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RCS MEDDH-288 (RI)

U S ARMY MEDICAL RESEARCH AND DEVELOPMENT TECHNICAL REPORT

ANNUAL PROGRESS REPORT, FISCAL YEAR 1972

U S ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE

Natick, Massachusetts

PUBLISHED JULY 1972

UNITED STATES ARMY
MEDICAL RESEARCH & DEVELOPMENT COMMAND

173

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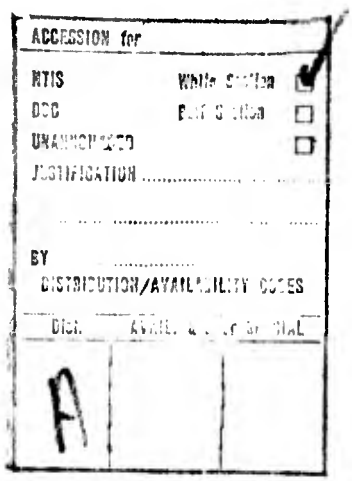

U S ARMY RESEARCH AND DEVELOPMENT

TECHNICAL REPORT

RCS-MEDDH-288 (R1)

U S ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE

NATICK, MASSACHUSETTS

ANNUAL PROGRESS REPORT

1 July 1971 - 30 June 1972

Approved for public release;
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UNITED STATES ARMY

MEDICAL RESEARCH & DEVELOPMENT COMMAND

FOREWORD

1. This has been a year of progress and change. The mission of USARIEM has been expanded to include an advisory/consultative capacity. Important contacts have been established or reestablished with the Command and General Staff College, Ft. Leavenworth, Kansas; the Medical Field Service School, Ft. Sam Houston, Texas; the US Army Infantry School and Ranger School, Ft. Benning, Georgia; the US Military Academy, West Point, New York; Ft. Carson, Colorado; Ft. Hood, Texas; Ft. McClellan, Alabama; Ft. Ord, California; and Ft. Rucker, Alabama; as well as other agencies, installations and headquarters.

2. Progress reported herein is the result of the efforts of USARIEM personnel under the guidance of our laboratory directors with the able assistance of Support Office personnel, several of whom are new. Dr. Sumner Robinson, M.D., replaced LTC Wayne O. Evans, MSC. LTC Evans is now Special Assistant to the Commanding Officer. Dr. John L. Kobrick, Ph.D., replaced Dr. E. Ralph Dusek. LTC L. H. Hartley, MC, was replaced by MAJ R.P. Hogan, MC, who, in turn, has been replaced by MAJ Samuel R. Giamber, MC. CPT Murray P. Hamlet, VC, formerly Research Veterinarian, AMRLA, replaced MAJ David K. Hysell, VC. LTC Norman E. Clyde, MSC, replaced COL James D. Grindell as Executive Officer and Chief, Support Office, and COL LeeRoy G. Jones, MC, assumed the duties of Commanding Officer/Scientific Director following the departure of COL James E. Hansen, MC. Dr. David E. Bass, Ph.D.; Dr. Ralph F. Goldman, Ph.D.; Dr. Milton Landowne, M.D.; Dr. Milton Mager, Ph.D.; LTC William H. Doolittle, MC, as well as the Support Office Branch Chiefs, Mr. Botsch, Mrs. Donnelly, CPT Miller, 1LT Moore, and Mrs. Zolner all remain in positions previously occupied. 1LT Carl J. Weinschenk replaced CPT Fred McKellar as Chief, Supply Branch and our Chief Medical NCO, SFC Kenneth Tackett has been replaced by 1SG Talmage Mathis.

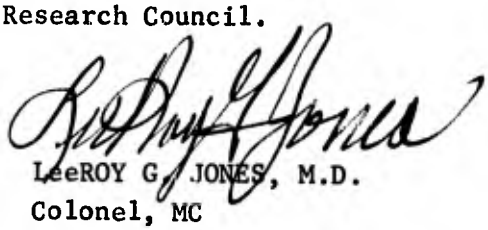
3. We are happy to welcome Dr. Michael Haisman, Ph.D., from the Army Personnel Research Establishment (APRE), Surrey, England, who is working in the Military Ergonomics Laboratory on an exchange program under which Dr. James A. Vogel, Ph.D., of USARIEM is a visiting scientist with the APRE for two years. Dr. Baruch Givoni, Israel, spent three months with us in mid-year working in the Military Ergonomics Laboratory. Dr. Takemasa Shiraishi, M.D., Ph.D., of Tokyo Medical College, a Neurophysiologist, arrived in June to begin work in the Biochemistry-Pharmacology Laboratory under the National Academy of Science Research Associateship Program, and arrangements have been finalized for the arrival of NIH International Fellow, Dr. S.C. Manchanda, M.D., of the All India Institute of Medical Sciences, New Delhi, India, to begin work at USARIEM in January 1973.

4. The second annual course on Research in Environmental Medicine, given by USARIEM staff and consultants, was provided for fifteen visiting officers including Research Fellows and Preventive Medicine Residents from WRAIR, representatives of the US Navy and Army Research Laboratories, as well as for new investigator and technical personnel from USARIEM.

5. We express special appreciation to Major General Richard R. Taylor, Commanding General, COL Richard F. Barquist, MC, Deputy Commander and the staff, US Army Medical Research and Development Command; to General Dean Van Lydegraf, Commanding General, and COL William B. Levin, QMC, Commanding Officer, US Army Natick Laboratories, and to the several civilian scientists who serve as consultants to USARIEM.

6. This work was authorized under the following DA Technical Projects: In-House Laboratory Independent Research (3A061101A91C); Research in Biomedical Sciences (3A061102B71R); and Military Environmental Medicine (3A062110A827).

7. In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care", as promulgated by the Committee on the Guide for Laboratory Animal, Resources, National Academy of Sciences-National Research Council.



LeeROY G. JONES, M.D.
Colonel, MC
Commanding

TABLE OF CONTENTS

Project No: 3A062110A827

Title: Military Environmental Medicine

(83101)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6120	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8A. DISP'N INSTR'N	8B. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☑ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	045
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)

(U) Medical Problems in Military Arctic Operations (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

003500 Clinical Medicine; 005900 Environmental Biology; 016200 Stress Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
65 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	6.0	221.0
	CURRENT 73	6.0	230.0

19. RESPONSIBLE DOD ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Doolittle, William H. LTC
TELEPHONE: 317-353-9157
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Gregory, Roger T. MAJ
NAME:

21. GENERAL USE

Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Cold; (U) Cold Injury; (U) Trenchfoot; (U) Military Environmental Medicine; (U) Acclimatization; (U) Therapeutic Techniques & Equipment; (U) Hypothermia

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Identify and quantitate physiologic effects associated with cold weather military operations, and exploit these changes to enhance operational performance and to treat or prevent adverse changes.

24. (U) I. Clinical and animal experimental programs to (a) maintain epidemiologic cold injury surveillance; (b) evaluate various methods of treatment of cold injury; (c) evaluate blood flow, nerve conduction velocity, serum enzymes as predictors in freezing injury; (d) evaluate efficacy of various methods of rewarming from accidental clinical hypothermia; (e) evaluate aviator performance as it relates to survival over a range of temperatures, clothing, and aircraft configurations. II. Identify and quantitate appropriate physiologic, pathologic and biochemical changes associated with occupational exposure to cold, cold/altitude, isolation, and varying photo-periods by measurement of (a) pulmonary function; (b) physical fitness; (c) biologic rhythms; (d) cardiovascular function; (e) immunologic function; (f) neurologic, psychomotor, and behavioral function by animal experimentation and in chamber and field investigations with human subjects.

25. (U) 71 07 - 72 06 Peritoneal dialysis with warm fluids resulted in a 78% return of cardiac output compared to a 50% return in hypothermic animals rewarmed by external means. Peritoneal dialysis has been used in 3 clinical cases of accidental hypothermia with encouraging results. A more efficient method of internal rewarming from experimental hypothermia is under investigation using arteriovenous shunt. Some detrimental effects of extreme cold upon peripheral function in the absence of clinical freezing have been identified. Use of electromyographic techniques has increased reliability in forecasting extent of ischemic injury. Autonomic conditioning has resulted in an increase in functionability and comfort during cold exposure and in alleviation of symptoms in a small number of cases of primary Raynaud's disease and other cases of uncomplicated cold hypersensitivity.

* Available to contractors upon originator's approval.

GENERAL BACKGROUND

Cold Injury, be it frostbite, immersion foot, or accidental hypothermia, modifies "present for duty" rolls only slightly in peacetime training units even in severe arctic climates. A moment's reflection on events in wartime can put cold injury in quick perspective. In World War II, from 1942-1945, 7,514,000 man days were lost due to cold injury. Translated to a division of 15,000 men, this means the division in lost to combat for 16 months of those three years. The mean maximum termperature in European operations between December '44 and January '45 was 33.5°F and the mean minimum was 22.6°F. Even in the Aleutians, the minimum temperatures were only -12.2°F. In Korea, average daily temperatures in coldest months were between 10° and 30°F, with minimums lasting one or two days down to -20°. Average hospital stay for cold injuries of all types in WWII was 83 days. In the Korean war, where over 8,000 cold injuries were generated, it was 37 days.

Personal protective equipment has changed and improved but we now contemplate and in fact train field units in arctic and subarctic areas where temperatures exceed -40°F and are sustained at these levels for weeks at a time. Despite new protective equipment, the potential medical problem in combat in such areas is staggering. Efforts to evaluate and effectively treat cold injuries and to shorten hospitalization must continue to have high priority in cold oriented medical research.

The following studies address this problem.

Title of Study: Clinical Evaluation of Peritoneal Dialysis and Resuscitation From Profound Hypothermia

Investigator: Roger T. Gregory, MAJ, MC

Favorable results from experimental studies using peritoneal dialysis with a warmed dialysis solution have encouraged the development of a clinical protocol to evaluate this technique further. Three cases of accidental hypothermia have been treated by peritoneal dialysis during the winter. Only one case was under control of this Laboratory. The remaining two were treated in civilian and/or Public Health Service hospitals as a result of dissemination of reports from here. The one case developing at Bassett AH had numerous complicating features including diffuse skin disease and pre-existing hyperosmolality which precluded careful documentation of the resuscitative efforts. The other two cases, one with a documented core temperature of 76°F and one with a temperature below 94°F (low reading thermometer not being available) were successfully resuscitated with peritoneal dialysis. Details of these resuscitative efforts were somewhat imcomplete. The one patient with a recorded core temperature of 76°F showed a cardiac arrhythmia which reverted to normal with peritoneal dialysis but the rates of rewarming were not carefully enough documented to be reliable. Further evaluation of this technique in clinical cases is necessary, and is planned for ensuing winters. Cooperative efforts with civilian treatment facilities have been encouraged.

Title of Study: Evaluation of Cardiovascular Effects of Arteriovenous Shunt Rewarming Following Induced Hypothermia in the Dog

Investigator: Roger T. Gregory, MAJ, MC

Accidental hypothermia is a well recognized clinical problem which is not confined by geography. The mortality in clinically identified cases of accidental hypothermia, in which external means of resuscitation have been attempted, exceeds 60% in most reported series. Internal or core rewarming appears to have certain advantages over the widely recommended external methods of rewarming. Isolated cases of an efficient method of internal rewarming utilizing total extracorporeal circulation with heat exchanger have been described. Although successful, this technique has not found wide acceptance because of the limited availability of the expertise and equipment required for the application of total extracorporeal circulation in an emergency situation.

The present study was designed to evaluate a more simple method of hematogenous rewarming in which expensive equipment is not required and to evaluate the cardiovascular and hematological effects of the maneuver.

The core temperature of nine mongrel dogs was lowered to 25°C for three hours after which rewarming was accomplished using an arteriovenous shunt. A disposable Miniprime heat exchanger was connected by cannulae to the right femoral artery and vein; water at varying temperatures was pumped in counter-current fashion through the opposite side of the heat exchanger using a constant temperature circulator.

Results suggest that this is an effective method of rapidly increasing core temperature with little effect on peripheral temperatures. The rates of atrial, esophageal, and rectal rewarming were 1.1°/min, 0.4°C/min, and 0.3°C/min, respectively. No significant hemolysis, as determined by plasma hemoglobin, resulted from the use of the heat exchanger. In addition, red blood cell fragility was unaltered, and peripheral smear evaluation revealed no changes associated with thermal injury to red blood cells. Heart rate and mean arterial pressure returned to prehypothermic levels after rewarming, while cardiac output improved from 42% to 76% of the prehypothermic levels immediately upon rewarming.

This additional simple technique of resuscitation from accidental hypothermia can increase the therapeutic armamentarium for this disastrous, not uncommon accident of northern operations. Clinical study of this technique deserves consideration.

Title of Study: Evaluation of Various Rewarming Techniques Following Induced Hypothermia

Investigator: John F. Patton, CPT, MSC

As previously reported, peritoneal dialysis has been evaluated as a method of resuscitation in induced hypothermia in the dog. Analysis of these data is now complete. Cardiovascular function was measured in anesthetized dogs prior to the induction of hypothermia, after 3 hours of hypothermia, during which cardiac temperature was at 25°C, and following external rewarming or core rewarming by peritoneal dialysis. Rate of rise in cardiac temperature was greater with peritoneal dialysis (4.5°C/hr) than with external rewarming (3.2°C/hr) and resulted in only a slight rise in skin temperature when compared to external rewarming. Typical electrocardiographic T-wave inversion during hypothermia became normal in the dialysed group during the warming but in 7 of 10 animals rewarmed externally, the T-wave failed to return to normal. Cardiac output, total peripheral resistance, and left ventricular work remained depressed in both groups immediately upon rewarming but significant improvement developed in the peritoneal dialysed group by 12 hours post-hypothermia. In addition, the mean arterial pressure was depressed in the externally rewarmed dogs 12 hours after hypothermia but not in those rewarmed by dialysis.

Peritoneal dialysis appears then, to be an effective, practical method of rewarming and when compared to external rewarming resulted in earlier return towards prehypothermic cardiovascular function. A question which remains, however, is the ability of peritoneal dialysis to effectively remove substances from the blood during the hypothermic period and whether the peritoneal membrane is altered following rewarming.

Studies were performed on 10 mongrel dogs to evaluate the efficiency of peritoneal dialysis during and following hypothermia by measuring the peritoneal clearance of urea and potassium. Preliminary analysis of the data suggests that the efficiency of the peritoneal membrane is decreased slightly during hypothermia but after rewarming, peritoneal clearances return to control levels.

In addition to the above, certain complications which have been reported with prolonged clinical use of peritoneal dialysis, i.e.,

hyperglycemia, protein loss, hypernatremia, water loss, were not observed in the present study where peritoneal dialysis was used as a method of rewarming.

Additional studies comparing rate of recovery of renal and peritoneal clearance will be conducted.

Title of Study: Use of Peripheral Nerve Response to Forecast Tissue Loss in Frostbite Injury; Evaluation of Sequelae Following Cold Injury; Effects of Cold Exposure on Common Clinical Neuropathies

Investigator: Henry C. Marshall, Ph.D.

Background:

Assessment of the electrical activity of peripheral nerves has been found to be a useful and reliable corollary of peripheral function. In addition, because of the frequency of sensory and motor complaints in the cold, because of the frequency of other forms of nerve dysfunction apparently related to protracted cold exposure without freezing and because of the changes in nerve function with freezing injury, this modality of evaluation has become increasingly important.

In experimental freezing, as nerve responses are traced from healthy tissue into the area of freeze injury, there are deteriorating changes in amplitude, duration, and latency of action potential. These changes parallel the extent of injury until, in nonviable tissue, a recognizable action potential can no longer be observed. Analysis of these nerve responses provides a useful tool in the prognostication of recovery from freezing injury.

Progress:

Studies on patients in collaboration with Dr. John Boswick at Cook County Hospital in Chicago, were conducted during the winter 1971-72, and although the results have not yet been fully analyzed, these studies have emphasized the differences between the analysis of the acutely inflicted experimental frostbite and the more graded accidental frostbite normally incurred by humans. These differences in turn have shown the necessity for a critical interpretation of electromyographic results in prognosticating human ischemic injury. Refinement of these techniques is expected to provide essential corollary information in human frostbite as well as in other injuries resulting in loss of nutritive blood flow to peripher nerves.

Further examination of the neuroelectrical aspects of cold exposure and cold injury thus far supports the following points:

a. Cold injury results in action potential and conduction velo-

city changes that indicate intensity of injury.

b. Clinical assessment of the degree of freezing injury is not consistent in some instances with nerve response results.

c. Cold exposure without recognizable cold injury can result in changes in nerve conduction velocity and action potential characteristics.

d. Decrements in nerve response caused by cold injury can persist long after clinical evidence of injury has disappeared.

e. There are significant age group differences in response to cold exposure.

Using the frostnip model (a reversible, superficial experimental frostbite) prepared by Dr. Ralph Goldman, Ergonomics Laboratory, USARIEM, the following additional observations have been made on data which is still being analyzed:

a. Subjects having prior frostnip experience appear to have a resistance to the efforts of subsequent frostnip on neuroelectrical phenomena.

b. Cold block of nerve response occurs at different exposure temperatures in those who experienced frostnip as compared to those who did not.

c. Although nerve conduction velocity classically slows at a rate of 2 m/sec/°C, in the frostnip models it was seen to drop to a greater degree in some test subjects than anticipated from the predictive temperature-correction formula.

d. Those who did not exerience frostnip reached skin temperatures of -13 to -14° without freezing.

These findings may provide useful insights into the management of clinical freezing injury and in addition provide an important tool for identifying and managing non-freezing cold induced impairment of function. As an example of the latter, evaluation of patients with unusual responses to cold (primary Raynaud's phenomenon-"cold numb hand syndrome") has resulted in a treatment program consisting of

autonomic conditioning that has been demonstrated to modify cold response in afflicted patients.

Although the importance of these techniques and procedures is obvious in clinical cases, it is as important to identify the implications for screening of personnel for programs involving high degrees of digital dexterity for longer than usual times in severe cold and for prophylactically treating those people who must operate sophisticated equipment in seriously cold weather, where maximum digital dexterity is required. With increasing complexity of the fighting man's equipment, this last application may have far reaching impact on military operations in arctic environments.

Title of Study: Epidemiology of Frostbite in a Garrison Situtation

Investigator: William H. Doolittle, LTC, MC

Progress:

A total of 113 cases of frostbite were treated by AMRLA personnel during the winter 1971-72. Of these, 82 were military, 22 dependents, and 9 civilian beneficiaries of the Government. Of the military frostbite, 76% were first degree, 22% second degree, and 2% (2 patients) were third degree. Of the dependent/civilian injuries, 61% were first degree, 26% were second degree, 6.5% were third, and 6.5% were fourth degree injuries. In the military injuries, 36.6% were located on the ears, 24% were located on the fingers, and 24% involved the toes and feet. Injuries of the nose in the military population constituted 5% of the total injuries, or 4 patients. In the dependent/civilian population, 22.5% involved the ears, 38.7% involved fingers, and 25.8% involved toes and feet. Approximately 10% of the civilian/dependent injuries involved the tongue. 7.3% of the military cold injuries were hospitalized (7 patients) and 22.6% of the civilian/dependent injuries were hospitalized (8 patients). The average duration of hospitalization for the military was 14.6 days; the average for the dependent/civilian population was 35.0 days, reflecting the greater severity of the injuries in the later group.

The basic purpose of this study, which was to identify host factors impacting on freezing injury, has been completed and comprises 292 soldiers with frostbite, with control data obtained from 3,766 soldiers derived from a population pool identical to that of the frostbite patients. Negroes were found to have 2.8 times greater incidence of frostbite than Caucasians. Persons born in warmer climates and those who had previous cold injuries had an increased incidence of frostbite. Caucasians with type O blood appeared to more susceptible than those with type A or B. Cigarette smoking increased the incidence of frostbite 1.4 times. Increasing rank, education, and experience in the subarctic were associated with a lower incidence of frostbite. Age, weight, and height, and a family history of hypertension or diabetes millitus had no effect.

Future Plans:

Continue epidemiologic surveillance, although detailed study as in the past will not be conducted.

Title of Study: Clinical Use of Xenon-133 to Predict Tissue Loss in Cold Injury

Investigator: William H. Dootlittle, LTC, MC

The difficulties in evaluating therapeutic modalities in frostbite have been amply detailed in the open literature and in previous reports. The use of radioactive xenon-133 to predict tissue loss in cold injury has been found to be efficacious in both experimental and clinical studies previously reported.

With the radio-isotope licensing of the local military facility (Bassett Army Hospital, Fort Wainwright) one case of frostbite was evaluated with radioactive xenon and showed improvement in blood flow following therapeutic efforts (see summany, Case No. 2, under the following study, "Evaluation of Low Molecular Weight Dextran in Treatment of Frostbite").

Further evaluation of this technique is planned in ensuing winters and hopefully collaborative studies with civilian facilities presented with the problem of frostbite will be developed.

Title of Study: Evaluation of Low Molecular Weight Dextran in Treatment of Frostbite.

Investigator: William H. Doolittle, LTC, MC

Background:

Attempts to improve post-thaw nutritional blood flow to the injured part constitute one important avenue of approach to treatment of freezing injury. Low molecular weight dextran has been shown experimentally to imporve tissue survival. Since 1968, Dextran has been used in a continuing program of evaluation. Numbers of cases have been small and until late winter 1971-72, no method for assessment of cases before treatment in a reliable fashion has been available here. Case No. 2 describes the first case from Fort Wainwright using Xe-133 with dextran to assess therapeutic results.

Progress:

Two cases of frostbite were added to the dextran study. Their summaries follow.

Case No. 1. A 46 year old male admitted approximately 0400, 4 December 1971, intoxicated, with closed fracture right tibia and fibula sustained in fall, and frostbite, both hands, during unprotected exposure for an unknown period at approximately -20°F. Distal phalanges were cyanotic and anesthetic bilaterally and doppler examination after rapid rewarming in a whirlpool at 105°F revealed no flow distal the distal interphalangeal joints to DIP joint to digits 3-5 on right hand and 2-4 on left hand. Patient was selected for inclusion in Dextran Protocol. He was treated with 1.5 gm/kg Dextran in the first 24 hours and then 0.5 gm/kg for the next 6 days. Creatine phosphokinase levels were elevated above 300 units. Flow by doppler was recorded with dextran running, in all finger tips. Finger tip sensation returned but subsequently the distal phalanx of the left 5th and 3rd and right 5th and 4th digits mummified and were amputated. There was ultimate loss of volume of other involved digits and some limitation of motion. There was no adverse reaction to dextran.

Case No. 2. A second patient was a 24 year old caucasian male found "passed out" without hand protection at approximately -20°F with exposure for unknown period. His hands were cold, firm and pale before

rewarming and then showed cyanosis of the distal phalanges of the right 5th finger and the left middle and ring fingers. Xenon-133 blood flows on the distal phalanges of the right and left 5th digits showed no flow. He was treated as above. Measurable blood flow in these digits was obtained two days after beginning dextran. The subsequent course was uneventful although the patient lost some volume of the volar fat pad of the left 4th digit and had mild contractures of the left 4th and 5th DIP joint. At later follow up (3 months post injury) nerve conduction velocity was reduced in affected digits and sensation impaired. X-rays at this time showed borderline periarticular erosions of the PIP joint of the 3rd, 4th and 5th digits.

Future Plans:

Additional clinical study of Dextran is necessary with serial blood flow measurements and is planned for future winters.

Title of Study: Therapeutic Value of DMSO in Experimental Frostbite

Investigator: John T. Boyce, CPT, VC

Background:

The investigation of therapeutic regimens for frostbite is based on the concept that some part of tissue loss in frostbite is due to progressive, post thaw impairment of tissue perfusion, nerve function, and or other undefined factors. For example, it has been demonstrated here that tissue loss could be predicted by measuring blood flow in the damaged area. It follows that if these changes develop post-thaw, it may be possible to reduce tissue loss with appropriate therapy. DMSO is known to penetrate biological membranes to reduce edema, to block pain sensation, and has been used at least once clinically in frostbite. Therefore, we are evaluating its therapeutic value in experimental freezing injury.

Work thus far completed tends to support the following statements:

1. In a situation which produces 4+ (100%) tissue necrosis in control animals, experimental animals who had topical 90% DMSO applied twice daily, manifested tissue necrosis ranges from 0 to 3+; however, xenon-133 blood flow recorded 12 hours after DMSO application is not significantly improved.

2. In the same situation using 68.4% DMSO, tissue necrosis ranges from 1 to 3+, and the xenon-133 blood flows show trend of improvement.

Future Plans:

The evaluation of DMSO will be completed and attempts will be made to further characterize blood flow changes associated with varying strengths of DMSO. In addition, the therapeutic value of combinations of other agents with DMSO will be evaluated. Because the post thaw tissue damage probably results from a combination of factors, the ideal therapeutic regimen will likely address more than one of these factors. The specific combination which will be most efficacious will, in part, be dependent on when, after thaw, therapy is instituted.

(83102)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OB 6122	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	046
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Prediction of the Biological Limits of Military Performance as a Function of Environment, Clothing and Equipment. (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*
016200 Stress Physiology; 013400 Psychology; 011700 Operations Research

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	1.3	121.2
FISCAL YEAR CURRENT 73	0.8	90.0

19. RESPONSIBLE DOD ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME:* USA Rsch Inst of Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Goldman, Ralph F. Dr.
TELEPHONE: 955-2831
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Stroschein, Lee Mr.
NAME: Breckenridge, John R. Mr. DA

21 GENERAL USE
Foreign Intelligence Considered

22. KEYWORDS (Precede EACH with Security Classification Code)
(U) Environmental Tolerance; (U) Performance Limits; (U) Heat Stress; (U) Cold Injury; (U) Military Tactics

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Develop mathematical equations and computer programs to synthesize available information on military task requirements, with the interaction between the man and his clothing, equipment and environment, to predict mission performance capability and identify areas where additional information is necessary.

24. (U) Relevant military clothing and equipment characteristics, environmental parameters, physiological factors and mission requirements have been reviewed and available tabulations will be continually updated. Predictive models of heat production and loss have been developed and limiting criteria in terms of maximum work capacity as well as with reference to comfortable, tolerable or unsafe extremes of body heat storage or debt are being evaluated. Systems for predicting individual comfort and/or unit mission performance decrements or tolerance time is being developed from these models. Predictions of military performance limits are being continually validated by controlled physiological chamber and small scale field studies as well as by participation in appropriate field maneuvers. The results guide military clothing design, suggest tactical doctrine and indicate potential environmental casualties.

25. (U) 71 07 - 72 06 Effects of load, manner of carriage and terrain have been used to predict actual march times with sufficient accuracy that the effects of load reduction, carriage or alternative march rates can be reasonably estimated using the available model. Little correction has been found necessary for use in extended operations; i.e. 36 hours of continuous wakefulness. Adjustment factors for heat losses associated with activity levels have been studies, with current emphasis on body armor systems since these factors have been developed for standard and CW protective systems. Major improvements in the model include prediction of heart rate as well as body temperature responses, and the effects of heat acclimatization on them. Models for cold exposure have been programmed and are being evaluated by chamber and field studies.

