated in relation to the military value of Atabrine. Since suppressive Atabrine therapy came into general use, clinical attacks of falciparum malaria have been almost eliminated and deaths from malaria have become extremely uncommon. There is no question concerning the general superiority of Atabrine over quinine, both for suppression and for clinical treatment of malaria.

7. Detailed information and instructions in regard to the possible toxic effects of Atabrine and the management of men for whom it is considered contraindicated should be disseminated to medical officers, especially those in direct charge of patients. In all discussions of the toxicity of Atabrine, its great military usefulness and the low incidence of all types of serious reactions to it should be emphasized. Discussions of its role in various disease conditions should be avoided in the presence of patients. Public discussions should be discouraged. At this time, the relation between Atabrine and the atypical lichen planus complex is classified as RESTRICTED.

8. It is recommended that the contents of this letter be communicated to medical consultants and that they be instructed to inform and advise all medical officers concerned.

Prognosis

The prognosis of both atypical lichen planus and eczematoid dermatitis was excellent, especially when Atabrine was discontinued and the patient was hospitalized and evacuated from the Tropics. Once these facts were appreciated and acted upon, the period of recovery was significantly shortened. Patients with severe eczematoid dermatitis were prone to relapse, especially if treatment was delayed until the lesions were well established on the hands, feet, or both. Perhaps 5 to 10 percent were left with a semipermanent increased sensitivity to trauma and external allergens.
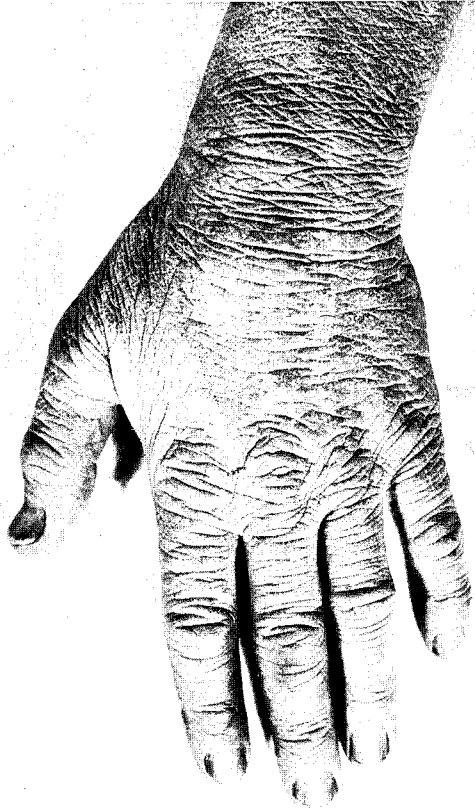
FIGURE 123.—Atabrine dermatitis, showing hyperpigmentation and thickening of skin which sometimes followed bilateral eczematoid lesions, particularly on the dorsum of the hands and feet.

Cases complicated by blood dyscrasia, severe hepatitis, or septicemia were usually fatal. These complications, which fortunately were uncommon, tended to occur in patients with severe generalized exfoliative dermatitis. Patients who recovered from them always had protracted courses.

Alopecia and sweating abnormalities cleared up spontaneously in almost all cases, though in some patients with deep obstruction of the sweat glands, severe intolerance to heat and apparently permanent anhidrosis developed. It was thought that the hyperpigmentation (fig. 123), which was frequently striking and sometimes disfiguring when the patients were received from overseas, would eventually disappear entirely, an expectation that has been largely fulfilled.

CHAPTER XXI

Psychosomatic Medicine

Colonel Albert J. Glass, MC, USA (Ret.)

Part I.   During Selection for Military Service

THE PSYCHOSOMATIC APPROACH

Psychosomatic medicine, as the term is used in this chapter, is broadly defined as a professional approach to disease and disability conceived as a mind-body whole. This viewpoint, which is held by most workers in the field of psychosomatic medicine,[1] is perhaps most clearly elucidated by H. Flanders Dunbar [2] who comments: "The term 'psychosomatic' is descriptive rather of the observer in his endeavor to apprehend than of the organism involved. Psyche and soma merely represent two angles of observation." Such a concept views every disease as psychosomatic since in all forms of illness the defensive reaction of the individual against threats from within or without involves the interrelationship of the resources of both psyche and soma operating together as a unity. In effect, disease is but another form of organismal adaptation.

World War II began during a favorable period in the development of the psychosomatic approach. The previous several decades had seen a growing interest in the influence of emotions upon bodily changes. There were many contributions demonstrating that somatic symptoms arose from psychic causes, and vice versa, but more important were the increasing efforts to discover the mechanisms involved. The year 1935 saw the publication of the monumental work by Dunbar, which surveyed the literature on psychosomatic interrelationships for the years 1910–33. In various symposia and professional meetings, the phenomena of total reaction in disease were discussed. In 1939, a regularly issued quarterly journal, *Psychosomatic Medicine,* came into existence. Despite such progress, the semantic confusion and the dichotomy inherent in the term "psychosomatic" fostered in many a continuation of the traditional separation of mind and body and permitted others to assume the complacent overgeneralization that psychosomatic medicine only restated an old and well-known axiom of medical practice.

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[1] (1) Weiss, Edward, and English, O. Spurgeon: Psychosomatic Medicine. Philadelphia: W. B. Saunders Co., 1943, pp. 1–15. (2) Menninger, W. C.: Psychosomatic Medicine on General Medical Wards. Bull. U.S. Army M. Dept. 4: 545–550, November 1945.

[2] Dunbar, H. Flanders: Emotions and Bodily Changes. 2d edition. New York: Columbia University Press, 1938.

Mobilization and war with their severe and unusual stresses created exceptional conditions for the recognition and utilization of psychosomatic concepts. There were produced numerous and obvious manifestations of mind-body interrelationships that remain latent under ordinary circumstances. This greater opportunity to notice the effect of emotions upon bodily changes could not fail to influence the professional thinking of most physicians engaged in wartime military practice. Another favorable circumstance lay in the close working relationship of psychiatrists with their medical colleagues. Not only was psychiatric opinion more readily obtained than in civil practice but informal discussions, among physicians of various medical disciplines who shared common frustrations, helped to dispel the skepticism and mysticism that so often surround psychiatrists and their concepts.

On the other hand, certain aspects of World War II military medicine militated against acceptance of the psychosomatic viewpoint. One deterrent arose from the specialization which, as in civilian medicine, was practiced in most large army hospitals; that is, the various separate clinical services and sections had each its own approach, and medical officers could readily avoid psychosomatic considerations by the transfer of patients whose manifestations did not fall within their specialized sphere. This attitude was illustrated especially by the almost universal efforts of medical officers to transfer to the psychiatric wards all patients who failed to exhibit a sufficient degree of so-called organic disease. It should be stated, however, that the large patient load often carried by the individual ward officer made understandable attempts to lighten this burden by removing puzzling or annoying patients.

The administrative necessity of adhering to a standard diagnostic code also fostered a one-sided attitude toward disease and disability. Then, as today, diagnosis mainly indicated tissue pathology or pathophysiology rather than the total reaction involved in the disease process for which there is as yet no adequate terminology.

Another obstacle came from the emotional difficulties that arose in many of the newly created medical officers by their transition from civil to military life. Physicians, like other participants in war, were separated from their loved ones, suffered economic losses, and endured varying degrees of hardship and danger. But apparently, these vicissitudes were not the major cause for their mental unrest. This mental unrest was due rather to a change from a status in which there was a high degree of independence, activity, and gratification in professional work and community prestige to the relatively restricted role of a subordinate medical officer who was often blocked from promotion, through no fault of his own, and who was frustrated by periods of delay and inactivity and by administrative procedures and other restrictions that seemed to be an inevitable part of military medicine. The psychic unrest thus created made it difficult for some medical

officers to evaluate objectively the manifestations of disease unless un-doubted structural changes were evident. Psychosomatic interrelationships were often either overlooked, owing to the close identification of the medical officer with the patient's psychological problems, or, if recognized, rejected as not being a legitimate reason for symptomatology.

In addition to these favorable and unfavorable influences, there were other factors that affected psychosomatic medicine in World War II. Various directives and regulations were issued that periodically altered the physical and mental standards for the utilization of manpower. Also, there were situational stresses of different types and intensity, from training to com-bat, which had a pertinent bearing upon the common clinical syndromes that were presented to the medical officer. In this chapter, consideration will be given to the development of psychosomatic concepts in relation to the following areas of the military effort; namely, (1) selection at induction or enlistment, (2) training and other service in the Zone of Interior, and (3) oversea duty and combat.

THE FIRST YEAR

The growth of psychosomatic insight during World War II is perhaps best illustrated by the change that occurred in medical thinking relative to the selection of men for military service. Here was a most difficult task, which not only involved the problem of choosing men capable of performing military duty from a physical, mental, and educational standpoint but which was further complicated by factors such as the motivation of the selectees concerned, the possibility of future compensation for disability, and the demands of a democratic society for equality in the distribution of deprivation and sacrifice. Rules of deferment for age, marital status, num-ber of dependents, essential occupation, and the like could be sharply de-fined. But, except for the obviously handicapped, no such clear-cut delinea-tion was possible by the known methods of medical selection. To meet this problem, MR (Mobilization Regulation) 1–9, War Department, 31 August 1940, was issued, prescribing physical and mental standards to be used as a guide for induction and enlistment. These regulations, however, soon came to be used mainly as a rigid directive because the civilian physicians and the new medical officers, who comprised the vast majority of medical exam-iners at local draft boards and Army induction stations, had little or no actual experience with the duties or conditions under which soldiers live and work. Moreover, they were strongly influenced by the unanimous opin-ion of prominent civilian and military medical authorities [3] who, placing

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[3] (1) Hillman, C. C.: Medical Problems Encountered in Military Service. Am. Int. Med. 13: 2205–2211. June 1940. (Also Army M. Bull. No. 53: 27–35, July 1940.) (2) Editorial: With Emphasis on the Word Selective. Mil. Surgeon 87: 265–266, September 1940. (3) Fox, L. A.: The Medical Officer's Responsibility in the Present Emergency. Army M. Bull. No. 55: 77–86, January 1941. (4) Bowman, K. M.: Psychiatric Examination in the Armed Forces. War Med. 1: 213–218, March 1941.

much emphasis upon the experience and statistics of World War I, called upon the examining physicians to exclude persons of substandard mentality and physique, on the grounds that they were both useless to the military and quickly joined the ranks of the compensable. Apparently, expert opinion at this time considered every inductee as a future combat participant, and it was considered axiomatic that modern war required only those with superior mental and physical stamina. Particularly emphasized was the careful detection and elimination of unstable persons and mental misfits.[4] Most of the psychiatric authorities held the optimistic belief that potential emotional breakdowns could be detected at induction by proper mental evaluation, and various outlines for such examination were suggested. Pratt,[5] in urging a thorough attempt to rule out mental breakdowns, quoted the British medical publication *Lancet* as advocating that medical officers turn down all men with a nervous disability, a suggestive family history, or a bad work record, and individuals who seemed otherwise doubtful. Kardiner,[6] however, was not at all certain that combat breakdowns could be predicted at induction and held that psychoneurosis was not in itself a contraindication to military service.

This emphasis upon elimination at induction in order to remove all possible failures and obtain the best of available manpower had its logical consequences. In October 1941, Selective Service Headquarters estimated that about 50 percent of selectees were disqualified for general military service because of physical, mental, and educational defects.[7] Medical causes for the first 900,000 rejections for general military service are shown in table 105.

Results of the first year's experience with medical selection confirmed an increasing awareness that men were being rejected by an unrealistic, compartmentalized, assembly-line type of examination in which each physician saw only a part of the whole and thus placed undue emphasis upon minor local bodily dysfunction or pathology.[8] Little consideration was given to the functioning of the individual as a whole person, and no attention was paid to superior motivation of special skills which might offset such unimportant defects as insufficient teeth or pilonidal sinus. The author, who served as examining physician to a local draft board during part of this period, could not adequately explain to himself nor to his layman colleagues the rejection, because of insufficient molar teeth or a small perforation of

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[4] (1) Sutton, D. G.: Naval Psychiatric Problems. Am. J. Psychiat. 97: 255–275, September 1940. (2) Circular Letter No. 19, Office of The Surgeon General, U.S. Army, 12 Mar. 1941, subject: Neuropsychiatric Examination of Applicants for Voluntary Enlistment and Selectees for Induction. (3) Madigan, P. S.: Military Psychiatry. Army M. Bull. No. 56: 61–69, April 1941. (4) Campbell, J. D.: Psychiatry and Military Service. Kentucky M. J. 39: 110–115, March 1941. (5) Porter, W. C.: Military Psychiatry and Selective Service. War Med. 1: 364–371, May 1941. (6) Cutler, E. C.: What Physicians Expect From Psychiatry. War Med. 1: 352–357, May 1941.

[5] Pratt, J. H.: Psychiatric Factors in Medical Examination. War Med. 1: 358–363, May 1941.

[6] Kardiner, A.: Neuroses of War. War Med. 1: 219–226, March 1941.

[7] Plans for Rehabilitation of Rejected Draftees. J.A.M.A. 117: 1364, 18 Oct. 1941.

