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CLINICAL INVESTIGATION SERVICE ANNUAL RESEARCH PROGRESS REPORT, FISCAL YEAR 1974

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Brooke Army Medical Center

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FOREWORD

During fiscal year 1974, marked progress was made toward the achievement of correlation and centralization of Clinical Investigation Service activities at Brooke Army Medical Center due to the continued support of the BAMC Commander, his administrative staff, and the professional medical staff.

The Clinical Investigation Service Laboratory became a reality in May 1974, when the conversion of one-half of Ward 43-A, Beach Pavilion, to laboratory bench and equipment areas was completed. Plans to convert the remaining portion of Ward 43-A, to include additional laboratory bench space and three administrative offices, scheduled for late FY 1975, will complete the centralization of Clinical Investigation Service activities. (The present administrative offices will move from the Main Hospital to Ward 43-A as soon as the remainder of that ward is converted.)

Funds for MEDCASE, Capital Equipment, and Consumable Supplies were instrumental in supporting the various protocols listed on the following pages and in outfitting the laboratory with the proper scientific instruments and equipment.

Forty-four protocols were registered in fiscal 1974: 8 were completed and 36 will be ongoing into fiscal year 1975. The statistical summary of registered protocols is given under Report of Total Activities of the Clinical Investigation Service.

Personnel support for the Clinical Investigation Service now includes the Chief, a Biochemist who administers the laboratory facility, a Computer Programmer, the Editorial Assistant and Secretary, and four enlisted specialists. The manpower survey, conducted in July 1973, recognized the need for an additional enlisted specialist and a clerk-typist. The former is scheduled to arrive in September 1974.

The preparation of this report would have been impossible without the most able and competent assistance of Mrs. Dodie Bratten, who has continued to give her excellent talents, assistance and loyalty to all Clinical Investigation Service activities.

R. Ansbacher

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Chief, Clinical Investigation Service

REPORT OF TOTAL ACTIVITIES OF CLINICAL INVESTIGATION SERVICE

DURING FISCAL YEAR 1974

A. Objectives

The Clinical Investigation Service was established at Brooke Army Medical Center 9 August 1971 to coordinate clinical investigation activities throughout the hospital complex. It is an independent service directly under the command of the Chief, Professional Services, and operates under the guidance of the Clinical Investigation Committee, composed of the chiefs of the various professional departments; and the Human Use Committee, composed of lay personnel.

The Clinical Investigation Service was established to promote, stimulate, coordinate, and provide support for clinical investigation and development activities within Brooke Army Medical Center, including design of experiments, typing and editorial services, and technical liaison with outside facilities.

B. Technical Approach

1. Manpower

a. The Chief, Clinical Investigation Service, devoted approximately 40% of his time during fiscal year 1974 to duties related to Clinical Investigation Service activities.

b. The Biochemist, Ph.D. Captain MSC, was instrumental in the establishment of a functional laboratory, and is in charge of the laboratory, both administratively and scientifically, assisting various investigators in their laboratory endeavors.

c. A Computer Programmer, Second Lieutenant Signal Corps, was assigned on 6 August 1973, and devotes his time almost exclusively to C-28-73, a cardiology protocol, plus assisting other investigators with statistical analyses of their data.

d. The Editorial Assistant and Secretary has devoted all her time to Clinical Investigation Service functions. She keeps a daily running budget for the service and for each individual protocol, orders all supplies and equipment, edits and types all manuscripts for publication prior to final review by the Chief and protocols prior to presentation to the Clinical Investigation Committee and Human Use Committee.

e. The E-6, Senior Medical Lab Technician, accepted a commission as a Second Lieutenant, MSC on 8 February 1974, and was therefore reassigned. He was replaced by an E-5 on 4 February 1974, who was promoted to E-6 on 9 April 1974.

f. The E-4, Medical Lab Specialist, left the Army on 7 March 1974 and plans to enter medical school. He was replaced by an E-5 on 19 February 1974.

g. An E-2 was assigned on 13 July 1973 and works primarily with the cardiology protocol, C-28-73. He was promoted to E-3 on 12 November 1973 and E-4 on 4 April 1974.

h. An E-2 was assigned on 22 April 1974 and is working in the newly completed laboratory facility.

i. The Manpower Survey Team, in July 1973, recognized the need for an additional enlisted specialist, who is programmed to start in September 1974, and a clerk-typist, who is at present unidentified.

2. Funding

The expenditures of the Clinical Investigation Service since its inception through FY 74 are given in Table 1.

C. Progress

The disposition of protocols registered with the Clinical Investigation Service through FY 74 is outlined in Table 2. Fifty-seven protocols will be ongoing into FY 75. The termination rate of registered protocols has fallen dramatically since the inception of the Clinical Investigation Service in August 1971.

During FY 74, 34 manuscripts eminated directly from investigative protocols registered with the Clinical Investigation Service: 28 have been accepted for publication and 6 are awaiting publication. In addition, 72 other manuscripts were reviewed and submitted for publication of which 31 were accepted and 41 are awaiting publication. Fifty-two resident papers were submitted and reviewed by the Clinical Investigation Service for fulfillment of the residency training requirements: 22 of these eminated from registered protocols. In summary, 158 manuscripts were reviewed, read for editorial and scientific corrections, and cleared by the Clinical Investigation Service.

During FY 74, 41 presentations were reviewed and cleared by the Clinical Investigation Service for National and International Medical Meetings and most of the material came from protocols registered with the Clinical Investigation Service.

Table 1. Clinical Investigation Service Expenditures FY 1972-1974.

TYPE	FY 72	FY 73	FY 74
MEDCASE		$ 50,100.00 (5 Protocols) $ 33,750.00 (Laboratory) $ 83,850.00	$ 35,431.98 (3 Protocols) $ 38,016.22 (Laboratory) $ 73,448.20
Capital Equipment			$ 1,757.40 (3 Protocols) $ 8,825.80 (Laboratory) $ 10,583.20
Consumable Supplies	$25,000.00 (4 Protocols)	$ 21,250.00 (15 Protocols) $ 7,150.00 (Laboratory) $ 28,400.00	$ 43,573.00 (1 Protocol-Contract) $ 25,197.59 (26 Protocols) $ 2,804.15 (Laboratory) $ 71,574.74
TDY		$ 1,800.00	$ 3,899.00
GRAND TOTALS	$25,000.00	$114,050.00	$158,505.14

Table 2. Clinical Investigation Service Protocol Disposition Through FY 74.

REGISTERED IN	FY 72	FY 73	FY 74	Total	GRAND TOTAL
FY 64-71	9 Ongoing to FY 73	6 Completed 1 Terminated 2 Ongoing to FY 74	2 Completed	8 Completed 1 Terminated	9 - FY 69-71
FY 72	40 Completed 22 Terminated 90 Ongoing to FY 73	32 Completed 25 Terminated 33 Ongoing to FY 74	13 Completed 7 Terminated 13 Ongoing to FY 75	85 Completed 54 Terminated 13 Ongoing to FY 75	152 - FY 72
FY 73		22 Completed 1 Terminated 21 Ongoing to FY 74	9 Completed 4 Terminated 8 Ongoing to FY 75	31 Completed 5 Terminated 8 Ongoing to FY 75	44 - FY 73
FY 74			8 Completed 36 Ongoing to FY 75	8 Completed 36 Ongoing to FY 75	44 - FY 74

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Peterson, H.D., and Burt, G.B., Jr.: The Role of Steroids in Prevention of Circumferential Capsular Scarring in Augmentation Mammoplasty. Plast Reconstr Surg, In Press.

Druepple, L.G. and Cox, W.A.: Simultaneous Bilateral Spontaneous Pneumothorax. Milit Med, 296-299, April 1974.

Seitter, G., III, Buker, R.H., Larson, A.W., and Cox, W.A.: Pulmonary Sequestration. Milit Med, In Press.

Cox, W.A. and Pauling, F.W.: A Simple Method of Managing Clotting Problems Following Cardiopulmonary Bypass. Ann Thor Surg, In Press.

Seitter, G., III, Buker, R.H. and Cox, W.A.: Chronic Traumatic Pseudoaneurysms of the Thoracic Aorta: Experience at Brooke Army Medical Center and Report of an Unusual Case. Milit Med, In Press.

Treasure, R.L., Rainer, W.G., Strevey, T.E. and Sadler, T.R.: Intraoperative Left Ventricular Rupture Associated with Mitral Valve Replacement. Chest, In Press.

Zumbro, G.L., Treasure, R.L. and Geiger, J.P.: Respiratory Obstruction in the Newborn Associated with Increased Volume and Opacification of the Hemithorax. Ann Thor Surg, In Press.

Treasure, R.L., Hopeman, A.R., Green, D.C. and Bedynek, J.L.: Traumatic Aortic Valve Regurgitation and Aortocardiac Fistula with Successful Primary Repair. Milit Med, In Press.

Ceccarelli, F.E.: Combined Transpyeloureterostomy and Ipsilateral Pyeloureterostomy and Orchiopexy by Testicular Artery Transection: Treatment in a Case of Prune Belly Syndrome. J Urol, 110:596-598, 1973.

Ceccarelli, F.E.: Peyronie's Disease. Current Therapy, 1973.

Squitieri, A.P., Ceccarelli, F.E. and Wurster, J.C.: Hypertension with Elevated Renal Vein Renins Secondary to Ureteropelvic Junction Obstruction--A Brief Report. J Urol, 111:284, 1974.

Wurster, J.C. and Ansbacher, R.: Sperm Antibodies in Vasectomized Men. Proceedings of the Kimbrough Urological Seminar, 20th Annual Meeting, 30 October-3 November 1972. Volume 6.

Lund, R.H.: Long-Term Survival and Morbidity Following Radical Prostatectomy. Proceedings of the Kimbrough Urological Seminar, 20th Annual Meeting, 30 October-3 November 1972. Volume 6.

Squitieri, A.P.: Bladder Tumors in Young Adults. Presented at the Western Section Meeting of the American Urological Association, Honolulu, Hawaii, 24-29 June 1973.

Treasure, R.L.: Intraoperative Left Ventricular Rupture Associated with Mitral Valve Replacement. Presented at the American College of Chest Physicians meeting, Toronto, Canada, 22 October 1973.

Treasure, R.L.: Scientific Exhibit "Thoracic Outlet Compression Syndrome: Diagnosis and Treatment," 59th Annual Clinical Congress, American College of Surgeons, Chicago, Illinois, 15-19 October 1973; 67th Annual Scientific Meeting, Southern Medical Association, San Antonio, Texas, 11-14 November 1973.

Bouzard, W.C.: Acute Dislocation of the Patella. Presented to the Society of Military Orthopaedic Surgeons, El Paso, Texas, November 1973.

Elton, R.C.: Burns of the Hand. Presented to the Society of Military Orthopaedic Surgeons, El Paso, Texas, November, 1973.

Haynes, R.J.: .22 Caliber Gunshot Wounds. Presented to the Society of Military Orthopaedic Surgeons, El Paso, Texas, November, 1973.

Haynes, R.J.: Pseudoarthrosis of the Tiba. Presented to the Society of Military Orthopaedic Surgeons, El Paso, Texas, November, 1973.

Barja, R.H.: Giant Cell Tumor. Presented to the Society of Military Orthopaedic Surgeons, El Paso, Texas, November 1973.

Elton, R.C.: Gunshot Wounds and Fractures of the Metacarpus. Presented at the Southern Medical Association Meeting, San Antonio, Texas, November 1973.

Jesunas, K.P.: Keratoacanthoma--Head and Neck Lesion. Presented at the Southern Medical Association Meeting, San Antonio, Texas, 13 November 1973.

Braud, L.L.: Rhinocerebral Phycomycosis. Presented at the Southern Medical Association Meeting, San Antonio, Texas, November 1973.

Gronski, H.W.: Carotid-Cavernous Fistula--A Complication of Maxillo-Facial Trauma. Presented at the Southern Medical Association Meeting, San Antonio, Texas, 11 November 1973.

Bouzard, W.C.: Scientific Exhibit "Reconstruction of the Thermally Injured Upper Limb," American Academy of Orthopaedic Surgeons, Dallas Convention Center, Dallas, Texas, 17-22 January 1974.

Gangai, M.P.: The Urologists Responsibility to the Infertile Male. Presented at the Kimbrough Urologic Seminar, Washington, D.C., 20-24, January 1974.

Gangai, M.P.: Surfing Injuries in Hawaii. Presented at the Kimbrough Urologic Seminar, Washington, D.C. 20-24 January 1974.

Uechi, M.: Retrograde Urethrography in Pelvic Trauma. Presented at the Kimbrough Urologic Seminar, Washington, D.C., 20-24 January 1974.

Conger, M.: Experiences with the Pereyra Procedure. Presented at the Kimbrough Urologic Seminar, Washington, D.C., 20-24 January 1974.

Pfaffenbach, D.D.: Abnormalities of Vertical Gaze. Presented at the San Antonio Ophthalmology and Otolaryngology Society Meeting, 6 March 1974.

Kaplan, J.A.: The Perioperative Management of Pericardial Tamponade. Presented at the Surgical and Orthopaedic Aspects of Trauma Seminar, Brooke Army Medical Center, Fort Sam Houston, Texas, 4-8 March 1974.

Seitter, G., III: Surgical Considerations in Traumatic Rupture of the Diaphragm. Presented at the Surgical and Orthopaedic Aspects of Trauma Seminar, Brooke Army Medical Center, Fort Sam Houston, Texas, 4-8 March 1974.

Treasure, R.L.: Penetrating Cardiac Trauma. Presented at the Surgical and Orthopaedic Aspects of Trauma Seminar, Brooke Army Medical Center, Fort Sam Houston, Texas, 4-8 March 1974.

Seitter, G., III: Atrial Myxoma. Presented at the Gary P. Wratten Symposium, Walter Reed Army Medical Center, Washington, D.C., 2 April 1974.

Larson, A.W.: Coronary Bypass Procedures on Patients with Printzmetal's Angina. Presented at the 4th Annual Meeting, Association of Army Cardiologists, Letterman Army Medical Center, 8-10 May 1974.

Zumbro, G.L.: Surgical Therapy of the Cardiac Manifestations of Marfan's Syndrome. Presented at the 4th Annual Meeting, Association of Army Cardiologists, Letterman Army Medical Center, 8-10 May 1974.

Treasure, R.L.: Intraoperative Left Ventricular Rupture Associated with Mitral Valve Replacement. Presented at the 4th Annual Meeting, Association of Army Cardiologists, Letterman Army Medical Center, 8-10 May 1974.

Elton, R.C.: Gunshot Wounds and Fractures of the Metacarpus. Southern Med J, In Press.

CHAPLAIN'S OFFICE

McSwain, D.W.: Ministering to the Amputee. Military Chaplain's Review, 1974.

HEALTH AND ENVIRONMENT SERVICE

Madorsky, D.D.: Venereal Disease: History, Public Health Control Programs, Present State of the Epidemic, Current Control Programs, Pathogenesis, and Methods of Teaching about Sexually Transmissible Disease. Three hour class presented to secondary school teachers at Incarnate Word College, San Antonio, Texas, 10 July 1973.

Madorsky, D.D.: Participated in panel discussion of Venereal Disease for the United States Junior Chamber of Commerce. Austin, Texas, 11 April 1974.

PHARMACY SERVICE

McAuley, R.J.: Establishment of the Limulus Test for <u>In Vitro</u> Pyrogen Detection. Presented at the 8th Annual Midyear Clinical Meeting of the American Society of Hospital Pharmacists, New Orleans, Louisiana, 10 December 1973.

PHYSICAL MEDICINE SERVICE

See, D.H.: Electromyography in Para Spinal Muscles Following Surgery for Root Compression. Presented at Annual Meeting of Physical Medicine & Rehabilitation and American Congress of Rehabilitation Medicine, Washington, D.C., 25 October 1973.

See, D.H.: Histologic and Electrophysiologic Studies in Guinea Pigs with Experimental Allergic Neuritis. Presented at Annual Meeting of American Academy of Physical Medicine & Rehabilitation and American Congress of Rehabilitation Medicine, Washington, D.C., 25 October 1973.

See, D.H.: Peripheral Neuropathy in Burn Patients. Presented at Burn Symposium, Southern Medical Association Annual Meeting, San Antonio, Texas, 14 November 1973.

See, D.H.: Rehabilitation of the Stabilized Patient. Presented at The University of Texas Health Science Center at San Antonio, 2 February 1974.

Gall, N.G.: Prediction of Rehabilitation Potential. Presented at The University of Texas Health Science Center at San Antonio, 2 February 1974.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effects of Different Major Connector Designs for Removable Partial Dentures on Speaking, Swallowing, Eating, and Resting Comfort

WORK UNIT NO.: C-35-73

PRINCIPAL INVESTIGATOR: Larry D. Campbell, D.D.S., Lieutenant Colonel, DC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the patient preference of different removable partial denture designs during speaking, swallowing, eating, and resting.

TECHNICAL APPROACH

Two metal removable partial denture frameworks, one maxillary and one mandibular, will be made for each of twelve dentists. During the study, the partial dentures will be altered systematically to produce a series of different commonly used designs. Four changes will be evaluated on the maxillary framework, and two on the mandibular. Questionnaires will be completed by the subjects during and after the study.

Manpower: None.

Funding: None.

PROGRESS

The last three subjects are being evaluated after which the data will be compiled.

Presented at the January 1973 Dallas Midwinter Dental Conference. The subject was "Transitional Immediate Dentures for Full Mouth Extraction".

Ongoing.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Post-Operative Localized Osteitis in Mandibular Third Molar Surgery.

WORK UNIT NO.: C-42-73

PRINCIPAL INVESTIGATOR: Sterling R. Schow, D.M.D., Major, DC

ASSOCIATE INVESTIGATOR: John A. Nespeca, D.D.S., Major, DC

OBJECTIVES

To determine the correlation between the incidence of localized osteitis following removal of mandibular third molar teeth.

TECHNICAL APPROACH

The population sample included patients treated for removal of mandibular third molars. Postoperative results were evaluated 4-6 days after completion of the surgical procedure. Parameters evaluated included localized osteitis (defined for purposes of this study as loss of blood clot with exposed bone and pain requiring further treatment), clinically obvious edema, and muscle trismus (evaluated clinically as the inability to open the teeth more than 2 cm. between the incisal edges of the central incisor teeth). Results were tabulated and graphed to show the incidence of postoperative sequelae, primarily localized osteitis, occurring in each of the situations evaluated.

Manpower: None.

Funding: None.

PROGRESS

The incidence of localized osteitis in females receiving oral contraceptives is markedly increased over those not so medicated.

C-42-73 (Continued)

Exposure of the external oblique ridge caused an increased incidence of localized osteitis. Suturing of the mandibular third molar mucoperiosteal flap should be avoided unless passive apposition of the flap in its desired position cannot be accomplished without suture.

Schow, S.R.: Evaluation of Postoperative Localized Osteitis in Mandibular Third Molar Surgery. Oral Surg, In Press.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Acceptability of Lateral Interocclusal Records by the Whip-Mix Articulator.

WORK UNIT NO.: C-25-74

PRINCIPAL INVESTIGATOR: L. James Bell, D.D.S., Major, DC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate clinically the use of lateral interocclusal records in setting the condylar elements of the Whip-Mix articulator; particularly to evaluate the acceptability of these records by the articulator.

TECHNICAL APPROACH

a. Obtain diagnostic casts on 25 dentulous patients.
b. Make right and left lateral interocclusal records on each patient.
c. Adjust and set the condylar elements of the Whip-Mix articulator for each patient with these records.
d. Evaluate these settings and analyze the settings as to their acceptability.

Manpower: None.

Funding: $385.30 Consumable Supplies FY 1974

PROGRESS

Eighteen patients have been evaluated. A new method of making interocclusal records has been designed and is being utilized.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A New Anesthetic for Use in Oral Surgery.

WORK UNIT NO.: C-33-74

PRINCIPAL INVESTIGATOR: John A. Nespeca, D.D.S., Major, DC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine onset of action, duration potency, side effects and other distinguishing features of Bupivacaine Hydrochloride (marcaine) in oral surgical procedures.

TECHNICAL APPROACH

Random usage of one of six anesthetic agents - Xylocaine 2% with or without epinephrine, Bupivacaine .25% with or without epinephrine, Bupivacaine .5% with or without epinephrine. Agents are all double blinded to doctor and to patient. Data is collected primarily on nerve block anesthesia, not on infiltrations.