*Available to contractors upon originator's approval.

DD FORM 1 MAR 68 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A, 1 NOV 68 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

Title of Study: Terrain Coefficients of Walking on Snow and Ice

Investigators: Michael F. Haisman, Ph.D. and Ralph F. Goldman, Ph.D.

Background and Approach:

A previous study (Soule and Goldman 1971) defined terrain coefficients for six different types of terrain, providing coefficients which allowed use of the basic Givoni-Goldman energy cost prediction equation for these terrains. A terrain coefficient is derived by comparing the energy cost of walking over the terrain with the energy cost of walking at the same speed on a treadmill. The present study aimed to produce a terrain coefficient for snow of various depths and also for ice. The study was carried out at two walking speeds, 0.67 and 1.12 m/sec (1.5 and 2.5 mph) on the level treadmill and on whatever snow depths were available in the Natick Laboratories area. Unfortunately, because of an unusually mild winter and a shortage of test subjects, data was obtained from only four subjects up to snow footprint depths of 17 cm.

Conclusions:

(1) The ratio of the energy cost of walking in the snow to energy cost of walking at the same speed on the treadmill increased linearly with increasing depth of footprint, so that at 17.0 cm. the energy cost rises three times.

(2) At this maximum snow depression, energy expenditure at 1.12 m/sec, with about 9 kg weight of clothing and respirometer, had reached rather high levels, in the region of 900 kcal/hr. This level of energy expenditure is approaching the maximum for healthy young men so that future investigations at greater snow depressions should involve only the slower walking speed (0.67 m/sec).

(3) Energy expenditure expressed per horizontal kilometer x kilogram body weight and clothing also increases linearly with snow depression. The regression agrees well with the study of Ramaswamy et al (1966) on Indian soldiers but lies above the data of Heinonen et al (1959) at 15 cm. snow depression.

Title of Study: Role of Body Fat in Response to Heat

Investigators: R. G. Soule, Ph.D. and R. F. Goldman, Ph.D.

Background:

Although Miller and Blyth reported (1955) a lack of insulating effect of body fat during internal and external heat load, most studies of men working in the heat suggest that a higher percentage of body fat reduces heat tolerance. However, during a recent field study, body fat and rates of rise of rectal temperature (T_{re}) were determined for over 200 men marching in the heat; no correlation ($r \simeq 0.01$) was found for the whole group, or for just the 10 fattest and 10 leanest. Clearly, additional clarification was needed.

Conclusions:

In the present study, 14 men, selected from a group of over 200 fit but "thin" or "fat" volunteers to provide a range of body fat from 11.9 to 30.5%, worked under 5 conditions: climatic chamber on a treadmill (25 min walk, 25 min rest, 25 min walk, 45 min rest) at 5.6 km/hr at, 1) 24°C, 50% RH in shorts; 2) 35°C, 50% RH in vapor barrier coveralls; 3) 49°C, 20% RH in shorts; outdoors in standard fatigues, ($T_a \simeq 27$°C, RH $\simeq$ 50%) on a blacktop circuit; 4) as a group at 5.6 km/hr; 5) individually, self-paced. The analyses were carried out on the T_{re} and heart rate responses (HR) during each work and each rest period. There was a significant correlation for the self-paced condition, with fatter men walking slower ($p < 0.05$) than thinner. There were few significant correlations between T_{re} (or heart rate) and body fat during rest or work. In both heat conditions [2) and 3)], the change in HR during the first 25 min walk was correlated with % body fat ($p < 0.05$), with fatter men having the greater increase; the only other significant correlation was for HR fall for the first rest period at 49°C, where fatter men started significantly higher. Thus, at least for conditions producing T_{re} of 39.1°C and HR $\simeq$ 145, relative fat had little influence on these responses to heat, except for a more rapid initial HR. This may not be true for less fit men than for these overweight soldiers. We conclude that it is not being fat per se that is a disadvantage in the heat, but the lact of physical fitness which usually accompanies being fat.

Title of Study: Energy Cost of Transporting Loads by Manpowered Auxiliary Devices

Investigators: Michael F. Haisman, Ph.D.; F. R. Winsmann; and R. F. Goldman, Ph.D.

Background:

Extensive studies of the various devices for carrying load on the back, various load position and the elusive goal of reducing the total weight carried by the soldier have led to the conclusion that, even though individual items can be successfully made less heavy, the total load the soldier has carried throughout history, and will carry in the future, is almost independent of the weight of the individual items, and there is no way to reduce the energy cost per pound of weight carried at a given speed. There are many ways to make load carriage more costly by improper positioning of loads, but each pound exerts a very predictable energy cost at a fixed speed of march. Thus, the only potential for conserving the energy of the soldier on the march would appear to be removal of the load from his back to an auxiliary device. While we are aware of the problems and have many objections to adding new line items of equipment which may be impractical under a variety of field conditions, nevertheless, investigations into the potential benefits of load carriage by man powered carts is, we feel, appropriate. Whether or not such devices are ever adopted would depend on the relative benefits and development problems which may arise should development be warranted by the results of these studies.

Conclusions:

Seven male volunteers, mean age 21 years, pushed 4 types of hand-carts at 1.56 m/sec, on a level treadmill and on an outdoor asphalt circuit. The carts (A, 4-wheel, B,C,D, 2-wheel) had the following wheel diameters: A, rear 30 cm, front 15 cm; B, 50 cm; C, 40 cm; D, 35 cm. Each cart was loaded to achieve a total weight of 50 kg. Three measurements of energy expenditure were made during each 30 minute walk. The mean value for all carts for the treadmill walks was 511 watts (S.D. 52), which was closely similar to the mean for the outdoor circuit 512 watts (S.D. 45). Cart A was found to require the lowest energy expenditure, 478 watts (S.D. 37) and Cart D the highest, 551 watts (S.D. 41). With Cart A, the energy cost for the load carried on the cart, independent of cart weight, was only 12% of what it would have been had the load been carried on the back. Thus, appreciable energy cost savings can be achieved with this type of device on a fairly level terrain.

Future Plans:

A study is planned for this summer to take the largest wheeled carts available (66 cm) into the field and evaluate the energy cost of pushing and/or pulling cart loads based on an individual soldier pushing the combat load carried by the other three members of his fire team; i.e. a total load on the cart of approximately 80 kgs. The terrain to be investigated will include light brush, gravel roads and sand. Since this concept was recently mentioned by officers at the US Army Rangers School, Ft. Benning, Georgia, who were most interested to learn that we had been studying the possibilities of this approach, a collaborative study with the Ranger Units at Ft. Benning is contemplated if promise is shown in these field studies.

Title of Study: Voluntary March Rate over Natural Terrains

Investigators: R.G. Soule, Ph.D.; M.F. Haisman, Ph.D. and R.F. Goldman, Ph.D.

Background:

Last year we indicated our plans for a field study to assess the validity of using the 425 kcal/hr ± 10% estimate of energy cost for the self-paced energy expenditure at which a man will voluntarily work, in combination with the coefficients which we have developed for various terrains, and differing load placements, in order to predict the time it will take a soldier to cover a given distance across a specified terrain.

Conclusions:

One to three mile segments of light brush, gravel road, blacktop and heavy brush terrains were selected to provide a continuous course consisting of 1.85 km blacktop road, 1.82 km gravel road, 1.2 km light brush, and 1.2 km heavy brush for a total distance of 6.1 km. Twelve men walked individually at their own "fastest possible" pace over this course, each starting at a different section (randomized) carrying a 30 kg or 15 kg pack or 3 kg in each hand in a burlap sack or 2 kg on each foot, as a heavily weighted boot. Times to traverse each terrain, predicted considering the above parameters compared with the actual measured times very closely as shown in the following table.

	30 kg		15 kg		3 kg/hand		2 kg/foot	
	Meas	Pred	Meas	Pred	Meas	Pred	Meas	Pred
Blacktop	21.2	21.3	18.5	19.1	18.5	19.0	18.4	17.8
Gravel	24.0	22.7	19.8	20.2	19.2	19.9	19.2	18.7
Lgt Brush	17.2	17.0	15.9	15.0	15.0	14.6	14.4	13.7
Hvy Brush	24.2	21.3	19.9	17.9	20.6	16.9	17.9	16.0

Although it appears that the heavy brush in this study was more difficult than allowed for by the terrain prediction coefficient ($\eta = 1.5$), the results are most encouraging and suggest that this approach is a reasonable way to predict the time troops will take to march given distances over specified terrains. The results also, of course, thoroughly validate our concept that 425 kcal/hr does represent the maximum voluntary hard work rate which troops will adopt if allowed to.

(83103)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6145	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	047
b. CONTRIBUTING				
c. COMPARABILITY	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code): (U) Effects of Environmental Stressors on Military Performance Interactions with Extended Operations, Unusual Activity-Rest Cycles (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 002300 Biochemistry; 012900 Physiology; 013400 Psychology; 005900 Environmental Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	1.8	145.0
FISCAL YEAR CURRENT 73	2.5	200.0

19. RESPONSIBLE DOD ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Francesconi, Ralph P. Dr.
TELEPHONE: 955-2877
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: R.F.Goldman, Dr.
NAME: R.D. Cahoon, Dr. DA

21. GENERAL USE
Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code): (U) Continuous and sustained operations; (U) Activity-rest cycles; (U) Heat; (U) Cold; (U) Altitude; (U) Motor performance; (U) Fatigue mental

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Rapid deployment of troops to desert, jungle, arctic, or mountain areas may require simultaneous adjustment to the adverse climate as well as to unusual activity-rest cycles or periods of sustained sleep loss. Such stressors, combined with the effects of rapid time-zone crossing and disrupted periodicities, may cause performance decrements and hence limit combat effectivness. Research will characterize these human limitations at biochemical, physiological, and behavioral levels, and investigate methods of attenuating the effects on military personnel.

24. (U) Thus the effects of these environmental stresses will be characterized on an interdisciplinary basis: a. metabolic (amino acid metabolism centrally and peripherally, circadian periodicities); b. physiological (reflexes, physical work capacity, self-paced work levels); c. behavioral (alertness, cognitive function, complex decision making).

25. (U) 71 07 - 72 06 Sleep Deprivation: Subjects worked on the self-paced treadmill for 1 hour every 6 hours during a period of continued wakefulness lasting a total of approximately 36 hours. Results indicated that voluntary hard work levels are not significantly affected during 36 hours of sleep deprivation. Cold Exposure: Final results of a study in which 6 test subjects were exposed to a 48-hour cold stress after a 7 day stabilization and control period demonstrate that cold exposure does not affect the periodicity of rectal temperature although absolute levels were reduced. Cold exposure increased the catabolism of the pivotal amino acids tryptophan and tyrosine as evidenced by decreases in levels of these amino acids in plasma as well as increases in urinary breakdown products. These metabolic alterations may be effected by increased adrenocortical activity during cold exposure.

*Available to contractors upon originator's approval.

DD, FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A, 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE.

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Title of Study: The Effects of Acute Cold Exposure on Circadian Periodicity in Man as Monitored by Alterations in Tryptophan and Tyrosine Metabolism

Investigators: Ralph Francesconi, Ph.D.; Aubrey E. Boyd III, MAJ, MC; and Milton Mager, Ph.D.

The term "circadian periodicity" has been coined to describe a wide variety of physiological, metabolic, and behavioral functions that display a remarkably consistent pattern of maximal and minimal levels of activity on a 24-hour basis. It has been demonstrated in man that a number of factors, e.g., environmental stressors, rapid transition across time zones, altered sleep-wakefulness cycles, sleep deprivation, encapsulation, may be responsible for the disruption or desynchronization of a number of these daily rhythms. It has been further demonstrated that such desynchronization of normal cycle patterns may be associated with general malaise, fatigue, and performance decrement. We have, therefore, focused our attention of the effects of various stressors on the periodicity of key metabolic and physiologic functions which may be related ultimately to performance.

In this study we achieved control periodicities by requiring six volunteer Army test subjects to remain for 5 days under strictly regulated conditions of diet and caloric intake, sleep-wakefulness cycles, ambient environmental conditions, clothing, and daily activity. This stabilization period was followed by a 48-hour control period, a 48-hour exposure to acute cold stress (58°F, shorts and socks only) and a 48-hour recovery period. Monitoring Rectal temperatures, monitored at four hour intervals during the waking hours demonstrated a well-defined periodicty which persisted during cold exposure, although significant depressions occurred during this period. Adrenocortical output was affected during cold exposure as evidenced by disruptions in the daily periodic oscillations of both plasma and urinary cortisol levels. Although total plasma amino acid concentrations were unaffected, there was a highly significant reduction of two important amino acids - tryptophan and tyrosine. Marked increases in the urinary output of two major metabolites of tryptophan - kynurenic and xanthurenic acids - suggested that the changes in plasma tryptophan was mediated through an increase in the activity of the catabolic liver enzyme - tryptophan oxygenase. In summary, we have demonstrated significant effects of acute cold exposure on tryptophan and tyrosine metabolism in humans. These effects seem to be mediated by

by catabolically-active hepatic enzymes known to be induced in humans by adrenocortical hormones. These results gain added significance since physiological changes in plasma tryptophan levels affect concentrations of brain serotonin, a substance intimately related to the control of human behavior and performance by the central nervous system.

(83104)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6123	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	048
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Biomedical Impact of Military Clothing and Equipment Design including the Section f Crew Compartment Environments (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

013300 Protective Equipment; 022400 Bioengineering

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
64 01		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:

b. NUMBER:*

c. TYPE: d. AMOUNT:

e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	2.6	188.7
FISCAL YEAR CURRENT 73	3.0	231.0

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL

NAME: Jones, LeeRoy G. COL

TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst of Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME:* Breckenridge, John R. Mr.

TELEPHONE: 955-2833

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Goldman, Ralph F. Dr.

NAME: DA

21. GENERAL USE

Foreign Intelligence not Considered

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Protection; (U) Biophysics; (U) Military Clothing; (U) Heat; (U) Cold; (U) Wind

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Investigate heat and moisture exchange in the Man-Clothing Environment systems, to provide a basis for improving thermal protection and recommending environments for crew compartments in military vehicles, and for increasing soldier effectiveness.

24. (U) Analysis of materials, uniforms and/or equipment items on heated "sweating" flat plates and copper manikins indicate the nature of changes in heat and moisture exchange produced by such items. Results provide guidance for military designers and identify stressful items or environments. These can be verified with soldiers under controlled chamber environments or in field studies.

25. (U) 71 07 - 72 06 Study of the increase in insulating value with reflective layers was continued on various fabric systems, and using ski suits with several lining constructions, reflective arctic clothing liners, and handwear and footwear items incorporating metallized layers. Copper manikin insulation tests were run on 3 fireman's turnout coats for National Bureau of Standards; four wet suits were also evaluated in water for the Navy, and 25 different combinations of sleeping bags and pads, with and without clothing on the manikins, were measured for AMC developers. The capabilities of a production model Engineer Ordnance Demolition (EOD) suit to protect from -40°F to 110°F have also been investigated using a sectional manikin. Two types of Japanese mukluk-style footwear, standard US military footwear, and commercial footgear were evaluated on the sectional copper foot. Studies have been initiated on the difficult problem of direct translation from "static" copper manikin values of clothing insulation and sweat evaporative impedance, to the actual values of these two parameters when the uniform is worn by an active soldier. Such "pumping coefficients" have been derived empirically for a number of standard uniform systems using data from extensive physiological chamber studies of active men.

*Available to contractors upon originator's approval.

Title of Study: Relationship Between Clo Values of Footwear and Foot Cooling Time-Constant for Human Male Subjects

Investigator: Leander A. Stroschein

Background and Approach:

The relationship between the insulation properties of footwear ("clo" values) and foot cooling-time is the major element for a predictive model of foot cooling. The basic approach was to use data from a previous study (Foot Cooling Rates as a Function of Footwear) and verify this relationship with data from another study (Onset of Extremity Cooling). Only four critical points: big toe, little toe, heel, and instep were considered. A specialized curve fitting program was developed for a Wang 700 series calculator to fit the general $A + Be^{kt}$ equation to the raw data, where k is the desired cooling time-constant and A is the equilibrium temperature (T_e). The clo versus k relationship for subjects wearing the same type footwear was determined, using a statistically derived mean of k.

Progress:

The determined values for the big toe and little toe in seven types of footwear were 145 and 180 min/clo, respectively. The relationship tends to be linear, ranging from 0.5 to 1.6 clo over the toe cap for five types of footwear, but two other types showed a marked offset or discontinuity in the curve. For this reason an investigation of the measured clo values of the footwear using the copper foot was carried out and will be reported separately. The time-constants for the cooling-time prediction at the heel and instep are extremely variable causing the present processing techniques to become unstable. This variability must be caused by the subject shifting his foot position within the footwear varying the cooling rate by each position change.

The present processing technique provides an interesting by-product, i.e., computed heat flow (q). Values of q thus far computed appear to be reasonable values that one might expect for the various footwear used. These computed values of q can be verified by measured values from small heat-flow plates in future studies.

Future Plans:

Future studies will be in four major areas: 1) the correction of clo values for effective wind speed, 2) curve fitting techniques to detect onset of cooling, 3) data smoothing techniques to deal with artifacts such as altered foot position within the footwear, and 4) verifying the computed heat flow (q) values with measured values.

(83105)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6146	72 07 01	DD DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO. / CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	044
b. CONTRIBUTING				
c. (CONTRIBUTING)	CDOG 141 (2a)			

11. TITLE (Procode with Security Classification Code): (U) Prevention and Treatment of Disabilities Associated with Military Operations in the Cold (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012900 Physiology; 005900 Environmental Biology; 003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE

FISCAL YEAR	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
PRECEDING 72	3.0	207.9
CURRENT 73	3.8	260.0

19. RESPONSIBLE DOD ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Newman, Russell W. Dr.
TELEPHONE: 955-2801
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Goldman, Ralph F. Dr.
NAME:

21. GENERAL USE
Foreign Intelligence Considered

DA

22. KEYWORDS (Procode EACH with Security Classification Code): (U) Cold Injury; (U) Frostbite; (U) Thermoregulation; (U) Microcirculation; (U) Acclimatization; (U) Performance Decrement; (U) Psychomotor Skills

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Procode text of each with Security Classification Code.)

23. (U) Measure and describe: the effects of cold on military performance, the effects of local and/or general cold exposure in inducing damage or reducing man's efficiency; the biological defenses which minimize, delay or repair the damage,from cellular to the intact organism level (soldier, animal, or model).

24. (U) A multi-faceted approach will emphasize: (1) actual or potential biochemical histological, and/or physiological changes associated with the site of cold injury; (2) techniques for initiating and strengthening natural defenses against the effects of cold (conditioning, acclimatization, indoctrination) and study of their practical limitations and (3) types and extent of military performance adversely affected by cold (manual dexterity, target detection, vigilance, problem solving). Studies will use animal or human subjects, as appropriate.

25. (U) 71 07 - 72 06 It was found that wetting the finger, by water, exposing to blowing snow or pre-heating the hand, enhanced the susceptibility to frostnip, while cooling the forearm or dehydrating the skin by bicarbonate soaking decreased frostnip. Alcohol ingestion prior to exposure appears to protect against frostnip, but smoking does not change the incidence. Air temperature was found to be more important than wind speed in frostnip, raising questions about the present wind chill index. Frostnip experience with a large number of exposures now allows the skin temperature immediately before freezing to be characterized at levels which appear associated with different environmental conditions, with and without supercooling. Finger heat losses were compared to whole hands and showed greater loss per unit of area, with the greatest proportional loss in the finger tips. A mathematical model was developed for foot cooling and tested against various types of footwear; prediction was good except when foot position was changed in the boot.

*Available to contractors upon originator's approval

Title of Study: Effect of Skin Hydration on Finger Cooling

Investigators: G.W. Molnar, Ph.D.; A.L. Hughes, M.D.; O. Wilson, M.D.; R.F. Goldman, Ph.D.

Background:

In our extensive experience with induction of frostnip in the laboratory, using the frostnip apparatus reported previously, as reported last year pre-exposure to heat did not reduce susceptibility to frostnip, but in fact increased susceptibility. This had been tentatively attributed to the wet skin induced by the heat. The studies were continued with dry versus wet finger exposures, and by introduction of blowing snow (freezing moisture droplets) into the air stream.

Conclusions:

The middle phalanx of a finger of seven subjects was exposed in duplicate tests, once dry and once wet, to a wind stream of 6.8 m/sec at -15.0°C. Both non-Newtonian and Newtonian cooling were somewhat faster for the wet than for the dry skin. The difference can be ascribed to an increment of heat transfer by evaporation from the wet skin. The actual time difference to reach the super-cooled temperature at which the wet skin started to freeze, however, was only 0.7 minutes greater for the dry skin. Freezing occurred in 6 of the 7 cases of wet skin (cold-induced vasodilatation supervened in the seventh case), but only 2 cases with dry skin. It is concluded that water in the corium precipitates crystallization at a higher supercooled temperature than supercooling can proceed to in the dry skin without crystallization.

The studies with blowing snow were even more impressive, with frostnip appearing in an extremely short exposure, far before what one would have anticipated.

Title of Study: Effect of Environmental, Physiologic, Pharmacologic and Local Tissue Alterations on Susceptibility to Frostnip

Investigator: Donald C. Fink, CPT, MC

Background and Approach:

Continuing the established method of investigating frostnip (experimental frostbite) carried out in previous years, several factors were investigated to determine their effect on altering frostnip susceptibility.

Progress:

Ingestion of alcohol prior to frostnip exposure appears to exert a protective effect and prevents tissue cooling from the exposed finger and enhances cold induced vasodilatation (CIVD). Smoking neither inhibits nor enhances frostnip. Both wetting the skin and soaking to increase finger water content greatly increase incidence of frostnip, as does addition of blowing snow to the air stream to which the finger is exposed. Analysis of relative importance of wind and temperature in production of frostnip showed temperature to be much the more important factor. For a given windchill, a low temperature with little wind produces a much greater incidence of frostnip than when the skin is exposed to a higher temperature with more wind at the same windchill. Bicarbonate soaking of the finger, which has been shown to exert a dehydrating effect on the stratum corneum, results in a much lower incidence of frostnip as compared to a soaking in plain water or exposure of the unsoaked finger. Exposure to freezing temperatures was found to greatly reduce nerve conduction under the affected skin with very rapid recovery in those fingers cooled but not frostnipped, while recovery required a period of days in fingers which were frostnipped. Cooling of the forearm prior to freezing a finger produced a decreased incidence of frostnip, by stimulating CIVD in the finger via an axon reflex so that protection was afforded the finger prior to frostnip challenge. Heating the hand before and during the frostnip exposure of the finger greatly increased the incidence of frostnip. Heat messages to the spinal cord overwhelm the cold message from the finger and blocks the axon reflex.

Title of Study: Finger Heat Loss in Relation to Water Temperature in a Water-Bath Calorimeter

Investigator: Russell W. Newman, Ph.D.

Background and Rationale:

Previous studies on hands and feet in the water-bath calorimeter have indicated that hands lose more heat than feet at all water temperatures used, presumably because: (1) fingers represent a greater proportion of hand surface area than do toes of foot surface area, and (2) probable differences in blood flow per unit of tissue. Both hands and feet show a marked increase in heat loss in water colder than 16°C, possibly caused by a relaxation of vaso-constrictor tone. This type of study was extended to include the fingers (excluding the thumb) over the same range of water temperatures and with different finger segments (distal only, distal + medial + proximal) in the calorimeter.

Conclusions:

Fingers showed the same marked heat loss increase in water below 16°C seen in the total hand and foot, and, presumably, for the same reason. Heat loss at all water-bath temperatures was directly related to the amount of finger exposed, i.e., a whole finger lost more heat than just the tip of a finger, and an entire hand lost more heat than just the four fingers. However, when size and shape are considered by expressing the heat losses as either per unit of surface area or mass, the distal segment lost far more heat than the middle or proximal segments, and whole fingers lost more heat than the entire hand. This is not a function of cold-induced vasodilitation (CIVD) which is more dramatic in fingers than in the remainder of the hand, because the differences persisted when CIVD was eliminated from the analysis. It may be a function of vasculature, but is more probably a simple matter of reverse-wicking in which most of the heat transfer occurs near the water level so that a short wick of a given diameter is more efficient for its size than a longer wick. The heat loss in the stirred water-bath was convective in nature, but the same result should occur if all or only the tips of the fingers are exposed to cold air to perform manual operations, including the conductive heat loss through contact with cold objects.

(83106)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6147	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	050
b. CONTRIBUTING				
c. [illegible]	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code): (U) Prevention and Treatment of Disabilities Associated with Military Operations in the Heat (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 016200 Stress Physiology; 013400 Psychology; 003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	4.0	180.4
	CURRENT 73	4.0	210.0

19. RESPONSIBLE DOD ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME: USA Rsch Inst of Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Fine, Bernard J. Dr.
TELEPHONE: 955-2855
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Mager, Milton Dr.
NAME: DA

21. GENERAL USE
Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code): (U) Heat Stress; (U) Heat Tolerance; (U) Heat Disabilities; (U) Body Temperature; (U) Military Disabilities

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) The objectives are the identification, prediction and prevention of heat-induced disabilities which critically impair the performance of military missions and the development of methods of treatment of casualties due to such conditions as dehydration, heat stroke and heat exhaustion collapse.

24. (U) The knowledge and techniques of relevant sciences and clinical medicine are applied to the solution of problems of military operations in hot environments. Approaches include: (a) assessing and predicting performance of tasks, e.g., vigilance, mental activity, march rate, in heat; (b) determining effects of heat on biophysical, physiological, biochemical and psychological functioning; (c) defining effects of such factors as solar load, clothing and equipment interference and soldier's work requirements on his tolerance limits; and (d) studying methods of prevention and treatment of heat casualties, and improving their applicability in military situations.

25. (U) 71 07 - 72 06 (1) Significant decreases in serum magnesium were found in normal Ss after prolonged exercise in the heat. These were related to sweat losses in the heat; (2) Ss at Ft. Polk, LA with heat exhaustion had marked respiratory alkalosis which may explain symptoms of heat illness seen in many patients who are not salt or water depleted; (3) Investigation of L-DOPA as a possible therapeutic agent in heat stroke has demonstrated a centrally mediated drop in rectal temperature in some normal males following oral administration; (4) Based on data from mice and men, it is postulated that glucopenia produced by insulin and 2-Deoxyglucose in the central nervous system affects brain centers that are involved with the control of peripheral heat production and is accompanied by a decreased utilization of available substrate; (5) Amount of body fat was found not to be related to rectal temperature responses of men working in the heat.

*Available to contractors upon originator's approval.

DD, FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A, 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE.