[8] Menninger, W. C.: Condensed Neuropsychiatric Examination for Use by Selective Service Boards. War Med. 1: 843–853, November 1941.

TABLE 105.—*Estimated number of registrants found to be unqualified for general military service because of physical and mental defects*

Defect or disease	Registrants unqualified for general military service	
	Number	Percent
Dental defects	188,000	20.9
Defective eyes	123,000	13.7
Cardiovascular diseases	96,000	10.6
Musculoskeletal defects	61,000	6.8
Venereal diseases	57,000	6.3
Mental and nervous defects	57,000	6.3
Hernia	56,000	6.2
Defective ears	41,000	4.6
Defective feet	36,000	4.0
Defective lungs (including tuberculosis)	26,000	2.9
Miscellaneous	159,000	17.7
Total	900,000	100.0

an eardrum, of husky, alert, well-motivated men who were capable of performing strenuous activity and the acceptance of sickly, timid selectees whose entire sedentary life had been supervised carefully by an indulgent mother. As the causes for military rejection became common knowledge,[9] artificial values of health became established in the community, creating guilt and embarrassment for those rejected (the so-called 4–F group) and permitting poorly motivated persons consciously and unconsciously to exploit minor defects and subjective symptoms in order to avoid military service.

REEVALUATION OF INDUCTION STANDARDS

The disclosure of the excessive rejection rates marked the beginning of a critical reevaluation of induction standards, and with increasing needs for manpower after the outbreak of hostilities, there was a gradual policy change in the direction of considering the individual as an integrated functioning being rather than as a collection of tissues and organs. As early as July 1941, when the first 6 months of selective service operations indicated the trend toward high rejection rates, Darnell[10] made a plea for medical examiners to utilize MR 1–9 more as a guide rather than as a comprehensive directive. Also, at this time, Meehan[11] pointed out that military induction standards were designed to obtain individuals of superior qualifications for

[9] Koontz, A. R.: Has Psychiatry Failed Us in World War II? Mil. Surgeon 101: 204–208, September 1947.

[10] Darnell, J. R.: Concerning Physical Standards for Selective Service. Army M. Bull. No. 57: 18–27, July 1941.

[11] Meehan, J. W.: Health of the Nation's Manpower. Army M. Bull. No. 57: 13–17, July 1941.

1 year's service and that they should not be construed as an index of health. Meehan indicated the unrealistic nature of current dental standards by quoting from the medical statistics of the Provost Marshal General of 1875, which noted that the availability of breech-loading guns and metallic cartridges made unnecessary the biting and tearing of paper required with the old-fashioned cartridges, and thus obviated enlistment requirements for incisor teeth. In February 1942, War Department Circular No. 43 reduced the dental and visual requirements to conform more with the selectee's overall ability to function. Dental elimination rates promptly began to fall, followed somewhat later by a decline in rejections for defective vision.

The efficiency of selection from the psychiatric standpoint also came under critical scrutiny. Aita,[12] Menninger and Greenwood,[13] and Smith[14] all strongly condemned the 2- to 5-minute psychiatric examination usually performed at induction stations as being superficial and of little practical value. They called for a more comprehensive survey of the background and the current status of the inductee. In July 1942, Porter,[15] "taking stock" of the mounting psychiatric rejection rate, warned against overzealousness in psychiatric screening, seriously questioned the ability to predict psychological failure, and advocated measures such as reassignment and rehabilitation instead of rejection and discharge.

As the war progressed, it was apparent that the rejection of a high percentage of men at induction stations had failed to prevent the later appearance of numerous soldiers who were seemingly unable to perform even noncombat duties. Williams[16] argued that the quality of men selected was proof of the adequacy of induction methods, which could accordingly be measured by the relative numbers of inductees subsequently discharged for reasons of physical and mental disability. A corps area (later service command) with a high rejection rate for all causes or for a particular cause should have given to the Army such a well-selected group or category that its respective discharge rate would be small, but in a survey of the nine corps areas in the United States, Williams found much inconsistency. Only two of the corps areas followed the expected rule. The best correlation of rejection and discharge rates was for visual defects; the poorest correlation, for hernia, for defects of the ear, nose, and throat, and for neuropsychiatric and musculoskeletal defects.

Consequent to the mounting evidence that induction methods were not producing the desired results, various suggestions and policy changes were

[12] Aita, J. A.: Problem of Neurologic and Psychiatric Examination During Military Mobilization; III. Consideration of Guides for Examination. Proc. Staff Meet. Mayo Clin. 16: 307–313, 14 May 1941.

[13] Menninger, W. C., and Greenwood, E. D.: The Psychiatrist in Relation to Examining Boards. Bull. Menninger Clin. 5: 134–138, September 1941.

[14] Smith, L. H.: Psychiatric Aspects of Military Medicine. M. Clin. North America 25: 1717–1759, November 1941.

[15] Porter, W. C.: Military Psychiatry. War Med. 2: 543–550, July 1942.

[16] Williams, G. D.: U.S. Army Induction Board Experience November 1940–September 1942. Army M. Bull. No. 65: 105–135, January 1943.

proposed. Halloran and Farrell [17] and Moersch [18] called for more intensive efforts to weed out potential mental disorders at induction. Bloomberg and Hyde [19] published figures indicating that rigorous prior elimination of neurological and psychiatric disorders reduced the discharge rate. The majority of observers, however, were inclined to doubt the predictive value of induction examinations and advocated liberalization of physical and mental standards to include the current effectiveness of the individual rather than the future possibility of disability. This attitude was also dictated by the growing shortage of manpower. Koontz [20] caused all roentgenograms of registrants rejected for tuberculosis to be reviewed by a panel of experts. This procedure resulted in a 31-percent reclassification to full military service. Another 19 percent were considered borderline cases requiring further study, following which many were declared fit for induction.

Rowntree,[21] Chief Medical Officer, Selective Service System, called for a reexamination of all previous rejectees. He cited one study in which 53 percent of those reexamined were found capable of military service. Rowntree also gave current selective service data which demonstrated the effect of age upon acceptance for military service, as follows:

Age	Percent accepted
45	15
36	30
21	70
20	74
19	82
18	84

Reynolds [22] noted the benefits of obtaining objective information in medical histories from civilian sources and gave results of using such a method in Pennsylvania. He recommended this procedure as of special value with individuals previously hospitalized for tuberculosis or for neuropsychiatric disease. A routine procedure, operational in the State of Maryland since the beginning of Selective Service, checked the name of each selectee against a roster of prior State hospital admissions.[23] A similar program had been instituted in New York, N.Y.[24]

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[17] Halloran, R. D., and Farrell, M. J.: The Function of Neuropsychiatry in the Army. Am. J. Psychiat. 100: 14–20, July 1943.

[18] Moersch, F. P.: The Psychoneuroses of War. War Med. 4: 490–496, November 1943.

[19] Bloomberg, W., and Hyde, R. W.: Survey of Neuropsychiatric Work at Boston Induction Station. Am. J. Psychiat. 99: 23–28, July 1942.

[20] Koontz, A. R.: Cases Rejected for Army Service on the Basis of Chest Films Alone. Mil. Surgeon 91: 440–442, October 1942.

[21] Rowntree, L. G.: Wartime Problems of Selective Service. Mil. Surgeon 92: 149–162, February 1943.

[22] Reynolds, C. R.: The Medical and Epidemiological Management of Selective Service Men Rejected for Military Service. Mil. Surgeon 92: 140–148, February 1943.

[23] Koontz, A. R.: Keeping Men With Psychiatric Records Out of the Army. Mil. Surgeon 91: 313–314, September 1942.

[24] (1) Kopetsky, S. J.: Validity of Psychiatric Criteria for Rejection for Service With the Armed Forces: Study of Cases of 696 Registrants With Psychiatric Diagnoses From New York City Selective Service Area. War Med. 6: 357–368, December 1944. (2) McBee, M., and Stevenson, G. S.: Role of Psychiatric Social Worker in Selection of Men for the Armed Forces. Am. J. Psychiat. 99: 431–434, November 1942.

Cardiovascular manifestations.—Also noted were many instances of mind-body relationships that were characteristic of the induction examination itself and that had a pertinent bearing upon acceptance or rejection. Of particular importance were various abnormal cardiovascular manifestations. Kilgore [25] and Lowry [26] found that examination excitement produced such variations of pulse rate and blood pressure in young men applying for military service that recordings were deemed to be of little value at any given time. Both of these observers recommended that, as a better guide to determining the cardiovascular status, examiners should consider general appearance, coordination, posture, color, and strength and endurance as judged by action in the present and the past. Lowry pointed out that similar abnormal cardiovascular findings may be present in men who have served successfully for many years. He explained the fluctuations as being due to the incomplete development of young men, causing them to be highly responsive to sympathetic stimulation.

Wilburne and Ceccolini [27] reviewed blood pressure findings in 25,000 consecutive induction examinations. Using 150 mm. Hg systolic and 90 mm. Hg diastolic as the upper limit of normal, they found that even after rest periods hypertension occurred at the rate of 0.96 percent, as compared with 0.47 percent for insurance examinations and 1.6 percent for examinations of young college students. In this large series, they found that from 18 to 20 percent of selectees had elevated blood pressures on initial readings if the current standard of 140 mm. systolic was used. Rest periods from 15 to 30 minutes reduced the blood pressure of the vast majority of cases to normal levels. The most marked instance of lability was an initial blood pressure of 230/112 which, after 35 minutes of rest, decreased to 146/80. Orenstein,[28] using a standard of 140/90, found hypertension without other cardiovascular or renal findings to be three times more common among Negro selectees than among their white counterparts. Rogers and Palmer [29] discussed the relationship of transient, nervous hypertension to so-called essential hypertension. Examination of candidates in an officer procurement center indicated that 14 percent had mild, variable hypertension with no organic changes at the initial examination. These individuals frequently displayed signs of a nervous pressor reaction, such as tachycardia and sweating. Their reaction to the cold test was greater than normal but less than in early, mild, definite hypertension, and responses to exercise and position were not significant. Prognosis, as revealed by a followup of 25 cases, was excellent. Wilburne and Ceccolini concluded that even early signs of essential hypertension need not be disqualifying, and they recommended ac-

[25] Kilgore, E. S.: The Heart in Military Service. J.A.M.A. 117: 258–260, 26 July 1941.

[26] Lowry, E. F.: Evaluation of Heart Signs in Navy Recruiting. Mil. Surgeon 90: 37–44, January 1942.

[27] Wilburne, M., and Ceccolini, E. M.: Note on the Incidence of Arterial Hypertension in 25,000 Army Examinees. Army M. Bull. No. 68: 118–125, July 1943.

[28] Orenstein, L. L.: Hypertension in Young Negroes. War Med. 4: 422–424, October 1943.

[29] Rogers, W. F., and Palmer, R. S.: Transient Nervous Hypertension as a Military Risk; Its Relation to Essential Hypertension, New England J. Med. 230: 39–42, 13 Jan. 1944.

ceptance of applicants with variable hypertension above the standard limits under the following conditions: A negative family history of death from cardiovascular disease under 60, absence of pronounced tachycardia, normal fundi, an age of 40 years or younger, and a response to cold test of less than 20 systolic and 15 diastolic.

A reevaluation of rejectees for cardiovascular reasons [30] resulted in 17.3 percent being resubmitted as fit for military service. From this reevaluation, Fenn and his associates found that cardiovascular disease accounted for 10 percent of rejectees between the ages of 18 and 38. The common categories were as follows: Rheumatic heart disease, 50 percent; hypertension, 21 percent; neurocirculatory asthenia, 5 percent; and sinus tachycardia, 4 percent. These observers recommended that blood pressure standards be raised to 160/90 in nervous persons and that the pulse limits be placed between 40 and 120. In regard to neurocirculatory asthenia, it has been noted by British observers that this phenomenon was far less frequent than in World War I.[31] Similar observations were noted in the United States.[32]

Neurocirculatory asthenia.—Starr [33] reported on a ballistocardiographic study of draftees who had been rejected for neurocirculatory asthenia. He found that abnormalities of the circulation could be demonstrated in 75 percent of the cases and recommended the use of the ballistocardiograph for the detection of malingerers who feigned symptoms of this type. Starr was of the opinion that neurocirculatory asthenia was in no sense a disease for it affects neither health nor duration of life. He considered that the syndrome constituted a maladjustment of the circulation, no doubt precipitated by emotion but primarily a predisposition which, like clumsy movement of muscles, usually dates from early life and may be hereditary. He noted that many of those studied had selected certain light occupations and avoided others because they were aware of being made worse by emotion and by physical stress, which explained why they "quit" or broke down when placed at heavy work in the service.

Albuminuria.—Another example of psychosomatic interrelationships was the frequent occurrence in the young inductees of albuminuria without apparent cause. This phenomenon had been observed for many years and was variously described as benign, orthostatic, or psychogenic. It posed a chronic and annoying problem in evaluation for military service. Kidney disease was often suspected, and many individuals were rejected. Young,

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[30] Fenn, G. K., Kerr, W. J., Levy, R. L., Stroud, W. D., and White, P. D.: Reexamination of 4,994 Men Rejected for General Military Service Because of Diagnosis of Cardiovascular Defects. Am. Heart J. 27: 435–501, April 1944.