Manpower: None.

Funding: $992.69 Consumable Supplies FY 1974

PROGRESS

One hundred patients have been treated with Bupivacaine as the local anesthetic. The results indicate that the duration of anesthetic symptoms are prolonged from 8-12 hours. The onset is clinically acceptable but the postanesthetic analgesia is still in question. Currently, data is being collected under more stringent circumstances to validate the results.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Topical Vitamin A Acid in Lamellar Ichthyosis.

WORK UNIT NO.: C-39-72

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: George B. Skipworth, M.D., Colonel, MC

OBJECTIVES

To evaluate and utilize an effective topical preparation in a selected number of dermatoses which are generally unresponsive to other therapeutic modalities.

TECHNICAL APPROACH

Preparation will be applied topically to the affected area initially t.i.d. to the end point of cutaneous irritant dermatitis. Frequency of application is adjusted to several schedules, depending on response. Patients will be closely followed with periodic medical photographs and skin biopsies when indicated.

Manpower: None.

Funding: None.

PROGRESS

Two young patients are currently being treated and continue to show excellent control of their thick, scaling dermatosis with the once daily application of 0.2% Vitamin A acid cream.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Application of the Fluorescent Antibody Technique to the Investigation of Various Dermatoses.

WORK UNIT NO.: C-44-72

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Major, MC

ASSOCIATE INVESTIGATOR: John E. Sattgast, M.D., Major, MC

OBJECTIVES

To demonstrate the presence or absence of skin auto antibodies or antibodies in the epithelium or sera of patients with a variety of bullous and nonbullous dermatoses.

TECHNICAL APPROACH

1. Four mm skin biopsies are sectioned, tagged with fluorescent conjugate, and viewed under UV microscope.

2. Work is performed in the Dermatology Service.

Manpower: None.

Funding: $200.00 Consumable Supplies FY 1973.
$277.90 Consumable Supplies FY 1974.

PROGRESS

112 separate specimens have been examined either by direct or indirect immunofluorescence. The service continues to be offered to any physician desiring immunofluorescence of a patient's skin specimen or serum sample.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Use of Hydroxyurea in Patients with Disabling Psoriasis.

WORK UNIT NO.: C-58-72

PRINCIPAL INVESTIGATOR: Bobby L. Limmer, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the therapeutic efficacy and side effects of the antimetabolite hydroxyurea in patients with disabling and incapacitating psoriasis with or without arthritis.

TECHNICAL APPROACH

All patients who, in the opinion of the Dermatology Staff, have disabling, severe psoriasis and have not responded to previous conventional therapy are eligible for treatment with hydroxyurea. The patients will have a pretreatment evaluation including a history and physical examination and various laboratory procedures to evaluate hematologic, hepatic, pulmonary and renal status. The drug will be discontinued or not begun if a serious abnormality is detected. The therapeutic efficacy will be evaluated by the erythema and scaling thickness of plaques, number of lesions, and photographs over an 8 week period.

Manpower: None.

Funding: None.

PROGRESS

Four patients have been treated with hydroxyurea during the past four years. All patients have improved during the initial 3-6 months of treatment after which new lesions have appeared in spite of continued

C-58-72 (Continued)

hydrea therapy. All patients have been taken off hydrea, either because the therapeutic benefit was no longer felt to be worthy of the risk involved or because methotrexate was substituted to control psoriatic arthritis.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: POMP Combination Chemotherapy of Adult Acute Leukemia.

WORK UNIT NO.: C-93-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the frequency of remission induction in adult acute leukemia.

TECHNICAL APPROACH

Eighty-nine adults with acute leukemia were treated with a combination of 5-mercaptopurine (Purinethol), Vincristine (Oncovin), Methotrexate and Prednisone (POMP) for remission induction and maintenance.

Manpower: None.

Funding: None.

PROGRESS

The overall response rate was 53% and the complete remission rate was 40%. The median duration of maintained complete remission was 24 weeks. The median survival time for all patients was seven months. For the patients who responded, the median survival time was 13 months. Age and previous therapy were major factors influencing the response of the patients in this study. Side effects other than myelosuppression resulted in liver function abnormalities, minor gastrointestinal intolerance, and paresthesias. POMP chemotherapy is effective remission induction and maintenance therapy for adults with acute leukemia under the age of 50 and who had not had prior chemotherapy.

C-93-72 (Continued)

Rodriguez, V., Hart. J.S., Freireich, E.J., Bodey, G.P., McCredie, K.B., Whitecar, J.P., Jr., and Coltman, C.A., Jr.: POMP Combination Chemotherapy of Adult Acute Leukemia. Cancer 32:69-73, Jul 73.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Arabinosyl Cytosine and Hydroxyurea in Combination Therapy for Acute Adult Leukemia.

WORK UNIT NO.: C-97-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effectiveness of the DNA polymerase inhibitor, arabinosyl cytosine, to induce complete remission in adult patients with acute leukemia when combined with the nucleotide reductase inhibitor, hydroxyurea.

TECHNICAL APPROACH

This is a Southwest Oncology Group Study.

The original protocol was revised 11/1/72 as follows:

Hydroxyurea 800 mg/M^2 orally/daily every 4 hours for 16 hours (5 doses) followed in 8 hours by ARA-C 100 mg/M^2/IV push (given 24 hours after first dose of HU and 8 hours after last dose of HU). This cycle is repeated each day (or 24 hour interval) until marrow blasts disappear.

Patients with AGL, AMML and AML not previously treated with ARA-C or HU are eligible for study.

Manpower: None.

Funding: None.

PROGRESS

Seven patients have been registered and evaluated. One patient who relapsed on day 263 with 14% blasts was re-treated with the same

C-97-72 (Continued)

induction regimen for 10 days and achieved A-1 marrow within 32 days. She remains in remission on the same maintenance regimen 82 days later.

Nausea and vomiting was severe in one patient, necessitating a 25% reduction in HU dose. The marrow suppressive effect has been evident by day 10 and was much more prolonged in the one patient with Hodgkin's Disease treated two years earlier with combined radiotherapy and chemotherapy.

"Four patients achieved A-1 marrow and this experience is therefore quite positive," so stated Dr. Stuckey at the Southwest Oncology Group meeting 13-15 February 1974, University of Arizona, Tucson, Arizona.

Terminated due to transfer of principal investigator.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase I Protocol for the Evaluation of Combined Radiotherapy and Chemotherapy for Stage II-B, III-A, and III-B Hodgkin's Disease.

WORK UNIT NO.: C-98-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To test the ability of patients to tolerate total nodal radiotherapy following MOPP chemotherapy.

TECHNICAL APPROACH

The study was begun with three cycles and subsequently escalated to four cycles of MOPP. One hundred sixty patients have been entered, but only 108 can be evaluated.

Manpower: None.

Funding: None.

PROGRESS

The complete response rate overall is 82% in 108 patients. An estimated 80% of the patients have remission times lasting longer than 52 weeks from the end of treatment.

This study will be continued by the Southwest Oncology Group. However, due to transfer of the principal investigator, it will be terminated at Brooke Army Medical Center.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase I Study of Guanazole.

WORK UNIT NO.: C-103-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effective dose and anti-tumor effectiveness of Guanazole, a ribonucleotide reductase inhibitor.

TECHNICAL APPROACH

Guanazole is administered as rapid intravenous injection twice weekly for three weeks, and continued if an anti-tumor response is observed.

Manpower: None.

Funding: None.

PROGRESS

The major toxic manifestations from this drug are myelosuppression, fever, and somnolence. The twice weekly bolus study was associated with severe myelosuppression at a level of 20 gm/M^2/day.

Due to shortage of Guanazole, project was terminated.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy with Dimethyl-Triozeno Imidazole Carboxamide (NSC-45388) and Adriamycin (NSC-123127) in Soft Tissue and Bone Sarcomas.

WORK UNIT NO.: C-105-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the efficacy of combination chemotherapy with ICT and Adriamycin in patients with soft tissue and bone sarcomas.

TECHNICAL APPROACH

Adriamycin is administered intravenously once every three weeks. ICT is administered intravenously daily for 5 days each 3 weeks; the first daily dose of each course is administered on the same day as the Adriamycin.

Manpower: None.

Funding: None.

PROGRESS

Of 120 patients entered, 100 were evaluable. Five complete and 36 partial remissions were observed for a response rate of 41% including: synovial cell sarcoma 2/2; rhabdosarcoma 3/5; undifferentiated sarcoma 6/13; fibrosarcoma 5/11; osteogenic sarcoma 8/18; liposarcoma 3/7; neurofibrosarcoma 4/10; leiomyosarcoma 6/16; angiosarcoma 1/5; chondrosarcoma 0/4; and miscellaneous sarcomas 0/2. Median duration for complete remission was 5+ months and for partial remission 3-1/2+ months. Toxicity was

C-105-72 (Continued)

limited predominantly to vomiting, alopecia and myelosuppression. Leukocyte depression was next by median day 15 with prompt recovery permitting retreatment at a three week interval in all but 8% of the cases. Combination therapy of the Adriamycin and DIC appears to be effective and promising regimen in the treatment of metastatic sarcomas.

Gottlieb, J.A., Baker, L.H., Quagliana, J.M., Luce, J.K., Whitecar, J.P., Jr., et al.: Combination Chemotherapy with Dimethyl-Triozeno Imidazole Carboxamide and Adriamycin in Soft Tissue and Bone Sarcomas. Cancer 30:1632-1638, Dec 72.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy of Multiple Myeloma

WORK UNIT NO.: C-109-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the frequency of remission induced by a four drug induction regimen (melphalan, prednisone, procarbazine, vincristine).

TECHNICAL APPROACH

Four drug remission induction regimen.

Manpower: None.

Funding: None.

PROGRESS

Analyses indicate that there is no improvement in response rate from the addition of either procarbazine or vincristine to melphalan-prednisone.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Three Combination Regimens (OAP, DOAP, COAP) for Remission Induction and Remission Maintenance Therapy for Adult Acute Leukemia.

WORK UNIT NO.: C-112-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare the effectiveness of the three drug regimen and estimate the effectiveness when cytosine arabinoside is given by 120 hour infusion.

To compare two maintenance regimens: intermittent remission reinduction vs. intermittent reinduction plus continuous 6 MP.

TECHNICAL APPROACH

Each of the three regimens are administered every two weeks. Vincristine is administered intravenously once every two weeks. Prednisone is administered orally for five days every two weeks. Cytosine arabinoside is administered intravenously as a 120 hour continuous infusion every two weeks. Cytoxan is administered as a single rapid intravenous injection daily for five days every two weeks. Daunomycin is given as an intravenous injection once every two weeks.

Manpower: None.

Funding: None.

PROGRESS

This study of 337 patients revealed no significant difference between the three treatment regimens in terms of frequency of remission induction. An important finding was that the 106 patients

C-112-72 (Continued)

treated by larger institutional contributors had a remission rate of 55%, whereas the remaining 150 patients had a frequency of complete remission of only 29%.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination (Cytoxan, Vincristine, Methotrexate, 5-FU and Prednisone) Chemotherapy of Solid Tumors in Adults.

WORK UNIT NO.: C-113-72

PRINCIPAL INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the influence of a five drug combination on a variety of diffusely metastatic solid tumors.

TECHNICAL APPROACH

Eight week course of daily oral cytoxan and prednisone and weekly intravenous vincristine, methotrexate and 5-FU.

Manpower: None.

Funding: None.

PROGRESS

Although survival of the complete responders is statistically significantly longer than all other patients, the total absence of any difference between partial responders and even patients with increasing disease is disappointing.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Minocin Treatment of Gonorrheal Urethritis.

WORK UNIT NO.: C-129-72

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: Frank L. Foreman, M.D., Captain, MC

OBJECTIVES

To ascertain the best therapeutic dose of Minocin for treatment of acute gonorrheal urethritis in outpatients.

TECHNICAL APPROACH

Evaluation of Minocin capsules in the treatment of gonorrheal urethritis in adult males. Two dosage schedules are utilized with the drug randomized so that the physician does not know what dosage the patient will be receiving.

Gram stains, cultures, and VD-G Dri-DOT test will be done pre-therapy, at 48 hours and 7 days post-therapy. Blood will be drawn to determine serum levels of Minocin. These samples will be evaluated by Lederle Laboratories.

Manpower: None.

Funding: None.

PROGRESS

Approximately 100 patients have been studied to date. Data analysis will begin in early FY 1975.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Evaluation of the Efficacy of Dopamine in the Treatment of Cardiogenic Shock.

WORK UNIT NO.: C-130-72

PRINCIPAL INVESTIGATOR: George M. McGranahan, Jr., M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare Dopamine as a therapeutic agent in the treatment of cardiogenic shock agents presently available -- Isoproterenol, Norepinephrine.

To measure the hemodynamic response to Dopamine infusion.

TECHNICAL APPROACH

Only patients with cardiogenic shock will be candidates for the study. Cardiogenic shock will be defined as a systolic pressure less than 90 mm Hg in a patient who exhibits one or all of the following signs: (1) urine output less than .5 cc/min.; (2) poor peripheral perfusion manifested by pallor, cool extremities and/or cyanosis; (3) decreased cerebral perfusion manifested by confusion and obtundation.

Manpower: None.

Funding: None.

PROGRESS

Due to recent publications concerning the use of Dopamine in the treatment of cardiogenic shock, it is felt that there is no need to pursue a similar study at Brooke Army Medical Center.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Therapy of Bowen's Disease with Topical 5-Fluorouracil.

WORK UNIT NO.: C-143-72

PRINCIPAL INVESTIGATOR: Bobby L. Limmer, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effectiveness of topically applied 5-fluorouracil in the treatment of Bowen's disease.

TECHNICAL APPROACH

Eighteen patients with Bowen's disease were treated with topical 5-fluorouracil. The medication was applied to the lesion twice daily for 2-6 weeks until adequate reaction occurred consisting of inflammation, erosion, or ulceration of the lesion. The patients were seen weekly in the Dermatology Clinic. Photographs were taken prior to and after therapy and weekly during the course of therapy. Biopsies were done before and after therapy to determine the histologic as well as the clinical response to fluorouracil.

Manpower: None.

Funding: $479.00 TDY FY 1974

PROGRESS

Eighteen patients with Bowen's disease have been treated with topical 5-fluorouracil. None of these 18 patients have developed invasive squamous cell carcinoma in sites of Bowen's disease prior to, during, or after 5-FU therapy. Three patients have had other non-actinically

C-143-72 (Continued)

induced malignancies consisting of mixed tumor of the parotid gland, squamous cell carcinoma of the larynx, and squamous cell carcinoma of the penis. Three females with multifocal Bowen's disease of the vulva have also had squamous cell carcinoma in situ of the cervix.

5-fluorouracil topically would appear to offer an alternative mode of therapy for Bowen's disease in which initial surgical approaches would be difficult or mutilating (penectomy, vulvectomy, excision and grafting of extensive facial lesions, etc.). However, close follow-up is imperative since a significant incidence of recurrence is to be anticipated.

Completed.

Presented before the Military Dermatology Section, American Academy of Dermatology Meeting, Chicago, Illinois, 4 December 1973.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Study of Tobramycin.

WORK UNIT NO.: C-147-72-1

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the clinical efficacy of the aminoglycoside tobramycin in the treatment of serious gram-negative infections.

TECHNICAL APPROACH

Hospitalized patients will be acceptable for admission to the study with the following infections: (1) urinary tract infections as established by greater than 100,000 colonies of bacteria per ml of urine in a properly collected voided specimen, or a significant colony count from catheterized urine; (2) gram-negative pneumonia as manifested by typical radiological and bacteriological findings; (3) gram-negative sepsis and bacteremia; (4) severe surgical infections; (5) neonatal sepsis with and without meningitis.

Routine hematology, urinalysis and urine cultures, SMA-12, and BUN or creatinine will be accomplished before, at least once weekly, and following completion of therapy.

Dosage for adults and children will not exceed 6 mg/kg/24 hours. Serum concentrations as determined in the laboratory will dictate changes in dose schedule.

Manpower: E-4 (6 months).

Funding: None.

C-147-72-1 (Continued)

PROGRESS

Since initiation of this protocol, 14 patients have been treated with tobramycin for infections due to sensitive gram-negative rods. All sensitivity testing was determined by Kirby-Bauer technique. There were no allergic reactions and no toxic manifestations were noted following the administration of tobramycin. Following a dose of 3 mg/kg body weight per 24 hours divided into 3 eight hourly doses, the serum concentration 30 minutes after infusion ranged between 3 and 6 mcg/ml; at a dose of 5 mg/kg body weight administered in divided doses every 8 hours, levels were between 6 and 10 mcg/ml--all of these levels were well below previously established levels of oto- or nephrotoxicity for this drug. Again, during the treatment with tobramycin, no patient experienced deterioration in renal function and no ototoxicity was detected. Urine samples taken 1 hour after administration demonstrated levels between 50 and 100 mcg/ml using 3 mg/kg and using 5 mg/kg were greater than 100 mcg/ml. All patients had a satisfactory clinical response. One patient with a Pseudomonas urinary tract infection presented an interesting problem of rapid tobramycin elimination. This patient was initially treated with 3 mcg/ml/24 hours with urinary drug levels of 6 mcg/ml and serum levels of less than 1 mcg/ml. On increasing the dose to 5 mg/kg the corresponding levels in the urine did not change; however, the serum level increased to 2.9 mcg/ml. Because multiple antibiotics which were ineffective against his isolated organism had been demonstrated, the dose was increased to 7 mg/kg body weight with concomitant serum levels of 1.4 mcg/ml and urinary levels of 1.7 mcg/ml, and this patient is considered the only clinical failure. Why higher serum levels were never achieved and why urinary levels did not increase with increasing dosage is not clear and reflects the variable handling of an aminoglycoside by different patients. Although unusual, this problem has been described previously, and it is suspected that hepatic detoxication may be playing a role; however, this remains to be proven.

We intend to continue this study until a total of 20 patients have been treated.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Tobramycin-Carbenicillin and Gentamicin-Carbenicillin in the Treatment of Acute Infections in Cancer Patients.

WORK UNIT NO.: C-147-72-2

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the clinical efficacy of a combination of Tobramycin-Carbenicillin and Gentamicin-Carbenicillin for treatment of systemic infections in cancer patients with compromised defense mechanisms.

TECHNICAL APPROACH

The study was done in a single blind fashion so that only the pharmacy and the investigator knew which of the two drugs were being given. Patients were assigned a consecutive number in this protocol so that they were matched to either a combination of tobramycin-carbenicillin or gentamicin-carbenicillin in a random order. Indications for starting patients on the study were an acute febrile episode and a neutropenia of less than 1000 WBC/mm^3. Appropriate cultures were taken prior to starting antibiotic therapy. The dose of tobramycin and gentamicin was 5 mg/kg/24 hrs, IV piggyback, given at 8 hour intervals. The dose of carbenicillin was 5 gm IV piggyback q4H, or 30 gm/24 hrs. Serum levels of tobramycin and gentamicin were determined at least twice during therapy, and determinations were done one hour after an IV dose. The bacillus spore assay was used to determine antibiotic levels after adding penicillinase to the serum to destroy the carbenicillin activity. Urine levels of both drugs were also determined using this same technique.

Manpower: E-6 (6 months)

Funding: None.

C-147-72-2 (Continued)

PROGRESS

Eighteen cancer patients, who were immunosuppressed and who had acute bacterial infections, were sucessfully treated with a combination of either tobramycin or gentamicin and carbenicillin. No significant side effects were noted. We were unable to detect any significant differences between the response to either combination with the possible exception of mean duration of fever after initiation of antibiotic therapy. One possible explanation for this difference appeared to be the randomization of patients with acute leukemia.

On the basis of this study, tobramycin appears to be equally as effective in the treatment of acute bacterial infections in cancer patients as is gentamicin.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Determination of Patch Test Reaction Time.

WORK UNIT NO.: C-5-73

PRINCIPAL INVESTIGATOR: Daniel B. Clarke, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

OBJECTIVES

To determine the significant patch test reaction times and locations with known allergens included in a standard patch test screening tray.

