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US ARMY
MEDICAL RESEARCH LABORATORY
FORT KNOX, KENTUCKY 40121

ANNUAL PROGRESS REPORT, FY 1971

RCS MEDDH-288(R1)

30 June 1971

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UNITED STATES ARMY
MEDICAL RESEARCH AND DEVELOPMENT COMMAND

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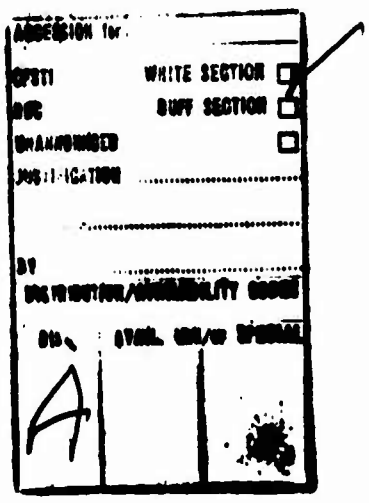

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US Army Medical Research Laboratory
Fort Knox, Kentucky 40121

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2b. GROUP

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13. ABSTRACT

The research and development effort at the US Army Medical Research Laboratory, Fort Knox, Kentucky, is concerned with studies in sensory psychophysiology, the biological effects of laser radiation, and methodology related to the preservation, transfusion, collecting, processing, and shipment of human blood.

The progress during Fiscal Year 1971 and the current status of the various work units are reported herein.

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UNCLASSIFIED

Security Classification

14 KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Psychophysiology						
Visual Performance						
Human Factors						
Auditory Performance						
Motivation						
Psychomotor Skills						
Hearing Loss						
Color Vision						
Disorientation						
Target Discrimination						
Depth Perception						
Stereoscopic Vision						
Temporary Threshold Shift (TTS)						
Fibrinolysis						
Hormones						
Enzyme Synthesis						
Antibody						
Antigen						
Blood Banks						
Blood Groups						
Blood Donors						
Blood Transfusion						
Blood Preservation						
Adenine						
Inosine						
Sickle Cell Disease						
Australian Antigen						
Australian Antibody						
Methylene Blue						
Automation						
Incompatible Blood Transfusion						
Carboxyhemoglobin						
Histocompatibility						
Protein Biosynthesis						
Cell Membrane Integrity						
Membrane Stabilizers						
Logistics						
Biophysics						
Instrumentation						
Laser						
Diseases of Animals						
Annual Progress Report						

AD _____

HEADQUARTERS
US ARMY MEDICAL RESEARCH LABORATORY
Fort Knox, Kentucky 40121

ANNUAL PROGRESS REPORT, FY 1971

RCS MEDDH-288(R1)

30 June 1971

FY 1971 Projects:

3A061101A91C
In-House Laboratory Independent Research

3A061102B71P
Basic Research in Support of Military Medicine

3A061102B71R
Research in Biomedical Sciences

3A062110A821
Combat Surgery

SUMMARY

The research and development effort at the US Army Medical Research Laboratory, Fort Knox, Kentucky, is concerned with studies in sensory psychophysiology, the biological effects of laser radiation, and methodology related to the preservation, transfusion, collecting, processing, and shipment of human blood.

The progress during Fiscal Year 1971 and the current status of the various work units are reported herein.

FOREWORD

The mission of the laboratory has remained unchanged during the past year. Notable accomplishments toward these goals are outlined.

In the area of blood banking research, trace amounts of methylene blue added to optimal concentrations of inosine and adenine in CPD blood will extend the shelf life of bank blood to 6 weeks; whereas the levels of 2,3-DPG--a measure of hemoglobin function--are maintained very well, ATP levels are not affected significantly. The salivary anti-A and anti-B isoantibody system in group O males has been found to be distinct from the serum antibody system and cannot be applied in differentiating the group O universal donor with dangerous levels of serum anti-A and anti-B.

An automated procedure applicable to the field study of sickle cell hemoglobin screening in large populations has been developed; the cost per test for reagents averages $0.03. The first large field study in Vietnam returnees with reference to the incidence of Australian antigen has been completed. The translation series "Selected Contributions to the Literature of Blood Groups and Immunology" (1962 - 1971) and comprising seven parts has been completed.