[31] Jones, M., and Scarisbrick, R.: Effort Intolerance in Soldiers: A Review of Five Hundred Cases. War Med. 2: 901–911, November 1942.

[32] Dunn, W. H.: Gastroduodenal Disorders; An Important Wartime Medical Problem. War Med. 2: 967–983, November 1942.

[33] Starr, I.: Ballistocardiographic Studies of Draftees Rejected for Neurocirculatory Asthenia. War Med. 5: 155–162, March 1944.

Haines, and Prince [34] stated that in their experience one out of every four rejections by Army induction boards for albuminuria was established by careful clinical and laboratory tests to be of orthostatic origin, with no renal lesions present. They emphasized the value of obtaining urine specimens after subjects had been placed in an exaggerated lordotic position. From their studies, they were convinced that albuminuria of this origin is harmless and disappears with age. A careful study of this problem was also made by Ahronheim [35] in the examination of air cadets. He found that 554 out of 1,000 men displayed albuminuria in one or both specimens taken before and after the routine intravenous withdrawal of blood. Of those who fainted during blood removal, 100 percent exhibited albuminuria in subsequent specimens. Ahronheim noted that similar observations had been made on college students [36] and on frightened cats.[37] He gave support for his thesis that this type of albuminuria was of psychogenic etiology by citing the following incidents: (1) a cadet fainted during blood withdrawal and fell, striking his head and causing a bloody laceration. Of the 17 onlooking candidates awaiting their turn, 15 exhibited albumin in the urine specimens collected at this time. (2) A pilot who emerged unharmed from a nerve-racking crashlanding had 3+ albuminuria, which cleared by the next morning. (3) Subjects with albuminuria were given a placebo of a bright color and bitter taste to drink and were told that it was a potent medicine. In over 50 percent of the cases, the albuminuria promptly cleared. Ahronheim also found that this phenomenon decreased with age and that higher age groups did not respond to emotional stimuli by albuminuria.

REVISED STANDARDS

Toward the latter part of 1943 and in early 1944, the increasing evidences of failure in medical selection had become crystallized into overt admissions of error in aims and methods. A semiofficial editorial [38] pointed out that current neuropsychiatric incidence was three times that of World War I, despite the fact that neuropsychiatric rejections were three to four times greater than in World War I. Farrell and Appel,[39] emphasizing the limitations of psychiatric screening, recognized that psychiatric breakdowns in combat could not be predicted at induction since the breakdowns were a complex resultant of failures in group relationships, in leadership, and in training, complicated by fatigue, hunger, and other physiological

[34] Young, H. H., Haines, J. S., and Prince, C. L.: Orthostatic Albuminuria: The Importance of Its Recognition by Medical Examining Boards. Mil. Surgeon 92: 353–365, April 1943.

[35] Ahronheim, J. H.: Emotional Albuminuria. War Med. 5: 267–270, May 1944.

[36] Diehl, H. S., and McKinlay, C. A.: Albuminuria in College Men. Arch. Int. Med. 49: 45–55, January 1932.

[37] Starr, I., Jr.: The Production of Albuminuria by Renal Vasoconstriction in Animals and Man. J. Exper. Med. 43: 31–51, January 1926.

[38] Neuropsychiatric Disease: Causes and Prevention. Bull. U.S. Army M. Dept. 1: 9–13, October 1943.

[39] Farrell, M. J., and Appel, J. W.: Current Trends in Military Neuropsychiatry. Bull. U.S. Army M. Dept. 2: 44–50, July 1944.

factors. These authors urged consideration of preventive measures rather than elimination. Policy changes were instituted that completely reversed the former concept of screening out all potential breakdowns. War Department Technical Bulletin (TB MED) 33, issued on 21 April 1944,[40] pointed out that the acute need for manpower made imperative the induction of all men who had a reasonable chance of adjusting themselves to the service. This change was incorporated into MR 1–9, in June 1945. In several studies of successful combat and noncombat soldiers,[41] individuals were found to have performed satisfactory or superior service despite a background of psychoneurotic predispositions.[42] Doubts about the value of medical screening became widespread, and to some [43] it now seemed best to induct all but the halt and the blind—the obviously incapable—and rely upon basic training as a practical test of fitness.

It was evident that a more sensible viewpoint was needed in the medical selection of men for military service. Steps were taken in that direction by borrowing methods employed by the Canadian Army, which had been reported on favorably by Meakins [44] and by Kubie.[45]

The Canadian Army system, known as PULHEMS, was a survey of seven physical and mental qualities numerically graded from one to four, the higher numbers indicating increasing dysfunction in the particular category: P represented overall physical endurance and capacity; U referred to the upper extremities; L, lower extremities; H, hearing; E, eyes or vision; M, mental ability or intelligence; and S, emotional stability. This method embodied the psychosomatic viewpoint of considering the entire individual, yet paying attention to local defects. It had the advantage of considering in one spectrum the overall capabilities and incapabilities of the individual. It was introduced in the American Army on a small scale in the spring of 1942 and came to be more widely used in 1944 and 1945.[46]

[40] War Department Technical Bulletin (TB MED) 33, 21 Apr. 1944, subject: Induction Station Neuropsychiatric Examination.

[41] (1) Sheps, J. G.: A Psychiatric Study of Successful Soldiers. J.A.M.A. 126: 271–273, 30 Sept. 1944. (2) Needles, W.: The Successful Neurotic Soldier. Bull. U.S. Army M. Dept. 4: 673–682, December 1945.

[42] During the postwar period, there appeared various reviews and reflections upon the results of routine induction examinations, particularly the failures of psychiatric screening (see Menninger, William C.: Psychiatry in a Troubled World. New York: MacMillan Co., 1948, pp. 134–152). Fry (see Carmichael, L., and Mead, L. C. (editors): The Selection of Military Manpower, a Symposium. Washington, D.C., National Research Council, 1952. A Study of Special Groups by Clements C. Fry, pp. 133–148) found that 70 percent of individuals who had been psychiatric patients while in college had rendered satisfactory or better than average service during World War II, the majority as officers. J. R. Eagan, L. Jackson, and R. H. Eanes (A Study of Neuropsychiatric Rejectees. J.A.M.A. 145: 466–469, 17 Feb. 1951) found that, of men who had previously been rejected for psychiatric reasons, 79.4 percent performed their duties well, although the number of discharges for disability for the group as a whole was three times the Army's average. N. Q. Brill and G. W. Beebe (Follow-Up Study of Psychoneuroses; Preliminary Report. Am. J. Psychiat. 108: 417–425, December 1951) in followup studies of psychiatric breakdowns during military service concluded that 50 percent of them could not have been predicted by the most thorough psychiatric examination.—A. J. G.

[43] Bloomberg, W.: Plan for Screening, Induction, and Utilization of Man Power. Am. J. Psychiat. 105: 462–465, December 1948.

[44] Meakins, J. C.: "Pulhems" System of Medical Grading. Canad. M.A.J. 49: 349–354, November 1943.

[45] Kubie, L. S.: Special Aspects of Procedures and Organization for Induction and Discharge in the Canadian Army. War Med. 5: 373–377, June 1944.

[46] (1) Developments in Military Medicine. Bull. U.S. Army M. Dept. 7: 602, July 1947. (2) Supplement to Mobilization Regulations No. 1–9, Physical Profile System, 22 May 1944, revised June 1945.

Six categories (PULHES) were employed in the U.S. Army, in what became known as the Physical Profile Serial System.[47]

To summarize briefly, it may be said that the selection experiences of World War II induced an appreciation of the human being as a complex, integrated organism whose future performance could be assessed not by a narrow localized measure but only through recognition of somatic and psychic interrelationships as well as of sociological and cultural factors.

Part II.   During Training and Service in the Zone of Interior

PSYCHOSOMATIC DISORDERS DURING TRAINING

A primary mission of the World War II military program was the difficult task of transforming raw selectees into an effective fighting force. For the majority of new soldiers, this process comprised several distinct phases; namely, basic training, advanced or specialized training, unit training with battle indoctrination, and often participation in large-scale maneuvers and preparation for oversea movement. Considerable variation of the training program was necessary during the later years of the war because urgent needs for infantry and other replacements often permitted time only for basic training and preparation for oversea shipment. In addition, large numbers of troops remained in the Zone of Interior to perform the various necessary logistic and support tasks.

Although each of the phases just mentioned had its distinctive physical and emotional stress with consequent characteristic adjustment problems, the initial or basic training produced the largest number of medical and behavioral disorders. Basic training constituted the critical period of transition from civilian to military life. Here, the trainee was required abruptly to accommodate himself to separation from home, to regimentation, to lack of privacy, to enforced competition, to new dietary habits, often to sexual deprivation, and to the use of firearms and explosives, in addition to unusual and strenuous physical exertion and exposure to a relatively primitive field environment.[48] Other types of training also produced discomfort, frustration, and physiological strain which, when added to uncertain or defective

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[47] In September 1950, the Physical Profile Serial System was adopted as a common standard for all branches of the armed services (Jacobs, E. C.: Medical Screening of Military Man Power: Utilization of the Physical Profile Serial System. Mil. Surgeon 112: 112–118, February 1953; also AR 40–115, 20 Aug. 1948, subject: Physical Standards and Physical Profiling for Enlistment and Induction), and its soundness was confirmed during the Korean War. With liberal induction standards and emphasis upon proper assignment, rejection and discharge rates were not excessive. Psychiatric breakdowns increased in number during the severe battle phases, but accent upon rehabilitation and return to duty reversed the World War II experience of disability. In fact, the discharge rate for neuropsychiatric disease declined during the Korean War.— A. J. G.

[48] Menninger, William C.: Psychiatry in a Troubled World. New York: Macmillan Co., 1948, pp. 56–80.

motivation and complicated by the cultural acceptance of disease as an honorable reason for the avoidance of obligations, produced clinical syndromes that defied the usual diagnostic and treatment procedures. In general, such psychosomatic disorders were of three related types, all of which had in common a persistence of somatic complaints.

First, there was a purely psychogenic group in which little or no objective evidence of significant structural or functional pathology could be demonstrated. The patients of this group stubbornly clung to bodily symptoms and, as noted by Menninger,[49] were found almost as often on the medical and gastroenterology wards as on the psychiatric wards. Indeed, the bulk of overt psychological disorders had one or more chief complaints of headache, stomach trouble, chest pain, weakness, palpitation, backache, dizziness, arthralgia, skin rash, or diarrhea.[50]

Second, there were those well-known clinical entities generally regarded as having an emotional component in either etiology or clinical course, such as peptic ulcer, hypertension, asthma, various dermatological syndromes, migraine, and rheumatoid arthritis, which responded relatively poorly to treatment or promptly recurred upon preparation for, or after return to, duty.[51]

The third and perhaps most numerous group included personnel who persistently voiced residual somatic complaints following subsidence of the acute phase of almost any injury, illness, surgical procedure, or even physical strain. Thus, there were syndromes of painful discomfort with or without limitation of function following mild lower back injury,[52] minor head injury,[53] foot strain,[54] rheumatic fever,[55] infectious hepatitis,[56] surgery for

[49] Menninger, W. C.: Relationships of Neuropsychiatry to General Medicine and Surgery in the Army. Mil. Surgeon 96: 134–138, February 1945.

[50] (1) Brussel, J. A., and Wolpert, H. R.: The Psychoneuroses in Military Psychiatry. War Med. 3: 139–154, February 1943. (2) Altman, L. L.: Neuroses in Soldiers: Use of Sodium Amytal as an Aid to Psychotherapy. War Med. 3: 267–273, March 1943. (3) Pulsifer, L.: Psychiatric Aspects of Gastrointestinal Complaints of the Soldier in Training. Mil. Surgeon 95: 481–485, December 1944. (4) Casey, J. F.: Disciplinary Problems in a Military Neuropsychiatric Hospital. Mil. Surgeon 97: 312–317, October 1945. (5) Incidence of Somatization Reactions in Psychoneurotic Disorders. Bull. U. S. Army M. Dept. 5: 383–384, April 1946.

[51] (1) Study of Psychosomatic Dermatological Syndromes. Bull. U.S. Army M. Dept. 5: 18–20, January 1946. (2) Davis, D. B., and Bick, J. W., Jr.: The Diagnosis of Migraine in Flying Personnel. Mil. Surgeon 98: 17–20, January 1946. (3) Zanfagna, P. E.: Perennial Bronchial Asthma: Analysis of One Hundred Cases. Bull. U.S. Army M. Dept. 3: 100–103, April 1945. (4) McFarland, M. D.: Hypertension in an Army General Hospital. Mil. Surgeon 97: 209–215, September 1945. (5) Sweeney, J. S.: Gleanings From the Medical Service of a General Hospital. Mil. Surgeon 97: 7–13, July 1945.

[52] Weiss, I. I.: A Study of Camptocormia With Presentation of 3 Postspinal Cases. Mil. Surgeon 97: 462–474, December 1945.