TECHNICAL APPROACH

Chemicals composing a proposed international standard patch test screening tray will be used. Subjects known to be reactive to one or more of the above chemicals by previous diagnostic patch testing will be entered in the study. One horizontal row of six patches with a known amount of allergen will be placed on the extreme upper and one on the extreme lower back. Under each row of allergen patches will be one row of six control patches. Estimation of reactivity will be: - negative; + erythema; ++ erythema and vesicles; +++ erythema, vesicles and spreading; IR irritant rection. Data will be analyzed to determine minimal significant reaction time for the involved chemicals in each location.

Manpower: None.

Funding: None.

PROGRESS

Twenty-five patients have been studied. Twenty-five additional patients will be studied.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of the Efficacy and Safety of Petrin W-2197 Orally. (Cooperative study with Letterman and Fitzsimons)

WORK UNIT NO.: C-13-73

PRINCIPAL INVESTIGATOR: Troy H. Williams, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine whether W-2197 orally favorably influences the clinical symptomatic course of anginal patients by altering the frequency and severity of anginal attacks and nitroglycerin requirements; to determine the most effective dose range of the drug; to determine the effect on exercise stress induced ECG changes in anginal patients; to determine patient tolerance of drug.

TECHNICAL APPROACH

This will be a double-blind placebo-controlled, single crossover trial of W-2197 in anginal patients with two 8-week treatment periods. The double-blind study is preceded by a single-blind phase. A period during which placebo is administered is followed by a period of varied dose administration to evaluate the individual patient's dose requirement prior to commencing the double-blind study. Also, a placebo period separates the dose individualization section of the study from the double-blind crossover portion of the study in order to re-establish baseline information.

Manpower: None.

Funding: None.

PROGRESS

The Defense Department would not allow Government Hospital to accept funds from a drug company.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Study of Cefazolin Sodium.

WORK UNIT NO.: C-22-73

PRINCIPAL INVESTIGATOR: Layne O. Gentry, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: William L. Moore, M.D., Lieutenant Colonel, MC
Jay Sanford, M.D.

OBJECTIVES

To evaluate the efficacy of cefazolin sodium in the treatment of susceptible gram-negative bacterial infections.

TECHNICAL APPROACH

Hospitalized patients with the following infections were admitted to the study: (1) urinary tract infections as established by greater than 100,000 colonies of bacteria per ml of urine in a properly collected voided specimen, or a significant colony count from catheterized urine; (2) continuation of antibiotic therapy following intravenous cephalothin.

Culture and sensitivity data proving susceptible infection were obtained before, during and after therapy as indicated. CBC and platelet count were obtained before therapy, at least once a week during therapy, and following completion of therapy. Urinalysis was done before therapy, once a week during therapy, and upon completion of therapy. SMA-12 was done before and after therapy and at least once a week during therapy. BUN and/or creatinine was done at more frequent intervals as indicated.

Manpower: E-6 (6 months)

Funding: None.

C-22-73 (Continued)

PROGRESS

Forty patients with urinary tract infections have been treated with Cefazolin. Two of twenty-six patients suffered a relapse after five days of therapy but were successfully treated with ten days of therapy.

Additional data obtained from this study are being evaluated, and a manuscript is being prepared.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Gastrointestinal Candidiasis in Cancer.

WORK UNIT NO.: C-25-73

PRINCIPAL INVESTIGATOR: Layne O. Gentry, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

OBJECTIVES

To study the role of immunoglobulins in serum and gastrointestinal secretions in systemic candidiasis.

TECHNICAL APPROACH

Patients on the Oncology Inpatient Service will have routine weekly serologic tests for candidiasis in the Infectious Disease Laboratory using the following methods: immunoelectrophoresis, latex agglutination, immunodiffusion. The following cultures will be obtained: mouth and pharyngeal; rectal swa[illegible]; sputum; scrapings of all mouth lesions; and material obtained [illegible] endoscopy. Esophagograms will be done when esophageal candidiasis is suspected. Endoscopy will be performed to document the presence or absence of lesions in the pharynx and esophagus.

Patients undergoing chemotherapy on the Oncology Inpatient Service will have weekly determinations of serum IgA, IgG, and IgM levels. Saliva from patients undergoing chemotherapy will be collected, immediately frozen, and tested for IgA levels; secretions from the duodenum and jejunum will be obtained at endoscopy, immediately frozen, and later tested for IgA levels.

Manpower: E-4 (6 months)

Funding:	$ 546.95	Consumable Supplies	FY 1974
	$ 360.00	TDY	FY 1974
	$2,214.00	Consumable Supplies	FY 1973
	$ 890.00	PEMA	FY 1973

C-25-73 (Continued)

PROGRESS

Either the immunodiffusion or counterelectrophoresis tests when combined with the latex agglutination test are useful in detecting invasive candidiasis. Colonization with Candida species is responsible for positive serologic tests, and in a few patients will cause the latex agglutination titers to increase. In the patient with heavy colonization or invasive candidiasis, a positive immunodiffusion or counterelectrophoresis test and with a rising latex agglutination titer, strongly suggests that a progressive and serious Candida infection is present and that systemic antifungal therapy may be indicated. Candida krusei infections will not be detected by any serologic test using Candida albicans antigen. Severe immunosuppression and early effective antifungal therapy may result in false negative serologic test results.

Presented at the American Society for Microbiology meeting, 12-17 May 1974, Chicago, Illinois.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Cyproheptadine in the Management of Patients with Idiopathic Chronic Immunic Complex-Induced Glomerulonephritis: A Controlled, Double-Blind Cooperative Study.

WORK UNIT NO.: C-27-73

PRINCIPAL INVESTIGATOR: Philip W. Rogers, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Richard H. Merrill, M.D., Major, MC
Daniel A. Nash, Jr., M.D., Major, MC
David B. Olin, M.D., Major, MC

OBJECTIVES

This study was designed to arrest chronic complex-induced glomerulonephritis in humans by preventing antigen-antibody complex deposition in the capillary loops in the glomeruli.

TECHNICAL APPROACH

Patients with glomerular filtration rate greater than 20 ml per minute and with the demonstration of immunoglobulin deposition in the kidney in a granular pattern on renal biopsy are admitted to the study. The patients are given a placebo or cyproheptadine (Periactin®) in a double blind manner as determined by Merck, Sharpe and Dohme Laboratories. The patients are followed for one year with close observation of glomerular filtration rate, liver function studies, serum complement and complete blood count. At the end of one year, a repeat renal biopsy is performed and immunofluorescent studies again performed and compared with the initial biopsy.

Manpower: None.

Funding: None.

C-27-73 (Continued)

PROGRESS

Three patients have been admitted to this study locally with a total of 44 patients admitted by other centers. One of our patients was dropped from the study because of the development of extrapyramidal manifestations directly attributable to Periactin®, and a second patient was dropped from the study because of a protocol violation. From the number of patients admitted and followed thusfar, it appears that Periactin® may decrease the amount of protein excretion resulting from the renal disease; however, little change in renal function has been observed. No definitive conclusions can be made at the time of this report.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Simultaneous Determination of Instantaneous Aortic Flow, High Fidelity Intracardiac Pressures, Intracardiac Phonocardiography, Echocardiographic Dimensions, and Derived Indices in Man.

WORK UNIT NO.: C-28-73

PRINCIPAL INVESTIGATOR: Joseph P. Murgo, M.D., Major, MC

ASSOCIATE INVESTIGATORS: George M. McGranahan, Jr., M.D., Colonel, MC
Hal A. Martin, M.D., Major, MC
James F. Dorethy, M.D., Major, MC

OBJECTIVES

1. To develop new techniques in cardiac catheterization, especially in the area of multi-solid state sensor catheters including high fidelity pressure sensors and electromagnetic flow meters. To utilize high speed biplane angiography and external echocardiography in conjunction with such techniques.

2. To utilize these techniques to define sophisticated parameters of ventricular function in patients with various cardiac diseases.

3. To develop specialized computer-assisted analyses of the data derived from such studies.

4. Detailed description of multiple specific objectives are to be found in the original protocol.

TECHNICAL APPROACH

All patients (adult) coming to routine right and left heart catheterization are evaluated in the usual manner by a cardiac fellow prior to catheterization. This evaluation includes strip chart echocardiography to determine the patient's suitability for certain aspects of the protocol. During catheterization, a special custom designed triple-tip right-sided catheter is introduced into the right heart such that simultaneous high fidelity pressures are measured from the pulmonary artery, right ventricle and right atrium.

C-28-73 (Continued)

A second, more conventional catheter is also introduced into the pulmonary artery for purposes of blood specimen withdrawal, etc. The left heart is catheterized using a multiple sensor custom-designed catheter such that high fidelity left ventricular and left atrial pressures are measured as well as ascending aortic electromagnetic flow velocity. Patients are studied during both rest and supine exercise; and in some protocols, depending on the patient's disease, they are studied utilizing a variety of other stresses. Following the collection of hemodynamic data, the patients undergo external echocardiography while simultaneously measuring pressures and flows, and the study is terminated using biplane ventricular angiography and coronary arteriography if indicated. All patients also undergo an aortic root angiography for the purposes of determining aortic root diameter which is necessary to convert flow velocity to flow itself. An on-line Honeywell 316 computer presently exists in the laboratory and is capable of sampling all pressures, electrocardiograms and flow simultaneously. This computer will print out the results of all of these parameters immediately, simplifying the data analysis immensely. Specially designed research programming for the computer to perform sophisticated calculations will be added in the near future. The angiograms and echocardiograms are analyzed using specialized Hewlett-Packard digitizers and programmable calculators.

Manpower: 2LT (12 months)
E-3 (12 months)

Funding:			
	$29,354.25	PEMA	FY 1974
	$ 862.40	Capital Equipment	FY 1974
	$43,573.00	Consumable Supplies (Contractural Svc)	FY 1974
	$ 1,195.68	TDY	FY 1974
	$43,300.00	PEMA	FY 1973

PROGRESS

Since last year's report, significant progress has been made in the design and development of specialized catheters. There has been an advance from the double high fidelity differential pressure catheter to triple pressure sensors for the right side as described above, and a double high fidelity pressure sensor on the left side to include an electromagnetic flow velocity probe. An abstract regarding the technical characteristics of these techniques is currently being written and will be submitted to

the American Heart Association for consideration for the annual meeting in November 1974. A second abstract regarding the specialized computer program for continuous echocardiographic volumes and pressure volume loops is also currently being written and will be submitted to the same meeting and, in addition, to the Conference of Engineering in Medicine and Biology. Over 180 patients have been studied thusfar using the techniques described above and significant progress has been made in describing the characteristics of ventricular ejection in man first defining a control population of patients who are found to have no cardiac disease and also in patients with various degress of arteriosclerotic heart disease, and finally some very significant findings in a group of nine patients with idiopathic hypertrophic subaortic stenosis. Approximately eight to ten manuscripts are in preparation to be submitted for publication regarding both the techniques and the results using these techniques.

"The Normal Left Ventricular-Aortic Pressure Relationship in Man using a New Twin-Tip High Fidelity Catheter" presented at the Tenth International Conference on Medical and Biological Engineering, Dresden, German Democratic Republic, August 1973.

Nine seminars regarding the techniques and results of our efforts were presented to various medical universities in Europe at the following institutions and cities: The University of Zurich, Switzerland; Frankfurt University, Dusseldorf University and Essen University, all in West Germany; a seminar sponsored by Lamieris Instrumenten B. V. in Utrecht, Holland; two seminars in Oslo, Norway at the university hospitals in that city; one seminar in Helsinki, Finland; and a seminar in London which was attended by approximately 75 physicians from hospitals and universities throughout England.

"Continuous Left Ventricular Volume, Circumferential Fiber Shortening Rate and Pressure Volume Loops by Echocardiography and a Multisensor Catheter" presented at the 46th Scientific Sessions of the American Heart Association, 8-12 November 1973, Atlantic City, New Jersey. Accepted for publication.

"Aortic Flow Velocity and the Left Ventricular Aortic Pressure Gradients in Patients with Normal Aortic Valves" presented at the 46th Scientific Sessions of the American Heart Association, 8-12 November 1973, Atlantic City, New Jersey Accepted for publication.

C-28-73 (Continued)

"New Techniques in Cardiac Catheterization, Including Multisensor Catheters and Echocardiography" presented at the Texas Heart Institute, December 1973.

Participated as a faculty member for a three-day course entitled "Three Days in Cardiology--The Hemodynamic Basis of Heart Sounds and Murmurs" sponsored by the University of Pittsburgh Medical School and the American Heart Association, April 1974, Mariott Inn, Pittsburgh, Pennsylvania.

"Left Ventricular Ejection Dynamics--The Role of the Peripheral Circulation" presented at the Fourth Annual Army Association of Cardiology Meeting, Letterman Army Medical Center, May 1974.

"The Dynamic Pressure Flow Relationships in Idiopathic Hypertrophic Subaortic Stenosis" presented at the Fourth Annual Army Association of Cardiology Meeting, Letterman Army Medical Center, May 1974.

"Clinical Usefulness of Systolic Time Intervals" presented at the Fourth Annual Army Association of Cardiology Meeting, Letterman Army Medical Center, May 1974.

Murgo, J., et al.: Echocardiographic detection of supravalvular aortic stenosis. Circulation, July 1974.

Murgo, J., et al.: Ventricular ejection mechanics--how the left ventricle works. Circulation.

Murgo, J., et al.: Simultaneous aortic flow velocity, left ventricular aortic pressure gradients and mitral motion in hypertrophic subaortic stenosis. 46th Scientific Sessions of the American Heart Association.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Cephalothin and Alkalinized Cephalothin.

WORK UNIT NO.: C-29-73

PRINCIPAL INVESTIGATOR: William L. Moore, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: Layne O. Gentry, M.D., Lieutenant Colonel, MC

OBJECTIVES

To determine by a controlled clinical trial whether the incidence of phlebitis is less with intravenously administered alkalinized cephalothin than it is with non-alkalinized cephalothin.

TECHNICAL APPROACH

This controlled clinical trial will be a cross-over study in which a comparison will be made of the incidence of phlebitis associated with the intravenous administration of the study drug (alkalinized cephalothin) and the control (non-alkalinized cephalothin). Both the study preparation and the control preparation will be administered in a similar fashion to each patient. Patients selected to enter this study will be inpatients. Adults of either sex who have suspected or confirmed bacterial infections that would ordinarily require IV cephalothin are eligible for the study. Patients to be excluded from the trial should be those who have a history of hypersensitivity to cephalosporins and patients who are receiving anticoagulant therapy. Laboratory studies appropriate for the patient's care will be obtained. Evaluation of results will be done from patients who complete the study, and both infusion sites will be included in the analysis of the results.

Manpower: None.

Funding: None.

C-29-73 (Continued)

PROGRESS

No significant difference between the two drugs was detected.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Skin Window Studies in Trichophyton Hypersensitivity.

WORK UNIT NO.: C-39-73

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

OBJECTIVES

To evaluate the type of cellular response in patients with tinea pedis as revealed by the skin window technique, utilizing trichophyton antigen.

TECHNICAL APPROACH

Twenty-five patients from the Dermatology Clinic with tinea pedis, diagnosed either by KOH positivity or culture, will undergo skin window studies. An area on the volar aspect of the subject's forearms is cleaned with alcohol. 0.1 cc of trichophyton antigen is injected in an intradermal location at two sites on one forearm and 0.1 cc of diluent on the other forearm. A 4 mm diameter abrasion is created over one injected site by scraping the skin with a #15 Bard-Parker blade until bleeding points are seen. A sterile, cardboard-backed coverslip is securely placed over the abrasion and changed at 24 and 48 hours. The coverslips are air dried, stained with Wright stain, and mounted permanently on glass slides. The slides were evaluated for basophile count at 24 and 48 hours.

Prisoners at the California Medical Facility were the subjects in cooperation with LAIR.

Manpower: None.

Funding: None.

C-39-73 (Continued)

PROGRESS

All the data has been collected and is being analyzed.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Calcium Metabolism During Acute Renal Insufficiency.

WORK UNIT NO.: C-40-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Daniel Nash, M.D., Major, MC

OBJECTIVES

To determine the mechanism of hypercalcemia seen in some cases of acute renal insufficiency.

TECHNICAL APPROACH

All patients with acute renal failure will be surveyed. They will be divided into two groups in an alternate manner. The usual dietary and chemotherapeutic modalities for treating acute renal failure will be employed. Hemodialysis and peritoneal dialysis will be reserved for those patients who are uremic or in whom fluid and potassium balance cannot be controlled by conservative means. Serum phosphorus will be maintained below 6 mg% in one group, and the second group will go untreated. For those able to eat, 1000 mg calcium and 1500 mg phosphorus will be offered. Percutaneous renal biopsies will be examined by light microscopy, electron microscopy, and immunofluorescent microscopy. Patients with acute renal insufficiency will have three 6-hour dialyses a week. Serial determinations will be done to detect any manifestations of hypercalcemia. In addition, serum parathyroid hormone will be measured and an attempt will be made to correlate the hypercalcemia that is frequently seen following acute renal insufficiency with increased parathormone secretion.

In those patients developing hypercalcemia in the diuretic phase, efforts will be made to suppress parathormone secretion by calcium infusion or phosphorus depletion. When possible weekly eye examination will be performed to document early metastatic calcification. Skin biopsies will be analyzed for calcium.

C-40-73 (Continued)

Manpower: None.

Funding: None.

PROGRESS

No progress has been made on this particular protocol because of the lack of availability of ionized calcium electrode. This electrode is now available at the Institute of Surgical Research and the study will begin.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Association of Immune Complex Renal Disease in Hepatitis.

WORK UNIT NO.: C-41-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Gerald A. Hiatt, M.D., Major, MC

OBJECTIVES

To determine the incidence of immune complex glomerulonephritis in acute hepatitis.

TECHNICAL APPROACH

Patients with hepatitis admitted to the Gastroenterology Service are being screened to determine the incidence of immune complex renal disease. Each patient will have bi-weekly analysis of hepatic, renal, and immune systems. All patients found to have evidence of renal disease will be further evaluated by renal biopsy which will be studied by the techniques of light microscopy, electron microscopy and immunofluorescence microscopy. If immune complex renal disease is proven, an attempt will be made by immunofluorescent technique to document that the immune complexes are indeed due to the hepatitis associated antigen. The ability of the kidneys to dilute and concentrate will be determined. Immunocompetence will be established by skin tests. Immunoelectrophoresis will be performed on those patients with abnormal protein electrophoesis. The presence of hepatitis associated antigen and antibody in serum and urine will be detected by radioimmunoassay. Complement levels will be measured, and any anticomplementary activity will be assayed. Latex fixation test and antinuclear antibody test will be performed and an LE preparation if indicated.

Manpower: None.

Funding: None.

C-41-73 (Continued)

PROGRESS

Approximately 15 patients have thusfar been screened, with no objective evidence of renal disease.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Immunofluorescent Study of Various Renal Diseases.

WORK UNIT NO.: C-43-73

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

A characteristic fluorescent pattern in various forms of glomerulonephritis has been defined. In many instances, when the light microscopic findings are difficult to interpret, immunofluorescence may reveal a pattern which is commonly associated with a characteristic abnormality on light microscopy.

TECHNICAL APPROACH

Needle biopsy of patient's kidney will be bisected for H-E staining and for immunofluorescent staining. Specimens for fluorescence are sectioned at 4u on a cryostat and placed on a nonfluorescent microscope slide. The slide is labelled and section covered by 1 or 2 drops of fluorescent-tagged conjugate. The slide is then incubated at room temperature for 30 minutes, after which the conjugate is rinsed from section and the slide suspended in a phosphate buffered water bath for 60 minutes. A cover slip is placed on the section and viewed under a UV microscope using an excitor filter (UG5 Sehoft filter) and a UV absorbing filter (Wratten 2B).

Manpower: None.

Funding: $408.30 Consumable Supplies FY 1974

PROGRESS

Due to lack of specimens, this protocol is terminated. However, the Dermatology Service will continue to offer this service to any physician desiring fluorescence of renal biopsy specimens.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effects of Gentamicin or Tobramycin and Carbenicillin on the Fungal Flora of Hospitalized Patients.

WORK UNIT NO.: C-1-74

PRINCIPAL INVESTIGATOR: Layne O. Gentry, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

OBJECTIVES

To study the effects of broad spectrum antibiotic therapy as a cause for the increased incidence of fungal "carrier state" and/or fungal infection in hospitalized patients.