In the area of psychophysiology, behavioral tasks have been used successfully to differentiate central and peripheral visual phenomena; one involves the use of the Stroop paradigm with bilingual presentations naming words in one language and interfering words in another. In the application of the "dancing arabesque", wherein an achromatizing lens is moved in front of the eye to correct its chromatic aberration producing an effect of dissociative movement, the resulting phenomenon is clearly retinal. Data derived from the growth and recovery functions of temporary threshold shifts (TTS) after 48 hours of continuous noise exposure provides confirmation of an asymptotic TTS; the slow recovery from low values of TTS under these conditions has important implications in understanding the processes producing temporary and permanent threshold shifts.

Progress in laser research continues. In the evaluation of functional visual impairment incident to ruby laser injury, trained rhesus monkeys exposed to relatively large lasing doses may recover as much as 50% of their preexposure acuity; smaller radiation doses result in greater recovery. Q-switched ruby laser radiation induced skin burns using darkly pigmented pigs and CO_2 laser burns in white pigs have provided additional data for use in safety standards. Experiments with the Q-switched erbium laser in rhesus and owl monkeys affirmed that ocular damage is limited to the cornea. With currently available energy levels, corneal damage threshold data for the gallium arsenide laser has

been obtained with the diode cooled to 77° K; when operated at room temperature, the energy was inadequate to induce ocular damage. Corneal damage threshold data for the CO_2 laser has been obtained in rabbits, rhesus, and owl monkeys for a 0.1 to 1.0 second exposure. The research activities of the Joint Laser Safety Team are being coordinated with Air Force and Navy programs.

TABLE OF CONTENTS

Project No. 3A061101A91C	In-House Laboratory Independent Research
Task No. 00	In-House Laboratory Independent Research
Work Unit No. 145 (a)	Biological Control of Calcium Absorption
Work Unit No. 145 (b)	Laser Instrumentation Design for Military Hazard Evaluation
Work Unit No. 146	Effect of IV Infusions and Hypotension on Regulation of Serum Ionic and Total Calcium Concentration and on Serum Inorganic Phosphate Concentration
Work Unit No. 151	Transplantation Antigens in Keratoplasty

Investigators:

WU No. 145(a)	Robert L. Morrissey, CPT, VC David K. Hysell, MAJ, VC Willie L. Janik, CPT, VC
WU No. 145(b)	Joseph C. Rosenbaum, M.S. Kenneth A. Conard, B.A.
WU No. 146	Robert L. Morrissey, CPT, VC
WU No. 151	Anthony J. Luzzio, Ph.D.

*Terminated 1 Sep 1970; work unit number reassigned to another study.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1 AGENCY ACCESSION	2 DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0B 6079	70 09 01	DD DR&E(AN)636

3 TYPE SUMMARY	4 KIND OF SUMMARY	5 SUMMARY SCTY	6 WORK SECURITY	7 REGRADING	8A GRP'N INST'N	8B SPECIFIC DATA-CONTRACTOR ACCESS	9 LEVEL OF SUM
70 07 01	H. TERMINATION	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10 NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61101A	3A061101A91C	00	145 (a)
b. CONTRIBUTING				
c. CONTRIBUTING				

11 TITLE (Project code with Security Classification Code)

(U) Biological Control of Calcium Absorption (18)

12 SCIENTIFIC AND TECHNOLOGICAL AREAS

002600 Biology

13 START DATE	14 ESTIMATED COMPLETION DATE	15 FUNDING AGENCY	16 PERFORMANCE METHOD
69 02	CONT	DA	C. In-House

17 CONTRACT/GRANT

a. DATE EFFECTIVE: NA — 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 70	.1	3
	CURRENT 71	.5	14

19 RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20 PERFORMING ORGANIZATION

NAME: Pathology Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)
NAME: Morrissey, R. L., CPT
TELEPHONE: 502-6243937
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Hysell, D. K., MAJ
NAME: Janik, W. L., CPT DA

21 GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22 KEYWORDS (Provide EACH with Security Classification Code)

(U) Biochemistry; (U) Biology; (U) Clinical Medicine; (U) Physiology; (U) Radiobiology

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

23. (U) To determine the mechanisms involved in regulating the rate of intestinal calcium absorption; to provide for the rationale approach to the treatment of certain disabling disorders of calcium metabolism encountered in military medical practice.