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Title of Study: Epidemiologic Study of Heat Stroke at Ft. Polk, Louisiana

Investigators: George A. Beller, MAJ, MC, and A. E. Boyd, MAJ, MC

Background:

Heat stroke is relatively uncommon. When it occurs, however, it is one of the most serious medical emergencies seen in military recruits undergoing intense physical training in a hot humid environment. The presence of a "heat ward" at Ft. Polk, LA., to which heat casualties are immediately transported from the field, afforded a unique opportunity to study clinical heat stroke in a high risk population.

Progress:

During the years from 1969 to 1971, there were 13 cases of heat stroke evaluated at Ft. Polk, LA. The mean rectal temperature on admission in these patients was 107.6^{o}F. The prevalence of heat stroke was greatest during the 3rd week of basic training. The mean weight of these soldiers was far greater than would be expected for their mean height and age, thereby confirming previous observations by others that obesity is a risk factor in heat stroke. Eighty-five percent of these patients were engaged in marching activities when initial symptoms of heat stroke developed. Treatment was prompt in all cases, using conventional therapeutic measures. Interestingly, all 13 patients survived without obvious sequelae despite marked hyperpyrexia.

Conclusions:

With only 13 documented cases reported over a three year period, heat stroke is not a major medical problem at Ft. Polk. In addition, it appears that mortality can be eliminated and morbidity reduced by institution of vigorous treatment soon after the development of symptoms and signs of this heat illness.

Title of Study: The Role of Primary Respiratory Alkalosis in Heat Exhaustion in Military Recruits

Investigators: A. E. Boyd, III, MAJ, MC, and George A. Beller, MAJ, MC

Background:

Hyperventilation has been described as a normal physiologic response to heat stress. In order to evaluate the role of hyperventilation in the pathogenesis of heat exhaustion, all heat casualties evacuated to the Fort Polk, LA heat ward during a 2 week period were studied by the investigators, who were also responsible for the primary medical care of the patients.

Progress:

There were 17 patients with heat exhaustion and one with heat stroke in whom detailed clinical data, and arterial and venous blood samples were obtained immediately upon admission. Of the 17 patients with heat exhaustion, 11 presented initially with syncope, 16 had severe muscle cramps, 9 had frank tetany and all were hyperventilating (mean respiratory rate 26/min) on entry. The mean admission rectal temperature in the group was 100.4 ± .25°F. Mean arterial pH and pCO_2 values were, respectively, 7.62 ± .03 and 23.5 ± 2 mmHg, while the mean arterial lactate and pyruvate concentrations were in the normal range, indicating the presence of a marked primary respiratory alkalosis in this group. On the other hand, the only patient seen with heat stroke had an arterial pH of 7.28 associated with hyperlactemia. The mean serum sodium, potassium, creatinine and magnesium concentrations were normal in the heat exhaustion patients. Only 2 patients appeared to be severely dehydrated as reflected by clinical signs, hypernatremia and azotemia.

Conclusions:

Volume depletion is considered an important etiologic factor in heat-exhaustion syndrome. This study suggests that many of the manifestations of heat exhaustion may be the result of an exaggerated hyperventilatory response to heat stress in patients who are not salt or water depleted. Although hyperventilation can lead to hyperlactatemia in some clinical states, it does not appear to be a significant problem in hyperventilation associated with heat stress.

Title of Study: The Role of Hyperventilation in Man's Response to Heat

Investigators: A. B. King, MAJ, MC and S. M. Robinson, Ph.D.

Background:

Hyperventilation is a frequent accompaniment in situations of severe heat stress, particularly in unacclimatized individuals. We have reported previously that when men are exposed to the heat, and voluntarily hyperventilate, an increase in core temperature is noted. This hyperthermia is related to the hypocapnia accompanying the hyperventilation and is associated with a fall in blood flow to the skin and a transient decrease in sweat rate. Ongoing studies have been designed to evaluate involuntary hyperventilation when men were exposed to extreme conditions of heat and humidity.

Progress:

The increase in ventilation (measured by a fall in end-expiratory % CO_2) in response to a rising rectal temperature was studied in subjects at a temperature of 49°C/38°C (dry bulb/wet bulb). A linear relationship was obtained for each individual when the change in rectal temperature was compared to the change in % CO_2, and is referred to as thermal sensitivity. The mean for the group was 0.8% CO_2/1°C, with individual sensitivities ranging from 0.3 to 4.4% CO_2/1°C. Further experiments revealed that thermal sensitivity is not affected by acclimatization to heat, thus suggesting that the decreased incidence of hyperventilation in acclimatized individuals is related to a reduced temperature stimulus rather than a diminished thermal sensitivity.

Title of Study: Metabolic Aspects of Thermoregulation

Investigators: Milton Mager, Ph.D; Sumner Robinson, Ph.D. in collaboration with Norbert Freinkel, M.D., Northwestern University Medical School

Background:

Thermoregulatory dysfunction or failure is manifested by a number of disabilities potentially affecting a variety of military activities. Included are those disabilities caused by heat, e.g., heat stroke, heat exhaustion, heat syncope. Rational therapy is hindered by a lack of knowledge of the mechanisms underlying these syndromes, particularly of the biochemical and neurochemical relationships. Our interests have been directed to defining the impact of the metabolic milieu on thermoregulation, with emphasis on the hypothermia noted in man with hypoglycemia, particularly insulin hypoglycemia. It has not been established whether this phenomenon results from limitations in the extracellular concentrations of all fuels or from selective deprivation of glucose within the cells. Moreover, it has not been clarified whether the hypothermia is triggered by primary actions on peripheral thermoregulation mechanisms or on thermoregulatory centers in the central nervous system. We postulated that 2-deoxy-D-glucose (2-DG) might provide an effective experimental tool for examining the above question. 2-DG blocks intracellular glucose utilization, and thereby causes intracellular glucopenia sufficient to activate the sympatho-adrenomedullary system and cause concomitant hyperglycemia and hypothermia.

Progress:

We have infused standard amounts of 2-DG into normal male volunteers to compare thermal regulatory changes with concurrent excursions in plasma glucose, immunoreactive insulin and growth hormone. Following 2-DG infusions, rectal temperatures in normal humans fell to nadir levels in 2 to 2-1/2 hours coincident with maximal increases of plasma growth hormone. Temperatures remained below basal values for six hours despite increases in plasma glucose and insulin and urinary catecholamines. The findings indicate that the hypothermia is conditioned by intracellular glucopenia rather than the availability of circulating glucose or glucoregulatory hormones.

We have also injected graded quantities of 2-DG into the cerebral ventricles or peripheral veins of mice to assess the relative change in rectal temperature initiated by cerebral as opposed to peripheral glucopenia. Reductions in rectal temperatures were elicited by injection of 2-DG via either route. However, hypothermic potencies were greater with the intracerebral administration, indicating that exclusion of glucose from central rather than peripheral sites plays a major role in the hypothermia. Oxygen consumptions were reduced with 2-DG, and the changes generally paralleled the decrease and return of rectal temperature to normal values. It is postulated that the glucopenia produced by 2-DG in the CNS affects centers in the brain that are involved with the control of peripheral heat production, and is accompanied by a decreased utilization of available substrate.

Future Plans:

The relationship of the hypothermia of cellular glucopenia to possible central thermoregulatory neurotransmitters will be determined by attempting to blunt the effects of 2-DG (or insulin) with various adrenergic blocking agents.

(83107)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6148	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L.	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.21.10.A	3A062110A827	00	051
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code): (U) Prevention and Treatment of Disabilities Associated with Military Operations at High Terrestrial Elevation (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012600 Pharmacology; 005900 Environmental Biology; 013400 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	6.0	347.8
FISCAL YEAR CURRENT 73	6.0	300.0

19. RESPONSIBLE DOD ORGANIZATION
NAME:* USA Rsch Inst Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Beller, George A., MAJ, MC
TELEPHONE: 955-2887
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Landowne, Milton Dr.
NAME: Kobrick, John L., Dr. DA

21. GENERAL USE
Foreign Intelligence Not Considered

22. KEYWORDS (Precede each with Security Classification Code): (U) Hypoxia; (U) Disabilities; (U) Performance; (U) Mountain Sickness; (U)Combat Effectiveness; (U)Pharmacology; (U)Vision; (U)Sensory Processes

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Exposure of soldiers to high terrestrial elevation results frequently in reduced efficiency as well as disabilities which are incompatible with the successful completion of military operations. The purpose of this unit is to investigate methods of prevention and treatment of these performance decrements and disabilities.

24. (U) Studies will be conducted in animals and man to (1) determine the mechanisms of the disorders which occur at altitude; (2) assess and predict the performance of perceptual and cognitive taska, e.g., target detection, decision making, speed of reaction; (3) evaluate the efficacy of pharmacological agents in preventing or reducing performance decrements and illness; (4) enhance the rate of adaptation to this environment.

25. (U)71 07 - 72 06 Animal - There was no significant change in myocardial contractility in intact conscious dogs following two weeks of chronic hypobaric hypoxia, although resting cardiac output and stroke volume decreased. Human - At altitude, arterial PO_2, O_2 saturation and content were persistently higher on a high carbohydrate diet, due to increased ventilation. Plasma renin activity and urinary aldosterone excretion were diminished during three days at altitude. A portable CO_2 breathing apparatus was utilized by subjects at altitude and resulted in increased alveolar ventilation. A double blind field study of the efficacy of acetazolamide in the prevention of AMS was undertaken. Forty-eight hour exposures in the hypobaric facility corroborated former findings of engorgement, increased diameter and tortuosity of retinal vasculature. These changes did not immediately abate after return to normoxia. Decrements in vigilance in an Army Radio Communications Network Monitoring task above 13,000' were reduced by using highly motivated, radio-trained personnel. Critical evaluation of CO_2 rebreathing methods for estimating cardiac output disclosed sources of variability.

*Available to contractors upon originator's approval.

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Title of Study: Effects of Chronic Hypoxia on Myocardial Contractility

Investigators: George A. Beller, MAJ, MC; Samuel R. Giamber, MAJ, MC; and J. T. Maher, Ph.D.

Background:

It has been shown that following 10 days to 2 weeks exposure to a hypoxic environment there is a fall in cardiac output which is the result of a progressive decrease in stroke volume. It has been suggested that one mechanism to explain this diminished stroke volume during chronic hypobaric hypoxia is a direct depressing action of hypoxia on myocardial contractility. The aim of this study was to determine whether the contractile state of the canine ventricular myocardium is depressed following prolonged exposure at an altitude of 14,000 feet in a hypobaric chamber.

Progress:

Seven dogs underwent left heart catheterization during a sea level control period, and following 14 days at altitude. Preliminary results show no significant diminution of myocardial contractility following the prolonged hypoxic stress.

Conclusions:

The observed decrement in cardiac output and stroke volume associated with chronic hypoxic stress is probably not secondary to a depression of the left ventricular contractile state. Decreased ventricular function, as reflected by cardiac output, is most likely due to a diminished filling pressure of the left ventricle related to contraction of plasma volume.

Future Plans:

Further investigation of possible alterations in myocardial contractility in man is warranted since results in the dog model may not be applicable to humans.

Title of Study: Effects of Ouabain During Normoxia and Hypoxia in Intact Conscious Dogs

Investigator: G. A. Beller, MAJ, MC

Background:

Decreased resting cardiac output and work performance has been demonstrated in both man and animals following exposure to chronic hypobaric hypoxia. Digitalis glycosides exert a positive inotropic effect on the myocardium, characterized by an increased dp/dt during systole. These cardiactive compounds might be effective in either the prevention or reversal of this hypoxic-induced decrement in cardiac performance. Experimental hypoxia studies in anethetized animals, however, have shown a lowered threshold for digitalis toxic arrhythmias. Because anesthesia alone may alter the myocardial action of digitalis, a study of the toxic effects of ouabain (a rapidly acting cardiac glycoside) was undertaken in 7 conscious dogs during normoxia and acute hypoxia. It was felt that if, in unanesthetized animals, hypoxia was associated with a significant increase in myocardial sensitivity to ouabain, then this would either preclude the use of digitalis in human field studies at altitude or indicate that the usual dosage of the drug be reduced.

Progress:

Hypoxia experiments were performed in the hypobaric chamber controlled at 446 mmHg pressure (14,000 feet), 2 weeks following a normoxic sea level study. During both studies a 7.5 μg/kg intravenous loading dose of ouabain was followed by an ouabain infusion (3 μg/kg/min) to electrocardiographic evidence of toxicity. Arterial pH, PO_2, PCO_2, and O_2 saturation were determined prior to ouabain administration, at the onset of cardiac toxicity, and 15 minutes following the appearance of toxicity. During both normoxia and hypoxia, toxic doses of ouabain were associated with a significant rise in arterial pH, fall in PCO_2, and rise in PO_2 and O_2 saturation. During normoxia the mean arterial pH rose from 7.39 ± 0.04 (S.E.) to 7.70 ± 0.06, arterial PCO_2 fell from 42 ±2 to 15 ± 3 mmHg, PO_2 rose from 83 ± 6 to 117 ±9 mmHg. During acute hypoxia the mean arterial pH rose from 7.47 ± 0.02 to 7.70 ± 0.09, arterial PCO_2 fell from 33 ± 2 to 15 ± 4 mmHg, PO_2 rose from 40 ± 3 to 58 ± 16 mmHg. The mean toxic dose of ouabain was significantly less ($P < 0.05$) during hypoxia (72 ± 14 μg/kg) than normoxia (79 ± 12 μg/kg).

Conclusions:

In conscious dogs, under conditions of both normoxia and hypoxia, toxic doses of ouabain produced a striking respiratory alkalosis secondary to a profound hyperventilatory response to the drug. Increased sensitivity to the arrhythmogenic effects of ouabain during acute hypoxia was also demonstrated.

Title of Study: Control of Water and Electrolyte Metabolism at Altitude by the Renin-Aldosterone System

Investigators: R. P. Hogan, MAJ, MC; T. A. Kotchen, MAJ, MC; A. E. Boyd, MAJ, MC; L. H. Hartley, M.D.; T.K. Ki, M.D.; J.W. Mason, M.D.

Background:

Plasma volume is known to decrease over the first few days at altitude and dilution studies have suggested that intracellular volume rises over the same period of time. It has been suggested that increased pressure on brain cells caused by increased intracellular volume, increased cerebral blood flow, and/or increased venous tone may cause the symptoms of acute mountain sickness. Intracellular fluid shifts may occur secondary to alkalosis or withdrawal of mineralocorticoid support. Alkalosis results from hyperventilation at altitude, and decreased aldosterone secretion has been demonstrated in mountain sojourners. However, plasma renin activity has been said to remain normal or to rise slightly on exposure to hypoxia, raising doubts about the control of aldosterone secretion at altitude. A study was undertaken to clarify the relationship between renin and aldosterone at altitude and to look for possible relationships between water and electrolyte metabolism and the occurrence of acute mountain sickness.

Progress:

Ten male volunteer test subjects between the ages of 19 and 23 were studied for 72 hours in a hypobaric chamber at a simulated altitude of 12,000 feet. Subjects consumed a controlled 160 meq sodium, 60 meq potassium diet throughout the study.

Plasma renin activity and urinary aldosterone excretion were decreased. Subjects retained potassium, lost sodium, and had mild water and weight losses. Increased insensible loss was primarily responsible for the negative water balance. Test subjects who experienced the most severe symptoms of acute mountain sickness also showed the greatest decrease in aldosterone excretion at altitude.

Conclusions:

It is concluded that aldosterone secretion at altitude follows usual control mechanisms, contrary to previous reports. It is postulated that the observed depression in renin release is secondary to

decreased renovascular resistance and increased renal blood flow. It is further postulated that fluid and electrolyte shifts secondary to aldosterone withdrawal may be etiologically related to acute mountain sickness.

Future Plans:

A crossover drug study utilizing fludrocortisone and acetazolamide while assessing symptom frequency and severity at altitude is planned for the future.

Title of Study: The Use of Acetazolamide in the Prevention of Acute Mountain Sickness

Investigators: S. Robinson, Ph.D.; D. Horstman, Ph.D.; W. O. Evans, LTC, MSC; and A. Cymerman, Ph.D.

Background:

The efficacy of acetazolamide in the prevention of the symptoms of acute mountain sickness (AMS) has been suggested by several laboratory and field studies. Experimental design in these investigations has generally consisted of random assignment of subjects to drug or placebo groups, followed by exposure to simulated altitude or rapid transport to high terrestrial elevations. A difficulty inherent in this approach is the probability that both the placebo and drug groups contain individuals who are resistant to the effects of high altitude, thus detracting from an evaluation of the full potential of the drug under investigation. We were afforded the unique opportunity of studying acetazolamide in a cross-over design in a field situation, with volunteers from the 4th Infantry Division (Mech) from Fort Carson, Colorado. These men were in training for "Stride the Divide", an adventure walk along the Continental Divide commencing on or about July 1, 1972. A second aspect of this study was to determine whether hypoxic sensitivity, i.e., the response to hypoxic gas mixes at sea level, could serve as a predictor of acute mountain sickness.

Progress:

Approximately 30 volunteer soldiers from Fort Carson participated in this study. The first climb and overnight stay was at Pikes Peak (14,100 feet), while the second climb was a week later at Mt. Elbert (14,430 feet), with the subjects remaining near the summit for two nights. Acetazolamide or placebo were administered for the two days prior to each of the ascents. Preliminary review of the data from symptom questionnaires, as well as the impressions of the investigators, revealed little evidence of AMS in the placebo and drug groups. Some subjects reported mild to moderate headaches after the climb, others were unable to sleep, and nausea and anorexia were also noted. Most of the symptoms seemed to be a reflection of the climbs and the attending fatigue rather than a response to altitude itself, since symptoms other than anorexia were minimal after the first nights at altitude. A number of possibilities to account for the lack of subjective symptomatology include (1) prior

residence at 6,000 feet at Fort Carson, (2) the possibility that the stay at altitude was not long enough to develop symptoms, and (3) the interaction of altitude and exercise. It is interesting to note that four members of the USARIEM investigative team, after residing at Fort Carson for only 4 days, successfully completed the climbs with the subjects and also developed few symptoms of AMS. It does not seem likely that this short a time at an altitude of 6,000 feet would acclimatize them for their ascent to 14,000 feet. Length of time at altitude does not appear to be a factor, for the subjects spent approximately 40 hours in the vicinity of the summit of Mt. Elbert. This study poses the intriguing question as to why so few symptoms of AMS were observed in these subjects at 14,000 feet.

Future Plans:

Studies will be designed to examine whether (1) the heavy physical work involved in climbing to altitude or (2) prior residence at 6,000 feet ameliorates the development of AMS.

Title of Study: Investigation of Auditory Vigilance in an Army Radio Communications System at Altitude

Investigator: Richard L. Cahoon, Ph.D.

Background:

One of the most important activities of the Army is communication. To communicate means to send and receive accurate information on a timely basis. In radio communications, the receiver must often monitor networks for long periods of time during which non-critical messages are being transmitted. It is his job to detect the critical message and to do so accurately.

Previous research in this Institute has shown that the ability of the soldier to remain alert to changes in an auditory stimulus is significantly impaired under hypoxia. Thus, it is reasonable to hypothesize that the auditory monitoring task involved in radio communication will show a decrement when the operators are hypoxic.

Progress:

Two studies testing this hypothesis were performed. The method for both studies involved having subjects listen to a simulated radio communications network in which were embedded critical messages containing the subject's call sign and instructions to press one of five buttons on a panel in front of him. Other messages containing different call signs were mixed with the critical messages to provide a "background noise" to be ignored by the subject. The total task lasted two hours during which each subject received 36 critical messages. Four altitudes were studied: sea level, 13,000 ft., 15,000 ft., and 17,000 ft.

In the first study, permanently assigned volunteer test subjects were used. Their responses were analyzed for the percentage of correct detections, number of false detections, and reaction time. Significant decrements in correct detections occurred above 13,000 ft. These results paralleled those found in previous vigilance research in this laboratory, and suggested that Army monitoring tasks requiring sustained alertness will suffer in hypoxic environments.

The second study considered the effect of training and motivation on this process. TDY subjects were obtained from Ft. Devens, MA; half

the subjects were trained in radio communications and the other half were engineers. None had been used in previous research and all subjects participated on a purely voluntary basis, thus tending to favor naivete and high motivation. The subjects were paid for their participation.

As in the first study, the responses of these subjects were analyzed for performance decrements over the four altitude conditions. No decrements were found, i.e., they performed equally well at all altitudes, although individual differences in performance did arise.

Progress:

The data from research to date indicate that the vigilance decrements found in Army radio communications monitoring at high altitude can be reduced or perhaps eliminated by using highly motivated, well-trained personnel on such tasks. However, these results are the first to differ from a long series of vigilance studies which have shown significant decrements in this process at high altitude. Further study of this inconsistency is needed.

Future Plans:

Future studies will investigate other Army tasks requiring sustained alertness at high altitude. Groups with specified training and background will be used as test subjects to determine the interaction of these variables with vigilance performance.

Title of Study: Evoked Cortical Potential Correlates of Attention Under Hypoxia

Investigator: Richard L. Cahoon, Ph.D.

Background:

Analysis of vigilance decrements under hypoxia found in this laboratory have indicated that the process being affected involves attention to the stimulus. The data suggested that subjects were unable to attend to the stimulus source for extended periods of time at oxygen levels of less than 12.8% (13,000 ft).

To further investigate the process of attention under hypoxia, it is necessary to consider the neurophysiological responses to sensory stimulation that change with level of attention and with oxygen level. The evoked cortical potential is a useful index of such responses. It has become quite well established that when a stimulus of sufficient intensity is presented to the eye or ear, an electrocortical response of specified wave form can be recorded from the scalp. It is also a confirmed finding that this evoked response shows a greater amplitude for stimuli that are attended to than for stimuli that are ignored. The response of the evoked potential to hypoxia is not as well established.

The present study is investigating the visual evoked response of the brain at sea level and at 17,000 feet altitude while the subject is attending to the stimulus and while he is distracted from it.

Progress:

Two preliminary studies have been conducted. In the first, 15 enlisted volunteers served as test subjects. EEG electrodes were attached to the top and back of the head and the subject watched a photo stimulator strobe light which flashed at a rate of once per second. Averaged responses from 64 flashes were obtained from each of several stimuli including a series of incomplete figures which appeared with each flash and which required the subject's full attention to detect. Comparisons of evoked responses to these stimuli with those from the light alone showed no significant difference in amplitude or latency.

A second study used previously untested civilian volunteers to determine whether naive subjects would reflect a higher attention level in

their evoked potentials. In addition to the stimuli used in the first study, an attempt was made to produce potentials to double flashes in accordance with a technique developed by Ciganek to study the effects of distraction on this response. These data are being analyzed.

Future Plans:

A study will be run in the altitude chamber in which subjects' evoked potentials will be recorded at sea level and at 17,000 feet altitude. These responses will be measured while the subject is attending to the stimulus and while he is distracted from it to determine the effect of a hypoxic environment on the brain during these states. Stimuli to be used in this study will be determined from the analysis of data of the preliminary studies.

Title of Study: The Relationship of Oxygen Uptake and Cardiac Output and the Influence of Environmental Factors

Investigator: Milton Landowne, M.D.

Background:

We have previously demonstrated that the relationship between oxygen uptake ($\dot{V}O_2$) and cardiac output ($\dot{Q}$) in exercise is curvilinear, and can be described in terms of a limiting slope, A, which is dependent on the oxygen content of arterial blood, and a coefficient, C, describing the manner in which oxygen extraction increases with exercise of increasing severity.

Progress:

Additional data have been examined. These parameters (A and C) continue to furnish an apt and logical description not only of the relationship, but of the influence of several environmental factors. The summarized status (Table I) is based on an evaluation of material from 262 subjects and includes 17 groups of data from the literature. Exercise was carried out at several levels of severity either at a single or several sessions, performed by pedalling in the upright position in a bicycle ergometer or by walking on a treadmill, and cardiac output was determined by catheterization, indicator dilution or foreign gas inhalation techniques.

Where available, the data for each subject was fitted by an individual curve. Curve parameters A and C are summarized as the means and standard deviations of the subjects in a group or as mean differences and standard errors. When individual data were not available, curves were fitted to averaged data to provide group mean parameters, although characterizing curvature is obscured by averaging data points. The majority of cases provided four coordinate points for analysis (range 3-7), i.e., rest, and three levels of exercise.

The curve fitting procedure is exactly reproducible by computer analysis and has yielded good fits to experimental data. However, since the number of points per curve is small, and single values for biological data may show relatively large deviations and unless weighting factors are known, a "least squares" fit may be a biologically incongruous or impossible description. The constraint needed to fit

curves of appropriate form and direction has been obtained by a modified curve fitting procedure. This utilizes an empirical relation of B to A and derives C and A to minimize the sum of squares of deviations about the regression. The value of A thus obtained has a ration ± S.D. to the arterial oxygen content = 1.50 ± .19.

Plans:

We are continuing to seek for an expression and a derivation procedure which will overcome these relative limitations, i.e., will have the needed constraint to yield plausible values despite biological variability, will be free of empiricism and will provide estimates of limiting slope A which are closer to the arterial content as predicted by theory.

At the same time, since a larger number of points per individual would substantially improve the description of this relationship, we have undertaken to evaluate rebreathing methods for non-invasively determining cardiac output, in the hope that this may provide a means to obtain larger sample sizes.

TABLE I

Summary of Some of the Parameters for the Relation $\dot{V}O_2 = A\dot{Q} + (e^{-CQ}-1)B/C$, Where $\dot{V}O_2$ = Oxygen Uptake and $\dot{Q}$ = Cardiac Output, in Liters/Minute, Normalized to 70 kg Body Weight

	C(Min/L.)	A(l./l.)	N	Source
a.	Men in good health, < 30 yrs old:			
	.076 ± .026	.285 ± .04	63	Various *
	.071 ± .015	.270 ± .02	8	Ekblom 1968
	.083	.250	25	Hanson 1968 (G)
	.114	.261	9	Tabakin 1962 (G)
	.138 ± .047	.361 ± .05	16	Hansen 1966
b.	Men in good health, > 30 yrs old:			
	.081	.272	25	Hanson 1968 (30-39 yrs) (G)
	.098	.259	25	Hanson 1968 (40-49 yrs) (G)
c.	Athletes, < 30 yrs old:			
	.065 ± .030	.33 ± .025	4	Ouellet 1969
	.055	.253	9	Hanson 1963 (G)
d.	Athletes, > 30 yrs old:			
	.087 ± .037	.286 ± .044	14	Hartley 1969
	.054 ± .011	.255 ± .024	9	Grimby 1966
	Influence of Factors; Differences Experimental-Control			
a.	Altitude			
	.056 ± .033	-.065 ± .005 $p < .001$	6	ARIEM *
	-.005 ± .013	-.053 ± .01 $p < .01$	5	Stenberg 1966 *
	.033 ± .017	-.086 ± .012 $p < .0001$	16	Hansen 1966

	C(Min/L.)	A(l./l.)	N	Source
b.	Physical training:			
	-.029 ± .005 p = .004	.019 ± .02	5	Saltin 1966 *
	-.069 ± .035 p = .05	.018 ± .007	8	Ekblom 1968
	-.015 ± .008	-.004 ± .007	15	Hartley 1969
c.	Heat (43.3°C vs 25.6°C):			
	.041	.023	6	Rowell 1966 (G)
d.	β-adrenergic blockade:			
	.058	.109	9 + 7	Epstein 1965 (G)
e.	Females vs males:			
	.027 ± .008 p = .004	-.059 ± .011 p = .001	11 + 12	Astrand 1964 *

* = previously reported

G = group mean

Title of Study: Circulatory Transport of Carbon Dioxide at Rest and During Exercise

Investigator: Milton, Landowne, M.D.