TECHNICAL APPROACH

The study will consist of three groups of patients. All cultures will be collected in the routine manner, either under the supervision of or by a member of the Infectious Disease Service. Cultures will be done at three separate intervals in the Group II and Group III patients. The first cultures will be obtained either immediately before or immediately after starting the systemic antibiotic therapy. A record will be maintained so that the current and any previous courses of antibiotic therapy will be documented. The second set of cultures will be done after three days of antibiotic therapy. The third and final set of cultures will be taken three days after the termination of antibiotic therapy. Group I patients will have cultures taken on only one occasion, with a careful history of previous antibiotic therapy being documented. The method of the Myocology Section of the National Center for Disease Control in Atlanta, Georgia will be utilized for identification of fungi.

Manpower: E-4 (6 months)

Funding:			
	$1,519.14	Consumable Supplies	FY 1974
	$ 360.00	TDY	FY 1974

C-1-74 (Continued)

PROGRESS

The analysis of data has revealed a significant risk to patients hospitalized at Brooke Army Medical Center.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In Vitro Susceptibility of Candida and Torulopsis Species Isolated from Hospitalized Patients to Nystatin, 5-Fluorocytosine and Amphotericin B.

WORK UNIT NO.: C-2-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Preston B. Cannady, M.D., Major, MC

OBJECTIVES

To compare in vitro susceptibility of Candida and Torulopsis species isolated from patients who are receiving broad spectrum antibacterial or antifungal agents against similar species isolated from hospitalized patients who are not receiving such agents.

TECHNICAL APPROACH

Approximately 100 isolates will be tested against Nystatin, Amphotericin B and 5-fluorocytosine. Strains isolated from patients being studied at Brooke Army Medical Center will be used for sensitivity testing. One isolate of each species from a patient will be used. Repeat sensitivity testing will be done on only those organisms obtained from patients who have received one of the commonly used antifungal agents. Sensitivity testing by the tube dilution technique will be carried out in duplicate for each isolate.

Manpower: E-6 (6 months)
E-5 (6 months)

Funding: None.

PROGRESS

One-hundred-twenty strains of Candida and Torulopsis species isolated at Brooke Army Medical Center were tested against Nystatin, Amphotericin B and 5-fluorocytosine. Candicidin studies are

C-2-74 (Continued)

currently being conducted. This data is to be presented at the American Society for Microbiology meeting in 1975. Manuscript for publication of this data is in preparation.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Physiologic Evaluation of Pulmonary Status in Patients Undergoing Renal Dialysis.

WORK UNIT NO.: C-4-74

PRINCIPAL INVESTIGATOR: William W. Burgin, Jr., M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Robert B. Blumer, M.D., Lieutenant Colonel, MC
Richard H. Merrill, M.D., Major, MC

OBJECTIVES

To evaluate the pulmonary function in renal dialysis patients both pre- and post dialysis, to better ascertain the physiologic changes which take place in the lung.

TECHNICAL APPROACH

All patients in the dialysis program at Brooke Army Medical Center are being evaluated pre- and post dialysis as to the effect that dialysis has on pulmonary function capability and oxygen carrying capacity of the blood.

Manpower: None.

Funding: None.

PROGRESS

Equipment for the performance of this project is now on hand and the investigation will commence.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Study of Aminoglycoside Antibiotic BB-K8.

WORK UNIT NO.: C-8-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Leslie M. Burger, M.D., Major, MC

OBJECTIVES

(1) To evaluate therapeutic effectiveness of BB-K8 in the treatment of hospitalized adult patients with infections caused by susceptible pathogens.
(2) To establish an optimal therapeutic dosage schedule for BB-K8 which is safe and effective.
(3) To establish a side effect profile for the drug.
(4) To obtain information on the clinical pharmacology of the drug in diseased patients.

TECHNICAL APPROACH

BB-K8 will be given by deep intramuscular injection at an appropriate site at a dose not to exceed 7.5 mg/kg body weight every 12 hours. Each patient and his clinical record will be evaluated twice each day throughout the course of drug therapy. Patients with urinary infections will have repeat urine culture and colony count at 48 to 72 hours after initiation of BB-K8. Each patient will have daily urinalysis with microscopic examination; BUN and creatinine determinations will be performed every 48 hours throughout the period of drug administration. Audiograms will be performed on the 3rd, 6th and 10th days of therapy. Appropriate specimens will be forwarded to Bristol Laboratories for determination of BB-K8 concentrations. Appropriate post-treatment cultures will be obtained at the conclusion of BB-K8 treatment; repeat chest x-rays will be obtained and patients with septicemia will have post-treatment blood cultures obtained.

Manpower: None.

Funding: $71.30 Consumable Supplies FY 1974

C-8-74 (Continued)

PROGRESS

To date, no patients have been started on this antibiotic. However, important preliminary laboratory information has been obtained. In testing by tube dilution technique organisms resistant to stnadard aminoglycoside therapy, approximately 75% of these organisms are sensitive to BB-K8 by tube dilution sensitivities. Furthermore, the preliminary evaluation demonstrates that the Kirby-Bauer zone diameter size does not closely correlate with tube dilution sensitivity technique in determining susceptible or resistant organisms. It is planned to continue the work with this antibiotic with a projected population of 10 patients being treated. The patient selection has been recently liberalized by the Food and Drug Administration and should make completion of this project easier.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Clinical Study of Intravenous Veracillin (Sodium Dicloxacillin).

WORK UNIT NO.: C-9-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Preston B. Cannady, M.D., Major, MC
Barry E. Sieger, M.D., Major, MC

OBJECTIVES

To determine efficacy and safety of intravenous veracillin when used in the treatment of infections due to susceptible organisms.

TECHNICAL APPROACH

Every patient will be subject to the following laboratory evaluations: CBC to include WBC, differential, platelet estimation and hematocrit; liver function studies to include SGOT, alkaline phosphatase; renal function tests to include urinalysis, serum creatinine and BUN. All examinations must be performed at least with the 24 hours prior to starting, every fifth day of therapy, and within 24 hours after cessation of intravenous veracillin therapy. Cultures from the appropriate site will be repeated during and after cessation of therapy.

A standard dose of 1000 mg q6H IV is to be used in severe infections such as septicemia or pneumonia with doses of 250 or 500 mg q6H for urinary tract and severe wound or soft tissue infections. Serum killing levels will be determined using the patient's serum and measuring the killing effect after any given dose of veracillin against the bacteria responsible for that infection.

Manpower: None.

Funding: None.

C-9-74 (Continued)

PROGRESS

Since the institution of this protocol, three patients have been treated with intravenous veracillin. Indications for therapy have been extensive cellulitis in two and abscess in one. Clinical response occurred in all of the three patients treated; no allergic manifestations or drug toxicity has been noted.

While the initial information suggested that prolonged high blood levels might be present following the intravenous use of this drug, that has not been confirmed in the three patients studied with peak serum levels of 7 to 10 mcg/ml occurring 1 hour after infusion; levels obtained 5 hours postinfusion have fallen to levels of 2 mcg/ml or less. It is therefore felt that the antibiotic should be administered more frequently, probably every 4 hours and future patients to be treated with this drug will receive medication on 4 hourly intervals. We intend to continue this study until a total of 20 patients have been treated.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Clinical Study of Ticarcillin (BRL 228).

WORK UNIT NO.: C-10-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Barry E. Sieger, M.D., Major, MC
Preston B. Cannady, M.D., Major, MC

OBJECTIVES

To evaluate the effectiveness and safety of various dosages of ticarcillin in the treatment of infections in hospitalized patients where those infections are the result of susceptible organisms: E. coli, Proteus mirabilis, Proteus morgani, Proteus rettgeri, Proteus vulgaris, Providencia stuartii, Pseudomonas aeruginosa, Mima, Herellea, Enterobacter aerogenes, Enterobacter cloacae, Citrobacter freundii, and Serratia marcescens.

TECHNICAL APPROACH

Every patient will be subject to the following laboratory evaluations: CBC, platelet count and bleeding time; SMA-18 and creatinine phosphokinase; urinalysis; urine culture and susceptibility testing to be done when indicated. All examinations must be performed at least within 24 hours prior to starting, every 5th day of therapy and within 24 hours after cessation of therapy. Dosage: (a) Urinary tract infections (uncomplicated), 0.5 to 2.0 gm IM or IV q6-8hrs; (b) Urinary tract infections (serious/complicated), septicemia, soft tissue infections or respiratory infections, 200 to 300 mg/kg/day (12 to 20 gm) by intermittent 2 hour infusion q4-6hrs. Appropriate cultures will be obtained during therapy, and evaluation of treatment will be based on post-therapy cultures.

Manpower: None.

Funding: None.

C-10-74 (Continued)

PROGRESS

Since initiation of this protocol, three patients have been treated with intravenous ticarcillin. The indications for treatment in all patients were infections with Pseudomonas aeruginosa which was sensitive to ticarcillin using the 50 mcg sensitivity disc and Kirby-Bauer sensitivity testing technique. In all three cases, the infection was urinary tract in origin. All three patients responded well to the drug. There were no adverse reactions. Using a dose of 300 mg/kg/24 hrs, total dose divided into infusions given every 4 hours, produced blood levels of between 40 and 80 mcg/ml--a level well within the sensitivity of the organism. Concomitant urinary levels ranged between 2000 and 4000 mcg/ml. All these levels are within the anticipated levels for the dose of this antibiotic. Further evaluation of this antibiotic is to be done with a total treatment group of 30 patients.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Transfusion - Efficiency and Methods to Improve Current Results in Thrombocytopenia Patients.

WORK UNIT NO.: C-16-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To improve the quality of platelet transfusions in thrombocytopenic patients and platelet transfusion complications.

TECHNICAL APPROACH

Techniques for identifying platelet antibodies are used to select donor platelets which would have an anticipated normal survival in a recipient who had received multiple units of platelets prior to transfusion and had been shown to have platelet antibodies. The techniques of serotonin release assay, lymphocyte toxicity with HL-A typing serum and complement fixation are proposed to identify the platelet antibodies. The technique of chromium 51 labeled platelets to monitor platelet survival of the transfused platelets is to be used. The purpose is to identify a means of rapidly finding a compatible donor for a transfusion of platelets into a thrombocytopenic patient who may have previously shown the presence of platelet antibodies to random donor platelets.

Manpower: None.

Funding: None.

C-16-74 (Continued)

PROGRESS

Progress to date has been limited due to the lack of technical support and to the failure of Brooke Army Medical Center to obtain a Broad Spectrum License authorizing use of chromium 51 survivals of platelets. To date approximately 75 serum samples have been obtained for identification of platelet antibody. Serotonin release has recently been set up after approval of tritiated serotonin by the Radiation Control Committee and after modifications of the procedure are made to comply with the equipment available at Brooke Army Medical Center.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of Specific and Total IgE Globulin Levels in the Serum to Specific Skin Tests.

WORK UNIT NO.: C-18-74

PRINCIPAL INVESTIGATOR: Bryan R. Updegraff, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Robert Greely, M.D., Lieutenant Colonel, MC
Robert Lull, M.D., Lieutenant Colonel, MC
Charles Lewis, M.D., Lieutenant Colonel, MC

OBJECTIVES

To correlate the levels of specific circulating antibodies in the serum with intracutaneous skin tests in mountain cedar sensitive patients.

TECHNICAL APPROACH

A total of 50 patients will be selected from the Allergy Clinic. Ten patients will be placed in each of five groups based on reactivity of skin tests to mountain cedar antigen as graded from 0-4+. These patient's serum will be evaluated for levels of total and specific IgE and the results correlated.

Manpower: None.

Funding: $999.00 Consumable Supplies FY 1974

PROGRESS

Technique and materials for IgE determination have been established, and the patients are in the process of selection.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy of Minocycline in Patients with Staphylococcal Skin Infections.

WORK UNIT NO.: C-19-74

PRINCIPAL INVESTIGATOR: Stephen E. Rostan, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Stuart Salasche, M.D., Major, MC
Frank Rabey, M.S., Major, MSC

OBJECTIVES

To demonstrate the clinical and laboratory efficacy of minocycline in patients with staphylococcal skin infections compared to phenoxymethyl penicillin.

TECHNICAL APPROACH

Double-blind study comparing penicillin V and minocycline in the treatment of staphylococcus aureus in outpatients, 12 years of age or older.

Manpower: None.

Funding: $256.00 Consumable Supplies FY 1974

PROGRESS

Several patients have been studied but additional ones are needed to determine the efficacy of minocycline.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hypertension with Polycystic Kidney Disease.

WORK UNIT NO.: C-20-74

PRINCIPAL INVESTIGATOR: Daniel A. Nash, Jr., M.D., Major, MC

ASSOCIATE INVESTIGATORS: Andrew Nowakowski, M.D., Major, MC
Philip W. Rogers, M.D., Major, MC

OBJECTIVES

To study the volume status and the renin-angiotensin system in patients with polycystic kidneys and unexplained hypertension and to clarify the mechanism(s) of the hypertension frequently present in patients with polycystic kidneys.

TECHNICAL APPROACH

Patients with hypertension and adult polycystic kidney disease are evaluated to exclude extra-renal causes of the hypertension. Off all medications, renin activity and aldosterone levels are measured. This is done after a balanced state is reached on an intake of 60 to 100 mEq of sodium per 24 hours, and subsequently on a low sodium intake of 10 mEq/24 hours. The degree of hypertension is correlated with these alterations of the renin angiotensin aldosterone system and the sodium balance. Only patients with preservation of at least 75% of their normal renal function are studied. Selective renal vein renin assays are obtained if possible.

Manpower: None.

Funding: None.

PROGRESS

Six patients have qualified for this study and completed the hypertension evaluation. Three of the six had selective renal vein renin assays. Five of the six had normal peripheral renin activity and aldosterone responses when studied on the ideal (60-100 mEq) sodium

C-20-74 (Continued)

diet. All remained moderately hypertensive, without measurable evidence of blood volume expansion. Blood pressures normalized during the low sodium period in all but one patient. Four appeared to have blunted renin responsiveness. Most interestingly, two of three patients had significantly asymmetrical renal renin production. Although the data is not statistically significant, a multifactorial etiology for hypertension with polycystic kidney disease, involving relatively increased renin activity and an unmeasurable degree of volume expansion, is strongly suggested.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Radioactive Serotonin Release Assay and Lymphocyte Thymidine Uptake as a Means of Platelet Antibody Identification.

WORK UNIT NO.: C-22-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the relative specificities of these assays and to evaluate their clinical usefulness.

TECHNICAL APPROACH

Handlin and others have shown that platelet antibodies are capable of stimulating lymphocytes. The purpose of this protocol is to use a radioactive serotonin release assay method and lymphocytes stimulation method with thymidine uptake to identify platelet antibodies and to compare their selectivity as a method of identifying potential donors for thrombocytopenic patients.

Lymphocytes will be stimulated by serum from selected patients. Sera is incubated at 56° for 30 minutes and stored at -20°C; 0.1 ml of the platelet concentrate with approximately 10^8 platelet is incubated with 0.2 ml of the test serum at room temperature for 15 min.; 2 ml of freshly prepared platelet-poor plasma at pH of 6.5 are added and the mixture is centrifuged at 10,000 Xg for 10 minutes. The platelet button is resuspended in 0.3 ml of TC-199 and is used in this manner to stimulate lymphocytes.

Approximately 10-20 patients of each antibody type would be examined with the exception of drug induced antibody situations. Sera will be stored at -20°C. Samples will be studied at various dilutions to obtain the titer of the antibody. Sensitivity of both tests may thus be evaluated, as well as the specificity. Each serum should be tested against a battery of at least ten different platelet samples.

C-22-74 Continued)

Manpower: None.

Funding: $192.00 Consumable Supplies FY 1974

PROGRESS

Serum samples have been obtained. Two patients have been examined by the lymphocyte stimulation uptake method, and platelet antibodies have not been identified.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in the Presence of Varied Platelet Antibodies.

WORK UNIT NO.: C-23-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the capability of platelet function when stressed by a variety of platelet antibodies.

TECHNICAL APPROACH

Several authors have suggested that platelets function abnormally in patients who have an antibody directed against them. Platelet function studies, i.e. bleeding time, platelet aggregation, platelet Factor III release, are to be performed on patients who have been identified as having antibody in their serum. Purpose of this is to identify a patient who not only is thrombocytopenic from a platelet immune disease, but who has a bleeding diathesis due to poor function of the platelets which are present.

Platelet function will be examined, both from random donors and from the patients themselves who had evidence of on-going platelet antibody situation. Platelets of patients with the antibody will be examined when the platelet count is sufficient to warrant doing so. Serum from these patients will also be obtained. This serum will be incubated with normal platelets and the platelet function, after this incubation, will be examined. This platelet function will be examined in both the platelets of patients having the antibody, i.e., and in vitro incubation, and by examining platelets from a donor with serum taken from patients with platelet antibodies. Platelet function studies to be done include platelet factor three release after the method of Hardisty, platelet adhesion after the method of Bowie, platelet aggregation,

C-23-74 (Continued)

including ADP, epinephrine and collagen stimulation. Platelet antibodies will be identified by 1) the clinical situation, 2) failure to respond to platelet transfusion, 3) modification of serotonin release assay, 4) thymidine uptake. Approximately 10-20 patients of each antibody type will be studied.

Manpower: None.

Funding:			
	$196.00	Consumable Supplies	FY 1974
	$420.00	Capital Equipment	FY 1974

PROGRESS

Project has started.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Platelet Factor IV to Evaluate Hypercoagulable States.

WORK UNIT NO.: C-24-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To look at the plasma of patients who have a possible setting of hypercoagulability and to evaluate their plasma for platelet factor IV activity.

TECHNICAL APPROACH

Platelet Factor IV, which is an anti-heparin, has been shown to be released by platelet destruction in vivo. A method of assaying this factor using heparin titration has been reported by several authors. The purpose of this project is to evaluate the patients who have the potential of developing thrombophlebitis and pulmonary embolus by using the platelet factor IV assay.

The plan of this study is to evaluate the measure of platelet factor IV assay according to that outlined by Fuster, et al., in the General Mayo Clinic, February 1973, and to apply this procedure to the plasma of patients who have recent myocardial infarctions, who have pulmonary emboli, who have crush injuries or who have shown instance of increasing headaches or vascular disease associated with the birth control pill. This is a pilot study and is designed only to show that there is clinical applicability of the procedure. It should be noted that more definitive studies, such as fibrinogen turnover rates and platelet survival and turnover rates, are not to be done in this study. Fifty patients will be studied. Controls will be normal patients of various age ranges. Controls from various clinical conditions will be examined.

C-24-74 (Continued)

Manpower: None.

Funding: None.

PROGRESS

Progress to date reveals that the assay has been established with appropriate normals and abnormals obtained. Patients with marrow suppression have been studied to show that no platelet factor IV is available. Material for assay is being collected on patients presented to the hospital with pulmonary emboli and with thrombophlebitis. Inadequate number of patients studied for complete evaluation at this time.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ophthalmologic Manifestation of Candida Infection and Hypersensitivity to Candida in Rabbits.

WORK UNIT NO.: C-26-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To study the natural history of candida infection in the eye.

TECHNICAL APPROACH

Initially, 20 New Zealand white rabbits will be utilized for the study; the grouping of the rabbits and experimental procedures are outlined in the original protocol. At the time all animals are sacrificed, the eyes will be submitted for quantitative cultures which will be determined on the basis of number of organisms per gram of tissue obtained from one of the two eyes, and the second eye then will be submitted for histologic examination with specific biopsies of the retina and uvea. It will be necessary to process these tissues using hematoxylin and eosin as well as methenamine silver stains to define the nature and extent of the Candida infections produced in the rabbits.