24. (U) An attempt was made to detect an endogenous factor responsible for regulating the conversion of vitamin D_3 to 25-HCC. Sera from low calcium diet adapted and normal chicks were dialyzed against a common buffer. Normal chick liver tissue was then incubated with the two types of sera in the presence of radioactive vitamin D_3. Undialyzed serum from both sources was also tested in a similar manner. After incubation, the lipids were extracted and separated by thin layer chromtography. The ratio of radioactive polar metabolites: radioactive vitamin D_3 was measured as an assay for this hypothesized endogenous factor in serum.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated because of the departure from the laboratory of all investigators (Morrissey, Hysell, Janik).

* Available to cleared users when originator's approval is given.

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

A91C 00 145(a) (cont)

Detail Sheet #1

Progress:

This project was terminated due to personnel transfer to Fitzsimons. Results and conclusions are contained in the publications listed below.

Publications and/or Presentations:

Morrissey, R. L., D. K. Hysell, and W. L. Janik. Control of calcium absorption: Influence of Vitamin D_3 hydroxylation on the calcium binding activity of chick duodenal mucosa. USAMRL Report No. 888, Aug 1970 (DDC AD No. 715697).

Selected Bibliography:

Morrissey, R. L. Regulation of intestinal calcium absorption. Ph.D. Thesis, Cornell University, Jun 1970.

Morrissey, R. L., D. K. Hysell, and W. L. Janik. Calcium binding protein: Endogenous induction. USAMRL Report No. 859, Mar 1970 (DDC AD No. 712957).

Morrissey, R. L. and R. H. Wasserman. Adaptation, calcium binding protein (CaBP) and the intestinal absorption of calcium. Fed. Proc. 29: 847, 1970 (Abstract).

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6074	71 07 01	DD DR&E AR(A)18

3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. DOWN GRADING	7. REGRADING	8A. DISP'N INSTR'N	8B. SPECIFIC DATA - CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 22	D. CHANGE	U	U	NA	NL	[X] YES [ ] NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61101A	3A061101A91C	00	145 (b)
b. CONTRIBUTING				
c. MISSING				

11. TITLE (Put code with Security Classification Code)

(U) Laser Instrumentation Design for Military Hazard Evaluation (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002400 Bioengineering; 009600 Masers and Lasers

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

17. CONTRACT/GRANT

a. DA EFFECTIVE — EXPIRATION

b. NUMBER: NA

c. TYPE — d. AMOUNT

e. END OF AGRMT — f. CUM. AMT

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
FISCAL YEAR PRECEDING 71	1.8	26
FISCAL YEAR CURRENT 72	1.8	27

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Biophysics Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

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

NAME: Rosenbaum, J. C.

TELEPHONE: 502-6243111

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME: Conard, K. A.

NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Provide with Security Classification Code)

(U) Laser; (U) Hazards; (U) Instrumentation; (U) Military; (U) Krypton; (U) Flashblindness

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

23. (U) To design and develop specialized instruments for use in the study of the biologic effects of laser radiation as a means of evaluating the hazards to military personnel from this form of energy. This involves the perfection of instrumentation, measurement techniques, and specialized instrument maintenance in support of this research effort.

24. (U) 1) Develop techniques for the application of transducers and associated instrumentation in order to monitor instantaneous thermal transients in model biological systems resulting from absorbed laser energy. 2) Develop devices for the absolute measurement and continuous monitoring of laser energy. 3) Incorporate modifications for efficient utilization and improved versatility of the over-all laser systems.