Background:

A "non-invasive" technique for determining cardiac output has long been desired, and would make pertinent study of military tasks more feasible. The fundamental principle used to measure cardiac output or blood flow is based on the identity: Blood flow rate x arterio-venous (A-V) concentration difference of blood constituent = transfer rate of the constituent out of the blood. Early methods studied gaseous constituents, but have had mostly a limited use and have provided only approximate values. Renewed interest in methods using carbon dioxide and/or oxygen equilibration in the lung to evaluate the A-V blood differences of these gases has followed the development of analytical instrumentation with rapid response characteristics.

In order to assess circulatory performance during exercise, determinations of cardiac output are needed at a number of levels of exercise. The curvilinear relationship between oxygen uptake and cardiac output which this laboratory has developed, would be more readily applicable to military medicine if multiple, replicate determinations were readily obtainable with minimal encumbrance of the subject.

Progress:

This need, coupled with the capability which we have developed for rapid accurate curve fitting to simple exponential functions by computer, has led us to study two techniques proposed for the determination of cardiac output using respiratory measurements of carbon dioxide (CO_2). In these, arterial CO_2 tension (A) is represented by end-tidal CO_2 analysis, and mixed venous CO_2 tension (V) is determined from the equilibrium kinetics of a rebreathing procedure. Theoretical models (1,2) and experimental observations (3) have characterized the early phase of rebreathing terms of a multi-compartment mixing system reducible to an equivalent simple two compartment model. In the first technique (3) an extrapolation asymptote is calculated from successive expired CO_2 levels during less than 15 seconds of rebreathing after a single inspiration of air or of a low concentration of CO_2. In the

second technique (4) an actual plateau is sought or interpolated during less than 15 seconds of rebreathing after a single inspiration of a concentration of CO_2 greater than or near to the expected equilibrium. The difference (V-A) in CO_2 gas tension may be converted into a difference (v-a) in blood CO_2 content (see below) and cardiac output calculated as the ratio of the CO_2 production rate-determined immediately before the rebreathing procedure - to the v-a content difference.

Multiple replicated observations were made at rest and during exercise on two subjects. Although overall significant correlations were found between oxygen uptake and calculated cardiac output ($r \geq .86$), neither method provided good individual reproducibility. The range of V-A CO_2 difference was approximately ±50% of its mean value. The variability of end-tidal CO_2 contributes to the resting V-A variability. The initial concentration of CO_2 inspired tends to influence the V-A CO_2 difference. About 25% of the rebreathing trials with the first method produced no reasonable solution. In the second method, higher initial CO_2 concentrations were needed for plateau values to be obtained during exercise, and few such points were obtained. Reproducibility was much better for plateau than for extrapolated asymptote values.

Accurate conversion of (V-A) difference in CO_2 gas tension to (v-a) difference in blood CO_2 content requires a knowledge of the individually applicable blood CO_2 dissociation curve. In the face of other assumptions, the substitution of an appropriate "standard" curve probably need not add large error, although it does add some uncertainty to interpretation of the results in terms of actual blood flow. We have developed computer programs to make this conversion in terms of the blood CO_2 dissociation studies of Peters et al (5), Dill et al (6), and Rahn and Fenn (7) or the derivations of McHardy (8).

Plans:

From the above studies, the second or plateau method appears superior although less convenient, and warrants further evaluation using higher CO_2 concentrations (checking for possible influence of this CO_2 upon blood pressure).

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8. McHardy, G. J. R. The Relationship Between the Differences in Pressure and Content of Carbon Dioxide in Arterial and Venous Blood. Chemical Science 32:299-309, 1967.

Project No.: 3A061102B71R

Title: Research in Biomedical Sciences

Task: 05 Environmental Biochemistry

(82101)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6140	72-07-01	DD-DR&E(A) ...

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	H.Terminated	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	055
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141(a)			

11. TITLE (Precede with Security Classification Code)

(U) Disease Susceptibility of Soldiers in Harsh Environments (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002300 Biochemistry; 003500 Clinical Medicine; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING: 72	1.5	128.0
FISCAL YEAR CURRENT:		

19. RESPONSIBLE DOD ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Casey, Francis B. Dr.
TELEPHONE: 955-2861
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Bowers, Wilbert D. Dr.
NAME: DA

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Stress; (U) Disease; (U) Environmental Extremes; (U) Temperature; (U) Fatigue; (U) Immune Response; (U) Defense Mechanisms

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23.(U) Disease causes more combat noneffectiveness than do battle injuries. There is an Army requirements to study factors which influence disease susceptibility and to provide prophylactic and/or therapeutic measures (Institute of Land Combat/Advanced Materials Concept Agency material data sheet S/MD-14, dtd May 1969). Fatigue, exposure to temperature extremes or altitude increase susceptibility to disease and diminish the efficacy of therapeutic regimens. The objective of this research is to predict the combat effectiveness.

24.(U) Existing models will be used to establish the conditions and extent to which any one or combination of environmental extremes and fatigue alter resistance to bacterial and viral diseases relevant to military operations. Changes in the body's defense mechanisms (e.g., mucous membrane sensitivity, antibody production) resulting from acute cyclic, or chronic exposure to environmental stress will be studied by immunological and biochemical techniques. Studies will be conducted in laboratory animals and in human volunteers under simulated field conditions.

25.(U) 71 07 - 72 06 Studies have been undertaken using mice acutely heat stressed, cold stressed, and fatigued (sleep deprived) and injected with sheep red blood cells as an antigen representative of a disease causing agent. Antigen uptake and distribution was markedly altered in cold stressed mice, but not heat stressed animals. I^{125} specific antibody has been prepared and a radioimmuno assay devised to conduct studies on passively administered antibody turn-over. Reason for termination: This work is more appropriately funded under ILIR(01020).

*Available to contractors upon originator's approval

DD FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE.

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Title of Study: The Effect of Acute Exposure to Harsh Environments and Fatigue on Immunity to Disease

Investigator: Francis B. Casey, CPT, MSC

Background, Rationale, and Approach:

In line with the Army requirement to study factors which: (a) influence disease susceptibility and (b) to provide prophylactic and/or therapeutic measures (Institute of Land Combat/Advanced Materials Concept Agency material data sheet S/MD-14, dated May 1969) studies were conducted during FY 71 to determine alterations in the humoral immune response of animals exposed to heat, cold, and fatigue (sleep deprivation). As an adjunct to the previous investigation, a study of antibody protein decay in vivo was proposed for FY 72.

The plan was to label a specific antibody with a suitable radioisotope and follow the loss of specific antibody activity by means of a radioimmuno assay.

Progress:

High titer anti-sheep red blood cell (anti-SRBC) antibody was prepared in mice and subsequently labelled externally with I^{125}. A radioimmuno assay was developed by which specific antibody is absorbed onto sheep red blood cells and then titered by means of counting the radioactivity in a scintillation counter.

Future Studies:

Mice are to be passively administered the I^{125} anti-SRBC antibody by intravenous injection, serially bled daily over a ten day period, and the antibody titer determined by radioimmuno assay. Antibody decay rates will be compared for control animals and mice exposed to cold (8°C), heat (37°C) and fatigue (sleep deprivation).

Title of Study: An Investigation Into the Comparative Effect of Exposure to Harsh Environments on Phagocytosis and Antigen Distribution as Related to Defense Against Disease

Investigator: Francis B. Casey, CPT, MSC

Background, Rationale and Approach:

Disease causes more loss of combat effectiveness than do battle injuries. There exists, therefore, Army requirements: (a) to study factors which influence disease susceptibility, and (b) to provide appropriate prophylactic and/or therapeutic measures (Institute of Land Combat/Advanced Materials Concept Agency material data sheet S/MD-14, dated May 1969). It was to satisfy the former requirement that this study was initiated.

Investigations conducted by many workers to elucidate the physiology of stress have emphasized the role of thyroxine, catecholamines, and andrenocortical hormones. Studies undertaken to determine the effects of these substances on important lines of defense against disease agents have given results that varied so much that it has been impossible to use them to predict how an individual's immune capability to disease would be effected by exposure to physically stressful environments.

Progress:

Random bred mice were exposed to 37°C and 60-80% relative humidity or 8°C and 15-25% relative humidity for heat or cold stress, respectively. To induce fatigue, the mice were forced to stand and remain awake on small pedestals surrounded by water for 72 hours. Control animals for all experiments were housed at 22°C, with 15-25% relative humidity, for the duration of each study.

Animals were injected intraperitoneally with sheep red blood cell (SRBC) antigen externally labelled with S^{35}. The mice were sacrificed at various time intervals post injection, selected organs removed, digested in perchloric acid and hydrogen peroxide, and then transferred to scintillation vials with suitable cocktail for counting. Antigen uptake and distribution was assayed by the counts per minute (CPM) found to exist in an organ at each particular time interval.

The cellular location of the SRBC antigen within the organ was determined by both fluorescent antibody staining of frozen sections and autoradiography in both frozen and parafin embedded sections.

Progress:

Initially, peritoneal cells, spleen, liver, lung, kidney, intestine, and urine were examined for uptake of antigen. However, it was determined that only spleen, liver and peritoneal cells were specifically "capturing" antigen. The presence of the S^{35} in the other organs was non-specific and indeed S^{35}-SRBC did not show any greater presence in the other organs than did S^{35} alone. In the case of the liver and spleen, maximum antigen uptake was found to occur at four hours post-injection of S^{35}-SRBC, while the maximum uptake by peritoneal cells was found to occur at one hour. However, the magnitude of antigen uptake has found to follow a periodicity depending upon at what time of day S^{35}-SRBC injection was made. For this reason, in all the experiments reported here, animals were injected at 0800.

In the first series of experiments, mice were exposed to the harsh environments on the same day as antigen injection. No significant differences, with respect to antigen uptake by spleen, liver or peritoneal cells, were observed.

The remaining experiments were designed to determine if prior exposure to heat, cold or fatigue altered antigen uptake. Animals were exposed to the stressors either one or three days prior to antigen injection.

Heat stressed animals, whether stressed for one or three days prior to antigen injection did not demonstrate significant differences in antigen uptake.

Animals exposed to cold (8°C) either one or three days prior to the administration of antigen showed varying alterations in the uptake and distribution of labelled SRBC. The peritoneal cells (mostly macrophages) took up approximately 30% more antigen after one day exposure to cold and approximately 50% after three days of cold exposure when compared to control animals. On the other hand, both the spleen and liver took up less antigen after cold exposure. Following one day of cold exposure, spleen and liver took up approximately 20% less antigen. Following three days of cold exposure, spleen and

liver took up approximately 40% and 25% less antigen respectively. Therefore, it is apparent that cold exposure results in a shift in uptake from the spleen and liver to the peritoneal cells.

Studies on the effect of fatigue (sleep deprivation) are still in progress and the limited data available do not permit conclusions at this time.

Future Studies:

This investigation will be extended during the next year to determine: 1) if there are any alterations in the bactericidal effects of the macrophages and 2) if the shift in antigen uptake adversely effects the development of the immune response.

Data from all these investigations will add to our ability to more logically predict the disease defense capabilities of an individual to similar environmental extremes.

(82102)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OB 6123	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	056
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141			

11. TITLE (Precede with Security Classification Code)* (U) Bioenergetics Related to Heavy Physical Work Ability of the Soldier

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

002300 Biochemistry; 012900 Physiology; 005900 Environmental Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	0.8	74.2
	CURRENT 73	1.3	100.0

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst of Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst of Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Horstman, Donald H. Dr.
TELEPHONE: 955-2822
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Hubbard, Roger W. Dr.
NAME: Boyd, Aubrey E. MAJ DA

21. GENERAL USE

Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Work; (U) Endurance; (U) Fatigue; (U) Energy Metabolism; (U) Blood Flow; (U) Muscle Metabolism

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) In the mobile soldier, survival may depend on his ability to perform muscular work. He can do so only if his cells are able to produce the energy required for muscle contraction. Any decrement in performance must be a reflection of a decrement at the cellular level. The objective of this research is to identify and characterize those factors which limit the cells ability to meet the added energy requirements imposed by heavy physical work.

24. (U) This research will include both humans and animals subjected to either exhaustive exercise or graded levels of work. Areas to be investigated will include: (1) utilization of substrate by skeletal muscle; (2) release of substrate by adipose tissue; (3) effect of training and exercise on enzymes which regulate intermediary metabolism and mitochondrial respiratory efficiency; (4) possible advantages of high energy fuels during heavy physical work.

25. (U) 71 12 - 72 07. In exercising rats, ultrastructural and biochemical patterns are being characterized for both red and white skeletal muscle during aging and endurance training. Gross changes in body composition were not different between trained and sedentary animals, although performance of trained rats was superior to that of the sedentary. Since the spleen acts as a blood volume reservoir in the dog, hepatic blood flow during exercise may be different from that of man; therefore the suitability of using the dog as a model for substrate metabolism in man may be invalid. To test this hypothesis, hepatic blood flow, oxygen consumption and substrate turnover are being studied in exercising dogs before and after spenectomy.

*Available to contractors upon originator's approval.

DD FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A, 1 NOV 65 AND 1498-1, 1 MAR 66 (FOR ARMY USE) ARE OBSOLETE.

Title of Study: Energy Metabolism and Body Fuel Utilization During Sustained Physical Work

Investigators: Donald G. Therriault, Ph.D.; L. Howard Hartley, LTC, MC; George A. Beller, MAJ, MC and James A. Smoake, CPT, MC

Background and Rationale:

During rest, the skeletal muscle of man uses only about 30% of the oxygen consumed. However, during moderate to heavy work, muscle will account for 70-90% of the oxygen consumption. Clearly, during heavy work and even during moderate work, skeletal muscle uses most of the fuel that is consumed by the individual.

The nature of the fuel utilized by the contracting musculature during work has been a subject of debate for many years. Ten years or so ago, many believed carbohydrate to be the sole fuel for muscular activity. It subsequently has been shown conclusively that both carbohydrate and lipid serve as fuel for contracting muscles. However, there is still considerable uncertainty regarding the relative role of each substrate at any given work load.

Considerable evidence exists from human and dog studies to indicate that fat, in the form of free fatty acids, serves as a major source of energy for muscular activity. Though there may be no question as to the importance of free fatty acids during moderate work, little is known about the relative role of lipid metabolism during heavy work.

Recent studies in Sweden indicate that during heavy work, the glycogen store of the working muscle progressively decreases. It was shown that the capacity for prolonged heavy leg exercise in man is directly related to the glycogen store in the working muscle(s). These experiments seem to support the conclusion that the intensity of work affects the relative contributions of fat and carbohydrate to the working muscle. During moderate exercise fat is the main energy source. The closer the subject works to his maximum capacity the more important is carbohydrate; however, no assessment of the participation of lipids during these periods of heavy work has been carried out. Some of the questions that still remain unanswered are: Does the muscle utilize its endogenous stores of lipid? Is the muscle capable of extracting

and utilizing circulating free fatty acids? Since the muscle cells contain enzymes which readily oxidize long-chain fatty acids to carbon dioxide and water, it is difficult to understand why fatty acids cannot support heavy work in muscles, even when depleted of glycogen stores.

The eventual sources of energy for the resynthesis of ATP must be either fat and glycogen stores in the muscle cell, or fatty acids and glucose which can be taken up from the blood. The mechanisms which control the relative participation of each of these energy sources during heavy work remain a mystery which must be solved if we wish to eventually increase the capacity of the soldier to perform sustained heavy work.

Progress:

Three groups of dogs were run under different experimental conditions characterized by varying the work load or the running time. Lipid and glycogen analyses were carried out on biopsies from the biceps femoris muscle before and after exercise. In addition, arterial and venous triglycerides and free fatty acids were determined on plasma samples from dogs in one of the groups that had been previously catheterized. Under the conditons of these experiments, results revealed: (1) plasma triglycerides did not contribute significantly to the energy supply for muscle contraction, (2) plasma free fatty acid efflux into muscle was increased during mild exercise but significantly lowered during heavy exercise, (3) exercise did not affect the phospholipid level or its composition in the muscle, (4) muscle triglyceride levels may increase, decrease or remain unchanged, depending upon the work load imposed by the exercise.

A manuscript has been accepted for publication by the Journal of Lipid Research.

Future Plans:

No further work is comtemplated.

Title of Study: Hepatic Blood Flow in Exercising Dogs

Investigator: D. Horstman, Ph.D.

Background:

It has been suggested that exercise results in a marked reduction of hepatic blood flow in man whereas the opposite occurs in the normal dog. Since the spleen serves as a large blood volume reservoir in the dogs, the removal of the dog's spleen may result in a pattern of hepatic response similar to that observed in man. Therefore, the splenectomized dog may provide a more adequate model of exercising man and allow for more extensive and definitive studies of substrate metabolism as it limits physical work capacity. The immediate purpose of this investigation is to compare hepatic blood flow and related parameters in normal and splenectomized dogs during various intensities of exercise.

Approach:

Dogs are being trained to run on the treadmill. Chronic catheters are placed in the descending aorta, right ventricle, and hepatic vein. Oxygen consumption ($\dot{V}O_2$), arterial-venous oxygen difference, heart rate, cardiac output, and stroke volume are determined at various workloads up to and including maximal and supramaximal levels. Hepatic blood flow, oxygen consumption, lactate uptake, and glucose output are determined at rest and during exercise corresponding to 50, 75 and 100% $\dot{V}O_2$ max. The spleen is then removed and all measures repeated following recovery from surgery.

Progress:

To date, all methods and techniques, both surgical and experimental have been refined and made operative. Eight dogs have been trained to run on the treadmill and necessary baseline information has been obtained for these animals. Two dogs have been catheterized and (non-splenectomized) control experiments are presently underway, with splenectomy to follow. Two other dogs have been catheterized and are presently recovering from the procedure.

Future Plans:

If, as postulated, the splenectomized dog is an appropriate model for substrate metabolism in exercising man, then several studies which have been previously performed with normal dogs would bear repeating. For example, it is known in normal dogs that elevated blood lactate levels, brought about by severe exercise, inhibit the release of free fatty acids from adipose tissue. Whether this is the result of direct inhibition of lipolysis by lactate is open to question since an elevation of blood glucose levels has sometimes been reported in dogs, as opposed to man working at heavy loads. Glucose is a known, potent inhibitor of lipolysis. Therefore, the interrelationship of glucose, lactate, and free fatty acid metabolism during prolonged heavy exercise may better be studied in splenectomized dogs.

(82103)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6142	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	057
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Development of Cold Injury Models and Characterization of Frostbite, Non-Freezing Cold Injuries and Whole Body Heat Loss Common to the Soldier (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*
002300 Biochemistry; 005900 Environmental Biology; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	4.0	175.6
	CURRENT 73	3.6	200.0

19. RESPONSIBLE DOD ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Klein, Albert W. CPT
TELEPHONE: 955-2863
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Hamlet, Murray P. CPT
NAME: DA

21. GENERAL USE
Foreign Intelligence Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Arctic Military Operations; (U) Cold Injury; (U) Frostbite; (U) Thermoregulation; (U) Cryobiology

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Study factors involved in frostbite and other non-freezing injuries, as well as whole body heat loss in both animals and man, to provide a rational basis for treatment and prevention of those cold injuries sustained by the military.

24. (U) The following areas are being investigated in humans and animals: (1) the suitability of animal model systems to mimic those clinical cold injuries seen during military operations in cold climates; (2) cell destruction following frostbite; (3) physiological, ethnic and other factors associated with cold injury; (4) physiological changes in man subjected to whole body cooling; (5) due to recent knowledge acquired in understanding frostbite, it seems apparent that special emphasis must be placed on the study of the microcirculation following feeeze injury.

25. (U) 71 07 - 72 06 Electron microscopic evidence indicates that as early as 15 minutes following an experimental freeze-thaw model of cold injury, circulation to the affected capillaries becomes sluggish and stops entirely. While some studies have suggested blood platelets and their aggregates as possible sources of the capillary blockade, work is progressing on an in vivo microcirculatory model to positively ascertain the cause of the circulatory collapse. This work is being pursued from multiple approaches. A model using mitochondrial respiration as an assay for freeze-thaw damage has been shown to be reproducible and exhibits graded levels of mitochondrial dysfunction. This approach has indicated that with a given insult, 60% of the subsequent frostbite lesion is due to circulatory collapse and the initial 40% due directly to the freeze-thaw. Agents to reduce this dysfunction are being evaluated.

*Available to contractors upon originator's approval.

Title of Study: Mitochondrial Dysfunction as an Assay for Freeze-Thaw Injury

Investigators: A. W. Klein, CPT, MSC and D. Therriault, Ph.D.

Background and Aims:

There is a distinction between the primary or direct effects of acute freezing injury and the secondary or endogenously mediated injurious effects which produce local microcirculatory insufficiency. The primary biochemical lesion in any living cell is always followed by secondary responses and a separation between primary and secondary events is quite often difficult. Nevertheless, the greatest attention and effort should be directed toward the identification of the primary lesion. For this reason, the choice of the experimental model becomes all important in that experimental conditions should be such as to allow an analysis of the earliest lesion and in as uncomplicated a state as possible. On the other hand, many investigators have emphasized the role which microvasculature injury plays in determining whether or not frostbitten tissue will survive. The aims of this research have been: (1) to establish a model in which freezing injury is readily quantifiable based on decrements of tissue and mitochondrial respiration, (2) to establish the role of the microcirculation in the cold injury lesion as opposed to the direct effect that the freeze-thaw injury exerts upon the cell, (3) to determine if the direct freeze injury is reversible and if so to what extent, and (4) to elucidate the mechanism of the frostbite lesion.

Skeletal muscle of the rat hind limb has been used in these studies. Although skeletal muscle is not normally subjected clinically to freeze injury, it has a dense population of mitochondria and is richly perfused with microcirculation. Both these characteristics make it a desirable tissue upon which to study freeze-thaw injury.

Progress:

Morphological alterations of the mitrochondria illustrate a wide range of responses within a given cell. The extent of mitochondrial alteration parallels the decline in cellular respiratory rates. These findings support the concept that mitochondrial respiration and morphological integrity do indeed constitute a better model upon which to gauge the severity of a freeze insult than does gross tissue loss. A

specific freeze insult initially resulted in a 40% decrement of mitochondrial respiration. During the next two to twenty-four hours the remaining respiratory capacity of the mitochondria decreases to zero. This later portion of the lesion is that which has been attributed to microcirculatory collapse. When respiratory rates are plotted against time post-thaw, the steepest decline of the mitochondrial respiration capacity occurs between two and four hours.

Future Studies:

This model, which has proven to be predictable and accurate with respect to mitochondrial dysfunction, will be used to evaluate specific therapeutic agents which have potential for frostbite treatment.

Title of Study: Ultrastructural Studies of Muscle Cells and Vascular Endothelium Immediately Following Freeze-Thaw Insult

Investigators: W. D. Bowers, Jr., Ph.D. and R. W. Hubbard, Ph.D.

Background, Rationale, and Approach:

Prediction of tissue loss after frostbite injury has shown only limited success, although recent studies with xenon-133 and nerve impulse conduction at Arctic Medical Research Laboratory, Alaska, offer considerable promise. Various models for predicting tissue loss have been explored, and the system in which the mouse hind limb is frozen and rewarmed at controlled rates produces certain consistent alterations in the ultrastructure of muscle cells and their associated microvasculature. Mitochondrial disruption in muscle cells and capillary endothelial breakdown are common features of tissue subjected to a freeze-thaw cycle. It is reasonable to assume that the degree of microvascular damage observed in this laboratory and reported by others is paramount in determining whether previously frozen tissue will survive. Vessels remaining after fat cell isolation may provide endothelium for study. The contributions of several parameters which may independently contribute to the ultimate damage in tissues which undergo a freeze-thaw cycle were studied. Hypoxia, produced by applying a ligature for 30 minutes, chilling to 2°C for 30 minutes, and super cooling were utilized. These produced no detectable changes in ultrastructure of the muscle. In order to follow changes in vascular permeability associated with frostbite, horseradish peroxidase was injected into animals, as an electron microscopic tracer, at various time intervals post-thaw. Initial reestablishment of microcirculation associated with changes in vascular permeability and subsequent shutdown was anticipated.

Progress:

Horseradish peroxidase (HRP) was injected into the tail veins of mice 5, 20, 50 and 110 minutes post-thaw and the soleus muscle was removed, processed for demonstration of HRP, and subsequent electron microscopy. No HRP was detected in the capillaries of the frozen tissue although it was abundant in tissue from the control limbs of the same animals. Preliminary studies employing the same technique with injection of HRP just prior to thawing yielded the same results. If confirmed, this would tend to contradict the theory that vascular flow

is reestablished in all capillaries prior to shutdown. The phenomenon may, however, be unique to muscle.

This study also indicates that ultrastructural assessment of capillary damage as early as one or two hours post-thaw may provide an effective means of predicting tissue loss. It also raises the possibility of needle biopsy, with subsequent examination of endothelial cells, as a technique for predicting tissue loss.

Future Plans:

Additional animals will be processed to assess the vascular transport of horseradish peroxidase to thawed tissue. We also plan to study samples of material obtained by small needle biopsy using this model, and to study cellular organization in the frozen state by freeze-etching. Examination of isolated vascular endothelium is also a part of this protocol. Examinations of the microvasculature of the skin in this system and in higher animals are anticipated.

Title of Study: Tissue Damage Resulting from Freezing and Non-Freezing Insult: Changes in Membrane and Intercellular Lipids at Site of Local Cold Injury

Investigators: Donald C. Therriault, Ph.D. and Donald B. Mellin, B.A.

Background:

There has been a long standing argument as to whether cold injury to tissue is the result of direct damage of the cold to the cell or is the consequence of subsequent thrombosis and circulatory stasis producing necrosis secondary to anoxia. As has been demonstrated on many occasions, there appears to be a re-establishment of good blood flow following a freezing injury and it is only at some point subsequent to this that thrombosis occurs. The duration of this blood flow and time of onset of thrombosis are not clearly defined. This indicates that one or both of two events have occurred at the local level; (a) the release from tissue of a substance capable of producing coagulation; (b) an alteration in membrane structure that could induce coagulation, change permeability and thus affect the viability of the tissue.