[53] Denny-Brown, D.: Sequelae of War Head Injuries. New England J. Med. 227: 771–780, 19 Nov. 1942; 813–821, 26 Nov. 1942.

[54] (1) Cozen, L. N.: The Treatment of Painful Feet in the Army. Mil. Surgeon 91: 196–198, August 1942. (2) Burnham, W. H.: Army Foot Disabilities. Mil. Surgeon 95: 20–24, July 1944.

[55] Hench, P. S., and Boland, E. W.: The Army Rheumatism Centers. Bull. U.S. Army M. Dept. 5: 655–662, June 1946.

[56] Benjamin, J. E., and Hoyt, R. C.: Disability Following Postvaccinal (Yellow Fever) Hepatitis. J.A.M.A. 128: 319–324, 2 June 1945.

pilonidal sinus,[57] abdominal surgery,[58] elective orthopedic surgery,[59] removal of herniated nucleus pulposus,[60] and even diagnostic lumbar puncture.[61] In these cases, the persistent symptomatology could not be substantiated by clinical, X-ray, or laboratory findings, and one could only speculate regarding the probability of adhesions, scar tissue, or altered physiology as causative mechanisms.

Clearly, these complex medical problems required a total approach for proper diagnosis and treatment, but such a psychosomatic viewpoint was lacking in the early years of World War II. The newly commissioned medical officers had little practical knowledge of the military environment. It was difficult for them to appreciate that somatic symptoms could and frequently did represent the mental, physical, and cultural responses to the stress of a wartime military adaptation rather than the presence of structural or psychological disease. Also, there existed a general tendency to hospitalize military personnel for subjective complaints and relatively minor disorders. Large numbers of these ambulatory cases were admitted or retained in Army hospitals.[62] The secondary gain to be derived from illness and hospitalization soon became a familiar feature of military medicine, fixating symptomatology, vexing medical officers, and creating hostile and resentful patients.[63] The more thoroughly symptoms were investigated, the longer was the hospitalization and the more convinced became patients that they had valid medical reasons for relief from onerous duty or even for discharge from the service.

Under these circumstances of iatrogenic and hospitalistic trauma, an atmosphere was created that stimulated others in and out of the hospital to seek relief, via medical channels, for their unhappiness and discomfort. One observer, Eisendorfer,[64] commented: "Neurosis is as contagious as a virulent infection. For every neurotic patient hospitalized there are ten more with potential neuroses who do not require much stimulation to react in a similar manner." Altman and his associates [65] found:

Soldiers lack no opportunity and lose none in comparing notes while in the hospital. Enforced idleness, few recreational facilities, and prolonged hospitalization help to en-

[57] Rogers, H.: Pilonidal Sinus; The Indications for Treatment in the Military Service in Time of War. Mil. Surgeon 95: 454–457, December 1944.

[58] Bowers, W. F.: Observations in the First Six Months of the General Surgical Section of the 1,500 Bed Cantonment Type Station Hospital at Fort Leonard Wood, Missouri. Mil. Surgeon 91: 170–176, August 1942.

[59] (1) Pickett, J. C.: The Diagnosis and Treatment of Internal Derangements of the Knee Joint. Mil. Surgeon 97: 198–203, September 1945. (2) Cozen, L. N.: Malingering Among Soldiers: Orthopedic Aspects. Mil. Surgeon 92: 655–657, June 1943. (3) Willien, L. J.: Second-Year End Result of Arthrotomies of Knee. Bull. U.S. Army M. Dept. 4: 452–456, October 1945.

[60] Haynes, W. G.: Problem of Herniated Nucleus Pulposus in the Military Service. War Med. 3: 585–595, June 1943.

[61] Levin, M. J.: Lumbar Puncture Headaches. Bull. U.S. Army M. Dept. 2: 107–110, November 1944.

[62] Pignataro, F. P.: Experiences in Military Psychiatry. Mil. Surgeon 91: 453–460, October 1942.

[63] (1) Sarlin, C. N.: Psychiatric Consultations in the Army. Mil. Surgeon 97: 139–143, August 1945. (2) See footnote 49, p. 687.

[64] Eisendorfer, A.: Clinical Significance of Extramural Psychiatry in the Army. War Med. 5: 146–149, March 1944.

[65] Altman, L. L., Pillersdorf, L., and Ross, A.T.: Neuroses in Soldiers; Therapeutic Barriers. War Med. 2: 551–560, July 1942.

courage this tendency. Procedures, results of treatment, death in a ward, disposition of other soldiers or almost any other occurrence in the hospital rarely escapes them.

Frustrated medical officers defended themselves by blaming their patients for having "neurotic predisposition" or "functional overlay" or by such castigations as "misfits," "chronic complainers," "neurotics," "hysterics," or "slackers." There was a general tendency to refer these cases to the psychiatrist, as illustrated by Eisendorfer's report that 48 percent of all patients admitted to Tilton General Hospital, Fort Dix, N. J., for the first 6 months of 1943 were examined by the neuropsychiatric service for the purpose of either consultation, treatment, or disposition. But the psychiatry wards were also congested. Psychiatrists were loath to accept, as transfer patients, those who had extensive hospitalization because of either prolonged clinical investigation or residual complaints following disease, injury, or surgery. According to Altman and his coworkers, such patients were not only resistant to psychiatric exploration and treatment but were overtly hostile toward any effort to remove their favorable status of hospitalization with its expectation of medical discharge. No one wanted these patients who, in turn, resented their doctors. Thus, an impasse was created.

MEDICAL DISCHARGE

The simple solution to this impasse was medical discharge. Indeed, medical separation was not only the easy way out for both patient and medical officer but had been recommended by prominent authorities on the grounds that modern war demanded individuals of "superior mental and physical stamina."[66] Madigan,[67] considering the recruit's first year, concludes:

There is no place in the Army for the physical and mental weakling. The Army should not be regarded as a gymnasium for the training and developing of the undernourished and underdeveloped, nor a psychiatric clinic for the proper adjustment of adolescents who need emotional support.

These sentiments were echoed officially by Circular Letter No. 19[68] and supported by Billings,[69] Porter (p. 680), Harrison,[70] and other civil and military medical leaders. As a result, the medical discharge rate steadily mounted. It was further increased by the influence of War Department Circular No. 161, dated 14 July 1943,[71] which required the reevaluation and discharge of limited service personnel. In September 1943, the medical dis-

[66] See footnote 3(1), p. 677.

[67] See footnote 4(3), p. 678.

[68] See footnote 4(2), p. 678.

[68] Billings, E. G.: The Recognition, Prevention and Treatment of Personality Disorders in Soldiers. Army M. Bull. No. 58: 1–37, October 1941.

[70] Harrison, F. M.: Psychiatry in the Navy. War Med. 3: 113–138, February 1943.

[71] War Department Circular No. 161, 14 July 1943, sec. III, subject: Elimination of the Term *Limited Service* With Reference to Enlisted Men.

charge rate approached 70,000 per month, which approximately equaled the induction rate.[72]

A typical picture of this problem in the early years of the war is given by Kinsey[73] who analyzed 1,000 consecutive medical discharges from the Station Hospital, Camp Blanding, Fla., over a 6-month period in the latter part of 1942 and early 1943. The 12 leading causes for medical separation were as follows:

	Percent
Psychoneuroses (all types)	40.2
Duodenal ulcer	7.4
Psychoses (all types)	6.9
Arthritis	5.9
Asthma	3.8
Organic and central nervous system disease	3.6
Epilepsy	2.7
Rheumatic heart disease	2.6
Tuberculosis (pulmonary)	1.7
Deformities of extremities	1.5
Bronchitis (chronic)	1.3
Hernia (inguinal, indirect, reducible)	1.2

Similar findings were reported by Pignataro[74] from the Station Hospital, Camp Livingston, La., for 1941 and 1942. Kinsey commented that almost all the psychoneurotics had symptoms referable to the gastrointestinal tract or to the cardiovascular system. In most of the so-called organic categories, neurotic predisposition, functional overlay, or poor motivation were considered the primary cause of discharge. Peptic ulcer promptly recurred when patients were returned to duty. Depression and lack of interest were noted in most cases discharged for arthritis. Asthmatics all admitted that their illness occurred before induction but insisted that they could not perform physical work in the service and if forced to do so would suffer severe impairment of health. It was impossible to attempt a trial of duty for patients with minimal rheumatic heart disease as they began to complain upon leaving the hospital. The low incidence of discharge for orthopedic conditions is accounted for by the number of instances in which associated psychoneurotic disease was regarded as the primary reason for their medical disability.

When these men were questioned just before discharge, 60 percent said they should not have been inducted and could not be adjusted in the Army under any circumstances; 25 percent said they could have been adjusted if given a job to which they were accustomed upon entry in the Army but "they were too nervous to do any good now." Fifteen percent felt that they could have been adjusted if given the right commanding officer or "had been

[72] Disability Discharges. Bull. U.S. Army M. Dept. 2: 52–55, December 1944.

[73] Kinsey, R. E.: Study of 1,000 Cases Separated From the Army on Certificate of Disability for Discharge. Bull. U.S. Army M. Dept. 1: 64–75, October 1943.

[74] See footnote 62, p. 688.

given a break" or "if things had gone right at home." Paradoxically, the majority of these men planned to work soon after discharge in defense plants or on a farm. Kinsey came to the pertinent conclusion that the major problem in most of these individuals was one of adjustment to army life rather than incapacitating disease.

POLICY OF MAXIMUM UTILIZATION

As the foregoing reports indicate, medical officers, with time and experience, learned that the purely medical considerations of symptoms, diagnosis, clinical course, and treatment of illness or injury could not be disassociated from the physiological and psychological problems of military adjustment. Meanwhile, developing manpower shortages demanded the salvage of so-called weaklings and misfits, if only for limited duty. A reorientation of medical thinking began to make itself felt in late 1942 and early 1943 in a liberalization of standards for selection and induction. A policy of maximum utilization was officially adopted in November 1943 with the issuance of War Department Circular No. 293,[75] stating that no man should be discharged so long as he could render adequate service in the Army. This trend was further elaborated by War Department Circular No. 81, 13 March 1945,[76] which directed against medical discharge for minor conditions, such as flat feet, mild sacrolumbar strain, and mild psychoneurosis, when the primary cause was defective attitude, inadaptability, and so forth. It warned that the medical defect in itself was not a cause for discharge unless genuinely disabling and directed that such cases be returned to duty or be administratively separated. In the main, medical efforts to implement these changes toward maximum utilization of marginal personnel were developed in three major areas: (1) Prevention of hospitalization, (2) reconditioning, and (3) hospital practice.

Prevention of Hospitalization

As has been noted, there was early recognition of the adverse effects of hospitalization in creating or perpetuating an adverse adaptation to illness or disability. This deleterious effect was most pronounced in neurotic disorders or in patients with minor or purely subjective complaints. An obvious solution was the outpatient management and treatment of such cases. Quite early in the war, Army psychiatrists moved toward the development of such extramural management of adjustment problems among trainees. This concept and practice rapidly expanded to become the replace-

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[75] War Department Circular No. 293, 11 Nov. 1943, subject: Enlisted Men—Utilization of Manpower Based on Physical Capacity.

[76] War Department Circular No. 81, 13 Mar. 1945, sec. III, subject: Personnel—Administrative and Medical Disposition of Noneffective Personnel.

ment training center clinic system which achieved official recognition in 1943 [77] and became a prominent feature of military psychiatry in World War II. Its origin, development, and methodology have been well documented by Perkins.[78]

The concepts and methods of outpatient military psychiatry were soon reflected in many other areas of military medical practice. Rogers [79] argued against radical excision for pilonidal sinus disorders, pointing out that such procedure required prolonged hospitalization and convalescence during which activity was extremely limited, motivation was impaired, new symptoms developed, and return to duty became problematical. He favored conservative treatment with the patient on duty status.

For gastrointestinal and other complaints.—From an extensive experience (1,702 cases) at a large Army post, Loder and Kornblum [80] found that most cases referred for gastrointestinal complaints were best handled on an outpatient basis with roentgenologic studies. After negative findings by X-ray, 78 percent did not return to the clinic. These workers held that such beneficial results were due not only to reassurance of the patient but also to the reassurance of the referring medical officer, who could then adopt a firm and realistic attitude toward the repeated complainer.

The treatment on duty status of acute gonorrhea was successfully accomplished by Atcheson,[81] using sulfathiazole. Patients were evaluated periodically on an outpatient basis, and in 92 percent successful results were obtained with no increase in complications in comparison with patients hospitalized for gonorrhea. Similar excellent results were obtained by Campbell and Carpenter.[82]

An effective plan for avoiding the hospital atmosphere was developed in 1944 at O'Reilly General Hospital, Springfield, Mo., as reported by Josey.[83] All ambulatory admissions were placed in a group of wards known as the disposition section, which avoided the usual hospital regimen of nursing care and medication. These cases were thoroughly worked up in a nearby clinic building. A decision was then made for hospitalization, reconditioning, return to duty, or discharge from the service. Of approximately 5,000 patients admitted to O'Reilly General Hospital during a 6-month period, 52 percent were evaluated in the disposition section and 23 percent received final disposition to duty or discharge without further hospitalization.