25. (U) 71 01 01 - 71 06 30 1) The warranted plasma tube for the Krypton laser has been replaced and satisfactory outputs at the desired wavelengths have been obtained. This Krypton system has been incorporated into the flashblindness study. 2) The chiller obtained for the carbon dioxide laser water supply is not acceptable because of an inherent cyclic nature. It is anticipated that by overriding the cooling capacity of the chiller with controlled heat the desired stability will be achieved. 3) Adequate environmental control over the past few weeks has resulted in a very stable carbon dioxide laser output beam. Several animal experiments have been run and additional calibrations of the small apertured (0.05 mm) Eppley thermopile and the dual thermocouple scanner have been underway. These scanning techniques have shown that the ratio of peak power density to total beam power becomes very large at higher laser outputs.

* Available in microfiche upon a specific request

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A91C 00 145(b) (cont)

Detail Sheet #1

Progress:

Since being re-engineered the Model 41 CO_2 laser has performed very satisfactorily. Stable operation at low gas pressure is now possible and the total power output is above quoted specification. At the higher outputs the laser beam is highly peaked, having a measured $1/e^2$ beam diameter of less than 5 mm compared to the manufacturer's specified 10 mm $1/e^2$ diameter. The chiller purchased to control the water supply for the CO_2 laser should become acceptable with a planned modification to include a controlled heating element to precisely regulate the temperature. With current environmental controls and moderate weather, reasonable CO_2 laser output stability has been achieved, and a series of animal experiments performed.

The dual thermocouple scanning device has been modified several times to correct deficiencies. Larger thermocouples are now in use (0.001 inch versus 0.0005 inch) for ease of installation without apparent loss of resolution or sensitivity; the silver chloride window material exhibited transmission changes with time and has been replaced with a slotted metal reflector that shields the device while illuminating the couples; a temperature controlled combined reference junction and heat sink has been installed to minimize environmental effects.

An Eppley thermopile equipped with a 0.05 mm aperture centered over the receiver disc has also been employed as a CO_2 laser beam scanning device. Both this system and the dual thermocouple system are in the process of being calibrated.

A pyro-electric IR detector has been successfully tested for pulse length measurements in the millisecond region. The design and assembly of amplifiers for use with gold-doped germanium detectors for nanosecond pulse length measurements is underway.

The Model 52 Argon laser met the manufacturer's specifications at all wavelengths. Several exchanges with the manufacturer of matched optics (output window and total reflector) were necessary before the Model 52 Krypton laser performed to specifications. Subsequently the Krypton plasma tube failed and was replaced by the manufacturer. Recently a power supply malfunction has reduced outputs to unacceptable levels; corrections are underway.

Publications and/or Presentations:

None.

A91C 00 145(b) (cont)

Detail Sheet #2

Selected Bibliography:

Heard, H. G. Laser Parameter Measurements Handbook. New York: John Wiley and Sons, 1968.

Hudson, R. D., Jr. Infrared System Engineering. New York: John Wiley and Sons, 1965.

Jenkins, F. A. and H. E. White. Fundamentals of Optics. New York: McGraw-Hill, 1950.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION: DA 08 6000 | 2. DATE OF SUMMARY: 70 09 01 | REPORT CONTROL SYMBOL: DD-DR&E-RDA(5)

3. DATE PREV SUMRY	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	10. SMRA UNIT
70 07 01	[illegible]NA-	U	U	NA	NL	☐ YES ☐ NO	A	

11. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61101A	3A061101A91C	00	146
b. CONTRIBUTING				
c. CONTRIBUTING				

12. TITLE (Procede with Security Classification Code): (U) Effect of IV Infusions & Hypotension on Reg. of Serum Ionic & Total Calcium Conc. & on Serum Inorganic Phosphate Conc. (18)

13. SCIENTIFIC AND TECHNOLOGICAL AREAS: 3226 Pathology

14. START (Yr)	15. ESTIMATED COMPLETION DATE	16. FUNDING AGENCY	17. PERFORMANCE METHOD
69	CONT	DA	C. In-House

18. CONTRACT/GRANT: a. DATE EFFECTIVE: | EXPIRATION: | b. NUMBER: NA | c. TYPE: | d. AMOUNT: | e. KIND OF AWARD: | f. CUM. AMT.:

19. RESOURCES ESTIMATE

FISCAL YEAR	a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
PRECEDING 70	.1	4
CURRENT 71	.2	9

20. RESPONSIBLE DOD ORGANIZATION
a. NAME: [illegible], US Army Medical Research Laboratory
b. ADDRESS: Fort Knox, KY 40121

c. RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

d. GENERAL USE: SECRET INTELLIGENCE CONSIDERED

21. PERFORMING ORGANIZATION
a. NAME: Pathology Division
b. ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Morrissey, R. L., CPT
TELEPHONE: 502-6243937
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME:
NAME:

22. KEY WORDS (Procede each with Security Classification Code)
(U) Calcium; (U) Control Processes; (U) Ionic Calcium; (U) Phosphate; (U) Hypotension

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

23. (U) To study the effect on calcium homeostasis of intravenous infusions containing calcium, calcium binding agents, and heparin in normal and hypotensive dogs. This will provide a basis for understanding the mechanisms that lead to osteoporosis and related conditions as observed in military medical practice.

24. (U) Each of seven dogs would be exposed to the following conditions in a normalized sequence. Blood samples will be drawn in each case (12-14 samples over a 6-hour period, to monitor the concentration of ionic calcium, total calcium, and inorganic phosphate in the serum. a. No treatment; b. Saline (20 mg/kg VW); c. Heparin; d. Saline + Heparin + Calcium; e. ACD; f. ACD + Calcium; g. Saline + Heparin + Hypotension; h. Heparin + Hypotension; i. Saline + Heparin + Calcium + Hypotension.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated because of the departure from the laboratory of the investigator (Morrissey).

26. (Leave blank. Items will be typed upon publication.)

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A91C 00 146 (cont)

Detail Sheet #1

Progress:

This project was terminated due to personnel transfer. Results and conclusions are contained in the referenced publication.

Publications and/or Presentations:

Morrissey, R. L., N. I. Birndorf, C. E. Shields, and D. K. Hysell. Effect of heparinized saline infusion and hypotension on calcium homeostasis in the dog. USAMRL Report No. 887, Aug 1970 (DDC AD No. 715703).

Selected Bibliography:

None.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6117	71 07 01	DD DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8B. DISP'N INSTR'N	8A. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 02	D. CHANGE	U	U	NA	NL	[X] YES [ ] NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61101A	3A061101A91C	00	151
b. CONTRIBUTING				
c. CONTRIBUTING				

11. TITLE (Precede with Security Classification Code)

(U) Transplantation Antigens in Keratoplasty (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

303500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
67 09	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES EFFECTIVE — EXPIRATION

b. NUMBER: NA

c. TYPE — d. AMOUNT

e. KIND OF AWARD — f. CUM. AMT.

18. RESOURCES ESTIMATE	PRECEDING/CURRENT FY	a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
FISCAL YEAR	71	.1	15
	72	.1	12

19a. RESPONSIBLE DOD ORGANIZATION

NAME: MAJ, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Biophysics Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

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

NAME: Luzzio, A. J.

TELEPHONE: 502-6246630

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME:

NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede each with Security Classification Code)

(U) Cornea; (U) Injuries; (U) Transplantation; (U) Antigens; (U) Immune; (U) Military

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

23. (U) To acquire knowledge concerning the interactions between the immunological defense mechanisms of the host and the antigens of the donor transplant involved in rejection of corneal grafts. Information in this area will enhance successful transplantation of corneas in the treatment of military combat injuries.

24. (U) This research will be divided into two phases: 1) Preparation and characterization of purified proteins from aqueous extracts of corneas. 2) Performance of corneal heterografts in nonsensitized rabbits and in rabbits sensitized with the donor specific corneal proteins prepared in phase I. The following parameters will be studied to evaluate graft rejection in both groups: 1) time of onset of graft opacification; 2) clinical severity of the reaction; 3) incidence of the reaction.