When tissue freezes, it is subjected to numerous physico-chemical stresses due to the removal of free water from the system in the form of ice crystals and the consequent increase in the tonicity of the remaining intracellular fluid. One can readily visualize the removal of phospholipid due to an increase in the tonicity of intracellular fluid; such removal could cause changes in membrane structure and function that might disrupt normal coagulation processes. It is well established, for instance, that the removal of lipids from membranes leads to a loss of enzyme activity at the membrane. It is also known that certain phospholipids exhibit procoagulant activity. The foregoing provided the rationale for this study, the purpose of which was to investigate whether the freezing of tissue *in vivo* causes the release of lipids from cell membranes.

Progress:

Quantitative analysis of the individual lipid classes from blister fluid obtained from adult albino New Zealand rabbits was carried out; blisters were caused by freezing the ears. Ear tissue and plasma samples were also obtained prior to and after freeze-thaw, and quantitative analysis of the individual lipid classes was carried out on these samples as well.

Cell particulates (i.e. plasma membrane, nuclei, mitochondria) were isolated by differential ultracentrifugation prior to and at various post freeze-thaw intervals, and lipid analyses were made to determine the effect of freezing on cell membranes.

Preliminary analysis of the data indicates that freeze injury does not affect the lipid composition of the tissue or the various cell particulates. The plasma phospholipid composition remains unchanged after freeze thaw; however, the free fatty acid concentration is significantly elevated. The blister fluid contains both neutral lipid and phospholipid. The phospholipid composition resembles more closely that of plasma, indicating that the origin of blister fluid lipid is plasma, rather than tissue.

Future Plans:

The data will be further tabulated and a manuscript prepared for publication. No further research is contemplated.

Title of Study: Tissue Loss Evaluation Secondary to Cold Injury at Various Times and Temperatures

Investigator: A. W. Klein, CPT, MSC

Background and Aims:

Before one can test the efficacy of various agents for potential therapeutic value in frostbite, a baseline or a reproducible injury must first be established as a standard of reference. A search of the scientific literature concerning frostbite reveals numerous attempts at the development of a freeze injury model which would: (1) closely mimic the clinical lesion suffered by the soldier in the field and (2) be reproducible in its extent of tissue loss. With respect to reproducibility, only one report has indicated a successful model. (ref: Sjostrom, Bjorn, R. C. A. Weatherley-White and Bruce C. Paton. Experimental studies in cold injury - I. The individual response to a standard cold environment. J. Surg. Res. IV:12, 1964)

Essentially this study had two phases: (1) to attempt to correlate the various freeze-thaw parameters of frostbite with tissue loss and, (2) to test the reproducibility of the specific model cited in the literature.

Progress:

First phase progress gives correlation coefficients for the following combination of parameters: rates of freezing, time spent frozen, depth of freezing, rates of rewarming, total time spent below $10^{o}C$, and the amount of tissue lost. Rates of rewarming gave the only positive correlation to tissue loss. Mathematical attempts at predictive curve fitting were unsuccessful. The second phase involved slow freezing rates applied to a rabbit ear. The slow, controlled rates are the key factor. Sjostrom et al (op. cit.) are the only workers in this area to have described a model with reproducibility of tissue loss; these workers also stated that depth of anesthesia was directly predictive of tissue loss. Our work has also shown a relatively high degree of reproducibility, but totally fails to support the conclusion that tissue loss is related to depth of anesthesia.

Future Studies:

This approach will be further studied for eventual use in the evaluation of any frostbite treatment regime.

Title of Study: Voluntary March Rate During Extended Operations

Investigators: R. G. Soule, Ph.D. and R. F. Goldman, Ph.D.

Background:

The rate of energy cost for maximum voluntary "hard work" has been established to be 425 kcal/hr ± 10% for a fit 18-25 year old soldier (Hughes and Goldman) with march rate adjusted to load to reduce this level. Whether this constant march rate for a given load would be maintained for intermittent work over an extended period was unknown.

Progress and Conclusions:

In this study 10 subjects began, although only 6 completed, two separate 31 hour test sessions. Subjects did not sleep during the 31 hour period from the start of each session until the last work bout was completed. The men (21 year, 74.8 kg) volunteered to complete 4.8 km in 1 hour or less every 6 hours, until the 6 one-hour runs had been completed on a self-pacing treadmill. They carried either a 15 or 30 kg load, randomized by session. The distance walked during each 5 minute segment was recorded, as was the time to walk each 400 m. With 15 kg, the walk times for the 7th and 13th hours were faster, ($p < 0.05$) than at the 1st, 19th, 25th and 31st hours. At all hours, the time to walk the first 400 m. was significantly slower than all the others, which were not different from each other. There were no significant differences in either of these measures with the 30 kg load. However, there was a discrepancy between the difficulty of the work, as subjectively perceived by the men, and their measured heart rates at the end of each work bout. Thus it appears that the extended 31 hour operation, without sleep, is not sufficient to measurably change the voluntarily selected "hard work" rate, but does change the perceived work level.

Title of Study: Freezing Temperature of the Skin

Investigators: Ove Wilson, M.D.; Ralph F. Goldman, Ph.D. and George W. Molnar, Ph.D.

Background and Approach:

Supercooling of the skin invariably occurs before the skin freezes. At the moment of ice crystallization in the tissue, there is always a rise in the skin surface temperature as a result of the heat fusion. An analysis of this temperature change was carried out, including the extent of supercooling and the time before freezing occurred. Forty white male volunteers were investigated with one finger exposed to either 6.8 m/s (wind chill index 1425) or 9 - 10 m/s (wind chill index 1505-1550) at an air temperature of -15°C for 15 min. unless frost nip (experimental frostbite) occurred. Multiple exposures of the 40 subjects resulted in a total of 186 cases of frost nip.

Conclusions:

Three main types of cooling curves resulting in frost nip were observed: in type A (82%) there was no indication of circulatory heat input; in type B (13%) there was a flattening of the curve with small rises in finger temperature of less than 1°C, indicating a slight circulatory heat input, which tended to increase the time to freezing; in type C (5) there was clear evidence of CIVD, manifested as a rise in the skin temperature of 1°C or more before freezing took place but not established as CIVD cycle. The second type of cooling (B) with a flattening of the curve was somewhat more common at the lower wind speed.

As a result of the liberation of heat of fusion at crystallization, the skin temperature rose from the supercooled value at freezing to what may be termed the "apparent freezing point". The apparent freezing point, $T_{sf} = T_{sc}$, was found to be -2.5°C for the wind speed of 6.8 m/s and -3.6°C for 9-10 m/s.

Obviously, the freezing point of skin in the absence of supercooling varies with the rate of heat loss. However, no definite relationship can be drawn from the present results, since the two estimated freezing points were not sufficiently different. Greater separation in wind speeds or in air temperatures is necessary to establish the relationship between the rate of heat loss from the skin and its freezing point in the absence of supercooling.

(82107)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6149	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	058
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Development of Measures to Assess the Impact of Environmental Stresses on Critical Military Performance (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*
005900 Environmental Biology; 013400 Psychology; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	1.8	96.2
	CURRENT 73	3.4	190.0

19. RESPONSIBLE DOD ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME:* USA Rsch Inst of Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Cahoon, Richard L. Dr.
TELEPHONE: 955-2823
SOCIAL SECURITY ACCOUNT NUMBER: 015-30-4628

ASSOCIATE INVESTIGATORS
NAME: Kobrick, John L. Dr.
NAME: DA

21. GENERAL USE
Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Environmental Stress; (U) Military Performance; (U) Perception; (U) Cognition; (U) Motor Skills

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Severely debilitating effects of heat, cold and high terrestrial elevation are identifiable by end points of exhaustion, cold injury, or collapse. However, such exposures can have less dramatic but highly significant effects on the soldier's efficiency and on unit mission performance. It is the objective of this research to develop sensitive and appropriate measures of these effects.

24. (U) Biochemical, physiological, and psychological methods will be developed to assess military performance; tasks sensitive to the effects of heat, cold, wind, moisture, work, and hypoxia on the soldier's perceptual, intellectual, and motor abilities will be studied.

25. (U) 71 07 - 72 06 Electrocortical (EEG) measures were taken on subjects exposed to 14,000 ft altitude for a 30-hour period. The results indicated a large inter-subject variance, but no significant shift occurred in the frequency distribution over the exposure period. However, severity of acute mountain sickness symptoms, particularly headache, did correlate significantly with the percentage of EEG in the beta (>13 c.p.s. range. Beta appears to be a possible predictor of severity of cerebral symptoms of A.M.S. A task was developed to measure response time to visual signals occurring in peripheral positions throughout the visual field, and to assess the effects of stress exposure upon such performance. The task shows that response is not uniform throughout the field, with the poorest locations being the upper and lower medial periphery. Hypoxia exposure intensifies these losses in direct relation to severity. Increases in rate of stimulus occurrence appear to further reduce response efficiency, the greatest losses occurring early in the work session followed by gradual partial recovery. Reductions in stimulus brightness also reduce response efficiency in relation to the difficulty of detection.

*Available to contractors upon originator's approval

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Title of Study: Development of an Electro-Cortical Measure of Mountain Sickness

Investigator: Richard L. Cahoon, Ph.D.

Background:

Although a number of symptoms of acute mountain sickness have a cerebral component, a review of the electroencephalographic (EEG) literature reveals little or no attempt to correlate EEG variables with these symptoms. Studies relating EEG changes to hypoxia have concentrated on conditions created by short-term severe anoxia produced experimentally or by disease. As a result, there are no known electrophysiological measures of cerebral changes that can be related to symptoms of acute mountain sickness produced by less severe but more protracted exposure to environmental hypoxia - the very conditions which the soldier is most likely to encounter at high terrestrial elevation. The present study was designed to develop such measures by taking EEG measures on human test subjects exposed to high altitude for a period long enough for symptoms of acute mountain sickness to appear.

Progress:

A study was conducted in which six groups of four subjects each were exposed to a simulated altitude of 14,000 ft for 30 hours. During this period, two-minute EEG samples were taken from three positions on the head every four hours during the waking hours. A sea level control sample was obtained before each altitude exposure period.

All samples were tape recorded as analog electroencephalographic records for off line analysis at a later time. Records were analyzed for shifts in percentage of energy found in classical frequency bands (4-8 H_z, 8-13 H_z, >13H_z) and for changes in amplitude and dominant alpha frequency. Also, correlations were sought among the various parameters of the EEG and severity of mountain sickness symptoms.

Conclusions:

Large individual differences in EEG responses were apparent. No significant group shifts in the EEG parameters occurred during the exposure period. The correlations between symptoms and EEG parameters indicated a relationship between severity of headache and percentage of EEG energy

in the beta frequency range. Subjects with high levels of beta activity at sea level rated their headaches as very severe during exposure to high altitude. This correlation was also high at the end of the exposure period, i.e., subjects experiencing the most severe headachesat the end of the exposure period manifested the greatest amount of beta activity in their EEG. These results encourage further exploration of the potential use of degree of beta activity as a predictor of cerebral symptoms of acute mountain sickness.

Future Plans:

A study is in progress in collaboration with Dr. John Weil of the University of Colorado Medical School in which EEG's from eight test subjects are being compared at sea level and on Pike's Peak. A power spectrum analysis of the data will be more sensitive to smaller shifts in dominant frequencies than was possible in the past. In addition, sleep EEG's are being taken on six test subjects to determine whether changes occur in the pattern of sleep stages as a result of exposure to high altitude.

Symptom questionnaires will be completed by the test subjects at the time EEG samples are taken. Correlating the responses on these questionnaires with the power spectrum analyses of the EEG samples will test further the relationship between beta activity and severity of cerebral symptoms found in the present study.

Title of Study: Effects of Hypoxia on Peripheral Visual Response Time on Rapid Rates of Responding

Investigator: John L. Kobrick, Ph.D.

Background and Progress:

Previous research studies in this Laboratory have shown that the efficiency of detection of visual flash signals diminishes for more peripheral locations in the visual field, with the greatest impairments occurring in the upper and lower medial periphery. These losses became substantially greater under hypoxia, and in direct relation to the severity of exposure. However, the task as performed involved a slow response rate to minimize confounding of the initial data with possible fatigue effects, and as such did not test for the influence of task load on the performance. The present study was conducted to assess such work factors, and involved the same visual flash detection task used previously and performed under optimum viewing conditions. Ten subjects performed the task for four one-hour work periods in each test session, receiving a stimulus every four seconds continuously; these stimuli were randomly positioned in the visual field. Each period was followed by a ten-minute rest. Each subject completed one session at each of four hypobaric conditions (0; 13,000; 15,000; 17,000 feet equivalent), which were counterbalanced in order of occurrence. Data collection has been completed and the results are being analyzed.

Conclusions:

Preliminary inspection of the data indicates similar impairment patterns in peripheral visual response as previously obtained with this task, and an increase in these impairments in direct relation to the degree of hypoxia. However, analysis is not far enough along to assess the effects of work load on the performance.

Future Plans:

Study of effects of other stressors and more complex visual tasks.

Title of Study: Effects of Levels of Hypoxia on Response Time to Peripheral Visual Signals of Low Luminance

Investigator: John L. Kobrick, Ph.D.

Background and Progress:

An important aspect of military performance is the effectiveness of the soldier's visual perception, since vision constitutes the major human sensory modality. Previous research in this laboratory has shown that signal detection differs in inherent sensitivity in various zones of the visual field, the major losses occurring in the upper and lower medial areas, as measured by response time to the occurrence of flash signals. It was further shown that these losses increase in direct relation to the severity of exposure to hypoxia. However, the data were obtained under near-optimum detection conditions, i.e., bright signals seen against a contrasting dark background, and may not reflect performance under poorer viewing condition. Data collection has since been completed in a further study of response time to the same stimulus configuration viewed in darkness, but with the luminance of all stimulus lights set at just above threshold detectability for the least sensitive area of the visual field. An automated computerized system was developed to automatically program and activate the stimulus lights and record the data in digitized binary format. Ten subjects each performed the task for four hours at each of four hypobaric exposure conditions (0; 13,000; 15,000; 17,000 feet equivalent) in different orders of occurrence. The data are presently undergoing computer analysis.

Conclusions:

None available at this time.

Future Plans:

Replication of the present study at the opposite extreme of poor viewing conditions, i.e., very bright signals just detectable against a near-glare background.

Title of Study: Effects of Hypoxia and Acetazolamide on Visually Evoked Cortical Potentials

Investigator: John L. Kobrick, Ph.D.

Background and Progress:

In a previous study, visually evoked cortical potential records were obtained from subjects viewing colored stimuli at several peripheral positions in the visual field during exposure to both hypoxic and normoxic conditions. These data are presently being analyzed but do not allow sufficient resolution from noise to permit Fourier transform analysis. A far superior system has since been designed and fabricated in which background noise has been eliminated, records are permanently secured on magnetic FM tape, and the analog traces can be digitized and converted to ASK II in punched paper tape format. This will allow total computer analysis of future data over the entire period of experimental exposure conditions, with no loss of fidelity. A group of 15 subjects have been tested on the new system under normoxia conditions, in preparation for subsequent data collection under hypoxia exposure.

Future Plans:

Further investigation of this measure as a potentially very significant measure of central nervous system activity of the intact human during performance of critical tasks during exposure to stress.

(82106)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OB 6120	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☐ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	059
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)

(U) Biological Processes that Limit Heavy Physical Work Ability of the Soldier (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

012900 Physiology; 005900 Enviornmental Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	5.5	357.7
	CURRENT 73	5.5	400.0

19. RESPONSIBLE DOD ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Maher, John T. Dr.
TELEPHONE: 966-2886
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Giamber, Samuel R. MAJ
NAME: Huibregtse, William H. Dr. DA

21. GENERAL USE

Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Work; (U) Endurance; (U) Fatigue; (U) Cardiovascular; (U) Military Performance; (U) Blood Flow

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) The combat soldier often depends upon his ability to perform sustained and sometimes severe levels of muscular exertion. The objective of this research is to identify and characterize those biological processes that influence his capacity to perform heavy work, thereby providing a rational basis for improving the soldier's performance.

24. (U) In animals and/or humans subjected to either exhaustive exercise or graded levels of work, the following will be investigated: (1) chemical and physical factors which determine muscle blood flow; (2) sympathetic control mechanisms; (3) myocardial contractility consequent to training; (4) involvement of triiodothyronine in the metabolic alterations occurring with physical conditioning; (5) influence of elevated 2,3 diphosphoglycerate following training on the oxygen dissociation curve.

25. (U) 71 07 - 72 06 In man, (1) hemodynamic changes occurring during submaximal and maximal exercise were adequately quantitated by the utilization of noninvasive indirect measurements; (2) the capacity for prolonged exhaustive exercise does not appear to be bound by the limits of myocardial performance; (3) the ability to perform prolonged work is determined, at least in part, by the regulation of working muscle blood flow; (4) the heart rate/oxygen uptake relationship was altered during different techniques of exercise; (5) an equation has been derived which relates endurance time to the intensity of work performed. In animals, (1) 2,3 diphosphoglycerate (2,3 DPG) and the ratio of 2,3 DPG to the hematocrit are increased with physical training.

*Available to contractors upon originator's approval.

DD FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A, 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

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Title of Study: Systolic Time Intervals During Submaximal and Maximal Exercise to Exhaustion in Man

Investigators: J. T. Maher, Ph.D.; G. A. Beller, MAJ, MC; and L. H. Hartley, M.D.

Background:

An increase in heart volume and a prolongation of mechanical systole have been reported in young men at the onset of exhaustion resulting from prolonged exercise. From these findings, a depression of cardiac function prior to exhaustion and a causal relationship between the impaired cardiac performance and the observed decrement in physical work capacity were postulated.

More recent studies in this laboratory have shown that exhaustion in the rat is associated with a depression in the intrinsic contractile state of the myocardium, characterized by a reduction in both peak isometric tension and velocity of shortening.

In an effort to establish whether the depressed functional response found in isolated cardiac muscle from these exhausted animals could also be demonstrated in intact man, a noninvasive, indirect parameter of ventricular function, namely, measurement of the systolic time intervals, was used in this study to assess the cardiocirculatory responses of healthy young men to exercise to exhaustion in the supine position.

Progress:

Total electromechanical systole (QS_2), left ventricular ejection time (LVET) and the pre-ejection period (PEP) were measured from simultaneous recordings of the electrocardiogram, phonocardiogram and external carotid pulse tracing in 10 young men during prolonged submaximal and short-duration maximal supine exercise to exhaustion. The heart rate at, and time to, exhaustion were 155 ± 4 beats/minute and 78.0 ± 12.3 min, respectively (ave ± S.E.), for submaximal exercise and 171 ± 4 beats/min and 5.0 ± 0.5 min, respectively, for maximal exercise. Linear regression analyses were performed relating each of the systolic time intervals (STI) to heart rate. Within the heart rate range 120-170 beats/min, determination of the QS_2 and LVET for all subjects formed a homogeneous population

which was a linearly decreasing function of heart rate. While the PEP during submaximal exercise manifested a linear correlation with heart rate, decreasing on the average, with increasing heart rate, maximal exercise PEP showed no such correlation and appeared to be a constant with respect to heart rate in the above range. The QS_2 and LVET during maximal exercise were significantly longer at comparable heart rates than during submaximal exercise, while no such differences in the PEP between the two levels of exercise were demonstrated. Changes in the STI with changes in heart rate from rest to exercise were also examined. There was a large and significant ($P < 0.001$) decrease in QS_2, LVET and PEP from rest to the initial phase of exercise (HR = 120). As exercise continued, there was a further increase in heart rate accompanied by additional shortening of the STI except for PEP during maximal exercise.

Conclusions:

Results of this investigation suggest that hemodynamic changes occurring during submaximal and maximal exercise in normal man can be adequately quantitated by the use of noninvasive, atraumatic techniques. The changes in the systolic intervals in this study correlate well with changes known to occur during exercise from internal measurements, including stroke volume, afterload, and isovolumic contraction time. The findings, although indirect, do not support the concept of an abrupt alteration in ventricular performance prior to or at exhaustion. Since, this may not be the case in individuals with underlying cardiac disease, the data obtained here in normal subjects may provide a basis for uncovering mild to moderate degrees of cardiac impairment which may escape detection by less stressful levels of exercise.

Future Plans:

No definite plans with respect to further studies using this approach have currently been programmed.

Title of Study: Radiographic Changes in Cardiac Dimensions During Exhaustive Exercise in Man.

Investigators: J. T. Maher, Ph.D.; G. A. Beller, MAJ, MC; J. M. Foster; and L. H. Hartley, M.D.

Background:

Ekelund and colleagues studied healthy young men during prolonged exercise of constant intensity and observed a continuous fall in end-diastolic heart volume accompanied by a continuous increase in heart rate. However, in 6 of 10 subjects in the sitting position and 3 of 6 in the supine posture, these investigators found a significant increase in heart volume at the onset of exhaustion in spite of a further increase in heart rate. Since no concomitant increase in central venous pressure would be expected at this time, it was not unreasonable to postulate that myocardial function had been altered which in turn, and at least in part, may explain the accompanying decrement in physical work capacity.

It was the purpose of this study (1) to reexamine this hypothesis noninvasively, (2) to relate the findings to previously observed alterations in systolic time intervals during similar conditions of exercise, and (3) to permit a more complete understanding of the mechanical aspects of the heart's activity during prolonged exercise to exhaustion.

Progress:

Forty-inch ECG-synchronized anteroposterior X-rays of the chest were taken of 9 healthy young males at rest, during the course of supine bicycle exercise, and at exhaustion. Exposures were triggered in end-diastole during end-expiration. The workload was on the average 789 kg-m/min with a mean endurance time of 63 ± 7 (SE) minutes. Heart rates at rest and exhaustion were 61 ± 3 and 156 ± 3 beats/minute, respectively. There was a significant ($P<0.001$) decrease (9%) in the mean transverse cardiac diameter, corrected for magnification, from rest (137 ± 2 mm) to exhaustion (125 ± 2 mm). The end-diastolic cardiac diameter decreased linearly with respect to the increase in heart rate ($r = -0.45$) during the course of exercise ($P < 0.01$).

Conclusions:

Under the conditions of this study, the normal physiologic response of decrease in heart size with increase in heart rate was not altered. It is probable that the progressive fall in cardiac dimensions resulted both from an abbreviation of the diastolic filling time with increasing heart rate and the positive inotropism characteristic of the cardiac response to exercise. The consistent reduction in ventricular dimensions from rest to exhaustion was compatible with the progressive diminution in each of the systolic time intervals throughout the course of exercise, suggesting maintenance of normal myocardial function. Thus, the capacity of healthy young men for prolonged exhaustive exercise does not appear to be bound by the limits of myocardial performance.

Future Plans:

None.

Title of Study: Effect of Training on Myocardial Contractility as Defined by Force Velocity Relationship

Investigators: Sam R. Giamber, MAJ, MC and George A. Beller, MAJ, MC

Background:

Many circulatory effects of physical training are well known, e.g. decrease in heart rate, increase in heart and stroke volume, ventricular hypertrophy, elevation of cardiac output. Only recently however, have the effects of training been looked at in terms of possible alteration in contractility, i.e., the ability of the heart to perform work under a given set of circumstances. Changes have been noted in ventricular function curves and more recently the heart has been shown to have an increased resistance to hypoxia after training.

This study was designed to evaluate the effects of 8 weeks of training on a treadmill on the inotropic state of the dog's myocardium. The method used for evaluating the inotropic state is at the present time the most sensitive and most widely used. This method of evaluation is based on the fact that the velocity of contraction is inversely influenced by the load against which it is contracting, assuming that the preload or initial muscle length is kept constant. This method requires high "obtainable" fidelity intraventricular pressure tracings, obtainable by direct ventricular puncture with a short stiff catheter or more precisely by a transducer-tipped catheter. The rate of rise of the left ventricular pressure (dp/dt) was measured and recorded both on tape and paper. DP/DT is plotted against KP(K = 28) to produce a force velocity curve that can be extrapolated to 0 pressure to produce a theoretical maximum velocity of shortening (V_{max}). This V_{max} is most closely related to the inotropic state.

In addition to the above considerations concerning contractility, the resting cardiac outputs and concomitant aortic and ventricular pressures were measured in order to calculate stroke work and stroke work index. These latter entities will be plotted against filling pressure to determine if ventricular function is altered by training.

As a pilot study, we measured 2-3 diphosphoglycerate (2-3 DPG) levels before, during and after training. It has been shown that 2-3 DPG concentration is related to a rightward shift in the oxygen dissociation curve. This shift allows an increase in tissue oxygenation by "dumping" more oxygen for any given PO_2. Such a shift has been noted in numerous

conditions in which the common denominator is tissue hypoxia, elevated phosphate levels or endocrine changes. The most dramatic changes have been noted with ascent to high altitude.

Progress:

In this study, 9 dogs were run on a treadmill every other day, for 8 weeks. They worked at increasing work loads such that heart rate was approximately 200/min. Initial data on ventricular contractility has been recorded and calculated. It is also on magnetic tape and a program is being developed at MIT so that V_{max} can be calculated. The post-training evaluation has recently been completed, but data have not yet been calculated.

The data on 2-3 DPG are partially complete; there was a significant rise in 2-3 DPG even after adjustment for the rise in hematocrit that takes place with training.

	Mean 2-3 DPG		Mean DPG/Hematocrit	
Pretraining	2.24 ± .41	$P<.05$	.050 ± .01	$P<.05$
One month training	3.00 ± .23			
		$P<.05$		
2 month training	3.33 ± .32		.075 ± .01	

The dogs will be evaluated in one month (end of June) for loss of this induction of 2-3 DPG.

Conclusions:

2-3 DPG and 2-3 DGP/H_{ct} is increased with physical training in dogs.

Future Plans:

1. The data on contractility must be completed before any conclusions regarding alteration can be made.

2. A study with training of human subjects and evaluation of 2-3 DPG will be performed in the future. Oxygen dissociation curves will be determined in the human study.

Title of Study: Determination of Factors Limiting Submaximal and Maximal Exercise in Soldiers

Investigators: Malcolm A. Gleser, MAJ, MC and James A. Vogel, Ph.D.

Background:

In the modern Army, men are often called upon to do critical physical work for long periods of time. Fatigue or inability to continue work could cause serious consequences. It is, therefore, important to study the causes of fatigue of prolonged physical work. In previous years we have developed a reliable, reproducible model of prolonged work using the bicycle ergometer, making it possible to study work of precisely defined intensity. This year we have used this model to investigate some of the physiologic determinants of fatigue.

Progress:

The main determinant of endurance time (the length of time until fatigue develops) was found to be the intensity of work (i.e., the load against which the soldier worked). Endurance time (T) and load (L) were found to be related by the following equation:

$$\log (T) = A \cdot L + B$$

However, when this equation is modified to take into account the maximal aerobic capacity (max $\dot{V}O_2$) of each soldier and the relative load (load/max $\dot{V}O_2$) is used in the equation in place of absolute load, i.e.:

$$\log (T) = A_r \cdot (L/\max \dot{V}O_2) + B_r,$$

most of the differences between individuals are eliminated.