[77] Halloran, R. D., and Farrell, M. J.: Neuropsychiatrists in the U.S. Army; Their Functions in General and in Relation to Replacement Training Centers. Army M. Bull. No. 65: 151–156, January 1943.

[78] Medical Department, United States Army. Preventive Medicine in World War II. Volume III. Personal Health Measures and Immunization. Washington: U.S. Government Printing Office, 1955, pp. 171–232.

[79] See footnote 57, p. 688.

[80] Loder, H. B., and Kornblum, S. A.: Duodenal Ulcer in a Large Army Camp; Incidence and Statistical Analysis. Mil. Surgeon 96: 492–497, June 1945.

[81] Atcheson, D. W.: Duty Status Treatment of Acute Gonorrhea. Mil. Surgeon 96: 159–163, February 1945.

[82] Campbell, G., and Carpenter, G. R.: Treatment of Acute Gonorrhea in the Army. Am. J. Syph. 28: 406–412, July 1944.

[83] Josey, A. I.: Disposition Section for Ambulatory Patients. Bull. U.S. Army M. Dept. 5: 353–355, March 1946.

In the common problem of foot complaints, Pemberton [84] found that most of such cases could be cared for by the dispensary medical officer in order to avoid hospitalization and loss of time from training. Pemberton pointed out that recent inductees readily developed foot strain, particularly those who had led a sedentary life before service. However, these symptoms begin to subside in the fourth week of training, and at the end of 8 weeks the soldier can drill all day and hike from 15 to 20 miles without strain. Treatment is not required except for a hot footbath at night since continued use is part of the conditioning process. Placing such a patient off duty or on light duty only postpones the time of complete recovery. Pemberton also restated an obvious but important finding; namely, that flat feet are subject to strain in the same manner as other feet and may become painful, but relief depends upon treatment of the strain and not of the flat foot.

In staging areas.—Prevention of hospitalization was particularly important at staging areas before oversea shipment. Lipschutz [85] noted that soldiers arrive at all hours and the incidence of acute illness is unpredictable. He found that from 40 to 50 percent of sick call cases were primarily psychological problems. He noted that sick call was particularly crowded when a unit was alerted for oversea shipment. Under these circumstances, hospitalization justifies complaints and strengthens the connotation of disability. On the other hand, neglect, ridicule, and denial serve the same attitude. This situation required the vigorous resources of an outpatient clinic where the medical officers adopted a psychosomatic approach and made prompt decisions for disposition.

Reconditioning

The development of organized programs of physical and mental activity for convalescent and ambulatory patients marked another important advance in psychosomatic medicine in World War II. These programs began in 1942 as a spontaneous attempt to prepare hospitalized patients for return to duty. Pioneer efforts in this sphere are generally credited to the Army Air Forces hospitals along with British military hospitals.[86] The idea and the practice, in various forms, of active convalescent care were rapidly adopted by most American military hospitals both in the United States and overseas. Soon there appeared reports of these successful activities which now became known as reconditioning. Childress,[87] in noting the results of an active convalescent program begun in 1942 by the orthopedic service of Stark General Hospital, Charleston, S.C., found that supervised drilling and field exercises

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[84] Pemberton, P. A.: The Care of Soldier's Feet. Bull. U.S. Army M. Dept. 3: 110–117, January 1945.

[85] Lipschutz, L. S.: Symposium on Psychiatry in the Armed Forces; Neuropsychiatry in a Staging Area. Am. J. Psychiat. 100: 47–53, July 1943.

[86] (1) The Reconditioning Program. Bull. U.S. Army M. Dept. 1: 27–30, December 1943. (2) Rusk, H. A.: The Convalescent Training Program in the Army Air Forces. Tr. Am. Neurol. A. 70: 19–22, 1944.

[87] Childress, H. M.: Regulated Group Exercise for Convalescent Patients. Mil. Surgeon 91: 581–584, November 1942.

prevented anxiety neurosis, "jitters," and "hospitalitis." Thomas,[88] also in 1942, stressed the importance of such a program in maintaining the morale of patients. Piazza,[89] in discussing the benefits of reconditioning at Moore General Hospital, Swannanoa, N.C., in 1943, remarked that reconditioning was fast becoming as much a part of Army medicine as typhoid inoculation. To quote from this author:

> No longer need the patient stare aimlessly at the bare ceiling hour after hour, no longer need the ambulatory patient pace the ward floor or hospital corridor uselessly or spend his time lounging in the post exchange or Red Cross building thinking about his illness or injury, magnifying it to unendurable proportions to the point of becoming useless to himself and the service.

Convalescent reconditioning was formally recognized in the summer of 1943. In August 1943, Maj. (later Lt. Col.) Walter E. Barton, MC, was appointed the first director of the newly created (June 1943) Reconditioning Division, Professional Service, Office of The Surgeon General, and in September 1943, Circular Letter No. 168[90] provided for the establishment of convalescent reconditioning programs at all Army hospitals. The Surgeon General's Office laid down broad guidelines for the operation of reconditioning in hospitals, as follows:[91]

> 1. Reconditioning to be successful must begin the moment convalescence begins. This may be while the patient is still confined to bed.
>
> 2. The mental attitude of every member of the hospital staff toward reconditioning is extremely important. There must be at all times the expectancy that the patient will return to duty.
>
> 3. Transfer of the patient from the hospital atmosphere to the reconditioning section as soon as he is not dependent upon active medical treatment is of paramount importance in restoring health.
>
> 4. In reconditioning sections, men spend their mornings in calisthenics, ward fatigue, outdoor drills, and marches. Afternoons may be spent in games and sports adapted to the physical strength of patients. In the evenings, movies, camp shows, group singing, quiz programs, and other opportunities for free choice of recreational outlets should be provided, with a more liberal use of town and weekend pass privileges.

The typical operation of reconditioning procedures in Army hospitals in World War II is illustrated in the reports from Lawson General Hospital, Atlanta, Ga.,[92] and Oliver General Hospital, Augusta, Ga.[93] As suggested by the Surgeon General's Office, convalescent patients were divided into four classes, as follows:

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[88] Thomas, H. M., Jr.: Convalescent Care and the Morale of Patients. Mil. Surgeon 93: 453–457, December 1943.

[89] Piazza, F.: The Reconditioning Program at Moore General Hospital. Mil. Surgeon 96: 81–84, January 1945.

[90] Circular Letter No. 168, Office of The Surgeon General, U.S. Army, 21 Sept. 1943, subject: Convalescent Reconditioning in Hospitals.

[91] See footnote 86(1), p. 693.

[92] Titus, N. E.: Rehabilitation Program at Lawson General Hospital. Bull. U.S. Army M. Dept. 1: 88–93, April 1944.

[93] Bilik, S. E.: Reconditioning Problem at Oliver General Hospital. Bull. U.S. Army M. Dept. 2: 81–93, July 1944.

Class I: Convalescents capable of being toughened by full physical activity.

Class II: Patients capable of limited physical activity requiring graded training to prepare for progression to Class I.

Class III: Ambulatory patients handicapped to varying degrees by residua of illness or injury.

Class IV: Bed patients.

Classes I and II patients were housed in the reconditioning sections, generally troop barracks or the back wards of the hospital, where the usual hospital atmosphere of nursing and medication was avoided. Patients were given uniforms and fatigue clothing instead of hospital garb; they were marched to meals and were responsible for policing their barracks or wards, which were inspected regularly. They were drilled and commanded by convalescent officer patients. A full day's program of activity was enforced. Failure to abide by the program brought denial of pass, restriction, and even confinement.

All observers agreed that convalescent training should be accomplished under medical supervision with one or more medical officers devoting full time to this work, one being in charge of the program. Patients were transferred to the reconditioning section with their completed clinical record. A final note was placed on the clinical record when convalescent training, which often culminated in a 15-mile hike, was completed. Most Class I and Class II patients required from 18 to 21 days of reconditioning. Candidates for medical discharge were moved early to a "CDD" (certificate of disability for discharge) barracks to avoid "contaminating" return-to-duty patients.

Further organization of the reconditioning program continued as the war proceeded. Not only were convalescent training facilities at existing general hospitals enlarged, but separate convalescent hospital centers were established.[94] The concept was extended to the management of psychiatric patients and successful results were reported by Rosner [95] at Dale Mabry Field, Tallahassee, Fla., and by Cotton [96] at Mason General Hospital, Brentwood, N.Y. On 6 September 1944, the Surgeon General's Office announced that one hospital in each service command would be designated as a neuropsychiatric reconditioning center to which any patient who was considered as having a remote chance of performing military service would be sent for a trial of reconditioning.[97]

Also initiated by the Surgeon General's Office was the *Reconditioning Newsletter* for monthly distribution to all Army hospitals in order to dis-

[94] Convalescent Hospitals. Bull. U.S. Army M. Dept. 2: 19–20, October 1944.

[95] Rosner, A. A.: The Neuropsychiatrist and Convalescent Training Program of the Army Air Forces. Bull. U.S. Army M. Dept. 2: 93–97, July 1944.

[96] Cotton, H. A., Jr.: Reconditioning Neuropsychiatric Patients in the Army. Mil. Surgeon 97: 450–455, December 1945.

[97] Reconditioning Notes. Bull. U.S. Army M. Dept. 2: 30–31, October 1944.

seminate widely new ideas, practices, and procedures. Reconditioning pro-
grams were further elaborated and divided into three basic components;
namely, educational, physical, and occupational therapy. In each of these
areas, technical manuals and training films were produced and distributed.[98]

The extent to which the reconditioning program became integrated as
part of the psychosomatic development of military medicine of World War
II is indicated by an open letter to hospital commanders from Maj. Gen.
Norman T. Kirk, The Surgeon General of the Army.[99] In this letter, General
Kirk points out: "If you treat only their bodies and forget their minds you
will have accomplished less than your full duty." The letter urges greater
efforts toward implementing the reconditioning program and comments
further: "Treatment of the whole patient, watching closely his progress,
encouraging him to participate, taking pride in his mental as well as physical
progress, is an essential of good medical care."

Psychosomatic Concepts in Hospital Practice

Gastrointestinal disorders.—The evolution of the psychosomatic view-
point in the management of inpatients is perhaps best illustrated by the
experience with persistent disorders of the upper gastrointestinal tract,
chiefly peptic ulcer, probably the most common cause of medical disability
in World War II.

Before the United States entered the war, there appeared numerous
reports of the unusual high rate of functional dyspepsia and peptic ulcer in
the Armed Forces of England, Canada, and Germany.[100] Willcox,[101] Payne
and Newman,[102] and others found duodenal ulcer to be the major cause for
medical invalidism in the British Forces. Curiously enough, it was noted
that peptic ulcer was only a minor problem of World War I, while neuro-
circulatory asthenia was a prominent disorder. The reverse situation ob-
tained in World War II. Jones and Scarisbrick,[103] on the basis of extensive
experience with cases of neurocirculatory asthenia, believed that the medical
profession of World War II viewed "effort syndrome" as a psychiatric dis-
order. They thought this change of attitude was responsible for the de-
creased incidence and argued against retaining the diagnosis, since almost
all cases of neurocirculatory asthenia could be readily placed in the psychi-
atric category.

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[98] (1) Boeckman, F. P.: The Reconditioning Program; The Army's Answer to the Manpower Shortage.
J.A.M.A. 125: 280–282, 27 May 1944. (2) Rankin, F. W., and Barton, W. E.: Present Status of Rehabilitation
in the U.S. Army. J.A.M.A. 125: 256–258, 27 May 1944. (3) Reconditioning of Patients. Bull. U.S. Army M.
Dept. 2: 23–24, August 1944.

[99] Kirk, N. T.: A Letter to Hospital Commanders. Bull. U.S. Army M. Dept. 3, February 1945.

[100] Pepper, O. H. P.: Disease Expectancy in the New Army. War Med. 1: 463–469, July 1941.

[101] Willcox, P. H.: Gastric Disorders in the Services. Brit. M.J. 1: 1008–1012, 22 June 1940.

[102] Payne, R. T., and Newman, C.: Interim Report on Dyspepsia in the Army. Brit. M.J. 2: 819–821,
14 Dec. 1940.

[103] See footnote 31, p. 683.

All British reports agreed that most cases of peptic ulcer originated in civilian life and were only brought forth or exacerbated by military life. Hurst [104] expressed a common viewpoint when he flatly blamed the increase of peptic ulcer upon "heavy Army food." With other observers, he advocated the rejection of individuals with peptic ulcer at induction and prompt medical discharge when found in the service except those military personnel who could obtain special food at regular hours. Hinds-Howell [105] recommended that even cases of functional dyspepsia should be discharged, but Hurst insisted that such patients could be benefited by early treatment directed to restore their ability to eat army food and face army life. Hurst pointed out that if treatment is not given early in such cases the result is "disordered action of the stomach," which he believed had replaced the effort syndrome of World War I.

In sharp contrast was the German attitude as expressed by Stehr,[106] who stated that only active peptic ulcer cases are unfit for work. Then, treatment is indicated, but such patients should not be kept too long away from physical activity because dietetic treatment was complemented by exercise and work. Stehr argued that the danger of recurrent ulcer or life-threatening hemorrhage is no greater during work than it is during rest. Schindler [107] disagreed with Stehr's back-to-work regime, considering it to be neither practical nor humane. He also advocated the discharge of all patients with peptic ulcer unless manpower needs became critical.