Manpower: E-5 (3 months)

Funding: $106.25

PROGRESS

Initially 20 rabbits were divided into 4 groups, each group containing 5 rabbits. The first group of rabbits were previously

C-26-74 (Continued)

vaccinated using a strain specific Candida antigen injected with Freund adjuvant and booster vaccinations given weekly until specific 'b' bands were present by immunodiffusion and latex agglutination titers 1:16 had been achieved. On day #1, all 20 rabbits received $2x10^6$ live Candida organisms. Then 10 days after the inoculation of organisms, the second group of 5 rabbits received 200 mg% of antigen prepared in a similar manner to the antigen used to vaccinate the original group. This was administered intravenously. Five days after the initial inoculation of organisms, the third group received an additional $5x10^5$ Candida organisms intravenously. The remaining 5 rabbits were used as controls. One rabbit died five days after the original inoculation probably as a result of laceration to the liver during pericardial aspiration of blood and at time of autopsy no evidence of candidiasis was present. At the end of the experimental time frame, all rabbits were sacrificed. Prior to sacrificing, funduscopic examination had demonstrated eye lesions in 3 rabbits. At time of autopsy, aspiration of eyes in all rabbits was done for culture for Candida. All of these cultures were negative. Examination of the tissues showed small scars in the kidneys of half of the rabbits, but it was obvious at autopsy that significant Candida infection had not occurred, even though the previous studies using the identical organism had demonstrated that the number of organisms injected in this study was only one log less than the LD-50 in a comparable group of animals. It was impossible at that point to determine whether the low degree of pathogenicity was due to a change in the virulence of the organism or if handling of the inoculum prior to injection had decreased the viable cell count.

From this first group of rabbits, the following information was obtained. First, vaccination could be easily accomplished with specific bands and high titers of latex agglutination reactions occurring. Second, inoculation of antigen separated by at least 10 days of time did not result in anaphylaxis. Third, technically blood sampling could be done on a weekly basis without any detrimental effects to the animals. Fourth, that with organisms of low invasivity, eye lesions did occur. Fifth, that the eye lesions when present were negative for culture for Candida albicans. Sixth, the photographic technique employed produced acceptable permanent records of these eye lesions.

With these factors in mind, the same strain of Candida was passed into an animal in massive concentrations producing lethal systemic candidiasis. After animal passage, the organism was recovered from kidney tissue and serologically documented to be the same serotype

C-26-74 (Continued)

as the initial organism injected. This organism was then grown in broth culture and injected into 20 virgin rabbits in a dose of $1x10^6$ viable organisms where viability was determined at the time of inoculation by dilution plate technique. The result of increasing the inoculum by one-half log following the transmission of this organism through an animal was devastating. All 20 rabbits died within six days of inoculation. Autopsy of these animals demonstrated widely disseminated systemic candidiasis. Although eye lesions did not develop, this probably reflects early death. Over 90% of the rabbits had massive myocardial Candida abscess formation. Current histologic studies are underway to define the myocardial lesions in these animals as well as the ophthalmic lesions produced in the original group. Complete histologic evaluation including electron microscopy is planned but is not available for this report. We plan to continue this study using the same model but adjusting the dose of inoculum of the organism which is now proven to be extremely virulent by dropping the size of inoculum two logs.

It is apparent that in these animals, disseminated candidiasis may take an acute form characterized by widely disseminated lesions, particularly cardiac lesions; a subacute form characterized by predominately renal lesions and renal failure, and, perhaps, a more chronic form of disease characterized by small abscesses and scars in the kidney and liver and associated with funduscopic abnormalities in the involved rabbits.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparative Study of Tobramycin and Gentamicin in Acute Urinary Tract Infections.

WORK UNIT NO.: C-27-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Layne O. Gentry, M.D.
Preston B. Cannady, M.D., Major, MC

OBJECTIVES

To evaluate and compare the effectiveness of these two aminoglycoside antibiotics in the treatment of acute urinary tract infections in hospitalized patients where those infections are the result of susceptible organisms.

TECHNICAL APPROACH

Every patient will be subjected to the following laboratory evaluations: Complete blood count and platelet estimate; SMA-12 plus 6; urinalysis and urine culture and when indicated susceptibility testing will be done. All examinations will be performed at least within 24 hours prior to starting antibiotic therapy, every 5th day of antibiotic therapy, and within 24 hrs after stopping antibiotic therapy. A follow-up specimen of urine will be obtained and cultured between 5 and 10 days following the course of antibiotic therapy.

A dose of 3 mg/kg/24 hrs will be given provided that creatinine clearance is in excess of 50 ml/min as estimated utilizing the serum creatinine. Adjustments of the dosage will be performed on the basis of the serum creainine and antibiotic levels as determined in the laboratory. All patients will receive a minimum of 5 days of antibiotic therapy of either tobramycin or gentamicin unless there are contraindications to complete this course.

Manpower: None.

Funding: None.

C-27-74 (Continued)

PROGRESS

Since initiation of this study, 22 patients have been treated on a randomized basis for urinary tract infection as the result of susceptible gram-negative organism where susceptibility was determined by Kirby-Bauer disc plate technique. Using a standard dose of 3 mg/kg/24 hrs divided into 3 doses given every 8 hours, the following results have been obtained. Serum levels of approximately 3-6 mcg/ml have been obtained. Urinary levels done simultaneously have ranged between 15 and 100 mcg/ml. All these levels have been adequate for the organisms tested. There has been no evidence of toxicity and no episodes of allergy have occurred to date. All 22 patients have had clinical and bacteriological cure although recurrence developed in 3 patients. This recurrence was related to repeated Foley catheterization and not to relapse with the original organism. The plan is to continue this protocol for a total of 40 patients.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Factor VIII Activity/Antigen Ratio in von Willebrand's Disease. I. Epinephrine Effect. (Collaborative study with WRAIR)

WORK UNIT NO.: C-30-74

PRINCIPAL INVESTIGATOR: Frederick R. Rickles, M.D., Major, MC (WRAIR)

ASSOCIATE INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

OBJECTIVES

To study the effect of stress on Factor VIII production and reactivity.

TECHNICAL APPROACH

To stimulate patients with epinephrine and measure Factor VIII antigen and coagulant activity as well as platelet factor activity by several methods. Plasma is to be collected over a two day period.

This study is being done in conjunction with Walter Reed Army Institute of Research.

Manpower: None.

Funding: None.

PROGRESS

Two patients have had initial plasma screens including antigen levels and Factor VIII activity. Factor VIII procedures have been standardized. Platelet function has not yet been attempted due to the lack of Ristocetin and gloss bead retention tubes commercially.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Antacid Therapy on Recurrence of Duodenal Ulcer.

WORK UNIT NO.: C-32-74

PRINCIPAL INVESTIGATOR: Richard W. Welch, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Armand Littman, M.D.

OBJECTIVES

To determine whether antacid treament in duodenal ulcer patients during asymptomatic periods prevents recurrences of complications.

TECHNICAL APPROACH

Males with typical history of ulcer distress and x-ray evidence of niche or duodenal bulb deformity will be selected. 40-50 or more patients will be studied. Treatment will consist of 4 tablets (0.5 gm each) 2 hours after each meal and at bedtime. One-half of the patients will receive DAA and the other half will receive a cellulose (Avicel). Each patient will be seen at 4 week intervals with routine inquiry concerning general health and ulcer symptoms. The frequency of hemorrhage, perforation, obstruction and recourse to surgical treatment will be assessed.

Manpower: None.

Funding: None.

PROGRESS

To date, there are 14 patients entered in the study, and no technical problems have been encountered. Because this is a prospective, randomized, double blind clinical trial, no advance inspection of the data is possible nor are any results known.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phytohemagglutinin Stimulation of Sarcoid Lymphocytes.

WORK UNIT NO.: C-36-74

PRINCIPAL INVESTIGATOR: Robert L. Pence, M.D., Major, MC

ASSOCIATE INVESTIGATORS: William W. Burgin, M.D., Lieutenant Colonel, MC
Robert L. Greely, M.D., Lieutenant Colonel, MC

OBJECTIVES

To study phytohemagglutinin (PHA) stimulation of lymphocytes from patients with sarcoid and to investigate possible suppression of lymphocyte response by plasma from sarcoid patients.

TECHNICAL APPROACH

20-30 patients with sarcoid admitted to the Pulmonary Disease Service or seen in the Pulmonary Clinic will be evaluated and treated in the usual manner. During the course of evaluation, 25-50 cc of heparinized blood will be taken to study their lymphocytes. The lymphocytes will be separated from whole blood by standard techniques and will be stimulated with PHA as well as SKSD and Monilia antigens, in the presence of homologous and autologous plasma. Lymphocyte response will be measured in terms of blastogenesis using thymidine incorporation with C^{14} or H^3 labeled thymidine. The degree of stimulation will be correlated with the extent of disease and the possible suppression of lymphocytes by sarcoid plasma can be verified. The sarcoid plasma will be saved and used in a similar way to study stimulation of lymphocytes from normals with the same antigen.

Manpower: E-5 (4 months)

Funding: $2,068.50 Consumable Supplies FY 1974
$ 475.00 Capital Equipment FY 1974

C-36-74 (Continued)

PROGRESS

The laboratory technique of lymphocyte stimulation has been set up and is functioning well.

Two patients have been studied to date, and both showed good lymphocyte stimulation with PHA. The lymphocyte response of both individuals was better with homologous plasma than with autologous plasma indicating possible suppression by autologous plasma.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Evaluation and Treatment of Male Infertility.

WORK UNIT NO.: C-39-74

PRINCIPAL INVESTIGATOR: Carlos E. Menendez, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Lieutenant Colonel, MC
Mauro P. Gengai, M.D., Colonel, MC

OBJECTIVES

To rule out any surgically or medically correctible causes of male infertility and to treat the idiopathic oligospermic or asthenospermic infertile patient with human chorionic gonadotropin.

TECHNICAL APPROACH

The patient will be subjected to an extensive medical work-up to rule out urological and endocrinological conditions as well as general medical conditions that can interfere with normal fertility, and if these are ruled out, the patients will be treated with human gonadotropin injections, 2500 units IM every week for 6-12 months with periodic repeat semen analyses.

Patients with idiopathic oligospermia will enter a prospective study designed to evaluate the effects of this agent on gonadotropin and testosterone levels in plasma, semen and fertility. An attempt will be made to relate semen changes and fertility with changes in the plasma levels of those hormones.

The female member of the couple will be evaluated to make sure she is potentially fertile.

Manpower: None.

Funding: None.

C-39-74 (Continued)

PROGRESS

Since the protocol has been approved, only one new patient has been investigated and therapy has not been started.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effectiveness of Immunotherapy in Mountain Cedar Pollinosis.

WORK UNIT NO.: C-43-74

PRINCIPAL INVESTIGATOR: Hobert L. Pence, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Robert L. Greely, M.D., Lieutenant Colonel, MC
Donald Mitchells, M.D., Major, USAF MC
Max I. Michaels, M.D., Colonel, USAF MC

OBJECTIVES

To evaluate the role and effectiveness of allergy injection therapy with Mountain Cedar pollen extract in the treatment of hay fever and asthma caused by the pollen of this plant.

TECHNICAL APPROACH

Approximately 40 patients with allergic rhinitis or asthma are to be studied to evaluate the effectiveness of specific allergy injection therapy in the treatment of these problems. In a double blind, controlled manner, these patients will be divided into two groups. One group will receive injection therapy with Mountain Cedar extract, and the other group will receive placebo, both in a manner routinely used for allergy injections. During the Mountain Cedar pollinating season (Dec., Jan., Feb.) the patients will send daily symptom scores to us. At the end of the season, the code will be broken, and the symptoms of the two groups will be compared and effectiveness of specific therapy determined.

Manpower: E-6 (3 months)

Funding: None.

PROGRESS

Forty patients have been selected and randomized and the extract and placebo is in the process of being mailed out to prepare the

C-43-74 (Continued)

patients for the coming season. Symptom index sheets have been put togethcr and are ready to use in the coming season.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Early Diagnosis of Urinary Tract Infections.

WORK UNIT NO.: C-44-74

PRINCIPAL INVESTIGATOR: Leslie M. Burger, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., Major, MC
Barry E. Sieger, M.D., Major, MC
Preston B. Cannady, M.D., Major, MC

OBJECTIVES

To evaluate several methods of rapidly establishing the presence of significant bacteriuria.

TECHNICAL APPROACH

One hundred unselected consecutive adult patients seen in the emergency room and walk-in clinic of Brooke Army Medical Center with urinary tract symptoms will be entered into the study. A questionnaire will be completed and clean catch, midstream urine sample obtained. The patient will be instructed to return to see one of the investigators the following morning when a first morning voided clean catch urine sample will be obtained. Each urine sample will be subjected to urinalysis, Gram stain of unspun urine, urine culture, nitrite test (Microstix®, Ames Company) and the glucose test (Uriglox®, KABI Laboratories). Therapy will be initiated as indicated after obtaining the first morning voided sample. Patients with significant bacteriuria will be asked to return after two days of therapy and again two days after the completion of therapy at which time a first morning voided clean catch, midstream urine sample will again be collected for urine culture, nitrite test, and glucose test.

Manpower: None.

Funding: $332.00 Consumable Supplies FY 1974

C-44-74 (Continued)

PROGRESS

The supplies have been ordered and the study will begin upon receipt.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Sperm Antibodies in Vasectomized Men.

WORK UNIT NO.: C-3-72

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the onset of sperm antibody production postvasectomy with special attention to serum uric acid values prior to and after vasectomy.

TECHNICAL APPROACH

Blood was obtained prior to, 6 weeks, 6 months, 12 months, and 24 months following bilateral vasectomy. The serum was removed after centrifugation of the clotted blood, and complement was destroyed by applying heat at 50°C for 30 minutes.

The macroscopic gelatin sperm-agglutination test of Kibrick, Belding, and Merrill and the sperm-immobilization test of Isojima, Li, and Ashitaka were used to determine the presence of sperm antibody activity in the sera. Pooled untreated rabbit serum served as the complement source. Fresh semen was obtained from sperm donors whose counts were consistently above 60 million spermatozoa per ml. coupled with motility greater than 70%. Uric acids were determined on the pre- and postvasectomy sera by the manual method as adapted by Technicon.

Eleven men had sperm antibody activity pre-, 3-4, 7, 10-11, 14 days and 6 weeks postvasectomy.

Manpower: Chief, Clinical Investigation Service (15 days)

Funding: $352.00 TDY FY 1974

C-3-72 (Continued)

PROGRESS

Thirteen men have been followed through 24 months postvasectomy. None had sperm-agglutinating activity prevasectomy, 6 were positive at 6 weeks (46%), 5 were positive at 6 months (38%), 8 were positive at 12 months (62%), and 8 were positive at 24 months (62%) with titers from 1:2 to 1:64. None had sperm-immobilizing activity prior to vasectomy, 4 were positive at 6 weeks (31%), 2 were positive at 6 months (16%), and none were positive at 12 or 24 months postvasectomy with titers from 1:4 to 1:16.

Serum uric acid levels on these 13 men pre-, 6 weeks, 6 months, 12 months, and 24 months postvasectomy showed no statistical differences (t-tests).

Of the 11 men studied prevasectomy and immediately postvasectomy, two demonstrated circulating agglutinins at 3-4 days, four at 7 days, six at 10-11 days, seven at 14 days, and nine at 6 weeks after the procedure was performed. Titers ranged from 1:2 to 1:8 early, and 1:4 to 1:128 6 weeks after vasectomy.

One man had circulating sperm immobilizins which developed 3 days postvasectomy which persisted through the six-week examination, and another man had immobilizins at the six-week check with titers 1:4 to 1:16.

Presented as part of "Biologic and Immunologic Consequences of Vasectomy" at the 9th Harold C. Mack Symposium, Regulation of Human Fertility, 5 October 1973, Detroit, Michigan (Wayne State University).

Presented as part of "Bilateral Vas Ligation: Sperm Antibodies" at the 21st Annual Meeting of the Pacific Coast Fertility Society, 27 October 1973, Palm Springs, California.

Presented as part of "Immunology of Infertility and Postvasectomized Men" as Consultant to the Department of Obstetrics-Gynecology, Scott and White Clinic, 23 March 1974, Temple Texas.

Presented as part of "The Significance of Sperm Antibodies in Vasectomized Men" at the 30th Annual Meeting of the American Fertility Society, 4 April 1974, Hollywood, Florida, and Brooke Army Medical Center Research Club, 14 May 1974.

C-3-72 (Continued)

Ansbacher, R.: Biologic and immunologic consequences of vasectomy, in Regulation of Human Fertility. Edited by K. S. Moghissi and T. N. Evans. Charles C. Thomas, Springfield, Illinois, 1974.

Ansbacher, R.: Bilateral vas ligation: sperm antibodies. Contraception 9:227-237, 1974.

Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Heart Valve Prosthesis in Pregnancy - Review of the Literature and Report of a Case.

WORK UNIT NO.: C-36-72

PRINCIPAL INVESTIGATOR: Warren N. Otterson, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To analyze the effect of heart valve prostheses on maternal morbidity and mortality, perinatal mortality, and general reproductive performance. In addition, it is hoped that a sound program of management, especially regarding the use of anticoagulant drugs, will evolve as a result of an extensive review.

TECHNICAL APPROACH

(1) To review all Brooke Army Medical Center and the world literature case reports in detail.

(2) To analyze each case relative to maternal and fetal outcome, and to evaluate the role of anticoagulants in patient management.

In addition, thoracic and cardiology literature is reviewed.

Manpower: None.

Funding: None.

PROGRESS

Comprehensive review is in the final stages of preparation.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maternal-Fetal Digoxin Levels.

WORK UNIT NO.: C-152-72

PRINCIPAL INVESTIGATOR: Warren N. Otterson, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the rate and amount of digoxin transferred to the fetus.

TECHNICAL APPROACH

Thirty patients in the labor area of the Robert B. Green Hospital and 12 to 16 patients at Brooke Army Medical Center will be given 0.25 mg of intravenous digoxin after informed consent is obtained. Upon delivery, maternal and fetal cord blood samples will be collected and analyzed for digoxin level. Since variable time will lapse between injection of digoxin and collection of blood samples, data on not only the comparability of the maternal fetal digoxin levels will be obtained, but the speed of fetal accumulation of digoxin noted.

The dose of digoxin is such that maternal levels at 2 hours, the accepted time when serum and myocardial level are comparable, is 1/100th of the usual therapeutic level. All patients given digoxin will be monitored by heart rate monitoring equipment. All RIA studies will be done at the University of Texas Medical School, San Antonio.

Manpower: None.

Funding: None.

C-152-72 (Continued)

PROGRESS

This study is terminated due to failure to obtain study samples from patients and their newborns and due to lack of cooperation with the University of Texas Medical School.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Endometriosis with Danazol.

WORK UNIT NO.: C-14-73

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To study the effects of Danazol therapy in the suppression of the discomforts arising from endometriosis.

TECHNICAL APPROACH

Four patients, ages 23-31, with proven endometriosis, diagnosed by laparoscopy or exploratory celiotomy and with symptoms of infertility, dysmenorrhea, pelvic pain, and dyspareunia were used in this study. Danazol, 800 mg/day, was administered.

Baseline studies included complete history and physical examination, CBC, urinalysis, SMA-6 and 12, serum FSH and LH. These studies were monitored while the patient was taking the medication.

Manpower: Chief, Clinical Investigation Service (6 days)

Funding: None.

PROGRESS

Four patients were studied. All were to continue the medication for 6 months without interruption. Two completed the full course; one discontinued it after 4 weeks and one after 3 months due to side effects.

C-14-73 (Continued)

Resolution of symptomatology and pelvic findings were dramatic. The four women became amenorrheic while on the medication, dyspareunia and pelvic pain cleared, and the pelvic organs became free and mobile without tenderness on motion or palpation. After cessation of therapy, reversion to the pretreatment state occurred in all.

Three have subsequently undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy within 8 months after completion of the Danazol therapy due to recurrence of their symptoms.

Side effects of Danazol therapy included an average weight gain of 9 pounds; severe headaches, migraine type, usually unilateral, with changing intensity from day to day; occasional dizziness and lightheadedness; unilateral tremor of the upper extremity; personality changes which included irritability and lethargy; and mild androgenic changes which included deepening of the voice and acne. These cleared after discontinuation of the medication and regular cyclic menses resumed.

CONCLUSIONS: The symptomatic improvement in these patients while on Danazol and the objective changes in the pelvic findings imply the possible efficacy of this medication for the treatment of endometriosis. However, the side effects noted and the fact that three women have had subsequent removal of their reproductive organs due to recurrence of their symptomatology and pelvic endometriosis indicate some caution in regarding this medication as a panacea.