We believe that the parameters A_r and B_r are related to the rate of anaerobic metabolism that takes place at any given relative load and that (T) is inversely related to the rate of anaerobic metabolism. Endurance training not only increases max $\dot{V}O_2$, but also changes parameters A_r and B_r in a direction suggesting decreased anaerobic metabolism and increased (T) at any given relative load. Our data support the hypothesis that anaerobic metabolism at submaximal loads is the result of insufficient vasodilation of the muscle blood vessels. In addition, the maximal ability of muscle vasculature to dilate seems to be the limiting factor in determining the maximal oxygen consumption of a given muscle.

Future Plans:

We plan to study the regulation of muscle blood flow in humans and animal models. It may be possible to achieve greater muscle blood flow during heavy submaximal work, thus decreasing anaerobic metabolism and increasing (T).

Title of Study: Changes in Serum and Sweat Magnesium Concentrations During Physical Work in the Heat

Investigators: George A. Beller, MAJ, MC; J. T. Maher, Ph.D.; L. H. Hartley, M.D.; D. E. Bass, Ph.D.; and W. E. C. Wacker, M.D.

Background:

It had been proposed in the literature that magnesium depletion might occur during prolonged physical exertion in the heat and could, therefore, be a factor in the development of heat illness. A study was, therefore, carried out to assess serial changes in serum magnesium concentration in 2 groups of healthy male volunteer subjects during treadmill exercise in a normothermic (21/14°C, dry/wet bulb) and hyperthermic (49/27°C, dry/wet bulb) environment.

Progress:

Under both normothermic and hyperthermic conditions, prolonged exercise (90 min) was associated with a significant decrease in serum magnesium concentration and a reciprocal rise in serum potassium concentration. The fall in serum magnesium was significantly greater under hyperthermic (9%) than normothermic (4%) exercise conditions, whereas the magnitude of serum potassium rise was not significantly different in the 2 studies.

Conclusions:

These data suggest that magnesium depletion might occur during prolonged periods of exertion, particularly in the heat, and may be related to sweat losses of this ion. Since magnesium depletion is associated with tetany and neuromuscular dysfunction, which are also observed in heat exhaustion, the role of this ion in the etiology or symptoms of heat illness merits further study.

Title of Study: Response of Plasma Free Fatty Acids to Lactate Infusion

Investigators: S. R. Giamber, MAJ, MC; A. E. Boyd, MAJ, MC; M. Mager, Ph.D.

Background:

Free fatty acids are an important source of energy to working muscles. It has been shown that at high work loads with concomitant high lactate levels, there is a fall in plasma free fatty acids. This fall was thought to be due to increased re-esterification rather than decreased lipolysis.

This study was undertaken to determine the effects of exogenous lactate on arterial free fatty acids, and glycerol levels. The exogenous administration of lactate would separate the effects of lactate from the other changes that occur with high level work.

Progress:

Six male subjects exercised for 90 min at 38 to 44% of maximal oxygen uptake, a work load which did not increase arterial lactate levels. During the final 30 min of exercise, sodium lactate (6 meq/kg) was infused intravenously, producing a peak plasma level of 9.01(SEM ± .34 μm/l). Serial arterial samples were collected during the exercise, infusion, and recovery periods. Plasma glycerol, FFA, lactate, pyruvate, glucose, insulin, and growth hormone concentrations were compared in the same individuals at a similar work load when they received a control $NaHCO_3$ infusion (4 meq/kg). Lactate and $NaHCO_3$ resulted in the same degree of alkalosis. During lactate infusion, both FFA and glycerol fell whereas with $NaHCO_3$ infusion, both continued to rise (see Table below).

TABLE

Plasma Constituent	Infusion Fluid: Lactate	Infusion Fluid: $NaHCO_3$	
FFA	.707 μm/ml	1.123.μm/ml	P< .05
Glycerol	.044 μm/ml	.064 μm/ml	

Insulin and growth hormone levels were not different in the three infusion periods.

Conclusions:

The rise in lactate appears to lower FFA by inhibiting exercise-mediated lipolysis rather than increasing re-esterification.

Future Plans:

Five subjects recently received lactate infusion while at rest. Results are not available at this time.

Title of Study: Response of Submaximal Heart Rate and Oxygen Uptake During Different Techniques of Treadmill and Bicycle Ergometer Exercise.

Investigators: W. H. Huibregtse,Ph.D.; J. T. Maher, Ph.D.; L.H. Hartley,M.D.

Background:

Heart rate has been observed to change for a given level of oxygen uptake under differing conditions of work. Since heart rate is used to predict maximal aerobic capacity and energy cost of doing work, such non-linearity has obvious implication to interpretation of data based on heart rate changes during work and exercise. This study was designed to measure the change in heart rate-oxygen uptake relationship during submaximal work on an ergometer.

Progress:

Two groups of subjects (total 32) have been compared for their response to differing modes of performing the same absolute work load on the bicycle. Indications derived from eight subjects initially were that heart rate increases with a different slope for equivalent levels of O_2 uptake depending upon the rate of pedalling (40, 50 and 60 rpm). These results were confirmed with a second larger group. Initial treadmill data served as a pilot study for a second group of subjects which indicated that under the work conditions employed there was no such differential effect of mode of working (changes in rate or slope of walking) on HR-O_2 uptake relationship.

Conclusions:

1. When using heart rate as an estimation of oxygen uptake or energy cost, the mode of work should be carefully prescribed.

2. The heretofore assumed linear relationship between heart rate and $\dot{V}O_2$ may hold only under some conditions. This second implication is based on previous data which demonstrate that maximal heart rates and oxygen uptake do not change with differing modes of bicycle or treadmill exercise. Assuming that both these results are accurate, then the paths described by heart rate changes from rest to maximal effort could not be linear.

Since our subjects were not taken to maximal effort, our data are not definitive on this point. Conversely, the studies by others who have maximal heart rates and oxygen uptake values are lacking the intermediate, graded values of these parameters.

Future Plans:

To repeat the study and include graded exercise to maximal oxygen uptake. Oxygen uptakes will be used as an independent variable for each subject by calculation from well-established prior data.

Title of Study: Effect of Endurance Training and Work Hypertrophy on the Biochemical Composition of Red and White Skeletal Muscle

Investigators: Roger W. Hubbard, Ph.D., and Wilbert D. Bowers, Ph.D.

Background:

The study is designed to characterize the changing ultrastructural and biochemical patterns found in red, white and mixed skeletal muscles of rats during ageing and different kinds of training (running vs. weight lifting). The purpose is to correlate these changes with the state of fitness and the type and degree of training received. When this is possible, then the role of other factors known to affect muscle performance and structure, such as neural and humoral agents, can be related to training. Thus, the reservoir of basic biochemical and structural knowledge already derived experimentally can be used to bridge the gap between the training in the laboratory and the soldier's training in the field.

Progress:

Although the analytical portions of this study are yet incomplete, the following observations have been made. Rats trained from one to three months by daily treadmill exercise gain weight more slowly than their sedentary controls (-15%). On the other hand, after three months of training, there is no effect of exercise on the muscle weights per 100 g body weight. In both the trained and sedentary rats, there is a 20% increase in muscle weight per 100 g body weight of the gastrocnemius and plantaris muscles, but no change in the soleus and anterior tibialis.

There is no training effect over the performance of weanling rats after three months of exercise, but there is more than 80% decrement in the performance of the corresponding sedentary controls. These results emphasize that degenerative changes in the sedentary "controls" may be of more importance than alterations in the composition of the trained "experimental" animals.

Preliminary ultrastructural studies suggest that the drastic degenerative changes in muscle mitochondria of exhausted skeletal muscle, reported by others do not occur under the circumstances of these experiments. Measurements of fiber to capillary ratio and fiber size in trained vs. untrained and young vs. old animals are in progress.

The biochemical data quantitating wet and dry weight, tissue water, DNA, protein, cytochrome C and total lipids are being measured.

Title of Study: Effect of Exercise and Training on Metabolic Shuttle Systems

Investigators: J. A. Smoake, CPT, MSC; R. W. Hubbard, Ph.D.; W. D. Bowers, Ph.D.; and J.M.R. Macaione

Background:

During heavy work, glucose is metabolized in the cytoplasm via the glycolytic pathway. In this process two moles of ATP are formed from the metabolism of glucose; also, one mole of NAD is reduced to NADH. It is necessary for the reduced NAD to be reconstituted for glycolysis to continue since NAD is present only in catalytic quantities. At least 3 mechanisms exist for the reoxidation of reduced NAD. These hydrogen accepting systems include the formation of lactate from pyruvate, the formation of dihydroxyacetonephosphate from alpha-glycerophosphate, and the formation of oxalacetate from malate. The second and third pathways are components of metabolic shuttle systems, which pass hydrogen ions into the mitochondria. Once in the mitochondria, malate is oxidized directly by the TCA cycle and the electron transport system with the formation of 3 ATP molecules; oxalacetate which is reformed from malate in the TCA cycle can migrate from the mitochondria to the cytoplasm where the cycle may start again. The alpha-glycerophosphate enters the mitochondria where it is converted back to dihydroxyacetonephosphate with the formation of 2 moles of ATP. Once reformed, the dihydroxyacetone phosphate diffuses back into the cytoplasm to begin its cycle again.

All of the pathways mentioned above for the oxidation of cytoplasmic NADH have been demonstrated in resting mammalian muscles. However, no studies have been done for the determination of functional changes of these enzymes and substrate pools during exercise of the intact animal, trained or untrained. The purpose of this study was to examine the enzymatic activities of lactic acid dehydrogenase, malic acid dehydrogenase, and glycerophosphate dehydrogenases (mitochondrial and cytoplasmic forms) and the substrates pools (pyruvate, lactate, GP, DHAP, malate and DAA) during and after exercise as well as at rest in trained and untrained rats.

Progress:

Rats were trained to run on a treadmill and were exercised 30 min. a day, 5 days a week for 12 weeks. The work was gradually increased from

the first to the fourth week until the rats were running 30 meters/min. at a 6° incline after the fourth week. One group was trained for 8 weeks; a second group was trained for 12 weeks. Untrained sedentary controls were maintained for both trained groups. At the end of the training regime each group was divided into 4 subgroups. Muscles (red and white) were taken from 6 animals which had not been exercised for 24 hours. Muscles were also taken from 6 animals which had been run on a treadmill for 30, 60 minutes or until exhausted. Immediately after the designated exercise period, the rats were anesthetized with Napentabarbital via heart puncture. The gastrocnemius and anterior tibialis from the left leg were dissected free from adjacent muscles and frozen in situ with Wallenberger clamps cooled in liquid nitrogen.

Untrained rats were exercised to exhaustion and for intermediate periods short of exhaustion, and muscles were taken in a manner similar to that with the trained rats. A group of untrained rats weighing 80-100 gm was treated in a manner similar to the other untrained controls.

All muscles were frozen at $-70^{\circ}C$ until they were assayed. The muscles have been assayed for the enzymes and their substrates.

Conclusions:

None, pending analysis of data.

Future Plans:

No future studies are being considered.

(82104)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA 0A 6143	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	060
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Development and Characterization of Models of Heat Injuries and Disabilities and Other Heat Response of the Soldier (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

005900 Environmental Biology; 003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 72	0.5	62.6
	CURRENT 73	0.5	60.0

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL

NAME: Jones, LeeRoy G. COL

TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME:* Robinson, Sumner M. Dr.

TELEPHONE: 955-2824

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Banderet, Louis E. Dr.

NAME: Maher, John T. Dr. DA

21. GENERAL USE

Foreign Intelligence not Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Disabilities; (U) Military Heat Stress; (U) Pathology Model; (U) Physiology; (U) Biochemistry; (U) Behavior; (U) Tolerance; (U) Heat

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Develop and characterize models, i.e., experimental equivalents or analogues, of heat stress and heat-induced injuries and disabilities in the soldier.

24. (U) Models will be produced using experimental animals, mathematical and physical stimulation, or human subjects. The injury, disability or response will be induced directly by heat or indirectly by chemicals or other agents. Physiological, pathological, biochemical, behavioral or other studies will then determine the nature and usefulness of the model in examining methods of prevention, amelioration, and treatment. Physical and mathematical analogues of heat responses will be produced and studied for predictive value in determining the soldier's tolerance to heat stress.

25. (U) 71 07 - 72 06 Studies in man on the alteration of heart rate and rectal temperature with acclimatization to heat have resulted in a model which estimates the importance of acclimatization for any given environment and clothing combination, suggesting optimal rates of induction (and indicating probable decay rates) of the acclimatized state as a function of days of exposure (or non-exposure).

*Available to contractors upon originator's approval.

DD FORM 1 MAR 68 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

(82105)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6144	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8b. DISP'N INSTR'N	8c. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.02.A	3A061102B71R	05	061
b. CONTRIBUTING				
c. CONTRIBUTING	CDOG 141 (2a)			

11. TITLE (Precede with Security Classification Code)* (U) Development and Characterization of Models to Study Acute Mountain Sickness and High Altitude Pulmonary Edema in Military Operations (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*
013400 Psychology; 012900 Physiology; 005900 Environmental Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
PRECEDING FISCAL YEAR 72	2.5	150.7
CURRENT FISCAL YEAR 73	2.4	150.0

19. RESPONSIBLE DOD ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Banderet, Louis E. Dr.
TELEPHONE 955-2857
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Horstman, D. H. Dr.
NAME: Maher, J. T. Dr.

21. GENERAL USE
Foreign Intelligence not Considered

DA

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Altitude; (U) Pulmonary Edema; (U) Mountain Sickness; (U) Acclimatization; (U) Hypoxia; (U) Performance; (U) Military Operations

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Development of models, i.e., predictive procedures, for identifying and characterizing those aspects of acute mountain sickness (AMS) and high altitude pulmonary edema (HAPE) relevant to the success of military operations at high terrestrial elevations.

24. (U) Models will be developed for studying (1) etiology of AMS and HAPE; (2) their symptomatology; (3) related functional deficits and disabilities; and (4) factors affecting recovery, in order to develop procedures for improving military effectiveness under high mountain conditions.

25. (U) 71 07 - 72 06 Unobtrusive behavioral measures, which permit assessment over relatively long periods of time, have been developed to quantitate changes indicative of AMS in the cage-roving squirrel monkey. This animal model is providing objective and quantitative behavioral indices of the time course and severity of AMS symptoms and will be used in the assessment of therapeutic regimens and acclimatization procedures. Other studies have demonstrated that reduced core temperatures which result when chair-restrained or cage-roving squirrel monkeys are exposed to hypoxia are due primarily to reduced oxygen consumptions. Rats treated with Persantin prior to exposure to hypoxia maintained greater levels of myocardial metabolites, e.g., adenosine triphosphate and creatine phosphate than controls. When six human test subjects were exposed to 12,000 ft. simulated altitude and exercised on a bicycle ergometer, four showed evidence of intravascular coagulation; such hematological changes were not observed in men exercising at sea level. This finding supports previous studies which implicate intravascular coagulation in HAPE.

*Available to contractors upon originator's approval

Title of Study: Validation of a Squirrel Monkey Behavioral Model for an Environmentally Induced Illness (Acute Mountain Sickness)

Investigator: L. E. Banderet, Ph.D.

Background:

Previous work at USARIEM has suggested that squirrel monkeys, in response to a hypoxic environment, exhibit physiological and behavioral changes which resemble acute mountain sickness (AMS) in man. For example, the first few days that squirrel monkeys are exposed to simulated altitude, food and water intake are reduced, activity is decreased, and the animals are relatively unresponsive to external stimuli. Accordingly, we have been investigating the appropriateness of the squirrel monkey as an animal model for AMS, so that drug regimens, acclimatization procedures, and the physiological basis for AMS can be studied in the laboratory under conditions too severe for human experimentation. Such a model requires that the physiological and behavioral changes which occur in response to altitude can be quantified.

Approach:

Squirrel monkeys were put in plexiglass chambers together with food and water, and altitude was simulated with gas mixtures. Behaviors which changed after ascent to altitude were noted as were behaviors which showed recovery following return to sea level. After these stress-sensitive behaviors were identified, a cage-chamber system with appropriate instrumentation was designed to allow assessment of these behaviors over a 2-3 week period of time.

Progress:

A cage-chamber system has been constructed which permits objective assessment of altitude-sensitive behaviors in the cage-roving squirrel monkey. This environmental system encourages playful activities and elicits behaviors such as climbing, swinging, and leaping. Within this setting, we have instrumented various measures so that qualitative and quantitative estimates of the animal's behavior, e.g., the animal's posture, location in the cage, type of motor activity, can be determined.

These automated measures maximize objectivity, permit unobtrusive measurement, and allow continuous day and night behavioral measurements of each animal. Food and water consumption, core temperature and body weight are measured once each day.

Using this cage-chamber, studies are being conducted to determine the validity of using the squirrel monkey as a model for AMS. These studies are designed to investigate the response of the squirrel monkey to different simulated altitudes, and to determine the effectiveness of treating squirrel monkeys exposed to hypoxia with acetazolamide, a drug known to reduce AMS in man.

Implications and Future Plans:

If these studies validate the use of this behavioral model, future studies will involve testing other pharmacological compounds that may provide a rationale for use in prevention and treatment of AMS.

Title of Study: Hypoxia-Induced Poikilothermia in the Squirrel Monkey

Investigators: L. E. Banderet, Ph.D., and D. Horstman, Ph.D.

Background:

Most species of mammals manifest decreased core temperatures when exposed to a hypoxic environment; thus, we have observed such temperature changes in cage-roving and chair-restrained squirrel monkeys shortly after acute exposure to hypoxia. Furthermore, when squirrel monkeys are chronically exposed to hypoxia, core temperatures are depressed during days 1-3 at altitude but recover with increased time at altitude. Since recovery of core temperature follows the time course of other physiological and behavioral measures of altitude acclimatization, we are interested in identifying the physiological correlates responsible for core temperature alterations during hypoxia.

Approach:

Six squirrel monkeys, previously chair-restrained and extensively habituated to the experimental setting, were tested with various gas mixtures to produce normoxia, two levels of hypoxia, and two levels of hypoxia plus hypercapnia. Oxygen consumption ($\dot{V}O_2$), CO_2 production (V_{CO_2}), and rectal (T_{re}) and skin temperatures (abdomen, leg, tail, and foot) were measured. From these measurements, heat content and storage, tissue conductance, and peripheral blood flow were estimated to determine whether decreased core temperatures result from decreased heat production, increased heat losses, or a combination of reduced heat production and increased heat losses.

Results:

Exposure to 11% O_2 resulted in a 20% decrease in $\dot{V}O_2$ and a 1.5°C reduction in T_{re}; exposure to 8% O_2 resulted in an additional 10% reduction in $\dot{V}O_2$ and a further decrease in T_{re} of 0.5°C. The addition of 5% CO_2 to the 8 and 11% O_2 gas mixtures resulted in partial recovery of both $\dot{V}O_2$ and T_{re}. When 21% O_2 was restored, an initial $\dot{V}O_2$ overshoot of about 20% above normal was observed accompanied by the rapid recovery of T_{re} to slightly above normal levels. Skin temperature responses to hypoxia were varied and individualized and do not appear to be a major contributory factor to the observed decreases in core

temperature. Thus, when squirrel monkeys are exposed to hypoxia, changes in body heat content can be accounted for by reduced heat production ($\dot{V}O_2$) since changes in T_{re} paralleled changes in $\dot{V}O_2$.

Future Plans:

The role of oxygen availability will be studied in a repetiiton of the experiments previously described with the inclusion of serial measurements of arterial pO_2, pCO_2, pH and O_2 saturation, blood pressure, heart rate and cardiac output. Furthermore, in separate experiments, skeletal muscle activity will be eliminated by gallamine infusion and respiration will be artificially controlled. Comparisons of $\dot{V}O_2$ (and T_{re}) under conditions of altered O_2 availability, without the interference of muscular activity, should indicate whether reduced metabolism is a function of O_2 availability or altered muscular activity.

Title of Study: Persantin in Hypoxia: Influence on Myocardial Function, Ultrastructure, and High Energy State

Investigators: J. T. Maher, Ph.D.; W. D. Bowers, Ph.D.; R. Francesconi, Ph.D.; and G. A. Beller, MAJ, MC

Background:

Acute exposure to hypoxia is associated with a transient increase in cardiac output lasting no more than a few days. However, following several days' exposure to a hypoxic environment, there occurs a fall in cardiac output to below the normal value, the result of a progressive decline in stroke volume despite a relative tachycardia. Restitution of stroke volume to sea-level values has not been accomplished by restoring filling pressure and blood volume to normoxic levels, which suggests an alteration of myocardial contractility as a causal factor. Indeed, data from this laboratory on chronically hypoxic dogs have indicated a reduction in myocardial performance; finally, metabolic and ultrastructural studies on cardiac muscle from chronically hypoxic animals have shown a marked depression of high energy phosphates and disruptive changes in fine structure.

In an effort to prevent or ameliorate the adverse effects of hypoxia on the myocardium, drugs of the dipyridamole group are currently being investigated. Characteristic of such agents is a striking vasodilating action upon the coronary system. These drugs have been shown to increase coronary sinus oxygen saturation without significantly altering myocardial oxygen consumption, and to exert a positive inotropic effect in man and animals.

Progress:

Hearts from control and experimental rats have been examined following exposure to hypobaric hypoxia. In the untreated animals, the hypoxic state caused a marked decrease in the myocardial stores of adenosine triphosphate and creatine phosphate. In the animals first treated with Persantin and then placed in an hypoxic environment, only a slight reduction in high energy phosphates was observed. Although samples of ventricular myocardium from both groups have been fixed and processed for electron microscopy, examination has not yet begun.

Conclusions:

A protective action of Persantin against the hypoxia-induced diminution of the myocardial energy potential has been demonstrated. The metabolic data suggest a resultant beneficial or preservative effect on ventricular performance.

Future Plans:

Hemodynamic studies will be performed to determine whether the protective action of Persantin on cardiac energy metabolism during hypoxic exposure gives rise to a functional advantage.

Title of Study: Intravascular Coagulation and Fibrinolysis During Exercise at Altitude

Investigators: R.P. Hogan, MAJ, MC and R.W. Hubbard, Ph.D.

Background:

In an earlier study at this Institute, it was found that two of the four test subjects studied demonstrated pathologically high levels of fibrin degradation products (FDP) 45 to 90 minutes after exercising at approximately 70% of maximum for 30 minutes while exposed to a simulated elevation of 11,000 feet. Levels were normal 18 hours later following eight hours of sleep, but were elevated again after another bout of exercise. Subjects were exposed to the same degree of hypoxia throughout the study. Other studies at this Institute have shown that significant elevations of FDP do not occur following exercise to exhaustion at sea level.

In an earlier protocol (Pilot Study: A proposed mechanism for the pathogenesis of high altitude pulmonary edema, by R.P. Hogan), a mechanism relating the production of high altitude pulmonary edema (HAPE) to specific abnormalities in the fibrinolytic system was proposed. Hultgren, Grover, and Hartley (Circulation, 44:759, Nov. 1971) recently postulated a similar mechanism.

Progress:

To obtain evidence for a clotting diathesis at altitude during exercise, six normal volunteer test subjects were studied in the hypobaric chamber at a simulated altitude of 12,000 ft. Three subjects exercised on the bicycle ergometer for three hours at approximately 50% of maximal oxygen uptake; the other three exercised intermittently for three hours at approximately 70% of maximal on a schedule of 10 minutes exercise followed by five minutes rest. Blood samples were taken before depressurization of the chamber, after one hour of rest at a simulated altitude of 12,000 ft., after each of three hours of exercise, and after a final hour of rest at altitude. Blood was analyzed for intravascular coagulation (protamine gelation test), fibrinolysis (staphylococcal clumping test and tanned red cell hemaglutination inhibition test), increased platelet aggregation and/or presence of circulating microclots (screen pressure filtration method), and free fatty acids. This protocol was repeated at sea level three weeks after altitude exposure.

Conclusions:

Four of the six subjects showed evidence of intravascular coagulation while exercising at altitude. None evidenced any abnormality after one hour of rest at altitude or as a result of exercise at sea level. It is postulated that the combination of hypoxia and exercise causes severe venous hypoxia and acidosis in the exercising extremities and that these circumstances result in a clotting diathesis. This lends further credence to the possibility that HAPE may result, following exercise at altitude, from partial pulmonary vascular occlusion by platelet thrombi or fibrin microthrombi. It is thought that individuals who are susceptible to HAPE do not develop fibrinolysis in response to intravascular coagulation at altitude.

Future Plans:

A group of individuals known to be susceptible to HAPE should be studied in the manner described above.

Project No: 3A061101A91C

Title: In-House Laboratory Independent Research

(81101)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OB 6121	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	K. Completed	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	020
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)* (U) Factors Limiting Military Performance at Sea Level and High Altitude and their Modification by Acclimatization and Adaptation (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

005900 Environmental Biology; 012900 Physiology; 016200 Stress Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:

b. NUMBER:*

c. TYPE: d. AMOUNT:

e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR — PRECEDING: 72	1.0	14.3
FISCAL YEAR — CURRENT:		

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL

NAME: Jones, LeeRoy G. COL

TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME:* Hartley, Loren H. Dr.

TELEPHONE: 955-2800

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME:

NAME:

21. GENERAL USE

Foreign Intelligence not Considered

DA

22. KEYWORDS (Precede EACH with Security Classification Code) (U) High Altitude; (U) Exercise; (U) Military Performance; (U) High Altitude Natives; (U) Atropine

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) High altitude environments are known to lead to decreased performance and disability. It is possible to minimize the effects of high altitude by acclimatizing individuals, but it is not practical to leave large numbers of troops at such locations. Hence, the purpose of these studies was to define the mechanism by which natural acclimatization occurs in an effort to develop ways of normalizing performance at altitude.

24. (U) This study was carried out in August and September of 1970. Subjects were examined at rest and during work to determine the extent of their disability. Cardiac output was measured to assess the importance of the heart in this disability. Muscle glycogen was measured to determine if this fuel which is used by the exercising muscle is deficient after ascent to altitude. Atropine was administered at high altitude to determine if the reduction in maximal exercise heart rate which occurs could be reversed and hence enhance working performance.

25. (U) 71 07 - 72 06 These studies have been completed and the results analyzed. Data will be presented in nine complete publications and two abstracts. Results may be summarized:

1. Cardiac output is decreased during maximal work at 2 days and during submaximal and maximal work at 10 days. a) the reduction in cardiac output is correlated with an increasing systemic vascular resistance.
2. Endurance time during submaximal work is decreased to a greater extent at 2 days than 10 days at altitude. a) muscle glycogen is equal at both times.
3. Maximal heart rate is reduced at 16,000 ft elevation. a) the reduction is partially reversed by atropine; b) the reversal of the depression of heart rate is not associated with improvement in working capacity.
4. The hemoglobin dissociation curve at high altitude is shifted to the right.
5. High altitude natives are superior to sojourners in the following respects: a) greater maximal cardiac output; b) better O_2 diffusion in lungs; c) lower blood lactate levels; d) higher hemoglobin concentrations.
6. High altitude natives have shifts in hemoglobin dissociation curve which are equal to the sojourners. This completes this study.