As the American Army mobilized, particularly after Pearl Harbor, the frequency and importance of persistent disorders of the upper gastro-intestinal tract soon paralleled the British experiences. Published reports indicated that from 30 to 40 percent of admissions to the gastrointestinal wards of Army hospitals were diagnosed as peptic ulcer, mainly of the duodenal type.[108] American observers, like their British colleagues, believed that in the majority of their ulcer patients the illness had originated in civil life.

As in England, there arose conflicting opinions on the cause of the frequency of peptic ulcer under wartime conditions. One group insisted that cases came from predisposed persons who had been traumatized by the Army diet and that psychogenic factors played little or no causative role. Thus, Kirk [109] reported that the concept of the emotional genesis of peptic ulcer was not suggested by his experience at Fort Sill, Okla. He found that

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[104] Hurst, A.: Digestive Disorders in Soldiers. Am. J. Digest. Dis. 8: 321–323, September 1941.

[105] Hinds-Howell, C. A.: A Review of Dyspepsia in the Army. Brit. M.J. 2: 473–474, 4 Oct. 1941.

[106] Stehr, L.: Die Beurteilung der Wehrdienst und Arbeitsfähigkeit bein chronisch Magenkranken. München. med. Wchnschr. 87: 1317–1322, 29 Nov. 1940. (Abstract in War Med. 1: 730–732, September 1941.)

[107] Schindler, R.: Gastroenterology in the Army; Methods of Examination and Disposition of Cases. War Med. 2: 263–276, March 1942.

[108] (1) Chamberlin, D. T.: A Plan for Standardization of Diagnosis and Treatment of Peptic Ulcer. Mil. Surgeon 93: 157–164, August 1943. (2) Kirk, R. C.: Peptic Ulcer at Fort Sill. Am. J. Digest. Dis. 10: 411–413, November 1943. (3) Berk, J. E., and Frediani, A. W.: Peptic Ulcer Problem in the Army. Gastroenterology 3: 435–442, December 1944.

[109] See footnote 108(2).

the incidence of peptic ulcer in psychoneurotic patients was not increased and concluded that intolerance to greasy foods was the greatest obstacle to satisfactory military service. He was partially supported by Chamberlin,[110] asserting: "It was not safe for a patient with ulcer to be on duty. He can do better in civilian life where he can regulate his hours and diet." However, Chamberlin also believed that contributing to ulcer breakdown were psychogenic factors which varied from simple dislike of the service, to difficult adjustment to army life, to toxic psychosis. Cheney,[111] in a study of 418 cases at Hammond General Hospital, Modesto, Calif., also failed to find an association between psychoneurosis and peptic ulcer. However, except for 31 cases, he noted that special diets made no difference in treatment and that a liberal diet made no patient worse.

A majority of American observers ascribed to psychogenic factors, as their major cause, ulcer breakdowns in military personnel. Flood,[112] on the basis of careful clinical studies at the Station Hospital, Fort George G. Meade, Md., concluded that the fundamental cause of chronicity of peptic ulcer in most cases was an associated anxiety state—in fact, an anxiety or fear reaction. Flood found that stable personalities responded well to treatment, whereas anxious patients did not. He advised psychiatric evaluation to rule out neurosis before considering return to duty of any patient with peptic ulcer. Morrison [113] came to similar conclusions from his extensive experience as gastroenterology consultant at an Army general hospital. He noted that gastrointestinal referrals were most common from the neuropsychiatric service. Conversely, psychiatric consultations were most frequently requested from the gastrointestinal wards. A major complaint of both types of patient was an inability to tolerate the Army diet. On this subject, Morrison made the pertinent observation that, for the personnel stationed in the United States, nowhere is there better food than in the Army. Only occasional meals are not satisfactory. Soldiers are not required to eat all that is offered and can practically select their own diet. Like others, Morrison noted the disappearance of gastrointestinal symptoms when patients learned of their contemplated discharge or when declared unfit for oversea duty. He concluded that the inability to tolerate an army diet was symbolic of maladjustment to military service. Sweeney,[114] in summarizing the lessons learned during his 2 years as chief of the Medical Service, Bushnell General Hospital, Brigham City, Utah, also found the underlying basis of peptic ulcer to be neurosis or anxiety state, remarking that relief from situational anxiety paralleled improvement in peptic ulcer. He cited the well-known phenomenon of the patient with a diagnosis of peptic ulcer

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[110] See footnote 108(1), p. 697.

[111] Cheney, G.: Peptic Ulcer and Nutrition. Mil. Surgeon 95: 446–454, December 1944.

[112] Flood, C. A.: Peptic Ulcer at Fort George G. Meade, Maryland. War Med. 3: 160–170, February 1943.

[113] Morrison, S.: Interservice Consultations in One Army General Hospital; Comments With Particular Reference to the Section on Gastroenterology. War Med. 7: 84–94, February 1945.

[114] See footnote 51(5), p. 687.

made overseas, supported by X-ray evidence, who becomes asymptomatic and negative roentgenographically after return to the Zone of Interior.

Berk and Frediani [115] in 3 years of experience in gastroenterology at Tilton General Hospital found further evidence for the psychological causation of acute breakdown of peptic ulcer. They cited patients who were asymptomatic until the day before induction or until their first Army meal. They also noted a remarkable subsidence when discharge was assured, or recrudescence when soldiers were informed of their impending return to duty. These workers found that the aggressive, conscientious, or perfectionist personality types so commonly described in civilian patients with peptic ulcer were infrequent in their military subjects, who were more apt to be slovenly, placid, and slow-moving men. An editorial in the *Military Surgeon*,[116] June 1943, perhaps best expressed the popular psychosomatic viewpoint relative to peptic ulcer in military personnel by commenting that some soldiers simply had no stomach for war.

Practically all observers agreed that, in general, treatment of peptic ulcer in military personnel gave unsatisfactory results and that discharge from the service was the preferable and, in fact, the inevitable disposition for most cases. Flood observed that in contrast with ulcer patients in civilian life, of whom two-thirds were relieved within 2 weeks of the usual conservative Sippy regimen, only one-third of military patients obtained relief and one-half continued to have symptoms even after 4 weeks of treatment. Followup X-ray studies confirmed that improvement occurred in only one-half of the cases. Best results were obtained in Regular Army personnel who were highly motivated for return to duty. Reeser and Guthrie [117] reported that 81 percent of ulcer patients were discharged from the service. Chamberlin [118] believed that patients with peptic ulcer were unfit for service, for "no matter how well peptic ulcer seems at induction or after operation, breakdown in the service is inevitable. For even when well such individuals can be expected to neglect therapy or diet." Berk and Frediani [119] returned to duty only 25 percent of Regular Army personnel, mainly men with uncomplicated cases who had some special military skill. They were against the promiscuous employment of gastric resection since this procedure did not alter the basic personal patterns nor did it remedy the emotional disturbance.

This almost uniformly gloomy prognosis for military patients with peptic ulcer was formally acknowledged in War Department Circular No. 46, 7 February 1945,[120] which directed that all enlisted men hospitalized for

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[115] See footnote 108(3), p. 697.

[116] Editorial: The Stomach in War. Mil. Surgeon 92: 663–665, June 1943.

[117] Reeser, R., Jr., and Guthrie, M. B.: The Management of Army Personnel With Peptic Ulcer; An Analysis of 200 Cases. Mil. Surgeon 98: 125–131, February 1946.

[118] See footnote 108(1), p. 697.

[119] See footnote 108(3), p. 697.

[120] War Department Circular No. 46, 7 Feb. 1945, sec. V, subject: Enlisted Men, Discharge for Chronic Peptic Ulcer.

chronic symptomatic peptic ulcer be considered for separation except those who possessed unusual qualifications for military service.

In the latter phase of the war, because of manpower shortages, occasional efforts were made toward rehabilitation of ulcer patients for duty. One such attempt was reported by Goldbloom and Schildkrout,[121] who were assigned to a staging area medical facility. They noted the high rate of medical discharges in 1943, including 10 percent for gastrointestinal disorders, mainly peptic ulcer. Stimulated by War Department Circular No. 293, 11 November 1943, which directed the retention of personnel who could render some type of effective service, they chose for study 100 cases of chronic disorders of the upper gastrointestinal tract. These patients originated mainly from units in the process of oversea movement, but some were from the station complement. They were given complete examination in the hospital, including roentgenographic and psychiatric evaluation. All were then assigned to duty on the post but were brought to the hospital messhall regularly for meals which were prepared under the supervision of the dietitian in cooperation with the gastrointestinal service. These patients were all followed by the outpatient service, and adjustments were made in duty assignments as required. Small group discussions were held to help the patients arrive at an understanding of their problems with respect to their digestive disorders, their adjustment in the service, and their personal difficulties. Of the 50 peptic ulcer cases, good results were obtained in 38 (76 percent). The 50 patients with chronic functional dyspepsia had poor morale and definite psychoneurotic background as contrasted with the ulcer group. Of these 50 patients, 30 (60 percent) seemed to function reasonably well on duty. Goldbloom and Schildkrout concluded that approximately 70 percent of the entire group could be salvaged for military service. A small number were maintained successfully on regular military rations, but in a majority of cases attempts at imposing a usual diet resulted in increasing pain and intolerance, forcing return to a special dietary regimen.

By the time the war ended, a good deal of understanding had been achieved insofar as mind-body relationships were concerned in peptic ulcer and chronic dyspepsia. (See pages 710–711.) Most patients in this category however, were found to be unusable on a duty status and were discharged from the service.[122]

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[121] Goldbloom, A. A., and Schildkrout, H.: Dyspepsia Regimen; A Method of Rehabilitation. War Med. 6: 24–26, July 1944.

[122] After the war, military gastroenterologists pursued the question of diet and the usability of personnel with peptic ulcer, who in other respects exhibited excellent military potential, since many such men had performed superior duty even under stressful conditions. Based on the work of E. D. Palmer, B. H. Sullivan, and E. L. Hamilton (Duodenal Ulcer in Military Personnel: Studies on Military Effectiveness of the Ulcer Patient. III. Review of 350 Cases of Recurrent Duodenal Ulcer. U.S. Armed Forces M.J. 3: 1123–1133, August 1952) and the later work of Sullivan and Hamilton (Peptic Ulcer in Military Personnel; Incidence and Management. U.S. Armed Forces M.J. 6: 1459–1468, October 1955), an entirely different approach was evolved, denying that army diet or any diet was a primary cause of ulcer breakdown and proposing that ulcer patients when improved could and should perform military service provided the psychological factors could

Elective surgery.—Another psychosomatic insight that gained wide recognition in World War II was an awareness that persistent symptomatology of neurotic type, similar to the well-known compensation neurosis, not infrequently may complicate the results of elective surgery. A typical sample is found in the report of Butsch and Harberson [123] on the results of elective surgery for varicosities of the lower extremities. In this series, 98 cases were chosen for operation because of complaints referable to the legs, obvious varicose veins and a competent deep venous circulation. The usual ligation and section procedure was performed. A 3-month followup study involving 35 cases revealed that only 10 had achieved symptomatic relief; the remaining 25 individuals complained of more difficulty with their legs than before the operation. The multiplicity of their complaints seemed incredible since careful examination of each soldier found 31 of the 35 subjects to have perfect surgical results with no instance of postoperative swelling. A correlation between maladjustment and the persistence of complaints was evident on psychiatric evaluation which further elicited unrelated symptoms, such as nervousness, headache, dizziness, gastrointestinal discomfort, and hyperhydrosis. In these cases, varicosities represented only an unimportant part of the soldiers' difficulties upon which operation had crystallized and fixated a rational reason for medical disability. These observers concluded that, when considering operation for varicosities, one should regard with suspicion the young soldier with a multiplicity of complaints. The presence of varicose veins is not in itself an indication for surgical treatment. One must consider the entire person—his past and current adjustment. A similar caution was sounded by Haynes [124] in advocating careful selection of cases for the surgical relief of lumbar herniated-disk syndromes. He warned against enthusiasm for the surgical approach in these cases and insisted that a "psychiatrically sound" soldier is a paramount prerequisite before considering operative intervention. Experience with elective surgery of the knee joint also exemplified the need for a careful selection of cases from the psychological standpoint. [125]

In contrast to this, Rosenbaum [126] deliberately employed elective surgery in a psychosomatic approach to improve effectiveness. He noted that, of 44 soldiers with strabismus, 35 were on a limited-duty status mainly because of their physical appearance and consequent inferiority feelings.

[123] Butsch, W. L., and Harberson, J. C.: Importance of Careful Selection of Soldiers for Ligation of Varicose Veins. Bull. U.S. Army M. Dept. 4: 226–230, August 1945.

[124] See footnote 60, p. 688.

[125] Selection of Cases for Arthrotomy of the Knee. Bull. U.S. Army M. Dept. 4: 4–5, July 1945.