Presented at the 22nd Annual Armed Forces Ob-Gyn Seminar, Las Vegas, Nevada, 16-21 September 1973.

Submitted to American Journal of Obstetrics and Gynecology for publication in Communications in Brief.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prospective Bacteriologic Study of Women Undergoing Hysterectomy.

WORK UNIT NO.: C-24-73

PRINCIPAL INVESTIGATOR: John W. George, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Lieutenant Colonel, MC
Warren N. Otterson, M.D., Colonel, MC
Frank Rabey, M.S., Major, MSC

OBJECTIVES

To elucidate the bacterial causes of postoperative febrile morbidity and to determine the role of anaerobes in febrile morbidity in women undergoing hysterectomy.

TECHNICAL APPROACH

Preoperative and 24-hour postoperative urines were obtained by transvaginal bladder tap and the freshly cut edge of the vaginal cuff was routinely swabbed following removal of the uterus. The subcutaneous layer was cultured during closure of the abdominal wound. The bacteriologic study was done on women undergoing 44 vaginal hysterectomies and 23 abdominal hysterectomies.

Manpower: None.

Funding: $603.27 Consumable Supplies FY 1973
None. FY 1974

PROGRESS

Of our 67 patients, 44 had positive cultures of either the urine, vaginal cuff, or both. However, only 18 of the 44 women (41%) who had vaginal hysterectomy and 8 of the 23 women (35%) undergoing abdominal hysterectomy developed febrile morbidity.

Escherichia coli, Enterococcus, and alpha and beta Streptococcus were the predominant organisms found.

C-24-73 (Continued)

The vagina appears to be a major source of organisms causing post-operative febrile morbidity. Routine culturing of the vaginal cuff at the time of surgery is indicated, since it was beneficial clinically, when febrile morbidity occurred, to know what organisms were cultured at the time of surgery.

Nine anaerobes were cultured intraoperatively, all Proprionibacterium species, and in one case this was the only organism associated with postoperative morbidity. Our microbiological system may not be sensitive enough. Continued surveillance for such organisms is indicated.

Presented at the 22nd Annual Armed Forces Ob-Gyn Seminar, 16-21 September 1973, Las Vegas, Nevada.

Submitted to Obstetrics and Gynecology for publication.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Clinical Application of the Oxytocin Challenge Test.

WORK UNIT NO.: C-34-73

PRINCIPAL INVESTIGATOR: Douglas E. Ewing, M.D., Major, MC

ASSOCIATE INVESTIGATORS: James R. Farina, M.D., Major, MC
Warren N. Otterson, M.D., Colonel, MC

OBJECTIVES

To determine if the oxytocin challenge test (OCT) is of value in predicting fetal outcome antepartum in high risk obstetrical patients.

TECHNICAL APPROACH

Fifty-eight patients from the prenatal clinic of BAMC were chosen to undergo oxytocin challenge tests. The sample included 40 patients considered likely to have placental insufficiency ("abnormal" group), and 18 randomly selected pateints considered normal.

All patients had one or more OCT's. Criteria for positive test were: a) uniform deceleration of the fetal heart rate that reflected the shape of the uterine contraction, b) onset of deceleration at or beyond the peak of the contraction, and c) repetition of a similar pattern during subsequent contractions. Those patients who displayed none of the above were considered to have a negative OCT. A test that could not be defined readily as positive or negative was termed "suspicious".

Individuals with a negative test had an OCT weekly thereafter, while those with a positive test had labors induced with amniotomy and infusion of oxytocin. All suspicious or unsatisfactory tests were repeated the next day.

Manpower: None.

Funding: None.

C-34-73 (Continued)

PROGRESS

Eighty-eight OCT's were performed on 58 patients. All, except 18 "normal" controls, had pregnancies complicated by hypertension, diabetes mellitus, suspected postmaturity, or suspected intrauterine growth retardation. Tests satisfactory for interpretation were obtained from all but one patient. Eight patients displayed late deceleration fetal heart patterns during oxytocin induced contractions (positive OCT); all subsequently had labors characterized by similar fetal heart patterns. No patient with a negative OCT had a labor characterized by fetal distress, and no intrauterine deaths occurred within one week following a negative OCT. The OCT was useful in the clinical management of patients considered likely to have placental insufficiency.

CONCLUSIONS: The OCT can be performed in obstetrical units where other tests of placental function may not be available. It has proved helpful in the clinical management of patients with suspected placental insufficiency.

Presented at the San Antonio Obstetrical and Gynecological Society Meeting, 12 September 1973.

Presented at the 22nd Annual Armed Forces Ob-Gyn Seminar, Las Vegas, Nevada, 16-21 September 1973.

Ewing, D.E., Farina, J.E., and Otterson, W.N.: The application of the Oxytocin Challenge Test. Obstet. Gynec. 43:563-566, 1974.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Sperm Antibodies in Celibate Men.

WORK UNIT NO.: C-5-74

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the incidence of sperm-agglutinating and sperm-immobilizing antibodies in the serum of celibate men.

TECHNICAL APPROACH

Blood was collected from nine Catholic priests, age range 27 to 54 years. History of nocturnal emissions was recorded from onset of puberty to the present.

The macroscopic gelatin sperm-agglutination test of Kibrick, Belding, and Merrill and the sperm-immobilization test of Isojima, Li, and Ashitaka were used to determine the presence of sperm-agglutinating or sperm-immobilizing activity after the complement in the sera had been destroyed by heating at 56°C for 30 minutes. Pooled rabbit sera served as the complement source, and donor semen, containing at least 60 million spermatozoa per ml. coupled with motility above 70% served as the antigen.

Manpower: Chief, Clinical Investigation Service (3 days)

Funding: None.

PROGRESS

All nine men, who entered the seminary at an average age of 18 years, recalled the onset of nocturnal emissions in their early teens, on the average of 4-5 per month with decreasing frequency after age 35.

C-5-74 (Continued)

(This substantiates the work of Kinsey, et al., reported in 1948 - Sexual Behavior in the Human Male.) None had demonstrable circulating sperm-agglutinating or sperm-immobilizing antibodies.

Presented as part of "Biologic and Immunologic Consequences of Vasectomy" at the 9th Harold C. Mack Symposium, Regulation of Human Fertility, 5 October 1973, Detroit, Michigan (Wayne State University).

Presented as part of "Significance of Sperm Antibodies in Vasectomized Men" at the 30th Annual Meeting of the American Fertility Society, 4 April 1974, Hollywood, Florida.

Ansbacher, R.: Biologic and immunologic consequences of vasectomy, in Regulation of Human Fertility. Edited by K. S. Moghissi and T. N. Evans. Charles C. Thomas, Springfield, Illinois, 1974.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Proposed Research Standards for Auto-Immune Antibody to Human Sperm, Collaborative Study, Part II.

WORK UNIT NO.: C-6-74

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To quantitatively assay seven test sera against the four proposed standards as determined by Collaborative Study, Part I (C-148-72).

TECHNICAL APPROACH

The four proposed standards and the seven test sera were each reconstituted with 0.25 ml distilled water and the decomplementation performed by heating at 56°C for 30 minutes. Dilutions were made with Baker's solution.

The macroscopic gelatin sperm-agglutination test and the sperm-immobilization test were used to determine the titer of sperm antibody activity in each sample. Complement source was pooled rabbit serum. Each sera was tested on three separate occasions using different sperm donors whose semen contained at least 60 million spermatozoa per ml coupled with motility above 70%.

Manpower: Chief, Clinical Investigation Service (4 days)

Funding: None.

PROGRESS

The four proposed standards had similar sperm agglutinating and sperm immobilizing activities as was demonstrated under C-148-72.

C-6-74 (Continued)

The seven unknown sera showed the following:

Sample	Agglutination Test	Immobilization Test
73/530 - A	Positive 1:256	Positive 1:2
73/530 - B	Positive 1:32	Negative
73/530 - C	Positive 1:4	Negative
73/530 - D	Negative	Negative
73/530 - E	Negative	Negative
73/530 - F	Negative	Negative
73/530 - G	Positive 1:64	Negative

(Reported as final serum dilution which was positive.)

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Use of Oxytocin Challenge Test in Monitoring High Risk Pregnancies.

WORK UNIT NO.: C-31-74

PRINCIPAL INVESTIGATOR: Bernard L. Hayden, M.D., Captain, MC

ASSOCIATE INVESTIGATOR: Joe Leigh Simpson, M.D., Major, MC

OBJECTIVES

To determine (1) if the oxytocin challenge test (OCT) alone can successfully predict the outcome of high risk pregnancies and (2) if the presence of meconium *in utero* signifies fetal distress.

TECHNICAL APPROACH

Selected third trimester obstetric patients will be admitted to the labor suite where an OCT, as described by Ewing, et al. (Protocol C-34-73), will be performed. These pregnancies will have been deemed high risk by two or more independent observers. All patients in these categories will have had ultrasound determinations of the fetal biparietal diameter performed at 20 weeks, or the initial visit if thereafter, and repeated in 3 weeks. The results of certain other parameters utilized in monitoring high risk pregnancies will be correlated with the results of the OCT. The following will be evaluated: Patients with diabetes mellitus; post-date fetuses; chronic hypertension; pre-eclampsia; suspected IUGR; elderly primagravidas; and history of unexplained stillborn.

Manpower: None.

Funding: None.

PROGRESS

Eighty-eight patients have been followed to date with the following diagnoses: 44 had gestational age greater than 42 weeks (postmaturity);

C-31-74 (Continued)

15 had suspected intrauterine fetal growth retardation; 10 had diabetes mellitus (6 Class A, 2 Class B, and 2 Class C); 7 had mild pre-eclampsia and 6 severe pre-eclampsia; 4 had chronic hypertension; 1 had a poor obstetrical history which included two prior stillbirths; and 1 had meconium noted in amniotic fluid prior to elective repeat cesarean section.

One hundred eighty-five oxytocin challenge tests were performed: 164 were negative, 15 suspicious, and 6 positive. Those fetuses with positive OCT's were products of pregnancies complicated by postmaturity (2), intrauterine growth retardation (2) or diabetes mellitus (2). All were delivered by cesarean section.

Nine mothers are still undelivered.

All fetuses were monitored during labor and none showed a heart rate pattern indicative of hypoxia. Eighteen postmature fetuses had meconium present at the time of amniocentesis and/or delivery, only one of which had a positive OCT. Twenty-six postmature infants lacked meconium, and one had a positive OCT.

During investigation of this high-risk group, no mother experienced an intrauterine fetal demise.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cefazolin as a Prophylactic Antibiotic in Vaginal Hysterectomy.

WORK UNIT NO.: C-37-74

PRINCIPAL INVESTIGATOR: Willie J. Lett, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: B. L. Davidson, Captain, MSC
Rudi Ansbacher, M.D., Lieutenant Colonel, MC
Guy D. Plunkett, M.D., Colonel, MC

OBJECTIVES

To compare the effectiveness of one dose of cefazolin to three doses of cephaloridine as a prophylactic antibiotic in vaginal hysterectomy.

TECHNICAL APPROACH

Each patient undergoing vaginal hysterectomy from March 1974 to February 1975 will be placed in a group receiving cefazolin, cephaloridine, or no medication. Patients will receive IM cefazolin or cephaloridine 1 hr prior to operation. Those on cephaloridine will also receive 1 gm immediately and 12 hrs postoperatively. 1 gm of vaginal cuff will be taken intraoperatively for aerobic and anaerobic cultures. Four blood cultures for anaerobic and aerobic organisms will be drawn in equally spaced time periods for 24 hrs in patients with a febrile postoperative course. Febrile morbidity will be defined as temperature elevation greater than 100°F after the first 24 hrs post-op on two occasions, 6 hrs apart. All febrile patients will have vaginal cuff cultures done on the day of diagnosis for aerobic and anaerobic organisms. Statistical comparison will be made between the three groups as to (1) febrile morbidity; (2) infection; (3) hepato or nephrotoxicity; and (4) length of hospital stay. Organisms isolated from the intraoperatively collected tissue will be compared to those isolated from blood cultures and vaginal cuff cultures of patients with febrile postoperative courses.

Manpower: None.

Funding:

$2,412.73	PLMA	FY 1974
$1,064.99	Consumable Supplies	FY 1974

C-37-74 (Continued)

PROGRESS

To date, 34 patients have been included in the study, which began on 1 March 1974. The double blind code will not be broken until March 1975.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laminaria: Two Outpatient Uses.

WORK UNIT NO.: C-38-74

PRINCIPAL INVESTIGATOR: Jose R. Ossorio, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Lieutenant Colonel, MC
Warren N. Otterson, M.D., Colonel, MC

OBJECTIVES

To determine if by the use of laminaria tents, sufficient dilatation of the cervix can be obtained in patients with stenotic or tight cervical ossa, so as to enable easier endometrial sampling by endometrial biopsy or jet washing, and easier insertion of intrauterine device in nulliparous patients.

TECHNICAL APPROACH

One hundred patients seen in the outpatient Gyn Clinic who are found to have tight cervical ossa which do not permit sounding with a regular uterine sound but who tolerate the introduction of a wire sound will have a size thin or extra thin laminaria tent inserted. The removal of the laminaria tent and the subsequent intrauterine instrumentation either for endometrial sampling or intrauterine device insertion will be accomplished 3 to 4 hours later as an outpatient procedure. The technique of insertion to be used will be similar to the one recommended by Hale and Pion.

Manpower: None.

Funding: $330.00 Consumable Supplies FY 1974

PROGRESS

Eighteen patients with stenotic cervical ossa have had laminaria insertion. None noted more than minimal discomfort. Endometrial biopsies were successful in all.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Incidence of Trichomonas Vaginalis in Women with Dysplasia of the Uterine Cervix.

WORK UNIT NO.: C-3-74

PRINCIPAL INVESTIGATOR: Douglas E. King, SP4

ASSOCIATE INVESTIGATOR: Richard C. Nau, M.D., Major, MC

OBJECTIVES

1. To investigate the incidence of Trichomonas vaginalis in cervical dysplasias of different severities.

2. To analyze non-random distributions of T. vaginalis incidence for:

   a. Cause-effect relationship between T. vaginalis and dysplasia.

   b. Cytologic confusion between changes caused by T. vaginalis and those of dysplasia.

TECHNICAL APPROACH

Cases used in the study were picked randomly using the following criteria: (a) Smear taken between 1967 and 1972; (b) Patient's age greater than 20 and less than 50. Those with abnormal cytology were broken down into two groups: atypical and dysplasias. The cases were evaluated to see if trichomonads had been identified and 50% of those with trichomonads were screened. 10% of the remaining slides with abnormal or negative cytology were screened at random to see if the diagnoses were correct. Chi squared tests of association were used to check the validity of the data. The distribution of negative and abnormal cytologies were graphed according to age groups and the difference analyzed. The same analysis on the incidence of Trichomonas vaginalis in women with minimal dysplasia compared with "slight, moderate and marked" dysplasia was done.

Manpower: None.

Funding: None.

C-3-74 (Continued)

PROGRESS

Patients with dysplasia have higher than expected incidence of Trichomonas vaginalis. However, the incidence is not significantly different when dysplasias of varying severity are compared.

CONCLUSIONS: a. The higher incidence of Trichomonas vaginalis in patients with dysplasia is probably explained by both being related to other population factors such as hygiene or sex habits.

b. Trichomonas vaginalis does not produce changes that should be confused with dysplasia.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Digoxin-Induced Changes in Urinary Sediment: Cytologic Evaluation for Adequacy of Digitalization.

WORK UNIT NO.: C-11-74

PRINCIPAL INVESTIGATOR: Keith Hallman, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Richard C. Nau, M.D., Major, MC
George M. McGranahan, M.D., Colonel, MC

OBJECTIVES

To correlate the digoxin levels in serum, epithelial maturation (estrogen-like effect) in urinary sediment, and the clinical status of the cardiac patient.

TECHNICAL APPROACH

Two hundred male patients will be divided into age-matched and investigational groups. Patients in the investigational group will be divided into five subgroups on the basis of standard digoxin therapy.

Specimens from members of the control and investigational groups will be submitted for routine urinalysis, urinary cytology, and SMA-12. Blood also will be drawn from members of the investigational group for levels of digoxin by radioimmune assay.

Manpower: None.

Funding: None.

PROGRESS

Fifty cytologic urinary tract preparations were examined and none showed any "estrogen-like" effects. Therefore, no further analyses were performed.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laboratory Parameters: Bacterial Meningitis.

WORK UNIT NO.: C-72-72

PRINCIPAL INVESTIGATOR: Ronald E. Keeney, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate our experience with consistency of laboratory data in diagnosing bacterial meningitis.

TECHNICAL APPROACH

Twenty bacteriologically proven cases of bacterial meningitis treated at Brooke Army Medical Center were reviewed retrospectively. The review was limited to patients between two months and forty-two months of age with meningitis caused by Neisseria meningitidis, Hemophilus influenzae, and Diplococcus pneumoniae.

Manpower: None.

Funding: None.

PROGRESS

There were nine patients with meningococcal meningitis, two with pneumococcal meningitis, and nine with Hemophilus influenza meningitis.

The elusiveness of Neisseria meningitidis in its etiology of bacterial meningitis was reaffirmed. Only one of eight patients with meningococcal meningitis had depressed CSF glucose, 3 of 8

C-72-72 (Continued)

had virtually no white blood cells in the CSF, 4 of 7 had elevated CSF protein, and 1 of 5 had negative CSF gram stain.

This elusiveness of diagnosis of bacterial meningitis is not limited to those cases caused by Neisseria meningitidis. Only 50% of all the cases in this series had markedly elevated peripheral white blood counts (>15,000 WBC/mm^3). Of the 17 patients in whom CSF glucose was measured on admission, nine had values >40 mg%.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chronic Mucocutaneous Candidiasis, Immunologic Observations A Role of Transfer Factor.

WORK UNIT NO.: C-73-72

PRINCIPAL INVESTIGATOR: Luis Canales, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate parameters of delayed hypersensitivity in patients with chronic mucocutaneous candidiasis. Previous work has shown that some of these patients have a factor(s) in their serum which inhibits the function of normal lymphocytes in vitro.

TECHNICAL APPROACH

Standard in vitro lymphocyte transformation to various specific and nonspecific antigens as developed in this laboratory are being utilized.

The response of normal cells to the addition of various dilutions of patient's sera is used to determine the presence or absence of severe inhibitory factors.

Manpower: None.

Funding: See C-4-70.

PROGRESS

Based on previous observations from this laboratory (Lancet, Sep 13, 1969), we have made some clinical trials of transfer factor in the therapy of chronic mucocutaneous candidiasis (CMC).

Complete immunological evaluation of this patient prior to this clinical trial revealed no delayed skin hypersensitivity to antigens

C-73-72 (Continued)

such as Monilia, PPD, mumps, SKSD and inability to sensitize him to DNCB. His lymphocytes transformed in vitro adequately to both mitogens (PHA and pokeweed) and specific antigens such as Monilia and Mumps. His humoral immunity has been found intact.

In order to reduce the antigenic load, a two week period of therapy was carried out with IV amphotericin B. Following this there was rapid clearing of the mucocutaneous lesions which continued to progress to complete clearing over a total period of 6 weeks.

Treatment with transfer factor was initiated approximately 48 hours after therapy with amphotericin B was terminated. Transfer factor was prepared by standard methods utilizing one unit of blood obtained from volunteer donors. Donors were selected by their positive skin and in vitro reactivity to Monilia antigen.

The dose of transfer factor was selected empirically to represent the amount of dialysate recovered from each unit of blood. This was administered by deep IM injection in the anterior thigh.

RESULTS: From July through February, 13 doses of transfer factor were administered. As stated above, at the beginning of therapy the skin lesions were almost entirely gone and did continue to improve for the next four weeks.

Within 48 hours of administering the first dose of transfer factor, there was a conversion of the skin test to Monilia antigen from negative to positive. With administration of transfer factor approximately every two weeks, the skin test remained positive for the next two months. It then reverted to negative in spite of the frequent administration of transfer factor of known potency.

Approximately three weeks after complete clearing of all lesions had been achieved, a new lesion was noted in the neck. Over the next six months these lesions continued to spread and by the end of the trial period the child had reverted to his original state in spite of continued transfer factor therapy.

DISCUSSION: We interpret the above experience as indicating the following:

The initial clearing of lesions we attribute to the administration of amphotericin.