*Available to contractors upon originator's approval

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(81102)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6138	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA - CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	D. Change	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	021
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)* (U) Historical Analysis, Development and Distribution of Military Environmental Medical Information (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

005900 Environmental Biology; 00600 Escape, Rescue and Survival

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:

b. NUMBER:*

c. TYPE: d. AMOUNT:

e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	0.3	18.8
FISCAL YEAR CURRENT 73	0.5	25.0

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL

NAME: Jones, LeeRoy G. COL

TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME:* Goldman, Ralph F. Dr.

TELEPHONE: 955-2831

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME: Evans, Wayne O. LTC

NAME: 955-2814 DA

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Training; (U) Military Information; (U) Military Tactics

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23.(U) Address collection and retention of available knowledge on the effects of heat, cold, work and high terrestrial elevations on military performance, evaluate techniques for its dissemination and improve the communication between the military man with an environmental problem and the scientists with relevant information.

24.(U) Analyze information on the impact of extreme terrestrial environments on past and present military operations; evaluate historical solutions to these problems. Develop effective liaison with US AMC, CDC, Navy and Air Force elements developing protective items or planning tactical operations where such problems can be anticipated, as well as with similar groups abroad. Expand dissemination by lectures at military academies and training courses, and preparation of material for military manuals. Ascertain present state of military environmental medicine knowledge and doctrine by Army Medicine Department of Personnel.

25.(U) 71 07 - 72 06 Improved communication with a large number of military groups has developed closer interaction with Arctic Test Center, Northern Warfare Training Center, the US PHS Alaska, Army Infantry School, Medical Field Service School, Fort Ord, Fort Hood, Fort Carson and its Recondo School, CBR School Command and General Staff College, etc., and suggested possible collaborative work on operational problems to be conducted over the next few years and an expanded lecture series and consulting service by USARIEM. Active participation on NATO Combat Clothing and Equipment Development Working Group Meetings, and with Commonwealth Working Groups is continuing. Visiting Scientists from UK, India, Japan and Israel have been arranged. Consultation to CDC (combat tactics under heat stress) is ongoing. Studies on performance (productivity and learning) under moderate environmental stress are being coordinated through participation in Technical Committees of the American Society of Heating, Refrigerating and Air-Conditioning Engineers.

*Available to contractors upon originator's approval.

DD FORM 1 MAR 68 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

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Title of Study: Approaches to Dissemination of Military Environmental Medical Information

Investigators: Ralph F. Goldman, Ph.D.; LeeRoy G. Jones, COL,MC, M.D. and all other USARIEM staff

Background and Approach:

The military commander frequently has problems or questions which can be answered by a research specialist in military environmental medicine, either from his base of expertise, his ongoing research program, or by access to the available scientific literature. Direct communication between these two types of individual with such widely different training, work environments and approaches to problem solving is frequently hampered by terminology barriers. Nevertheless, such communication is essential for the military commander to be able to attract and direct the interests of an investigator towards his problems of military operations in the field and, equally for the researcher to be able to orient his research program and to have the output of his research serve the people for whom it is being carried out. This work unit approaches the problem along three rather distinct lines: a) formal and informal instruction or participation in curriculum development at the various military training centers; b) liaison visits and briefings given at military bases with operational forces; c) information exchange, and occasional collaborative research, with other Department of Defense representatives and other countries, industry and universities. These approaches have the objective of defining "best" methods for communication between the laboratory and the "line".

Conclusions:

Formal lectures have been delivered as part of the military training programs at Walter Reed Army Institute of Research, Washington, DC; US Army Infantry School, FT Benning, Georgia; at the CBR School, FT McClellan, Alabama; at the Army Material Command Arctic Test Center, FT Greely, Alaska; at the Army Environmental Health Agency, Edgewood, Maryland; and to a special class at USARIEM for students drawn from a variety of military establishments. In addition, arrangements have been completed for participation in the course of instruction at Command and General Staff School next year, and other potential sites where USARIEM participation in training or provision of a curriculum material might be beneficial have been identified.

Copies of training films have been prepared which are available from USARIEM. A computer program detailing the latest USARIEM prediction model for physiological responses for men wearing protective uniforms was developed in a format compatible with ADP equipment at the CBR School, FT McClellan, and furnished to the school for use in its doctrine development and training programs.

Liaison visits and briefings have been given to the US Military Academy, West Point, NY; FT Carson, CO; FT Hood, TX; FT Benning, GA; FT Ord, CA; FT McClellan, AL; FT Greely, AK; FT Rucker, AL; and the Praesidio of San Francisco, CA and have resulted in improved communications between USARIEM and commands and surgeons stationed at these activities.

A special symposium on Physical Fitness in the Military was held at USARIEM to review the current state of knowledge, discuss the goals of physical fitness programs and evaluate the training and assessment procedures in use by various military forces; representatives from US Army, Air Force, Navy, Marine, and Canadian, United Kingdom and German Armed Forces participated. Continuing information exchange with counterpart elements at Edgewood Arsenal, at Naval Medical Research Institute, Bethesda, Maryland, at Wright-Patterson Air Force Base in Ohio, and with the Army Personnel Research Establishment and the Canadian Defence Research Establishment, Ottawa are routinely carried out. USARIEM scientists have participated (frequently at the invitation of the sponsoring element in the foreign country) in conferences on Clothing and Comfort in England, on Circumpolar Living in Finland, on Operational Aspects of Combat Clothing and General Equipment at the 10th Commonwealth Conference held in Canada, and with the NATO Combat Clothing and Equipment Working Group. Collaborative studies with counterparts from foreign countries have included visiting scientists from Israel, Sweden, Japan and England. Collaborative studies are being carried out with personnel at the University of Vermont, and at Kansas State University Institute of Environmental Sciences. Other information exchanges have been carried out by exchange of lectures with personnel at MIT, Boston University, the National Bureau of Standards, the American Society of Heating, Refrigeration and Air-Conditioning Engineers, the John B. Pierce Foundation Laboratories.

Future Plans:

It is felt that this work should be continued for one additional year a) to examine the continuing nature of some of the contacts estab-

lished, b) to evaluate the extent to which successful completion of the proposed collaborative studies with some of the military activities is accomplished, and c) to expand contacts within the Department of the Army and extend them on a broader base to Navy, Air Force, NASA, and other government activities where military environmental medical input would be of use to them, or where their problems would be helpful in solving research problems in military environmental medicine.

(81103)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OC 6139	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISS'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
	A. New	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	023
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)
(U) Development of Performance Measures for Simulated Military Team Tasks (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
013400 Psychology; 005900 Environmental Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
72 07		DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING	-	0	-
FISCAL YEAR CURRENT	73	1.3	93.0

19. RESPONSIBLE DOD ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION
NAME: USA Rsch Inst Env Med
ADDRESS: Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Banderet, Louis E. Dr.
TELEPHONE: 955-2857
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Stokes, James W. MAJ
NAME: 955-2856 DA

21. GENERAL USE
Foreign Intelligence Not Considered

22. KEYWORDS (Precede EACH with Security Classification Code)
(U) Performance; (U) Simulation; (U) Motivation; (U) Behavior; (U) Psychology; (U) Military Tasks; (U) Military Stress

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Military tasks requiring cognition, psychomotor ability, attention, information processing and transmission, and decision-making are inadequately evaluated in the laboratory by current measures of performance. This research will assess military team tasks in the laboratory and develop performance measures which are predictive to the field.

24. (U) Several task, subject, and situational variables which affect performance have been identified, e.g., task duration and complexity, subject's motivation, interest and proficiency with the task, knowledge of results, consequences of performance. Yet, many laboratory investigations of military performance have (1) studied isolated components of behavior (reaction time, psychomotor ability, arithmetic ability, hand strength), (2) measured behaviors unrelated to the field task, and (3) ignored or eliminated many of the task, subject and situational variables inherent in a military field task. As a result, such data often have little generality to tasks or situations other than those of the laboratory. To develop performance measures that are predictive to field operations, this research strategy will select critical military tasks, e.g., situations where human variability is maximal and the consequences of human error can be catastrophic. These tasks will be simulated in the laboratory; military personnel will be studied with environmental and temporal conditions similar to those in the field. Stress-sensitive behaviors which affect both individual and group performance on the simulated team task will be identified, measured, and tolerance limits determined for conditions of heat, cold, high altitude, and combinations of these stressors. With this means of performance assessment, more effective strategies for reducing performance disabilities can be evaluated.

*Available to contractors upon originator's approval.

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(81103)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6139	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	H, Terminated	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	023
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)* (U) Fundamental Research in Life Sciences of Intermediate and Long-Range Military Importance (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

016200 Stress Physiology; 005900 Environmental Biology; 002300 Biochemistry

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
70 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	2.5	79.8
FISCAL YEAR CURRENT		

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL

NAME: Jones, LeeRoy G. COL

TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME:* Robinson, Sumner M. Dr.

TELEPHONE: 955-2824

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Kobrick, John C. Dr.

NAME: Cymerman, Allen Dr. DA

21. GENERAL USE

Foreign Intelligence not Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U)Heat; (U)Cold; (U)Altitude; (U)Work; (U)Physiology; (U)Biochemistry; (U)Pharmacology; (U)Pathology; (U)Psychology; (U)Adaptation; (U)Metabolism

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) To increase knowledge of Life Sciences at all levels of function, from molecular levels to the total organism, in order to anticipate militarily relevant problems of the intermediate and more distant future.

24. (U) To support intriguing research in Life Sciences which does not normally have high mission priority, but which has unusually high scientific merit combined with potential military relevance.

25. (U) 71 07 - 72 06 In mice, cold exposure results in increased activities of the catabolic enzymes tryptophan oxygenase and tyrosine aminotransferase. These changes do not appear to be affecting the availability of the substrates tryptophan and tyrosine, or the brain monoamines norepinephrine (NE) and serotonin. In man, excretion of 3-methoxy-4-hydroxyphenylglycol, a metabolite of NE which may be indicative of brain NE activity, shows a diurnal variation, is increased during cold exposure and correlates with individual physical activity. Studies on changes in energetics with induced obesity have indicated little or no change in basal metabolic rate or work efficiency when correction is made for body weight. Reason for termination: the studies under this work unit have been transferred to mission funded projects.

*Available to contractors upon originator's approval.

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Title of Study: Effects of Cold Exposure on the Daily Periodicity of Central and Peripheral Amino Acid Metabolism in Mice

Investigators: Ralph Francesconi, Ph.D. and Milton Mager, Ph.D.

Background and Rationale:

There has been increased attention focused on the relationship between peripheral levels of amino acid and central nervous system catecholamines. For example, the amino acids tryptophan and tyrosine are the precursors to the central neurotransmitters serotonin and norepinephrine respectively. These compounds are known to have roles in behavior, regulation of body temperature, and sleep-wakefulness cycles. Recently, it has been demonstrated that increased levels of plasma tryptophan can effect concomitant increases in brain serotonin. Following up on our interest in the catabolism of these amino acids by liver enzymes, we wished to determine whether increased levels of these enzymes affected plasma and brain levels of tryptophan and tyrosine. Simultaneously, we hypothesized that the effects on tryptophan and tyrosine might also be reflected in levels of brain serotonin and norepinephrine.

Progress:

We had previously demonstrated that acute exposure of mice to cold stress (1-3°C) causes rapid increases in the activity of the liver enzymes - tryptophan oxygenase and tyrosine aminotransferase - thus, disrupting their normal circadian periodicity patterns. Presently, we are extending these studies to longer periods of cold exposure (up to 6 weeks), and concurrently measuring liver enzymes as well as plasma and liver levels of serotonin and norepinephrine. Preliminary results indicate that the rapid elevations of liver enzyme activity observed with acute cold exposure are attenuated with extended exposure. Recent data indicate that ultimately liver and plasma levels of amino acids as well as levels of amines in the central nervous system may be affected as a result of more prolonged exposure to cold. Experiments and data collection on this study are still in progress.

In a recent study we have demonstrated that 48 hours of starvation similarly effected marked alterations in the periodic oscillations of tryptophan and tyrosine metabolism. Interestingly, plasma levels of these amino acids dropped sharply after 12 hours of food deprivation;

however, during the ensuing 36 hours their concentration increased, probably as a result of amino acid mobilization and protein degradation. Upon refeeding, plasma levels of both tryptophan and tyrosine rapidly increased. The results indicated that the regulation of the catabolic liver enzymes, tryptophan oxygenase and tyrosine aminotransferase, is probably most affected by glucocorticoid hormones and protein intake respectively.

The aromatic amino acids, tryptophan and tyrosine, because of their unique roles in serotonin, norepinephrine, and thyroxine synthesis, and as essential amino acids in protein synthesis, are excellent models for studying the effects of stressors on amino acid (protein) metabolism.

Title of Study: Performance in a Stress Situation and Its Relationship to Catecholamine Metabolism and Affect State

Investigators: Allen Cymerman, Ph.D.; John C. Shershow, MAJ, MC; and Sumner Robinson, Ph.D.

Background and Rationale:

Recent studies have shown that epinephrine, norepinephrine, and their urinary metabolites are a reflection of man's response to physical and psychological stresses, not unlike those found in military life. Further, it has been suggested from laboratory and field reports that subjects who perform very well can usually be characterized as high norepinephrine excretors; conversely, those who do not perform well tend to be low excretors of norepinephrine. In this study, we are investigating the relationship of 3-methoxy-4-hydroxyphenylglycol (MHPG), a metabolite of norepinephrine, to several psychological parameters (mood and affect state) and physical activity. It has been suggested that catecholamine activity in the central nervous system can be evaluated by the excretory pattern of this metabolite.

Progress:

The determination of MHPG in urine by gas-liquid chromatography (GLC) has recently been perfected so that routine assay of nanogram quantities is feasible, and a large number of samples can be handled on a weekly basis. The use of a single urine aliquot for the simultaneous determination of four catecholamine metabolites--vanillylmandelic acid (VMA), MHPG, metanephrine, and normetanephrine--was evaluated and found incompatible with the GLC procedures. Presently, metanephrine and normetanephrine are assayed as 3-methylated catecholamines concurrently with VMA, while extraction and identification of MHPG requires a completely separate procedure.

MHPG excretion has been measured in 6 men exposed to cold. The subjects were placed on a liquid diet and housed in a controlled environment for five days, exposed to 56-57°F (cold) for two days, followed by two days under comfortable control conditions. Individual levels of physical activity were determined and psychological tests administered. The data obtained from this study are presently being analyzed. Preliminary results indicate that: (1) individuals can

be distinguished as high/low excretors of MHPG; (2) there may be a significant correlation with mood and affect state; (3) there is approximately a 50 percent increase in urinary MHPG after 48 hours exposure to moderate cold stress; and (4) there is a rhythm of MHPG excretion characteristic for the individual.

Future Plans:

Studies are being designed whereby subjects will be classified according to their excretion pattern of MHPG, i. e., high and low excretors;their performance will then be measured during situations of both physiologic and psychologic stress.

Title of Study: Carbon Dioxide Sensitivity and Personality

Investigators: John C. Shershow, MAJ, MC; Allen B. King, MAJ, MC; and Sumner Robinson, Ph.D.

Background:

Carbon dioxide sensitivity refers to the ventilatory response of a test subject to an increased level of CO_2 in his inspired air. We initially became interested in this measurement because of the possibility of its correlation with respiratory and body temperature responses to heat stress. Subsequently, it has appeared to have more value as an index of autonomic reactivity, and may be associated with differing personality characteristics.

Progress:

During the past year we have measured CO_2 sensitivity in an attempt to relate it to the response of subjects during exposure to environmental stress. We have used a simple rebreathing technique which measures CO_2 sensitivity by relating ventilation to the increase in alveolar CO_2.

Thus far, we find CO_2 sensitivity to have a strong association with certain personality traits. Using the Minnesota Multiphasic Personality Inventory (MMPI), we have found low responders to CO_2 to be significantly higher on trait depression, psychasthenia, psychopathia, and social introversion. We interpret these results as indicative of a psychophysiological relationship which manifests itself via the reticular activating system (which we detect with our test for CO_2 sensitivity), as well as being reflected in the "personality traits" measured by the MMPI.

Future Plans:

Future research will address the subject's CO_2 sensitivity variation over time (weeks to many months), and how personality varies with any such change. We also will consider altering CO_2 sensitivity, possibly by pharmacological means.

Title of Study: Effects of Extended Hypoxia and Cigarette Smoking On Visual Performance, Aqueous Outflow, and Intra-ocular Pressure

Investigators: John L. Kobrick, Ph.D., Ralph Rosenthal, MAJ, MC , and Budd Appleton, COL, MC

Background and Progress:

Data analysis has been completed in studies of eight human subjects exposed to two hypobaric equivalent altitudes of 10,000 and 15,000 feet for 48 hours each. Following 1, 20, 24, and 44 hours of exposure, measurements were made of dark adaptation thresholds, peripheral visual fields, aqueous outflow rate in the anterior chamber of the eye, and intra-ocular pressure. The effects of the two hypoxia levels on aqueous outflow in the anterior chamber were mixed, in that half of the subjects had slight flow increases, and the other half had moderate reductions or remained unchanged. These data are presently undergoing further analysis. The intra-ocular pressures showed little or no alteration. The data obtained at 10,000 feet exposure showed a moderate deterioration in dark adaption thresholds in the first test session compared to later measurements. Some recovery was evident with continued exposure to hypoxia, confirming both earlier findings that hypoxia disrupts dark adaptation, and more recent findings of Kobrick and Appleton on recovery of dark adaptation. The perimetry data showed moderate constriction in peripheral fields at 10,000 feet exposure with the greatest losses occuring in the superior medial vision areas. This confirms ealrier findings for peripheral color detection in which decrements were analogously distributed but substantially larger. Smoking at 10,000 feet had little effect on the data.

The data for 15,000 feet were much more clear-cut, showing decrements in both dark adaptation thresholds and peripheral visual fields. The added effect of smoking served to substantially increase these losses. The dark adaptation data showed an initial large impairment due to hypoxia, followed by gradual recovery after the first hour of exposure, confirming previous findings again as well as the data obtained at 10,000 feet. The effects of smoking were additive to those of hypoxia, and served to reduce any recovery trends seen. The results indicate that smoking at altitude can produce impairments greater than those caused by hypoxia alone. At higher altitudes, these effects are sufficiently increased to produce visual perception problems for troops

who may smoke in the field. These effects may moderate but not substantially recover with continuing hypoxic exposure. This finding is interesting in view of the fact that earlier studies from this Institute had revealed an additive effect of hypoxia and carbon monoxide on reduced ability of men to perform work at altitude. Since smoking is associated with an increase in carboxy-hemoglobin in the blood, smokers who must function at altitude may suffer an even greater decrement in visual performance than non-smokers under conditions where atmospheric carbon monoxide may be expected to be present, e.g., enclosed vehicles, tents.

(81101)

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OC 6136	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
	A. NEW	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	025
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)*

(U) Disease Susceptibility of Soldier in Harsh Environments (22).

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

002300 Biochemistry; 003500 Clinical Medicine; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
72 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
PRECEDING FISCAL YEAR		
CURRENT FISCAL YEAR 73	0,5	30.0

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med
ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Casey, Francis B. Dr.
TELEPHONE: 955-2861
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Bowers, Wilbert D. Dr. DA
NAME:

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Stress; (U) Disease; (U) Environmental Extremes; (U) Temperature; (U) Fatigue; (U) Immune Response; (U) Defense Mechanisms

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23.(U) Disease causes more combat noneffectiveness than do battle injuries. There is an Army requirement to study factors which influence disease susceptibility and to provide prophylactic and/or therapeutic measures (Institute of Land Combat/Advanced Materials Concept Agency material data sheet S/MD-14, dtd May 1969). Fatigue, exposure to temperature extremes or altitude are thought to increase suscepticility to disease and diminish the efficacy of therapeutic regimens, but the mechanisms of these effects are unknown. The objective of this research is to predict the combat effectiveness.

24.(U) Existing models will be used to establish the conditions and extent to which any one or combination of environmental extremes and fatigue alter resistance to bacterial and viral diseases relevant to military operations. Changes in the body's defense mechanisms (e.g., mucous membrane sensitivity, antibody production) resulting from acute, cyclic, or chronic exposure to environmental stress will be studied by immunological and biochemical techniques. Studies will be conducted in laboratory animals and in human volunteers under simulated field conditions.

*Available to contractors upon originator's approval.

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION*	2. DATE OF SUMMARY*	REPORT CONTROL SYMBOL
DA OA 6136	72 07 01	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY*	6. WORK SECURITY*	7. REGRADING*	8a. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 12 31	K. Completed	U	U	N/A	N/L	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6.11.01.A	3A061101A91C	00	025
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)*

(U) Development of a non-sedating analgesic for military use (22)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS*

012600 Pharmacology; 003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
69 07		DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: N/A EXPIRATION:
b. NUMBER:*
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 72	0.5	27.1
FISCAL YEAR CURRENT		

19. RESPONSIBLE DOD ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

RESPONSIBLE INDIVIDUAL
NAME: Jones, LeeRoy G. COL
TELEPHONE: 955-2811

20. PERFORMING ORGANIZATION

NAME:* USA Rsch Inst Env Med

ADDRESS:* Natick, Massachusetts 01760

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME:* Evans, Wayne O. LTC
TELEPHONE: 955-2824
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME:
NAME:

21. GENERAL USE

Foreign Intelligence Not Considered

DA

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Analgesia; (U) Drugs; (U) Clinical Testing; (U) Combat Casualties

23. TECHNICAL OBJECTIVE,* 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) A formal requirement has been established by the Combat Developments Command for an analgesic compound which will provide adequate relief from pain without producing sleep, mental confusion or a depression of vital bodily functions. The objective of this research is to help in the development of such a compound.

24. (U) It has been shown that a mixture of a stimulant of the amphetamine type when mixed with an opiate, such as morphine, will produce a potent analgesic compound which does not produce sleep, mental confusion or a depression of vital bodily functions as does morphine alone. Studies also indicate that a lower liability for physical dependence may be found for this mixture than for morphine alone. Further, side effects of nausea, headache or other bodily discomforts are reduced. Potential for abuse with this mixture has been evaluated in monkeys. In studies designed to determine potential for abuse of this mixture, monkeys when self-infusing, show signs of amphetamine toxicity. This suggests that the compound does have some potential for abuse. When evaluating the orally administered mixture of anileridine plus amphetamine by the ischemic arm pain test, we found that the mixture significantly enhanced the tolerance of pain as compared to a placebo or either compound alone. Preliminary findings also show an antidepressant effect from this mixture.

25. (U) 71 07 - 72 06 Findings of the analgesic and anti-depressive efficacy of opiate or opiod-amphetamine mixtures have been confirmed by the Addiction Research Center, NIMH Lexington, KY and VA Co-operative Analgesic Program, Palo Alto, CA. Further, sedation, hypothermia, hypotension, pupilary constriction, hypoventilation and bradycardia are also blocked by this mixture. A patent is in preparation for the orally effective mixtures designated E-2 by the NIMH. This completes research possible at this Institute.

* Available to contractors upon originator's approval.

DD FORM 1 MAR 68 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

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Research Performed While at USARIEM:

Angelakos, E. T., J. T. Maher, and R. F. Burlington. Arrest of spontaneous atrial activity by cold at different potassium concentrations. Archives Internationales de Physiologie et de Biochimie, 79:857-871, 1971.

Aoki, V. S. and S. M. Robinson. Body hydration and the incidence and severity of acute mountain sickness. J. Applied Physiol. 31(3):363-367, 1971.

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Bass, David E. Characteristics of acclimatization to work in the heat. Chapter in book entitled, "Encyclopedia of Sport Sciences and Medicine." New York: Macmillan Co., 1971 (pp 1581-85).

Bowers, W. D., J. J. Previte, and R. C. Daum. Ultrastructure of the liver in infected and endotoxin-poisoned mice exposed to cold. J. Infectious Diseases, 125:491-498, 1972.

Breckenridge, J. R. and R. F. Goldman. Solar heat load in man. J. Applied Physiol. 31:659-663, 1971.

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*In-press not included

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Gerben, M. J., J. L. House, and F. R. Winsmann. Self-paced ergometer performance: effects of pedal resistance, motivational contingency and inspired oxygen concentration. Percept. & Motor Skills 34:875-881, 1972.

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Maher, J. T., A. Goodman, R. P. Francesconi, W. D. Bowers, L. H. Hartley, and E. T. Angelakos. Responses of rat myocardium to exhaustive exercise. J. Applied Physiol. 222(1):207-212, January 1972.

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Molnar, G., R. F. Goldman, and O. Wilson. Analysis of the rate of digital cooling. J. de Physiologie 63:350-352, 1971.

Power, G. G., V. S. Aoki, W. H. Lawson, and J. B. Gregg. Diffusion characteristics of pulmonary blood-gas barrier at low temperature. J. Applied Physiol. 31(3):438-446, 1971.

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Witherspoon, J., R. F. Goldman, and J. R. Breckenridge. Heat transfer co-efficients of humans in cold water. J. de Physiologie 63:459-462, 1971.

ABSTRACTS

Research Performed While at USARIEM:

Boyd, A. E. III, S. R. Giamber, and M. Mager. Inhibition of lipolysis by lactate. Clin. Rsch XX(3):542, April 1972.

Boyd, A. E. III and G. A. Beller. The role of primary respiratory alkalosis in heat exhaustion syndrome. Clin. Rsch XX(3):573, April 1972

Hartley, L. H., J. A. Vogel, and J. C. Cruz. The effects of intravenous atropine on the decrement of maximal exercise heart rate induced by prolonged hypoxia. Circulation 44:175, 1971.

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PRESENTATIONS

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Boyd, A. E. III and G. Beller. The role of primary respiratory alkalosis in the heat exhaustion syndrome. American College of Physicians, Atlantic City, NJ, April 1972.

Boyd, A. E. III, S. R. Giamber, and M. Mager. Inhibition of lipolysis by lactate. American Federation for Clinical Research, Atlantic City, NJ, 29-30 April 1972.

Boyd, A. E. III and G. Beller. Acid-base change in heat exhaustion during basic training. Army Science Conference, West Point, NY, 20-23 June 1972.

Breckenridge, J. R. and R. F. Goldman. Human solar heat load. American Society of Heating, Refrigerating and Air Conditioning Engineers, New Orleans, LA, January 1972.

Burlington, R. F., J. A. Vogel, and B. K. Whitten. Adaptations to hypoxia in hibernating rodents. International Symposium on Environmental Physiology: Bioenergetics & Thermoregulation, Dublin, Ireland, 19-23 July 1971.

Cahoon, R. L. and E. R. Dusek. Auditory vigilance under hypoxia. International Congress of Applied Psychology, Leige, Belgium, July 1971.