[126] Rosenbaum, H. D.: Strabismus in the Army. Mil. Surgeon 95: 48–52, July 1944.

be satisfactorily alleviated. This viewpoint prevailed during the Korean War and has now become current operating policy in the Army. In a study (Yessler, P., Reiser, M., and Rioch, D. McK.: Blood Pepsinogen and Peptic Ulcer in Inductees. (To be published.)) on predisposition to peptic ulcer, followup examination of 16 young draftees in whom ulcer had been diagnosed early in the course of their military career showed that 15 remained on duty status after treatment and satisfactorily completed 2 years of military service.—A. J. G.

Surgical correction of the cosmetic defect produced increased self-esteem and self-confidence, and many were raised to a full-duty status. Indeed, two men volunteered and were accepted for Officer Candidate School.

Ocular disorders.—Psychosomatic considerations were also found to be prominent in other ocular disorders. Birge [127] described individuals with symptoms of persistent headache, photophobia, lowered vision, with loss of visual acuity up to 50 percent, burning and watering of the eyes due to increased autonomic activity of the lachrymal glands, sweaty palms, tremor, and often a history of nervousness. Such cases were found in persons awaiting shipment overseas and in those who had recently suffered the loss of one eye because of disease or injury, the other eye being normal. These patients received little benefit from spectacles or eye medication but required reassurance in psychiatric treatment. Similarly, McAlpine [128] noted the frequency of "functional" ocular disorders in military personnel. Common manifestations were blepharospasm, asthenopia, spasm of convergence and accommodation, and anomalies of conjugate deviation. Pupillary reactions were normal and amblyopia a relatively rare phenomenon. McAlpine found that such ocular difficulties arose as a result of the patient's inadequacy in coping with an unpleasant or difficult situation. Symptoms could be precipitated by a mild blow on the head or by a major situational problem.

Rheumatic fever.—In a few notable instances, a psychosomatic or total approach to illness was the basis initiating major changes in the overall management of complex disease entities. This is perhaps best illustrated by the report of Holbrook and van Ravenswaay [129] on the treatment and management of rheumatic fever. This had become a major problem of World War II with 400 cases originating monthly from Army Air Forces personnel alone. Generally, 85 percent of patients with rheumatic fever were medically discharged, many with cardiac neurosis. A new comprehensive program was begun in 1944, including measures of prevention, treatment, convalescent activity, and selective assignment to duty. Prevention was accomplished by the administration of prophylactic doses of sulfathiazole to personnel in areas of high disease incidence. Treatment procedures included the transfer of patients in litters to hospitals located in geographic areas of low incidence as soon as acute symptoms subsided (usually after the first few weeks). By this move, the likelihood of recurrence of rheumatic fever was markedly reduced (no recurrence in 1,000 cases). The transfer of patients also concentrated their care in the hands of experienced personnel who avoided the error of undue attention to the cardiac aspects of the disease. This diminished the incidence of cardiac neuroses that had hitherto been almost as important a cause for discharge and disability as

[127] Birge, H. L.: Ocular War Neuroses. Arch. Ophth. 33: 440–448, June 1945. (Abstract in War Med. 8: 181–192, September 1945.)
[128] McAlpine, P. T.: Hysterical Visual Defects. War Med. 5: 129–132, March 1944.
[129] Holbrook, W. P., and van Ravenswaay, A. C.: The Military Aspects of Acute Rheumatic Fever. Mil. Surgeon 96: 388–391, May 1945.

organic cardiac sequelae. In the new hospital, an active convalescence program was initiated with the quiescence of the rheumatic process. Objective tests of physical fitness were employed so that patients could measure their progress by a practical yardstick that they could see and understand. After convalescent activities, those with no sequelae were given a 12-day trial of simulated duty, including hikes, bivouacs, drill, and exercises, which demonstrated both to the patients and to their medical officers a realistic appraisal of physical ability to perform duty. Concurrent with this activity, job-assignment officers reviewed the patients' capabilities for the determination of a suitable military assignment. Then followed on-the-job training for such an assignment under medical supervision. After successful completion of the convalescent phase, patients with no demonstrable sequelae were returned to limited duty for 6 months in an area of the United States free of rheumatic fever. If found to be still without residua after this 6 months' assignment, they were returned to full duty. Patients found to have permanent cardiac damage but good cardiac reserve were given a permanent limited assignment in an area of low incidence in the Zone of Interior. Patients having in addition to permanent cardiac damage either impaired cardiac reserve or no useful assignment potential were medically discharged after maximum improvement. The overall results of this program demonstrated a decrease of medical separations in rheumatic fever patients from 85 to 25 percent, with a minimum of cardiac neuroses.

Peripheral nerve injuries.—Another striking example of the practical utilization of the psychosomatic viewpoint in the management of disease was furnished by the treatment regimen for peripheral nerve injuries established by Lewey and Bowles [130] at Cushing General Hospital, Framingham, Mass. Known as the work-furlough program, it was introduced to provide a practical incentive, during the long convalescent period, to improve the use of an impaired extremity by exercise. These patients, while still in the service, were given a 90-day work furlough. With the cooperation of civilian and welfare agencies, a full-time position was found for them in nearby factories or businesses. After 90 days, patients were again evaluated, usually at weekend periods, in order to avoid loss of time from work. If maximum improvement was found, such patients were medically discharged and could promptly resume their work and continue their new civilian adjustment. If further improvement was possible, they were given another 90-day furlough and reevaluated at the end of this period. By this method, active convalescence was carried on in an atmosphere that permitted a gradual transition to civil life, provided the practical incentive of pay, and fostered the return of self-esteem and self-confidence in persons who had temporary or permanent disability.

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[130] Lewey, F. H., and Bowles, G. K.: Work Furloughs for Patients With Peripheral Nerve Injuries. Bull. U.S. Army M. Dept. 4: 683–686, December 1945.

Part III.   During Oversea and Combat Duty

Oversea duty during World War II intensified the probability of exposure to a wide variety of frustrations, deprivations, and hazards. In addition to prolonged separation from home and family, there were encountered, either singly or collectively, such stressful circumstances as climatic extremes; monotonous diet, work, and recreation; isolated assignments in unusual geographic locations, such as tropical jungles or barren islands; threats of strange and ominous diseases, such as scrub typhus, schistosomiasis, malaria, and filariasis; and the intermittent terror and danger of combat. It may be assumed, however, that men who were sent overseas had achieved some degree of adjustability to military stress by virtue of their indoctrination and training experiences. Moreover, many of the weaker and presumably more vulnerable individuals had been eliminated from oversea duty by assignment limitation or discharge from the service for medical or administrative reasons.

Despite these qualifications, oversea service, particularly duty involving the cumulative effects of combat or isolated assignment, posed greater difficulties in adaptation than the transition from civil to military life or other vicissitudes of military service in the United States. Disturbances of adjustment under these circumstances were interwoven into the various clinical disorders that confronted each medical officer. The relationship of oversea stress to symptoms and disability was recognized by most medical personnel and facilitated acceptance of a holistic mind-body approach to the management of many disease and injury syndromes.

COMBAT FATIGUE

This growth of psychosomatic concepts in oversea medical practice is perhaps best exemplified by the evolution of understanding and methods of management in so-called combat exhaustion or combat fatigue. It will be recalled that this entity termed "shellshock" in World War I, was initially thought to be an organic brain disorder similar to, if not identical with, cerebral concussion. Later in World War I, it was commonly agreed that shellshock was the result of psychogenic trauma. Subsequently, the observation and treatment of veterans with chronic neurotic symptoms following shellshock gave further confirmation of its psychological origin, and the syndrome was designated as a traumatic neurosis. Thus, the pendulum has swung from a wholly organic to a completely psychological concept of causation. Early in World War II, the psychogenic viewpoint continued to prevail. But experience with combat psychiatric casualties soon made it evident that both psyche and soma were involved. It was found that most psychiatric casualties occurred when units were locked in heavy combat for several days in either offense or defense. Characteristic syndromes appeared

in which it was apparent that physical strain played a prominent role in reducing the individual's resistance to the psychological trauma of combat. Indeed, the very terms that came to be applied in such cases, namely, "combat exhaustion" and "combat fatigue," arose from this common finding of physical strain. Hanson [131] graphically described such casualties as follows:

> Their faces were expressionless, their eyes blank and unseeing, and they tended to go to sleep wherever they were. The sick, injured, lightly wounded, and psychiatric cases were usually indistinguishable on the basis of their appearance. Even casual observation made it evident that these men were fatigued to the point of exhaustion. Most important of the factors that produced this marked fatigue was lack of sleep. Under almost all combat conditions the infantryman gets too little sleep. The conditions of his existence— the almost continuous shelling, the strange night noises, flares, sentry and patrol duties, rain, snow, cold, heat, insects, and the ever present threat of the enemy—conspire to make his sleep at best intermittent and scanty. In spite of this lack of sleep he must undergo long periods of severe exertion, more often than not on a diet that is at best deficient in calories. Often the food is there for him, but he either cannot carry enough of it with him or is too frightened to eat the proper amount. Sometimes the type available has become distasteful through monotony.

Combat troops who were not psychiatric casualties also displayed this characteristic battle weariness, as witness Ernie Pyle's [132] moving account:

> For four days and nights they have fought hard, eaten little, washed none, and slept hardly at all. Their nights have been violent with attack, fright, butchery, and their days sleepless and miserable with the crash of artillery. The men are walking * * *. Their walk is slow, for they are dead weary, as you can tell even when looking at them from behind. Every line and sag of their bodies speaks their inhuman exhaustion. On their shoulders and backs they carry heavy steel tripods, machine-gun barrels, leaden boxes of ammunition. Their feet seem to sink into the ground from the overload they are bearing. They don't slouch. It is the terrible deliberation of each step that spells out their appalling tiredness. Their faces are black and unshaven. They are young men, but the grime and whiskers and exhaustion make them look middle-aged. In their eyes as they pass is not hatred, not excitement, not despair, not the tonic of their victory—there is just the simple expression of being here as though they had been here doing this forever, and nothing else.

The somatic component of combat fatigue was further demonstrated by the not infrequent finding, in these cases, of intercurrent disease, such as infectious hepatitis, malaria, diarrhea, and the like.[133] Here was evidence that so-called organic illness had undermined the ability of the individual to withstand the inroads of battle terror, since these patients had the usual symptoms of combat fatigue; namely, an inability to control their behavior in combat, overt manifestations of anxiety, startle reaction, and the almost invariable complaint of intolerance to the sounds and nearness of shellfire.

The fact that physical fatigue lowered the soldiers' ability to tolerate stress was also confirmed by the dramatic improvement of combat psychiatric casualties after 12 to 24 hours of sleep and food. With physical re-

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[131] Hanson, F. R.: The Factor of Fatigue in the Neuroses of Combat. Army M. Bull. Supplement No. 9: 147–150, November 1949.

[132] Pyle, Ernie T.: Here Is Your War. New York: Henry Holt & Co., Inc., 1943, pp. 247–248.

[133] Glass, A. J.: Combat Exhaustion. U.S. Armed Forces M.J. 2: 1471–1478, October 1951.

cuperation, overt signs of anxiety diminished or disappeared, confidence was restored, and the former psychiatric casualty was again capable of appropriate behavior in battle. This finding became the cornerstone of the successful forward management of combat psychiatric casualties, which returned to combat duty from 60 to 70 percent of patients after a 1- to 4-day treatment period.

It should be made clear that physical fatigue did not in itself produce psychiatric casualties. This fact was amply demonstrated by the many occasions in which units, advancing rapidly for days against slight enemy opposition and, therefore, enduring little emotional stress, had few or no psychiatric casualties even though conditions were such as to induce extreme physical fatigue. Conversely, a minority of psychiatric casualties occurred either immediately before battle or in the early stages of combat before any significant degree of physical strain was possible. Such patients were not considered to have genuine cases of combat exhaustion because the factor of physical fatigue was absent.

OTHER PROBLEMS

Combat fatigue represented an overt breakdown of adaptation to battle stress. Less obvious but more frequent manifestations of inability to endure the combat environment were a wide variety of symptomatic disorders presented to medical officers as evidence of incapacitating disease or injury. The following three major types of these clinical problems could be distinguished:

1. Persistent symptoms associated with negative findings of somatic disease.—This group included syndromes of constant headache; chronic lower back pain; recurrent digestive upset (dyspepsia) ; frequent episodes of weakness, giddiness, or faintness; painful feet; increased sweating, palpitation, or other manifestations of autonomic overactivity; and similar subjective disorders. Essentially, these complaints could be equated with some aspect of physical or mental discomfort suffered by most combat participants. Here, subjective discomfort was interpreted by the soldier concerned as indicating the presence of illness and, therefore, a legitimate reason for at least temporary removal from battle.

2. Persistent symptoms associated with minor objective findings of somatic disease or injury.—The important characteristic of this group was the disparity between the slight or moderate evidence of structural disease and the severity of the symptomatology. These cases posed diagnostic problems, for indeed there were findings such as scoliosis, shortening of one lower extremity, localized muscle atrophy, purulent discharge from a pilonidal sinus, deviation of the nasal septum with congested nasal mucous membrane and postnasal discharge, myopia, astigmatism or other visual refractive error, residua of an old knee injury, scars from trauma or sur-

gery, hypertrophic arthritis, and minor bruises and sprains. The symptomatology was focused upon and systematized around the particular physical finding. Current difficulties were blamed upon a recurrence or exacerbation of the previous disorder by virtue of strenuous exercise, minor injury, adverse climate, or primitive living conditions in the field. In this group, also, the drive for medical attention stemmed from a failure of combat adjustment rather than from a minor limitation of bodily function.