25. (U) 71 01 01 - 71 06 30 Rejection was accelerated in rabbits immunized with chicken albumin before grafting with chicken cornea. Graft rejection in rabbits presensitized with chicken gamma globulin proceeded at a slower rate. The data suggest that corneal rejection is elicited by a number of antigens present in the grafted cornea, and that one antigen-antibody system may manifest itself quite differently clinically from another specific immune system also present in the grafted host. These studies are being continued with additional purified blood serum proteins. Studies are also being conducted to characterize the number and nature of the various antigens present in cornea.

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A91C 00 151 (cont)

Detail Sheet #1

Progress:

A soluble (F1) and insoluble (F2) protein fraction has been isolated from chicken cornea by various extraction procedures. These fractions possess transplantation antigen activity as demonstrated by their ability to induce specific sensitization in rabbits resulting in accelerated rejection of a subsequent corneal graft. F1 and F2 consist of a mixture of proteins which stimulate the production of circulating antibodies capable of engendering a wide variety of immunological reactions in the presence of specific antigens in donor cornea. These studies have been extended to include the isolation and characterization of the individual components which comprise the soluble fraction. At least eleven different protein components exist in F1. They have been separated by column chromatography with DEAE Sephadex. Currently, these fractions are being collected and concentrated and will be analyzed further for identification and to determine their effect on graft rejection.

Immunodiffusion studies with F1 and antisera specific for purified chicken serum proteins suggest that the cornea contains blood serum proteins. These studies have been supported by the observation that rabbits pre-sensitized with purified chicken serum proteins reject subsequent grafts more violently and at a markedly accelerated rate than unmodified controls. F1 and F2 also elicited Forssman antibody in rabbits. However, even though the presence of Forssman antigen was demonstrated in donor cornea, rabbits with high circulating specific antibody, induced by sensitization with sheep red cells, did not reject corneal grafts in an accelerated manner. These findings imply that in xenogenic keratoplasty the cornea may include transplantation antigens and also other antigens which do not influence the fate of the graft even in the presence of high specific humoral antibody.

An additional implication of these findings is that soluble transplantation antigens diffuse from a graft and are primarily responsible for the sensitization of the host. Meanwhile the insoluble antigens persist within the grafted tissue where they act as targets for sensitized cells or circulating antibodies. The isolation and characterization of the eleven corneal protein components and studies to determine their relationship to the graft rejection phenomenon will add significant information to the meager knowledge available in this area of research.

Publications and/or Presentations:

A91C 00 151 (cont)

Detail Sheet #2

Leibowitz, H. M. and A. J Luzzio. Transplantation antigens in xenogenic keratoplasty II. Arch. Ophthal. 84: 645, 1970.

Luzzio, A. J. and H. M. Leibowitz. Immunochemical analysis of corneal antigens in xenogenic keratoplasty. Transplantation, 11: 383, 1971.

Selected Bibliography:

Elliott, J. H. and H. M. Leibowitz. Corneal immune rings associated with heterograft rejection. Arch. Ophthal. 73: 519, 1965.

Leibowitz, H. M. and A J. Luzzio. Transplantation antigens in keratoplasty I. Arch. Ophthal 83: 215, 1970.

Russel, P. S. and A. P. Monaco. The biology of tissue transplantation. New Eng. J. Med. 271: 502, 1964.

Project No. 3A061102B71P	Basic Research in Support of Military Medicine
Task No. 02	Biophysics
Work Unit No. 010	Mathematical Models for Predicting Laser and Thermal Injuries
Work Unit No. 013	Cellular Effects of Laser Radiation
Task No 06	Pathology
Work Unit No 056	Diseases of Laboratory Animals Used in Support of Military Medical Research
Task No. 08	Physiology
Work Unit No. 085	Military Performance: Psychophysiology of Vision
Work Unit No 088	Military Performance: Biomechanical Aspects
Work Unit No. 089	Military Performance: Auditory Perception and Psychophysics

Investigators:

WU No 010	Arnold J. Brownell, Ph.D. Joseph C. Rosenbaum, M.S.
WU No. 013	Edward S. Spoerl, Ph.D. Thomas J. MacVittie, CPT, MSC
WU No 056	John T. Ervin, MAJ, VC William L. Gooding, MAJ, VC William H. Shelton, CPT, VC Mark G. Burns, CPT, VC
WU No. 085	Isaac Behar, Ph.D. Gregory J. Lewis, CPT, MSC John P. Schielderup, B.E.E. Frederick W. Dyer, Ph.D. George S. Hacker, Ph.D.