C-73-72 (Continued)

This result is comparable to the administration of this same medication to this child on previous occasions. The prompt return of lesions in spite of a low antigenic load indicates a lack of beneficial effects from transfer factor even though there was conversion of the skin test.

Whether or not we delayed the appearance of a full blown clinical picture by the administration of transfer factor is difficult to decide. It is our impression from review of the records that this was the course followed after previous trials of amphotericin B on this patient.

The failure of transfer factor to convert the skin test after the initial success probably represents the return of too large an antigenic load for the effects of transfer factor to be manifested.

As others have reported, we consider transfer factor to have failed in the therapy of CMC on this child.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Immunologic Fetomaternal Interaction.

WORK UNIT NO.: C-8-73

PRINCIPAL INVESTIGATOR: Luis Canales, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR: Rudi Ansbacher, M.D., Lieutenant Colonel, MC

OBJECTIVES

To determine the mechanism(s) by which the fetus is protected from rejection during the course of pregnancy.

To evaluate the role immune mechanisms play (if any) in habitual abortions and infertility.

To determine the role of immune mechanisms in determining the onset of labor.

To determine the role (if any) that blocking antibodies may play in this phenomenon.

TECHNICAL APPROACH

A series of patients in various categories were selected by the Department of Ob-Gyn on the basis of diagnosis and willingness to cooperate with the study and stability of assignment to this area. Lymphocyte transformation studies were performed serially utilizing maternal lymphocytes as reactive cells and semen from the husband as stimulating antigen. Standard techniques for culture of lymphocytes as developed in this laboratory were utilized.

Manpower: None.

Funding: None.

C-8-73 (Continued)

PROGRESS

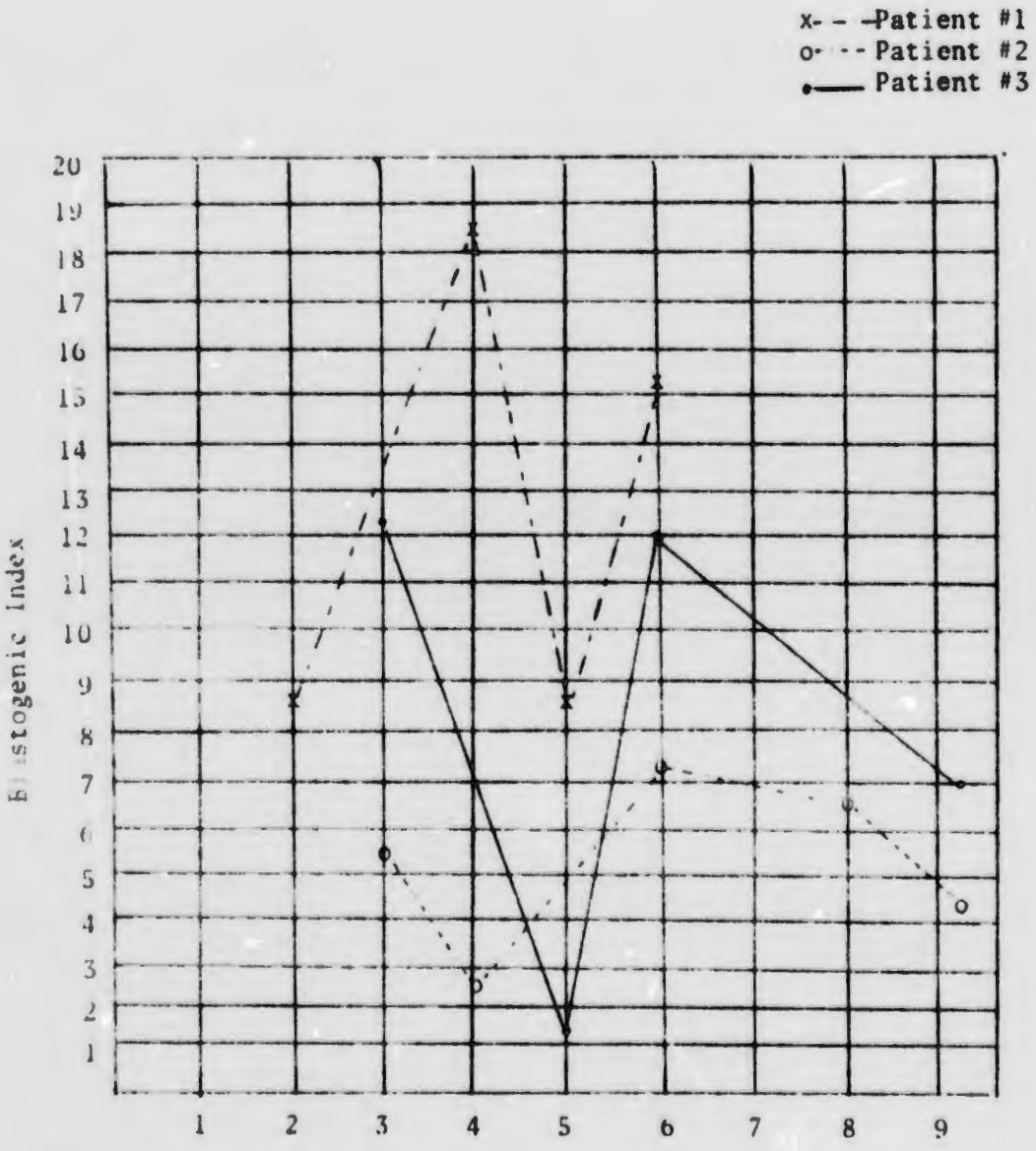
We were only able to follow three women throughout the duration of pregnancy. As seen in the graph, we could detect no relationship between the stage of gestation and the reactivity of maternal lymphocytes to paternal antigens.

We believe that the technique used may not have been sensitive enough for this purpose.

Completed.

C-8-73 (Continued)

Reactivity of Maternal Lymphocytes and Paternal Antigens (Semen) During Pregnancy



DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of Response of Lymphocytes to PHA as Affected by Prolonged Rupture of Membranes.

WORK UNIT NO.: C-37-73

PRINCIPAL INVESTIGATOR: Melvin Baden, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: M. Douglas Jones, Jr., M.D.

OBJECTIVES

To investigate the effect of labor and prolonged premature rupture of the membranes (24 hours) on radioactive thymidine incorporation by lymphocytes of newborn infants in response to phytohemagglutinins.

TECHNICAL APPROACH

The initial phase of this study will evaluate ten infants electively delivered by caesarean section to be used as controls. Ten infants born by vaginal delivery to primiparous women with less than 24 hours rupture of membranes and 10 infants with prolonged premature rupture of the membranes greater than 24 hours will then be investigated. Blood will be obtained from the fetal side of the placenta. The incorporation of radiothymidine in response to PHA will be measured in a scintillation counter after preparation of the lymphocytes by techniques already developed in this laboratory.

Manpower: None.

Funding: $88.80 Consumable Supplies FY 1974

PROGRESS

Steroid samples and statistical data is being evaluated by Dr. M. Douglas Jones, Jr., at the University of Colorado Medical Center, Denver, Colorado.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Cellular Immunity to the Varicella-Zoster Virus Employing a Newly Developed Microassay Technique.

WORK UNIT NO.: C-14-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., Colonel, MC
Monroe A. Vincent, B.S.
Sally A. Hensen, B.S.

OBJECTIVES

To examine the applicability of a newly developed microassay technique, which measures cellular immunity, specific to the Varicella-Zoster virus.

TECHNICAL APPROACH

In vitro assay of blastogenesis: lymphocytes are incubated with tissue culture cells persistently infected with varicella-zoster or other herpes group viruses. Uninfected cells were used as control with a blastogenic index (BI) calculated from cpm of C^{14} thymidine uptake for lymphocytes incubated with infected cells divided by uptake following incubation with uninfected cells.

This assay is being applied to study varied illnesses caused by herpes group virus.

Manpower: None.

Funding: $165.20 Consumable Supplies FY 1974

PROGRESS

The results indicate that patients with recurrent herpetic infection have a dissociation between the afferent and efferent mechanisms

C-14-74 (Continued)

of cellular immunity. They demonstrate normal or even enhanced lymphocyte transformation with HSV-1 antigen but decreased lymphocyte cytotoxicity. These data support the hypthesis that recurrent infection is a consequence of subtle cellular immune deficiency involving at least one of the efferent mechanisms.

Submitted to The Journal of Experimental Medicine for publication.

Presented at the Uniformed Armed Services Pediatric Seminar in March 1974 and received the research award presented by the American Academy of Pediatrics.

Presented at the Society for Pediatric Research meeting in Washington, D.C., 28 April - 2 May 1974.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cellular Immunity to Herpesvirus Hominis in the Compromised Host.

WORK UNIT NO.: C-15-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., Major, MC
Luis Canales, M.D., Colonel, MC

OBJECTIVES

To develop specific and reliable in vitro assays of both the afferent and efferent mechanisms of cellular immunity to Herpesvirus hominis (HVH) and to examine responses of patients with malignant disease or patients on immunosuppressive therapy.

TECHNICAL APPROACH

Cytotoxicity: Utilizing tissue culture cells persistently infected with Herpes-Simplex 1 as target cells, release of ^{51}Cr from these cells or controls was used as the index of lymphocyte reactivity.

This assay is being applied to study the immune responses of patients with varied illnesses caused by herpes group viruses.

Manpower: None.

Funding:			
	$1,206.78	Consumable Supplies	FY 1974
	$ 402.00	TDY	FY 1974

PROGRESS

The results indicate that patients with recurrent herpetic infection have a dissociation between the afferent and efferent mechanisms of cellular immunity. They demonstrate normal or even enhanced lymphocyte transformation with HSV-1 antigen but decreased lymphocyte cytotoxicity. These data support the hypothesis that recurrent infection is a consequence of subtle cellular immune deficiency involving at least one of the efferent mechanisms.

C-15-74 (Continued)

Presented at the Uniformed Armed Services Pediatric Seminar in Biloxi, Mississippi, March 1974 and received the research award from the American Academy of Pediatrics.

Presented at the Society for Pediatric Research meeting in Washington, D.C., 28 April - 2 May 1974.

"Cellular Immune Responses to Herpes-Simplex 1 (HSV-1) in Recurrent Herpes Labialis" submitted to The Journal of Experimental Medicine for publication.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Serum IgM and Its Predictive Value in Neonatal Sepsis.

WORK UNIT NO.: C-21-74

PRINCIPAL INVESTIGATOR: Melvin Baden, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: Amil Ortiz, M.D., Captain, MC

OBJECTIVES

To investigate the correlation between neonatal serum IgM levels and prolonged rupture of maternal membranes, maternal fever, and neonatal sepsis.

TECHNICAL APPROACH

Infants delivered to mothers with greater than 24 hours rupture of the membranes and/or fever off or on antibiotics will be identified from the admitting obstetrical history. As part of their admission evaluation and septic work-up, 0.5 ml of blood will be obtained, centrifuged with the removal of the serum which will be frozen and stored for later measurement of IgM. A control population of infants having blood obtained during day one of life for other reasons, i.e. electrolytes, bilirubin, etc., will also have 0.5 ml of blood obtained and handled as the above population of infants. Serum IgM will be measured using the Hyland immunodiffusion plate with antihuman IgM. All determinations will be done at one sitting in order to minimize variables.

Manpower: None.

Funding: None.

PROGRESS

Forty samples have been collected on infants with greater than 24 hours rupture of maternal membranes. Control samples will be

C-21-74 (Continued)

collected after which serum IgM determinations will be performed on all the samples during one day to minimize laboratory error.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Preparation and Purification of Dialyzable Transfer Factor for the Treatment of Selected Infectious Diseases.

WORK UNIT NO.: C-42-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., Major, MC
Luis Canales, M.D., Colonel, MC

OBJECTIVES

To evaluate the efficacy of transfer factor therapy for disseminated fungal or viral disease or for tuberculosis unresponsive to the usual forms of therapy.

TECHNICAL APPROACH

Dialyzable transfer factor is prepared by the method of Lawrence from heparinized whole blood of human volunteers sensitive to the infectious agent under consideration. One unit, equivalent to 85×10^6 lymphocytes, is administered by subcutaneous injection to the patient and his clinical course evaluated.

Manpower: None.

Funding: $1,092.41 Consumable Supplies FY 1974

PROGRESS

One patient with disseminated coccidioidomycosis has undergone a complete course of therapy with good response noted. *In vitro* assays of cellular immunity to coccidioides have become positive following therapy.

Three other patients with mucocutaneous candidiasis are presently being considered for therapy. Appropriate donors have been screened and assayed for cellular immunity to candida.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Alcohol Withdrawal and Sleep Deprivation in the Production of Seizures.

WORK UNIT NO.: C-126-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Thomas L. Feher, M.D.
Peter B. Dunne, M.D.

OBJECTIVES

Comparison of alcohol withdrawal and sleep deprivation in precipitating seizures.

TECHNICAL APPROACH

Data is being collected.

Manpower: None.

Funding: None.

PROGRESS

Due to pressure of clinical workload, no additional progress has been made.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: EEG and Other Correlates of Sleep Deprivation Seizures.

WORK UNIT NO.: C-127-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Thomas L. Feher, M.D.
Peter B. Dunne, M.D.
E. Liske, M.D.

OBJECTIVES

To compare sleep deprivation EEG's of patients who have had seizures following sleep deprivation and those who have not.

TECHNICAL APPROACH

Data is being collected.

Manpower: None.

Funding: None.

PROGRESS

EEGs have been reviewed by Dr. Liske. Correlation of the data and preparation of the manuscript are pending.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Neurology Workload Project.

WORK UNIT NO.: C-149-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine and compare workload of Neurology Services at Class I and Class II hospitals and compare these with comparable civilian studies.

TECHNICAL APPROACH

All patients seen in Neurology Services of Brooke Army Medical Center, Darnall Army Hospital, and Reynolds Army Hospital are being registered for a two week period. Information will be transferred to punch cards and card sorted. A second two week period will be studied at a later date and the data handled similarly. The two samplings will be compared for internal consistency. If they are internally consistent, they will be combined and the comparison made between the various hospitals and the civilian population.

Manpower: None.

Funding: None.

PROGRESS

Data has been collected and tabulated. Final analysis and comparison with civilian statistics has not been completed.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects on Attendees of a Course in Human Sexuality.

WORK UNIT NO.: C-34-74

PRINCIPAL INVESTIGATOR: Harry A. Croft, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Gilbert R. Kaats, Ph.D., Lieutenant Colonel, USAF
Edwin Cornelius, Captain, MSC
Tom Dolan, SP5

OBJECTIVES

To study the existence of and extent of change in attendees of a course in human sexuality in regards to sexual attitudes, beliefs, values, and behavior.

TECHNICAL APPROACH

At present, courses have been conducted on two occasions. To date, we have asked attendees to take only a pretest questionnaire, for purposes of modifying the questionnaire. Beginning in May, we will ask attendees to take pretest, 2 month post-test, and one year post-test surveys to measure any change present.

Manpower: None.

Funding: None.

PROGRESS

To date, we have been in the process of modifying both the course and the questionnaire. As soon as both are in final form, we will begin the actual research data gathering process.

Presented at the Army Preventive and Social Psychiatry Meeting, Denver, Colorado, 24-25 January 1974.

C-34-74 (Continued)

Presented at the 1st Annual Meeting of Sex Therapists, University of South Carolina Medical School, Charleston, South Carolina, 29 April 1974.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Gallium-67 as a Scanning Agent for Malignant Neoplasms.

WORK UNIT NO.: C-141-72

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR: John P. Whitecar, Jr., M.D., Lieutenant Colonel, MC

OBJECTIVES

To study the clinical usefulness of Gallium-67 as citrate for detecting and localizing the extent of malignant neoplasms.

TECHNICAL APPROACH

Patients are injected with 1-3 millicuries of Gallium-67 citrate, and whole body scans in anterior and posterior projections are obtained at 24, 48, and 72 hours.

Manpower: None.

Funding: None.

PROGRESS

Gallium-67 tumor localization studies have been performed on 89 patients. No adverse reactions have been associated with the injection of Gallium-67 citrate in these patients. The studies will be continued until the maximum of 100 are performed, and all results will be fully analyzed at that time.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of Cisternography Utilizing ^{111}Indium DTPA.

WORK UNIT NO.: C-35-74

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the safety and efficacy of ^{111}Indium DTPA for cisternography studies.

TECHNICAL APPROACH

Approximately 500 microcuries ^{111}Indium DTPA (supplied by Mediphysics, Incorporated) is administered by intrathecal injection. Images of the movement of this radiopharmaceutical within the subarachnoid space are obtained as appropriate with the clinical situation, generally at 2, 24, 48, and 72 hours. These images allow diagnosis of abnormal cerebral spinal fluid flow patterns and localization of obstruction to flow in the subarachnoid space.

Manpower: None.

Funding: None.

PROGRESS

Four patients have been studied with this radiopharmaceutical agent. No adverse reactions were noted. The image quality obtained in each case was excellent and contributed significant information to the patient's clinical diagnosis and management.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Survival Rates of Testis Tumors.

WORK UNIT NO.: C-39-64

PRINCIPAL INVESTIGATOR: Frank E. Ceccarelli, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

Part of worldwide investigation treatment study.

TECHNICAL APPROACH

A prospective evaluation of preoperative irradiation versus irradiation only for Class II and IV testis tumors.

Manpower: None.

Funding: None.

PROGRESS

Eighty-eight patients have been treated and preoperative irradiation seems to give better results.

No further investigation will be conducted at this hospital.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diastolic Augmentation Using an Intra-Aortic Balloon Pump.

WORK UNIT NO.: C-6-72

PRINCIPAL INVESTIGATOR: Robert L. Treasure, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Olyn M. Walker, MM.D., Lieutenant Colonel, MC
George L. Zumbro, M.D., Lieutenant Colonel, MC
George M. McGranahan, M.D., Colonel, MC

OBJECTIVES

Evaluation of an intra-aortic balloon pump (AVCO) providing diastolic augmentation increasing cardiac output in patients with low cardiac output due to myocardial infarction, severe cardiac disease, or following open heart surgery.

TECHNICAL APPROACH

The intra-aortic balloon is used in weening patients from cardiopulmonary bypass who are unable to generate satisfactory cardiac output. An intra-aortic balloon will be inserted in the descending aorta through a femoral arteriotomy and cardiac output increased by diastolic inflation of the aortic balloon by the AVCO pump timed by ECG. The effectiveness of this treatment will be determined by cardiac output, arterial and venous blood gases and pH; and urinary output. Blood trauma due to the balloon will be evaluated by serum hemoglobin.

Manpower: None.

Funding: None.

PROGRESS

To date this device has not significantly improved operative mortality in these critically ill patients. On the basis of our results, we feel that it is the best augmentation available for

C-6-72 (Continued)

long term support and appears to increase the cardiac output approximately 15% and improves coronary artery perfusion significantly. It is most useful following massive myocardial infarction and in low cardiac output following open heart surgery.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Compound Vascular Grafts.

WORK UNIT NO.: C-7-72

PRINCIPAL INVESTIGATOR: Robert E. Hansen, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: William A. Cox, M.D., Colonel, MC
Denton A. Cooley, M.D.

OBJECTIVES

Evaluation of a new dacron arterial graft with the interstices filled with cellulose. This is designed to stop blood loss through interstices in the heparinized patient. It is theorized that in time the cellulose will be absorbed and fibrous tissue invade the interstices of the graft.

TECHNICAL APPROACH

The new dacron arterial grafts were placed as aortic grafts after resecting a portion of the aorta in heparinized dogs. The grafts were evaluated for bleeding through the interstices in the heparinized animal at the time of surgery. Each animal was sacrificed at varying intervals postoperatively, weekly x 3, biweekly x 3, monthly x 3, 3 months, 6 months and 9 months. The grafts were examined to evaluate the rate of absorption of the cellulose and replacement with fibrous tissue, the rate of development, and the character of the neointima.

Manpower: None.

Funding: None.

PROGRESS

Forty-one of the new compound grafts were placed. Six different models were made as improvements were indicated by the experimental results. These improvements were necessary because of the stiffness of the graft, making it difficult to work with technically. Changes

C-7-72 (Continued)

in implantation porosity and biological porosity were made to prevent early and late bleeds through the interstices of the graft when the cellulose material had been absorbed. The animals were sacrificed at 2 weeks, 4 weeks, 3 months, 6 months and 9 months. There was no graft which was not associated with a major complication. Obstruction was seen to a lesser degree in the later series, and the incidence of early hemorrhage was reduced. Late hemorrhage was a problem in one of the later grafts, and perigraft hematoma continued to be a serious problem.