Francesconi, R. P., A. E. Boyd III, and M. Mager. Effects of acute cold exposure on the periodicity of tryptophan metabolism in humans. FASEB, Atlantic City, NJ, April 1972.

Givoni, B. and R. F. Goldman. Models for predicting the physiological effects of work and environment. J. B. Pierce Foundation Laboratory, New Haven, CT, 27 March 1972.

Gleser, M. A. and J. A. Vogel. Some physiological determinants of endurance time. FASEB, Atlantic City, NJ, April 1972.

Goldman, R. F. Load carriage and the infantryman. US Army Infantry School, Ft. Benning, GA, 14 June 1972.

Presentations (Cont'd)

Goldman, R. F. Physical agents, heat and cold. Occupational Medicine Course, Army Environmental Health Agency, Edgewood Arsenal, MD, 19 January 1972.

Goldman, R. F. Comfort and human tolerance to heat, work, and cold. Occupational Hazards and Protective Equipment for Firefighters, Policemen and Related Occupations, National Bureau of Standards, Washington, DC, 20 January 1972.

Hartley, L. H., J. A. Vogel, and J. C. Cruz. The effects of intravenous atropine on the decrement of maximal exercise heart rate induced by prolonged hypoxia. American Heart Association, Anaheim, CA, 11-14 November 1971.

Klein, A. Mitochondrial alteration in structure and function as an assay for freeze-thaw damage. 85th session of the American Association of Anatomists, Dallas, TX, 4-7 April 1972.

Kobrick, J. L. Recent research in peripheral vision. Seminar Chairman, Eastern Psychological Association Annual Meeting, April 1972.

Kobrick, J. L. Effects of hypoxia on visual performance. American Psychological Association Meeting, Washington, DC, September 1971.

Kotchen, T. A., J. W. Mason, L. H. Hartley, L. G. Jones, F. E. Waree, L. L. Pennington, and E. H. Mougey. Thyroid responses to the anticipation of exhaustive muscular exercise. Psychosymatic Society, Boston, MA, 14-16 April 1972.

Landowne, M. Cardiac and circulatory determinants of oxygen uptake during exercise. American Heart Association, Anaheim, CA, 11-14 November 1971.

Landowne, M., L. H. Hartley, and J. A. Vogel. Vascular conductance of muscle, primary determinant of maximal oxygen uptake in exercise. XXV International Congress of Physiological Sciences, Munich, Germany, 25-31 July 1971.

Presentations (Cont'd)

Maher, J. T., A. Goodman, W. D. Bowers, L. H. Hartley, and E. T. Angelakos. Myocardial function and ultrastructure in chronically hypoxic rats. American Physiological Society Fall Meeting, Lawrence, KS, 15-19 August 1971.

Maher, J. T., G. Beller, and L. H. Hartley. Systolic time interval during submaximal and maximal exercise to exhaustion in man. FASEB, Atlantic City, NJ, April 1972.

Mager, M. Enzyme analysis. N.E. Section, American Association of Clinical Chemists, Needham, MA, January 1972.

Marshall, H. C. A two-year study of effects of cold exposure and exercise upon peripheral function. Alaska Science Conference, University of Alaska, College, AK, 17 August 1971.

Marshall, H. C. Use of electromyographic techniques in the prognostication of ischemic injury. 9th Clinical Session of Northwest Association of Physical Medicine and Rehabilitation, Carmel, CA, 12-13 May 1972.

Patton, J. F. Cardiovascular function in the hypothermic dog following core and surface rewarming. Alaska Science Conference, University of Alaska, College, AK, 16 August 1971.

Patton, J. F. and R. T. Joy. Cardiovascular function after internal and surface rewarming of hypothermic dogs. FASEB, Atlantic City, NJ, April 1972.

Soule, R. G. and R. F. Goldman. Voluntary march rate during extended operations. Annual American College of Sports Medicine Meeting, Philadelphia, PA, 1-3 May 1972.

Soule, R. G. Voluntary march rate over natural terrain. FASEB, Atlantic City, NJ, April 1972.

Soule, R. G. and R. F. Goldman. Voluntary march rate during extended operations. American College of Sports Medicine Annual Meeting, Philadelphia, PA, 1-3 May 1972.

Presentations (Cont'd)

Stokes, J. W. and J. Mendels. A controlled trial of pyridoxine for premenstrual mood changes. 5th World Congress of Psychiatry, Mexico City, Mexico, 30 November - 5 December 1971.

Stokes, J. W., D. A. Chernik, G. Pandy, and J. Mendels. Effects of diazepam on growth hormone release during sleep. Association for the Psychophysiological Study of Sleep, 12th Annual Conference, Lake Minnewaska, NY, 3-7 May 1972.

Therriault, D. G., G. A. Beller, J. A. Smoake, and L. H. Hartley. Intermuscular energy sources in dogs during heavy physical work. American Oil Chemists Society, Atlantic City, NJ, 3-8 October 1971.

Webb, S. S., G. M. Smith, W. O. Evans, and N. Conant Webb. Toward the development of an orally-effective, potent, nonsedating analgesic. Annual Meeting of the National Research Council Committee on Problems of Drug Dependency, Ann Arbor, MI, 22-24 May 1972.

Wilson, O., R. W. Newman, and R. F. Goldman. Effects of alcohol, hot drinks, or smoking on hand and foot heat loss. International Symposium on Environmental Physiolgy, Dublin, Ireland, July 1971.

Wilson, O., R. F. Goldman, and A. L. Hughes. Skin temperature change with crystallization of ice on finger frostnip. 2nd International Symposium on Circumpolar Health, Oulu, Finland, July 1971.

Witherspoon, J. M. and R. F. Goldman. Integrating transient responses of man in heat. International Symposium on Environmental Physiology, Dublin, Ireland, July 1971.

Witherspoon, J. M. Thermoregulation during immersion in water from 20-45°C. International Symposium on Environmental Physiology, Dublin, Ireland, July 1971.

Research Performed Predominantly or Exclusively Before Joining USARIEM:

PUBLICATIONS:

Boileau, R. A., E. R. Buskirk, D. H. Horstman, J. Mendez, and W. C. Nicolas. Body composition changes in obese and lean men during physical conditioning. Med. Sci. in Sports 3(4):183-189, 1971.

Boyd, A. E. III, Lebovitz, H. E., and J. M. Feldman. Endocrine function and glucose metabolism in patients with Parkinson's disease and their alteration by L-DOPA. J. Clin. End. & Metab. 33:829-837, 1971.

Gleser, M. A. and M. F. Collen. Towards automated medical decisions. Computers and Biomed. Rsch 5:180, 1972.

Horstman, D. H. "Nutrition". Ergogenic Aids and Muscular Performance, Chpt 13, Editor: William P. Morgan, Academic Press, New York, NY (IN PRESS).

Klein, A. W., R. F. Becker, and M. R. Bryson. A method for estimating the distribution of alveolar sizes from histological lung sections. Trans. Amer. Micro. Soc. 91:195-208, 1972.

Mendels, J., A. Frazer, R. G. Fitzgerald, T. A. Ramsey, and J. W. Stokes. Biogenic amine metabolites in cerebrospinal fluid of depressed and manic patients. Science 175:1380-1381, 1972.

Mendels, J., A. Frazer, S. K. Secunda, and J. W. Stokes. Biochemical changes in depression. Lancet I:448-449, February 1972.

Ramsey, T. A., J. Mendels, J. W. Stokes, and R. G. Fitzgerald. Lithium carbonate and kidney function; a failure in renal concentrating ability. JAMA 219(11):1446-1449, 1972.

Stokes, J. W. and J. Mendels. Pyridoxine and premenstrual tension. Lancet I:1177-1178, May 1972.

Stokes, J. W., J. Mendels, S. K. Secunda, and W. L. Dyson. Lithium excretion and therapeutic response. J. Nerv. Ment. Dis. 154(1): 43-48, 1972.

Research Performed Predominantly or Exclusively Before Joining USARIEM (Cont'd)

PRESENTATIONS:

Malindzek, G. S., Jr., E. J. Kosinski, H. D. Greer, D. E. Roberts, and G. B. Orr. Laboratory computer assisted determination of coronary vascular tone in the anesthetized rhesus monkey. Biomedical Engineering Society, Baltimore, MD, April 1972.

Roberts, D. E. The contributions of baroceptor reflexes and beta-adrenergic receptors to its cardiovascular responses to epinephrine. Seminar presented to AMRLA and AHRC, AMRLA, Alaska, September 1971.

LECTURES AND SEMINARS

Bass, D. E. Effects of heat on man. Global Medicine Course, WRAIR, Washington, DC, 10 February 1972.

Beller, G. A. Exercise and your heart, Senior Citizens Group, Melrose, MA, (on behalf of the Massachusetts Heart Association, Inc.) 20 April 1972.

Beller, G. A. Ouabain-induced acute respiratory alkalosis in intact conscious dogs. Thorndike Memorial Laboratory, Boston City Hospital, Boston, MA, 26 April 1972.

Beller, G. A. Toxic effects of digitalis during acute myocardial hypoxia and ischemia. Boston University Medical Center, Boston, MA, 23 June 1972.

Boyd, A. E. III. Lactate inhibition of lipolysis. The Joslin Clinic Research Seminars, Boston, MA, 18 April 1972.

Boyd, A. E. III. Respiratory alkalosis in heat exhaustion during basic training. Army Science Conference, USMA, West Point, NY, 22 June 1972.

Cipriano, L. F. Exercise and altitude acclimatization. Boston University, Boston, MA, 9 December 1971.

Doolittle, W. H. Coronary care course. Staff, Fairbanks Memorial Hospital, Fairbanks, AK, October-November 1971.

Doolittle, W. H. Cold weather indoctrination. Officers, 171st Infantry Brigade, Fort Wainwright, AK, 15 October 1971.

Doolittle, W. H. Accidental hypothermia. Staff, Fairbanks Memorial Hospital, Fairbanks, AK, 28 October 1971.

Doolittle, W. H. Medical problems in the arctic. Six hour seminar for Residents in Aviation Medicine at AMRLA, AK, 4 January 1972.

Doolittle, W. H. Cold weather orientation. Staff, Cold Regions Research & Engineering Laboratory, Hanover, NH, 14 February 1972.

Doolittle, W. H. Investigations in freezing injury. Surgical staff, Mary Hitchcock Hospital, Hanover, NH, 15 February 1972.

Doolittle, W. H. Taped interview for radio program "Army Hour", 8 March 1972.

Lectures and Seminars (Cont'd)

Doolittle, W. H. Physiologic and pathologic changes during occupational cold exposure. National Institute of Occupational Safety & Health, Anchorage, AK, 9 March 1972.

Givoni, B. Models for predicting the psychological effects of work and environment. J. B. Pierce Foundation, New Haven, CT, 27 March 1972.

Goldman, R. F. Formulae, reference data and references. NATO Advance Study Institute on Human Factors, Bellagio, Italy, September 1971.

Goldman, R. F. Physiological factors in the design and use of clothing. NATO Meeting, Advanced Study Institute, Brussels, Belgium, 1-8 October 1971.

Goldman, R. F. Seminar on cold weather operations and cold injury. Arctic Medical Research Laboratory (USARIEM), Alaska, 14-16 November 1971.

Goldman, R. F. Seminar on cold weather operations and cold injury. Fort Greeley, AK, 17-19 November 1971.

Gregory, R. T. Cold weather orientation. Troops, Fort Wainwright, AK, October 1971.

Gregory, R. T. Cold injury and hypothermia. Professional staff, Bassett Army Hospital, Fort Wainwright, Fairbanks, AK, 1 & 8 October 1971.

Haisman, M. F. Assessing physical fitness in the British Army. Symposium on Physical Fitness, Dedham, MA, 10-12 October 1971.

Hamlet, M. P. Cold weather survival. Officers, 19th Aviation BN, Ft. Wainwright, AK, 26 January 1972.

Hartley, L. H. Adjustments of the oxygen transport system during residence at high altitude. 2nd International Conference on Red Cell Metabolism and Function, University of Michigan, Ann Arbor, MI, 29 April 1972.

Huibregtse, W. H. Frostbite. Potter Road Elementary School, Framingham, MA, 7 March 1972.

Lectures and Seminars (Cont'd)

Jones, L. G. USARIEM Missions and Operations, Headquarters, USAMRDC, Washington, DC, 11 April 1972.

Jones, L. G. USARIEM Missions and Operations. Executive Council, Algonquin Council, Boy Scouts of America, Natick, MA, 25 April 1972.

Jones, L. G. and R. F. Goldman. Seminar on USARIEM Missions and Operations. Special Operations Section, Department of Division Operations, Command and General Staff College, Fort Leavenworth, KS, 1 May 1972.

Jones, L. G. USARIEM Missions and Operations. Staffs of III Corps, Second Armored Division, First Cavalry Division (TRICAP), and MAASTER, Fort Hood, TX, 3-4 May 1972.

Jones, L. G. USARIEM Missions and Operations, Staff and Faculty, Medical Field Service School, Brooke Army Medical Center, Fort Sam Houston, TX, 6 May 1972.

Jones, L. G. USARIEM Missions and Operations, Staff and Faculty, United States Army Infantry School, Fort Benning, GA, 8 May 1972.

Jones, L. G. USARIEM Missions and Operations. Staff Silas B. Hayes Hospital, Fort Ord, CA, 18 May 1972.

Jones, L. G. USARIEM Missions and Operations. Directorate of Military Psychology and Leadership, United States Military Academy, West Point, NY, 21 June 1972.

Klein, A. W. Normal and stress fetal lung development with special reference to the surfactant system and R.D.S. Michigan State University Medical School, East Lansing, MI, May 1972.

Klein, A. W. Anatomical and pathological assessments of cell damage following a freeze-thaw insult. University of Maryland School of Medicine, Baltimore, MD, May 1972.

Maher, J. T. Careers in government service. Milford High School, Milford, MA, 9 March 1972.

Lectures and Seminars (Cont'd)

Maher, J. T. Science in government service. George S. Stacy Junior High School, Milford, MA, 19 May 1972.

Marshall, H. C. Some aspects of cold-induced neuropathies. Colloquium Institute of Arctic Biology, University of Alaska, College, AK, 15 October 1971.

Marshall, H. C. Practical aspects of cold weather research. Alaska Peace Officer's Association, Fairbanks, AK, 18 November 1971.

Marshall, H. C. Techniques in evaluation of clinical cold injury and compression syndromes. Professional staff, Bassett Army Hospital, Fort Wainwright, Fairbanks, AK, 10 December 1972.

Patton, J. F. Experimental studies on rewarming from hypothermia. Arctic Health Research Center, Fairbanks, AK, December 1971.

Robinson, S. M. High Altitude. WRAIR Meeting, Washington, DC, 14 February 1972.

Therriault, D. G. Energy sources during heavy physical work. The University of Connecticut, Storrs, CT, November 1971.

AGENDA

COURSE FOR WRAIR PREVENTIVE MEDICINE RESIDENTS/RESEARCH FELLOWS

HELD

15-19 MAY 1972

US ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE

NATICK, MASSACHUSETTS 01760

MONDAY, 15 MAY 1972

WORK

WELCOME	COL Jones
Foundations of USARIEM - historical	Dr. Bass
USARIEM: 1961 - tomorrow	COL Jones
Review of Work Physiology	Dr. Hartley
Panel Discussion: - Interdisciplinary Studies of Endurance Training	
BASIC research in Army Med R&D	Dr. Therriault
Biochemical aspects	Dr. Hubbard
Morphological aspects	Dr. Bowers
Physiological aspects	MAJ Giamber
Some determinants of endurance time	MAJ Gleser
DEMONSTRATION BASIC TECHNIQUES IN WORK PHYSIOLOGY	
Fitness for exercise - Energy expenditure in military personnel	Dr. Haisman

TUESDAY, 16 MAY 1972

COLD

Man in the cold, how it affects him and how he adapts	Dr. Newman
Military and civilian reactions to cold, (a Commander's experiences)	LTC Doolittle
Field operations in the cold (a Researcher's experiences)	MAJ Stokes

Wind Chill Movie	Dr. Goldman
Cold Weather Protective Clothing	Mr. Breckenridge
Computer model of cooling	Dr. Goldman

DEMONSTRATIONS: 3 GROUPS, 20 MIN AT EACH SITE:

Pool	a) Water immersion facilities and approaches
Chamber	b) Hand immersion heat loss
Chamber	c) Finger frostnip

Fundamental concepts of acute freeze injury	CPT Rabb Dr. Bowers Dr. Therriault CPT Klein
Discussion: Proposed solutions for soldiers in the cold	Class & Staff

WEDNESDAY, 17 MAY 1972

HEAT

Some aspects of Man's Physiological Response to Heat of Importance to the Health Individual	Dr. Bass
Clinical Problems of Heat Exposure	MAJ Boyd
Assessment of Heat Stress in the Field	Dr. Goldman
Class Discussion with Morning Session Presenters	Dr. Mager Moderator
Laboratory Studies in the Heat	MAJ King Dr. Robinson
TOUR LABORATORY STUDIES OF CLOTHING	Mr. Breckenridge
TOUR PREDICTING EFFECTS OF HEAT ON MAN	Mr. Stroschein
TOUR VALIDATION OF PREDICTIONS (NLABS CHAMBERS)	Dr. Goldman
Temperature Regulation in Man and Animals	Dr. Mager
Applying Research Output as Military Input	Dr. Goldman

THURSDAY, 18 MAY 1972

HIGH TERRESTRIAL ELEVATIONS

Man at High Elevations: Why are we interested? — MAJ Beller

TOUR OF HYPOBARIC CHAMBER

Laboratory Models in Investigating Hypoxic Stress

A. Cardiac muscle studies

1. Muscle mechanics — Dr. Maher
2. Biochemical alterations — Dr. Francesconi
3. Ultrastructural changes — Dr. Bowers

B. Intact animal studies — MAJ Beller

Discussion

DEMONSTRATIONS: 4 GROUPS: 15 MIN AT EACH SITE

A. Behavioral Models — Dr. Banderet
B. 3rd Floor Facilities — CPT Hamlet
C. Peripheral Visual Response — Dr. Kobrick
D. Cortical Evoked Potentials — Dr. Cahoon

Symposium on Mountain Sickness

A. Introduction and background — Dr. Landowne
B. Role of renin-angiotensin-aldosterone system — MAJ Hogan
C. Current Research on treatment — Dr. Robinson, MAJ King

Altitude and Performance

A. Altitude and cardiovascular performance — Dr. Hartley
B. Mountain Operations — LTC Evans

Round Table Discussion — Moderator - Dr. Robinson and presenters

FRIDAY, 19 MAY 1972

MILITARY PERFORMANCE

PERFORMANCE LIMITS	
Physiological	Dr. Goldman
Psychological	Dr. Cahoon
Individual	Dr. Fine
Problems of Rapid Transition, Circadian Rhythms	Dr. Francesconi
Approaches to Studying Performance	Dr. Kobrick
TASK SIMULATION DEMONSTRATIONS: 2 GROUPS, 15 MIN AT EACH	
GROUP A: Simulation of Control Operation	Miss Burnette
GROUP B: Simulation of Communication Net	Dr. Cahoon
Transfers from Model to Field	Dr. Goldman
Maneuvers - Research Realism vs Fun and Games	MAJ Stokes
Military Output as Research Input Discussion	Class
Concluding Comments	Dr. Goldman

SEMINAR PROGRAM

23 September 1971
Dr. Charles Matsumoto, Lilly Research Laboratories.
Some Investigations on an Amphetamine - Induced Hyperthermia in Rats.

14 October 1971
Dr. Loring P. Rowell, University of Washington.
Distribution of Blood Flow in Man Under Thermal Stress.

20 October 1971
Dr. Donald G. Therriault, Biochemistry and Pharmacology Laboratory, USARIEM.
Intramuscular Energy Sources in Dogs During Physical Work.

24 November 1971
Dr. Walter H. Abelmann, Harvard Medical School.
Responses to Orthostatic Stress in Health and in Heart Disease.

1 December 1971
Dr. L. Howard Hartley, Harvard Medical School.
The Neuroendocrine Response to Exercise.

8 December 1971
Professor D. W. Fawcett, Harvard Medical School.
Fine Structure of Muscle

15 December 1971
CPT Malcolm A. Gleser, Military Stress Laboratory, USARIEM.
Endurance Capacity Defined and a Hypothesis of the Role of Muscle Blood Flow in Exercise.

22 December 1971
Dr. Alfred Goldberg, Harvard Medical School.
Mechanisms of Growth and Atrophy in Skeletal Muscles.

12 January 1972
Dr. Harold Smookler, University of Pittsburgh.
The Role of the Sympathetic Nervous System in Development of Stress-Induced Hypertension in Rats.

19 January 1972
Dr. Peter Mazur, Oak Ridge National Laboratory.
Freezing Injury in the Living Cell.

26 January 1972
Dr. William N. Fishbein, Armed Forces Institute of Pathology.
Molecular Pathogenesis of Cryo-Injury and Cryo-Protection.

2 February 1972
Dr. N. Herbert Spector, Walter Reed Army Institute of Research.
Hypothalamic Control of Temperature and Feeding.

9 February 1972
Dr. Richard W. Hanson, Temple University.
The Role of Phosphoenolpyruvate Carboxykinase in the Regulation of Glyceroneogenesis in Mammalian Adipose Tissue.

15 February 1972
Dr. Lawrence R. Young, Massachusetts Institute of Technology.
Mathematical Models of the Human Operator.

16 February 1972
Dr. Thomas O'Donnell, Boston City Hospital.
Circulatory Dynamics of Heat Stroke - Experience at Parris Island, S.C.

17 February 1972
LTC William H. Doolittle, AMRLA
Frostbite and Hypothermia in Alaska.

23 February 1972
Dr. Russell L. Steere, U.S. Department of Agriculture.
High Resolution Stereo Electron Microscopy of Freeze Fractured and Freeze Etched Specimens with Emphasis on the Dog Heart Nexus.

25 February 1972
Dr. Robert F. Grover, University of Colorado Medical Center.
Cardiac Function at High Altitude.

8 March 1972
Dr. Carl Hittleman, University of Massachusetts Medical School.
Temperature, Skeletal Muscle Mitochondrial Functions and Oxygen Debt.

15 March 1972
Dr. Milton Mager, Biochemistry and Pharmacology Laboratory, USARIEM.
Thermoregulation of Mice and Men.

21 March 1972
Dr. Andree J. Lloyd, The University of Oklahoma Medical Center.
Time to be Tired.

29 March 1972
Dr. Russell W. Newman, Military Ergonomics Laboratory, USARIEM.
Sex Pheromones, Evidence in Mammals Including Man.

31 March 1972
Dr. L. E. Banderet and MAJ J. Stokes, USARIEM.
Exercise Ace Card IV.
Dr. S. M. Robinson and LTC W. O. Evans, USARIEM.
The Proposed WALK THE DIVIDE Exercise.

5 April 1972
FASEB Abstracts, USARIEM.

13 April 1972
Dr. Paul M. Hurst, State College, Pennsylvania.
The Role of Alcohol in Highway Accidents.

27 April 1972
MAJ Phillip C. Weiser, U.S. Army Medical Research and Nutrition Laboratory.
Prolonged Exercise: General Versus Latent Fatigue.

3 May 1972
Dr. Ove Wilson, Institute of Aviation Medicine, Malmslatt, Sweden.
Survival and Rescue of Astronauts in Polar Regions.

24 May 1972
Dr. Gin K. Gee, Corning Community College.
Shivering, Quantitation of Peripheral Cold Stimulus.

7 June 1972
Dr. Herbert Benson, Harvard Medical School.
Meditation: A Wakeful Physiologic Hypometabolic State.

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13. ABSTRACT

The research projects reported in this Annual Progress Report are as follows:

Project: Military Environmental Medicine (3A062110A827)

Work Units: Medical Problems in Military Arctic Operations (AMRLA)
Prediction of the Biological Limits of Military Performance as a Function of Environment, Clothing and Equipment
Effects of Environmental Stressors on Military Performance: Interactions with Extended Operations, Unusual Activity-Rest Cycles
Biomedical Impact of Military Clothing and Equipment Design Including the Selection of Crew Compartment Environments
Prevention and Treatment of Disabilities Associated with Military Operations in the Cold
Prevention and Treatment of Disabilities Associated with Military Operations in the Heat
Prevention and Treatment of Disabilities Associated with Military Operations at High Terrestrial Elevation

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13. ABSTRACT

Project: Research in Biomedical Sciences (3A061102B71R)

Work Units: Disease Susceptibility of Soldiers in Harsh Environments
Bioenergetics Related to Heavy Physical Work Ability of the Soldier
Development of Cold Injury Models and Characterization of Frostbite, Non-Freezing Cold Injuries and Whole Body Heat Loss Common to the Soldier
Development of Measures to Assess the Impact of Environmental Stresses on Critical Military Performance
Biological Processes that Limit Heavy Physical Work Ability of the Soldier
Development and Characterization of Models of Heat Injuries and Disabilities and Other Heat Responses of the Soldier
Development and Characterization of Models to Study Acute Mountain Sickness and High Altitude Pulmonary Edema in Military Operations

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11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY

13. ABSTRACT

Project: In-House Laboratory, Independent Research (3A061101A91C)

Work Units: Factors Limiting Military Performance at Sea Level and High Altitude and their Modification by Acclimatization and Adaptation

Historical Analysis, Development of Distribution of Military Environmental Medical Information

Fundamental Research in Life Sciences, of Intermediate & Long-Range Military Importance

Development of a Non-Sedating Analgesic for Military Use

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Adaptation	Military Tactics						
Altitude	Military Tasks						
Analgesia	Motivation						
Arctic Military Operations	Motor Performance						
Atropine	Motor Skills						
Behavior	Mountain Sickness						
Biochemistry	Muscle Metabolism						
Biophysics	Pathology						
Blood Flow	Pathology Model						
Body Temperature	Perception						
Cardiovascular	Performance						
Clinical Testing	Performance Decrement						
Cognition	Performance Limits						
Cold	Pharmacology						
Cold Injury	Physiology						
Combat Casualties	Protection						
Combat Effectiveness	Psychology						
Continuous and Sustained Operations	Psychomotor Skills						
Cryobioloby	Pulmonary Edema						
Defense Mechanisms	Sensory Processes						
Disabilities	Simulation						
Disease	Stress						
Drugs	Temperature						
Endurance	Therapeutic Techniques & Equipment						
Energy Metabolism	Thermoregulation						
Environmental Extremes	Tolerance						
Environmental Stress	Training						
Environmental Tolerance	Trenchfoot						
Exercise	Vision						
Fatigue	Wind						
Fatigue, Mental	Work						
Frostbite							
Head							
Heat Disabilities							
Heat Stress							
Heat Tolerance							
High Altitude							
High Altitude Natives							
Hypothermia							
Hypoxia							
Immune Response							
Metabolism							
Microcirculation							
Military Clothing							
Military Disabilities							
Military Environmental Medicine							
Military Heat Stress							
Military Information							
Military Operations							