WU No 088	Andree J Lloyd, CPT, MSC Marvin J Herbert, Ph.D. Lee S. Caldwell, Ph.D. George S Harker, Ph.D. John R Schjelderup, B.E.E. Bruce C Leibrecht, CPT, MSC E. Booker McClaskey, M.S.
WU No 089	James N Cronholm, Ph.D. James D. Mosko, Ph.D. John R Schjelderup, B.E.E.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1 AGENCY ACCESSION	2 DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OA 6072	71 07 01	DD-DR&E(AR)636

3 DATE PREV SUMRY	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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10 NO CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	02	010
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Mathematical Models for Predicting Laser and Thermal Injuries (18)

12 SCIENTIFIC AND TECHNOLOGICAL AREAS

002600 Biology; 009600 Masers and Lasers

13 START DATE	14 ESTIMATED COMPLETION DATE	15 FUNDING AGENCY	16 PERFORMANCE METHOD
62 11	CONT	DA	C. In-House

17 CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION

b. NUMBER: NA

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 71	1.7	76
FISCAL YEAR CURRENT 72	1.7	60

19 RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

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20 PERFORMING ORGANIZATION

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SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME: Rosenbaum, J. C.

NAME: DA

21 GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22 KEYWORDS (Precede EACH with Security Classification Code)

(U) Laser; (U) Models; (U) Injury; (U) Safety; (U) Military; (U) Skin

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

23. (U) To study the mechanisms of interaction of laser radiation with biological cells and tissues and to correlate these changes with respect to mathematical models that will serve to predict when laser injury can be expected to occur. This knowledge will be applied to the development of laser safety standards for military personnel employing laser systems. The mathematical models will be defined and modified to conform to the experimental requirement.

24. (U) The data from cutaneous burn studies (Project No. 3A061102B71R 01 103, Agency Accession No. DA OA 6103) will be correlated with those predicted by current mathematical models describing laser injury thresholds. The results will be analyzed to evaluate the thermal constants and thermal inactivation rates of skin. Model and tissue systems will be used to evaluate the appropriate heat flow equation in the mathematical models.

25. (U) 71 01 01 - 71 06 30 Mathematical equations describing heat flow in tissue resulting from exposure to a carbon dioxide laser beam with a Gaussian power distribution have been incorporated into the damage integral model. This mathematical model is being expanded to include rapid sequential pulsing of the radiation.

*Available to contractors upon originator's approval

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Detail Sheet #1

Progress:

Heat flow equations have been developed and the corresponding computer programs completed which describe thermal transients in tissue resulting from exposure to laser beams having a radially symmetrical power distribution. The equations also take into account the absorption characteristics of the laser radiation being considered. The mathematical models are being expanded to include the effects of rapid sequential pulsing of the radiation. Testing of the validity of the equations and the accuracy of the assigned thermal constants with both simple physical models and tissues has been delayed because of the nonavailability of the CO_2 laser.

Data from cutaneous burn studies (Project No. 3A061102B71R 01 103) using the CO_2 laser are now being generated. These data will be analyzed by means of the mathematical models to determine the appropriate thermal inactivation rate functions and constants for skin. The complete model can then be utilized to predict the extent of thermal damage in skin resulting from exposure to a wide variety of laser radiations and exposure conditions as well as other radiations and modes of thermal input to the skin.

Publications and/or Presentations:

None.

Selected Bibliography:

Davies, J. M. The effect of intense thermal radiation on animal skin. A comparison of calculated and observed burns. Quartermaster Research and Engineering Command Report T-24, 1959 (DDC AD No. 456794).