CONCLUSIONS: We believe the new bicomponent vascular prosthesis remains more a theoretical than a practical entity and that none of these materials demonstrated enough safety to begin clinical trials in humans.

Submitted to American Journal of Surgery for publication.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ethicon PolyTef Paste for Injection in Repair of Velopharyngeal Defects.

WORK UNIT NO.: C-20-72

PRINCIPAL INVESTIGATOR: S. R. LeMay, Jr., M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

Some patients with velopharyngeal defects can be corrected by adding bulk to the posterior pharyngeal wall to make closure of the velum possible in normal speaking. Further experience utilizing investigational drug injection to add bulk necessary to improve the speech is sought.

TECHNICAL APPROACH

The investigational drug, Mentor PolyTef Paste for injection, will be used by the investigator in accordance with the following criteria: Age: over 6 years. No sex selection. Generally good health. Complete physical examination. Accurate evaluation to include cineradiography of the velum and recordings pre- and post-operative. Evaluation by competent speech therapists. The PTEE will be injected into the posterior pharyngeal wall and/or palate to provide the bulk necessary to improve velopharyngeal closure. Complete records will be kept. Reports to Mentor will be made. As many available patients as fit the criteria will be injected.

Manpower: None.

Funding: None.

PROGRESS

Two patients have been injected to date. None have been injected in the past year. Sufficient number of patients may not be found

C-20-72 (Continued)

to make a series. However, this technique has been useful in the previous patients, and we will continue to utilize it as other suitable patients are found.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparative Analysis of the LOT Test and Type V Bekesy as an Indicator of Pseudohypacusis.

WORK UNIT NO.: C-24-72

PRINCIPAL INVESTIGATOR: Roy K. Sedge, Ph.D., Captain, MSC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To directly compare standard Bekesy tracings using 200-200 msec. on-off time with sweep-frequency LOT tracings using the 200-800 msec. on-off time criterion.

TECHNICAL APPROACH

One hundred pseudohypacusic subjects referred to the Auditory Evaluation and Treatment Clinic, Brooke Army Medical Center, were used in the experiment. The operational definition for pseudohypacusis employed the same criterion as Rintelmann and Harford. To preclude tester reliability, all pseudohypacusis subjects at the termination of testing had hearing levels of at least 20 dB from 500-2000 Hz.

Fifty pseudohypacusic subjects were grouped in a random fashion and tested under one of two conditions: 1) fifty were tested by conventional sweep-frequency Bekesy audiometry and 2) fifty subjects were tested by the sweep-frequency lengthened off-time procedure. Data in each group were tabulated and statistically treated.

Manpower: None.

Funding: None.

C-24-72 (Sedge)

PROGRESS

Two main conclusions were drawn from the data. First, although the sweep-frequency LOT enhanced the degree of separation between the pulsed and continuous signals, the amount of variability in both groups was high. Second, and in keeping with the first conclusion, the efficiency of the sweep-frequency LOT appeared to be greater than the conventional Bekesy procedure when applying the Rintelmann and Harford operational definition. However, the efficiency of the sweep-frequency LOT in identification of pseudohypacusics did not approach the efficiency of the LOT described by Hattler and Schuchman utilizing the arbitrary definition defined by Hopkinson. This observation was unexpected as the sweep-frequency LOT contained an additional psychoacoustic listening task not employed in the conventional LOT test. With the additional psychoacoustic parameter it was hypothesized that the sweep-frequency LOT would have as great or even greater efficiency in prediction of pseudohypacusic subject than the fixed LOT.

Implications were drawn concerning clinical utility, the need for operational definitions for the LOT, and the need for further research.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Autotransfusion at Surgery.

WORK UNIT NO.: C-78-72

PRINCIPAL INVESTIGATOR: Thomas L. Hudson, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the usefulness of intraoperative recovery of blood loss for reinfusion into the patient using the Sarns Model 6002 Modular Pump and Bentley disposable autotransfusion unit.

TECHNICAL APPROACH

Use Sarns Model 6002 Modular Pump and Bentley disposable autotransfusion unit.

Manpower: None.

Funding: None.

PROGRESS

Approximately twelve patients have been studied. The unit has proven its usefulness in sustaining blood volume in patients with large recoverable blood loss at the operating table thereby minimizing the requirement for banked homologous blood.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Carcinoma of Bladder.

WORK UNIT NO.: C-137-72

PRINCIPAL INVESTIGATOR: Frank E. Ceccarelli, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the various results of treatment for carcinoma of the bladder at Brooke Army Medical Center.

TECHNICAL APPROACH

Statistical analysis of all cases listed in the Tumor Registry at Brooke Army Medical Center with computerization will be accomplished.

Manpower: None.

Funding: None.

PROGRESS

This project has been terminated due to retirement of principal investigator.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Carcinoma of Testis.

WORK UNIT NO.: C-138-72

PRINCIPAL INVESTIGATOR: Frank E. Ceccarelli, M.D., Colonel, MC

ASSOCIATE INVESTIGATOR: Michael D. Uechi, M.D., Major, MC

OBJECTIVES

To evaluate the various results of treatment for carcinoma of the testis at Brooke Army Medical Center.

TECHNICAL APPROACH

Statistical analysis of all cases listed in the Tumor Registry at Brooke Army Medical Center with computerization will be accomplished.

Manpower: None.

Funding: None.

PROGRESS

This study has been terminated due to retirement of principal investigator.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Postoperative Venous Thrombosis in the Lower Extremities.

WORK UNIT NO.: C-7-73

PRINCIPAL INVESTIGATOR: Michael G. Zeigler, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To assess the usefulness of impedance phlebography in detecting postoperative venous thrombosis.

TECHNICAL APPROACH

The Codman 1PG impedance phlebograph was used in following consecutive patients undergoing abdominal operations in an effort to detect venous thrombosis in the lower extremities prior to clinical manifestations.

Manpower: None.

Funding:	$1,863.00	PEMA	FY 1973
	None		FY 1974

PROGRESS

The data on 23 patients was studied. It was concluded the impedance phlebography alone was not sufficiently reliable in following patients pre- and postoperatively, to allow adequate assessment of the presence of venous thrombosis. Its' value is related to the reproducibility of respiratory mechanics on repeated examinations as well as on continued cooperation from the patient. An attempt to reproduce these mechanics and thereby improve the ability to compare tracings was not successful.

C-7-73 (Continued)

Because of the unreliability of the technique, it is felt that further efforts would not be gainful. Further information in the literature would support this conclusion. The incidence of false positive and false negative determinations is simply too high to rely on the technique alone.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of 2-3 Diphosphoglycerate (2,3-DPG) and Arterial Venous pH Difference *in vivo*.

WORK UNIT NO.: C-32-73

PRINCIPAL INVESTIGATOR: Arthur W. Larson, M.D., Major, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To study the effects of Solu-Cortef and Solu-Medrol on 2-3 DPG levels *in vivo*.

2. To verify by a carefully controlled vivo laboratory experiment that A-V pH difference is an indication of low cardiac output.

TECHNICAL APPROACH

Both 2-3 DPG levels and A-V pH differences can be measured on the same dogs subjected to cardiopulmonary bypass pumping. Thirty dogs should be studied; 10 dogs with Solu-Cortef added to the pump, and 10 dogs with Solu-Medrol added to the pump. By total cardiopulmonary bypass any desired and accurately measured cardiac output can be studied.

Manpower: None.

Funding: None.

PROGRESS

This project has been terminated due to inability to get the 2,3-DPG tests performed.

Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Enflurane (Ethrane) on Cardiovascular Function.

WORK UNIT NO.: C-12-74

PRINCIPAL INVESTIGATOR: John R. Ritzman, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Joel A. Kaplan, M.D., Major, MC
Edward D. Miller, M.D., Major, MC

OBJECTIVES

To assess the effects of enflurane, enflurane with N_2O, and enflurane with muscle relaxant upon the function of the cardiovascular system using a non-invasive technique.

TECHNICAL APPROACH

Two groups of six healthy young volunteers were studied prior to minor elective surgery. No premedication was given. After control measurements were recorded, the patients were anesthetized with 50% N_2O and either 1% halothane or 2% enflurane. Cardiovascular measurements were made at the end of 30 minutes of stable anesthesia; then the N_2O was discontinued and repeat measurements were made 20 minutes later. End-tidal halothane or enflurane, arterial blood gases, blood pressure, and heart rate were recorded at each measurement period.

A simultaneous recording at 100 mm/sec was made of a carotid arterial pulse trace, phonocardiogram and electrocardiogram. The intervals measured were the QS_2 (total electromechanical systole), LVET (left ventricular ejection time) and PEP (Pre-ejection period) which were all corrected for heart rate. From these intervals, PEP/LVET, $1/PEP^2$ and the ejection fraction were calculated.

Manpower: None.

Funding: $1,297.70 Consumable Supplies FY 1974

C-12-74 (Continued)

PROGRESS

Both anesthetic agents caused a significant increase in the PEP/LVET ratio, and a decrease in $1/PEP^2$ and the ejection fraction, indicating myocardial depression at equipotent light levels of anesthesia ($P<.05$). The difference between halothane and enflurane was significant ($P<.05$) with halothane being more depressant. Discontinuation of N_2O led to a further depression of these parameters. Arterial blood gases showed no significant differences.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cardiovascular Effects of Continuous Spinal, Epidural and Nitrous-Oxide-Narcotic Anesthesia on Patients Undergoing Surgery for Hip Fractures.

WORK UNIT NO.: C-13-74

PRINCIPAL INVESTIGATOR: Daniel R. Bailey, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D., Major, MC
Joel A. Kaplan, M.D., Major, MC

OBJECTIVES

To determine the effects of spinal, epidural, and general nitrous-oxide-narcotic anesthesia on cardiovascular parameters including: cardiac output, total peripheral resistance, mean arterial pressure, CVP, and EKG in patients undergoing surgery for repair of hip fractures.

TECHNICAL APPROACH

A series of 30 patients will be randomly divided into three study groups of ten patients placed in each of the following groups: spinal, epidural, and narcotic groups. Patients in the spinal and epidural group will have a continuous catheter placed via the L3-4 or L4-5 interspace. After baseline recordings, EKG and CVP measurements will be made and the patients will receive an injection of cardiogreen dye for determination of baseline cardiac outputs via the indicator-dye-dilution technique. Continuous recordings of arterial pressure will be maintained. After baseline values are obtained, anesthesia will be induced. The narcotic group will be put into the surgical position prior to induction of anesthesia, and baseline measurements taken. Repeat cardiac output measurements will be made at intervals of 10, 30, and 60 minutes and every 30 minutes thereafter during the surgical procedure. Arterial blood gases will be measured prior to induction of anesthesia and then at 30 minute intervals during anesthesia. All patients will be closely monitored with continuous arterial pressures, CVP, EKG and urine outputs. Plasma volumes will be determined via the radio-iodinated serum albumin method prior to induction of anesthesia.

C-13-74 (Continued)

Manpower: None.

Funding:

$3,665.00	PEMA	FY 1974
$ 428.00	Consumable Supplies	FY 1974

PROGRESS

Equipment arrived in April 1974, and project is now underway.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Cardiopulmonary Bypass on the Renin-Angiotensin System.

WORK UNIT NO.: C-17-74

PRINCIPAL INVESTIGATOR: Daniel R. Bailey, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D., Major, MC
Joel A. Kaplan, M.D., Major, MC
Philip W. Rogers, M.D., Major, MC

OBJECTIVES

To determine renin and aldosterone levels of patients who undergo cardiopulmonary bypass.

TECHNICAL APPROACH

Ten consecutive, non-emergent adult patients undergoing cardiac surgery with extracorporeal circulation were anesthetized using the morphine technique (1-3 mg/kg). Mean arterial blood pressure, heart rate, central venous pressure, hematocrit, arterial blood gases, urine output, and plasma and urinary sodium, potassium, creatinine and osmolality were measured. Plasma catecholamines, renin, and aldosterone were also measured.

Manpower: None.

Funding: $1,329.74 Consumable Supplies FY 1974

PROGRESS

Results showed significant ($\geq$ 3-fold) increase in both renins and aldosterone pre- and during cardiopulmonary bypass.

C-17-74 (Continued)

The renin-angiotensin-aldosterone system plays an important role in blood pressure regulation and results in the excessive urinary excretion of potassium and the fall in plasma potassium seen during cardiac surgery.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prolonged Intercostal Block Analgesia After Thoracotomy.

WORK UNIT NO.: C-28-74

PRINCIPAL INVESTIGATOR: Joel A. Kaplan, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D., Major, MC
Edgar G. Gallagher, M.D., Lieutenant Colonel, MC

OBJECTIVES

To assess the effect of intercostal block using bupivacaine and dextran in patients who have undergon thoracotomy.

TECHNICAL APPROACH

Twenty thoracotomy patients will be studied over a six month period. Patients will receive a standard premedication of morphine 0.1 mg/kg and atropine 0.4 mg intramuscularly one hour prior to surgery. The study will be conducted in a double blind fashion. Two possible solutions will be injected: (1) Bupivacaine 0.75% - 12 cc, Dextran 40 - 12 cc and (2) Dextran 40 - 12 cc, saline 12 cc. There will be 20 numbers - 10 for each drug - which will be assigned in random fashion. After the block, the amount of ethrane needed for surgical anesthesia will be evaluated. Postoperatively the patient will be treated in the standard manner. The following data will be collected pre-op, 1 hour RR, 4 hour RR, 1 day post-op, 2nd day post-op, and 3rd day post-op: Blood gas; chest x-ray; vitalor PFT (VC, FEV_1, MEF); hematocrit; subjective evaluation - comfort, effective cough, move and turn, out of bed; objective evaluation - skin level unilateral spinal level bilateral; complications - pulmonary and block; narcotic dose and time; temperature.

Manpower: None.

Funding: $173.02 Consumable Supplies FY 1974

C-28-74 (Continued)

PROGRESS

Eight patients have been studied to date.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effects of Prolonged Acceleration ($+G_z$) on the Respiratory Exchange Ratio in Man.

WORK UNIT NO.: C-29-74

PRINCIPAL INVESTIGATOR: David W. Crim, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: F. Wesley Baumgardner, Ph.D.
Sidney D. Leverett, Jr., Ph.D.

OBJECTIVES

To determine the effects of prolonged acceleration ($+G_z$) on the O_2 uptake by the lungs and its relationship to the CO_2 that is exhaled. This study will try to answer the questions: what is happening to R during acceleration? and at what point is a steady state for R reached?

(This study is being performed at the School of Aviation Medicine, Brooks Air Force Base, Texas. The project was registered for record only.)

TECHNICAL APPROACH

Subjects will be placed on the USAF SAM centrifuge and monitored at 1, 2, 3, and 4 G_z for 10 minutes and at G_z for 5 minutes. A pneumotachograph will monitor flow (integrated to expired volume) and a mass spectrometer will monitor expired O_2 and CO_2 concentrations. This data will be analyzed by an Analog computer and give breath by breath readings for R.

Manpower: None.

Funding: None.

PROGRESS

Data has been collected but not analyzed.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Blood Lidocaine Levels in Man During Pentothal, Lidocaine, N_2O-O_2 Anesthesia.

WORK UNIT NO.: C-40-74

PRINCIPAL INVESTIGATOR: Philip R. Warren, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D., Major, MC
Joel A. Kaplan, M.D., Major, MC

OBJECTIVES

To evaluate this commonly used anesthetic technique and correlate the lidocaine dosages used clinically with the corresponding blood level.

TECHNICAL APPROACH

Samples are measured on a gas chromatograph and a mass spectrometer. The retention times and mass spectral characteristics for each local anesthetic (6 total) are measured and compared to a computer library search, providing qualitative and quantitative clinical information.

Manpower: None.

Funding: None.

PROGRESS

Clinical data have been collected. Following evaluation, a manuscript will be prepared.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: "VD-G Dri DOT" Serological Test for Gonorrhea

WORK UNIT NO.: C-144-72

PRINCIPAL INVESTIGATOR: David D. Madorsky, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare the "Gonosticon Dri-DOT" (formerly "VD-G Dri-DOT") Serological Test for gonorrhea with Thayer Martin cultures and smears in males who present for diagnosis of possible gonococcal urethritis.

TECHNICAL APPROACH

All men presenting for diagnosis of gonorrhea have a Gonosticon Dri-DOT Test and Thayer Martin Culture performed in addition to the smear. The test is performed on serum according to instructions and the end point is read. Results are compared to determine the efficacy of the test.

Manpower: None.

Funding: None.

PROGRESS

Data collection is complete but not tabulated. Publication will ensue.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Antigens in Fire Ant Venom.

WORK UNIT NO.: C-41-74

PRINCIPAL INVESTIGATOR: Frank K. James, Jr., M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., Major, MC
Donald P. Driggers, Captain, MSC

OBJECTIVES

To study the venom and/or its component parts and its effect on selective human volunteers known to be sensitive to the fire ant venom.

TECHNICAL APPROACH

The fire ant venom will be extracted from living fire ants, purified, diluted, and used as the basic skin testing material in patients. The commercially available fire antigen and synthesized fractions of the venom will also be utilized for comparative purposes.

Manpower: None.

Funding:	$115.00	Consumable Supplies	FY 1974
	$366.00	TDY	FY 1974

PROGRESS

This study is currently in the basic phase. Patients have been contacted in cooperating Allergy facilities for future skin testing and other appropriate immunologic studies. A Fire Ant Survey is currently in process at Fort Sam Houston under the direction of Captain Donald Driggers, 485th PM Company. The technique for milking fire ants to procure the pure venom, previously perfected by Dr. Blum, will be utilized in order to bring pure venom here for appropriate studies. (This is the only known source of pure fire ant venom.) In addition, synthetic alkaloids prepared from venom extracts by Dr. Blum will be procured from the University of Georgia.

C-41-74 (Continued)

Following completion of above, approximately 25 fire ant sensitive patients will be studied during the summer months with the agents listed in the above paragraph.

These initial findings will be presented by Colonel James to the annual meeting of the Association of Military Allergists (as part of the Annual Pulmonary Disease Symposium), Fitzsimons Army Medical Center, in September 1974.

Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Collaborative Study to Define Clinical Applicability and/or Utility of Carcindex (radioimmunoassay for carcinoembryonic antigen).

WORK UNIT NO.: C-7-74

PRINCIPAL INVESTIGATOR: Robert E. Lawson, Major, MSC

ASSOCIATE INVESTIGATORS: William A. Rutala, First Lieutenant, MSC
David Arbiter, M.D., Colonel, MC

OBJECTIVES

To identify the diagnostic and prognostic value of the Carcindex immunoassay procedure in endodermally derived neoplasias.

TECHNICAL APPROACH

Plasma specimens for CEA level determinations will be obtained from all hospital admissions. CEA test evaluation forms will be completed at the time of specimen collection. Specimens will be analyzed by split sampling.

Manpower: None.

Funding: None.

PROGRESS

Sixteen samples were tested which were consistently and significantly higher than those reported by Roche Research Center, Hoffman-La Roche Inc. The higher values are at present believed to be attributable to the ionic strength or pH of reagents which can result in falsely elevated plasma CEA levels.

Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Iodophor Handwashing in the Newborn Nursery.

WORK UNIT NO.: C-19-73

PRINCIPAL INVESTIGATOR: John Tyson, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Frederick P. Boehm, M.D., Captain, MC

OBJECTIVES

To determine the minimum duration of wash with Betadine and with pHisoHex necessary to insure satisfactory removal of Staph Aureus from the hands of nurses in the newborn nursery.

TECHNICAL APPROACH

Design:

a. Contamination of hands with Staph Aureus in amounts equivalent to those found under epidemic conditions.

b. Determination of percent reduction by pre- and post-handwashing cultures for 5, 10, 15, and 20 second handwashing periods with both agents.

Manpower: None.

Funding: None.

PROGRESS

This study was being performed at Reynolds Army Hospital, Fort Sill, Oklahoma. It has been terminated due to transfer of principal investigator.

Terminated.

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