3. Persistent symptoms during or following convalescence from an acute disease, injury, or battle wound.—These were a problem usually during hospitalization when it became evident that impending recovery would result in a return to combat duty. The symptoms of pain, discomfort, or limitation of function seemed to arise as residual complications of the acute illness. Thus, there were digestive disturbances and pain in the right upper quadrant following the subsidence of infectious hepatitis; painful scars or limitation of joint motion following wounds or indeed elective surgery; weakness, easy fatigability, and chills after recovery from a malarial attack; and headache, irritability, giddiness, and inability to concentrate after head injury, meningitis, or other acute cerebral syndromes. The gain through illness in these cases was substantial. It was apparent to patients and medical officers alike that continued incapacity was rewarded by evacuation to the United States or at least return to duty in a noncombat assignment.

The widespread prevalence of these psychosomatic problems and the difficulties that they presented in diagnosis, treatment, and disposition was a characteristic feature of military medicine in oversea theaters. Symptomatic disorders with negative or minor objective findings were mainly handled by the combat medical officer, particularly the battalion surgeon. Here, the physician was truly in a doctor's dilemma. It was easy to identify himself with the physical and mental strain of the soldier and his conscious or unconscious drive to obtain relief from battle. The field medical officer could readily convince himself that medical evacuation was justified in the interest of accurate diagnosis, which required laboratory and X-ray facilities available only in rear medical facilities. But to evacuate soldiers because of subjective complaints would only stimulate many others who were equally uncomfortable to attempt the medical escape route. Moreover, his line and medical superior officers would soon question a lenient evacuation policy that materially depleted the fighting strength. With time and experience, most combat medical officers came to adopt a realistic approach, with the objective findings of disease and the overall effectiveness of the individual their main consideration rather than the traditional reliance on symptoms and differential diagnosis. The fact that the combat medical officer shared to some extent the dangers and hardships of combat troops enhanced his ability to distinguish between discomfort and disease, lessened feelings of guilt for refusing medical evacuation, and facilitated an identification of

himself with the needs of the unit rather than with the desires of the individual.

Not infrequently, however, medical officers yielded to the demand of subjective symptoms and evacuated persistent complainers. That this prac- ⁄ tice was not rare is indicated by an editorial [134] which argued against evacuation from combat for slight wounds and subjective complaints. Medical officers were urged to ignore what the patient says and evaluate disability almost entirely on objective findings. A new concept, phrased "medical discipline," came into common usage. Loose medical discipline during an active battle period could readily deplete the combat command and overload medical evacuation channels at a time when hospitals were fully occupied with the wounded. These uninjured ambulatory patients were either neglected at forward hospitals or sent further along the evacuation chain to fixed hospitals at the rear. Return to combat duty from such distant medical facilities was not only difficult and time consuming but produced numbers of resentful, poorly motivated soldiers who had convinced themselves of the merit of their symptoms, were repeatedly on sick call, and, in general, rendered inadequate duty.

A similar but somewhat more complicated problem was produced by the symptomatic disorders that occurred during convalescence from acute injury and disease. Here, the hospital medical officer was mainly involved. These physicians had not shared the combat hazards of their patients and had developed positive relationships of varying degrees with patients during the acute phase of their illness. When these hospitalized patients complained of residual symptoms during convalescence or before expected return to duty and objective findings of disease or its complications were not elicited, further management and disposition became a difficult matter. Often, the medical officer recommended that the patient be given a noncombat assignment despite the absence of any physical limitations. Not infrequently, he would reassure the patient and himself by telling him to report to the battalion surgeon upon return to duty and request assignment to light tasks or further consideration of his symptomatology. This procedure almost invariably confirmed the patient's belief that he was not fully recovered from his illness or injury and created chronic sick call problems for the battalion surgeon. At times, the hospital medical officer, frustrated by the patient's unexplainable symptoms, responded with anger and accusations of malingering. Obviously, this approach helped neither the patient nor the physician. Many of these complaining patients were referred to the psychiatrist because of "functional overlay" or "neurotic predisposition." This discharge of responsibility was rightly regarded as a rejection by the patient, who insisted that his pain and discomfort were not "in my head" and remained resistant to any psychiatric insight or help. Maj. Gen. Morrison C. Stayer,[135]

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[134] Abuse of Medical Disposition Channels. Bull. U.S. Army M. Dept. 3: 34–35, February 1945.

[135] Stayer, M. C.: The Necessity of Making Decisions. (Editorial) M. Bull. Mediterranean Theat. Op., January 1945. (Cited in Bull. U.S. Army M. Dept. 3: 28–29, April 1945.)

Surgeon, Mediterranean Theater of Operations, U.S. Army, commented on this problem in an editorial aptly entitled "The Necessity of Making Decisions." He enjoined medical officers not to "pass the buck" to the battalion surgeons and insisted that they face up to their responsibility by informing patients that in view of negative disease findings they were considered fit for duty. As the deleterious effects of hospitalization became recognized, active convalescent programs were instituted, much like those that had been developed in the Zone of Interior. Kunkel [136] described a reconditioning program in an oversea general hospital, where patients being returned to the Zone of Interior were physically separated from those being readied for return to duty. The latter were dressed in fatigue clothing, quartered in tents, and given physical exercise and military training under the command of line officers. Kunkel noted that the patients who had been transferred from other general hospitals and had been excused from all military discipline were surly and arrogant and had developed symptom patterns against their return to duty. Effective reconditioning programs in oversea hospitals were also reported by Rathauser and Ulfelder,[137] and by Neu and Urban.[138]

SCRUB TYPHUS AND OTHER INFECTIONS

A special convalescent program for scrub typhus patients was described by Romeo,[139] who detailed his experience with 312 cases in a hospital in New Guinea, from July 1942 to September 1944. Scrub typhus had been considered to warrant a prolonged period of rest in bed after the acute phase. However, Romeo found that bed rest beyond the febrile period was productive of flaccidity and loss of muscle tone and fostered a fear of the disease and its sequelae. Patients at bed rest during convalescence exhibited tachycardia (55 percent), tremor of the hands (60 percent), and vertigo (25 percent), along with constipation, insomnia, and headache. With the institution of a program of properly graduated activity, apprehension was allayed and most patients recovered completely for full duty in less than 9 weeks.

A similar experience was recorded in the management of relapsing *(Plasmodium vivax)* malaria by Gordon, Lippincott, and their coworkers.[140] These authors treated 435 patients evacuated from the Southwest Pacific Area, a majority of whom had had repeated attacks of malaria. They dem-

[136] Kunkel, P.: Reconditioning Program in an Overseas General Hospital. Bull. U.S. Army M. Dept. 4: 586–590, November 1945.

[137] Rathauser, F., and Ulfelder, H.: Reconditioning Program in a Station Hospital. Bull. U.S. Army M. Dept. 5: 178–181, February 1946.

[138] Neu, H. N., and Urban, F. K.: Convalescence and Rehabilitation in a General Hospital in the Tropics. Mil. Surgeon 96: 377–385, May 1945.

[139] Romeo, B. J.: Convalescence From Scrub Typhus. Bull. U.S. Army M. Dept. 6: 167–173, August 1946.

[140] Gordon, H. H., Lippincott, S. W., and others: Clinical Features of Relapsing Plasmodium Vivax Malaria in Soldiers Evacuated From South Pacific Area. Arch. Int. Med. 75: 159–167, March 1945. (Abstract in War Med. 7: 414, June 1945.)

onstrated the value of an active reconditioning program in dispelling a commonly held anxiety of most patients that repeated attacks seriously compromised present and future health. An active reconditioning program coupled with work assignments on the post increased physical stamina, restored self-confidence, and removed the dread of the disease.

A special psychological problem became evident in soldiers who contracted filariasis. Coggeshall [141] described patients with filariasis in the Southwest Pacific Area who developed fear of permanent lymphedema from seeing natives with elephantiasis. Coggeshall developed the policy of explaining to each patient that the end result of filariasis was good, with eventual recovery. Patients were given a series of gradually increasing exercises and placed on full duty. The mental response was prompt and favorable. Men became less apprehensive even though an occasional flareup of edema or lymphangitis occurred. This observer concluded that soldiers with filariasis should not be permitted to deteriorate mentally and physically by prolonged hospitalization.

GASTROINTESTINAL DISORDERS

As in the Zone of Interior, disorders of the upper gastrointestinal tract were a conspicuous problem among oversea and combat troops. Peptic ulcer was apparently of minor importance in comparison with the more numerous cases of functional dyspepsia. Magnes [142] reported on the operation of an outpatient gastrointestinal service in England. He noted that "preinvasion jitters" brought on functional disorders and lighted up cases of quiescent peptic ulcer. Vomiting was a common symptom. Magnes confirmed the value of outpatient management in lessening invalidism and persistence of symptomatology.

Because of the frequency of gastrointestinal disorders in the Mediterranean theater, a special field facility was created for the diagnosis and treatment of these conditions. This unit, a platoon of a field hospital, was located at the evacuation hospital level, with an experienced gastroenterologist, a psychiatrist, and a radiologist on the staff. Cases were carefully but rapidly evaluated by means of roentgenographic, gastroscopic, psychiatric, and clinical studies. In reporting the results of this specialized hospital, Halsted [143] noted that, of 110 combat soldiers with chronic gastrointestinal complaints, 59 percent were found by gastroscopic examination to have normal mucosa while the remainder showed a mild superficial gastritis. No correlation was observed between the appearance of the gastric mucosa and

[141] Coggeshall, L. T.: The Problems of Filariasis. South. M.J. 38: 186–189, March 1945. (Abstract in War Med. 8: 61, July 1945.)

[142] Magnes, M.: A Gastro-Intestinal Outpatient Service. Bull. U.S. Army M. Dept. 3: 99–103, February 1945.

[143] Halsted, J. A.: Clearing Company for Gastro-Intestinal Disease. Bull. U.S. Army M. Dept. 3: 90–95, May 1945.

the severity of symptomatology. In one 4-week period, 263 cases were processed with an average hospitalization of 8.7 days; 80 percent were returned to duty and only 7 percent evacuated to a general hospital. A vast majority of cases (84 percent) were considered to be primarily of psychological origin. It was the experience of the author and other division psychiatrists that peptic ulcer occurred rather infrequently during combat, whereas syndromes referable to the upper gastrointestinal tract, including nausea, anorexia, and vomiting, were common. It appeared that situations of acute danger were less apt to provoke peptic ulcer than the chronic deprivations and frustrations of noncombat situations.

Blumgart and Zetzel (ch. XII, p. 310) have emphasized that some 90 percent of all cases of peptic ulcer occurring in the Army originated during civilian life. On the other hand, there were men who had endured the stresses of civilian life and the strains of military training and transport and only then, during oversea service, developed ulcers. The inference was drawn that, although there may well have been a psychogenic component in such cases, more severe strains were required for their inception. Evidence, though scanty, supported the view that this group responded well to treatment; of 54 patients returned to appropriate duty following therapy, only 8 had to be rehospitalized.[144]

SUMMARY

Medical practice in the relatively slow tempo of peacetime generally focuses upon the biological difficulties of the patient and usually ignores the sociological and psychological aspects of adjustment. The physician sees the patient in an office, clinic, or hospital, and confines himself to symptoms and complaints referable to bodily dysfunction or defect. Ordinarily, the physician has little time or opportunity to become familiar with the environment or milieu of his patient or its effects upon the symptoms or clinical course of the disease. War, with its characteristic situational changes, dramatically brings to the forefront the environmental aspects of man's struggle for existence. Thus, a byproduct of modern war has been advances in medicine stemming from a better understanding of environmental dangers, such as the control of infectious disease, sanitation, and the surgical treatment of injuries. These benefits were also evident in World War II, and in addition military medicine learned to appreciate psychological and sociological influences upon disease and adjustment. It was this experience in military medicine that made possible the growth of the psychosomatic viewpoint. Although psychosomatic concepts originated before World War II, they received a major impetus during the war years, for here was a vast laboratory of stress where physicians could observe firsthand the effects of

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[144] Report, Head, D. P., Wilen, C. J. W., and Fradkin, N. F., to Surgeon, MTOUSA, subject: Survey of the Peptic Ulcer Problem in MTOUSA, 1943–45.

mind-body interrelationships upon symptoms, treatment, and disposition in almost any disease and injury. It can be stated that World War II produced no evidence that a psychological trauma caused specific somatic disease. Amply demonstrated, however, was the fact that in order to obtain good clinical results in disease and injury it was necessary to take into account various pertinent aspects of the patient's individual reaction to environment, such as motivation, group and cultural attitudes, the influence of the treatment milieu upon the effectiveness of improvement or recovery, and personality characteristics of the sick or injured person.

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