Davis, T. P. A theoretical and experimental investigation of the temperature response of pig skin exposed to thermal radiation. University of Rochester Atomic Energy Project Report UR-553, 1959.

Fine, S., W. P. Hansen, G. R. Peacock, E. Klein, F. Hust, and Y. Laor. Biophysical studies with the CO_2 laser. NEREM (IEEE) Record, p. 166, 1966.

Fugitt, C. H. A rate process theory of thermal injury. AF Special Weapons Project Report No. 606, 1955 (DDC AD No. 212660).

Henriques, F. C. Studies of thermal injury. AMA Arch. Pathol. 43: 489-509, 1947.

Detail Sheet #2

Mixter, G., Jr., G. P. Delhery, W. L. Derksen, and T. L. Monahom. The influence of time on the death of Hela cells at elevated temperature. In: Temperature, Its Measurement and Control in Science and Industry. New York: Reinhold Publishing Corp., Part 3, pp. 177-182, 1962.

Vos, J. J. A theory of retinal burns. Bull. Math. Biophys. 24: 115-128, 1962.

Wood, T. H. Lethal effects of high and low temperatures on unicellular organisms. Adv. Biol. Med. Physics, 4: 119-165, 1956.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6076	71 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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	02	013
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Cellular Effects of Laser Radiation (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002600 Biology; 009600 Masers and Lasers

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
52 07	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	2	131
	CURRENT 72	2	108

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

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TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Biophysics Division

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

NAME: Spoerl, E. S.

TELEPHONE: 502-6247145

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: MacVittie, T. J., CPT

NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Laser; (U) Injury; (U) Hazards; (U) Military; (U) Preventive; (U) Therapeutic; (U) Electron Microscopy; (U) Cell Culture

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

23. (U) To define the extent of injury to human tissues associated with exposure to laser radiation and to define and evaluate the hazards to military personnel. Cell processes affected by absorption of laser radiation will be studied in order to provide useful knowledge concerning the principal physiological and biochemical changes induced. This, in turn, will lead to the development of better preventive and therapeutic measures.

24. (U) Cell processes and structures selected for the suitability of their responses to radiation and to heat will be studied in various ways. Effects upon membrane transport, sugar catabolism, and cell division will be examined in mammalian cells and tissues and in microorganisms. A variety of biochemical analyses will be employed. Microsurgery of cell organelles and electron microscopy of cell structures will be used to correlate structural and functional effects.

25. (U) 71 01 01 - 71 06 30 Monolayers of mammalian cells have now been carried through a long series of subcultures, indicating a stable cell line and cultural conditions. The cells have not yet adapted fully to growth in suspension, required for the large numbers used in some experiments. Freeze-etch and thin section preparations of these cells have been examined with the electron microscope to develop and improve techniques for measuring ultrastructural changes induced by laser radiation and acute thermal stress. Measurements of the transport of various compounds into other cells under varying conditions have been made in studying functional alterations. Knowledge of thermosensitive cell activities and structures can lead to the development of compounds which interrupt lethality or lead to repair, matters of high importance in protecting from laser injury.

*Available to contractors upon originator's approval

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Detail Sheet #1

Progress:

To characterize effectively the injuries which may occur in human tissues, studies with mammalian cells have had first priority during the past year. Monolayer cultures of strain KB cells are now routinely available for study. Development of a system for culture of these cells, initiated during the latter part of FY 1970, was slowed late last summer as a consequence of incubator malfunction at high ambient temperatures. Equipment changes, including incubator improvements and room cooling procedures, were made to produce a more appropriate growth facility. Problems of airborne contamination and the lack of sterile transfer areas were resolved with other equipment changes. Attempts to adapt monolayer cultures to a suspension type growth have not yet been successful. This more efficient method of culture would permit continued large harvests of cells under uniform growth and sampling conditions and provide a system highly suited for studies to correlate alterations in ultrastructure with cell processes sensitive to laser radiation.

Along with the development and stabilization of a mammalian cell culture system, biochemical and cytological procedures have been standardized for the measurement of cell growth and cell cycle sequences--by nucleic acid and protein assays--and the use of freeze-etch preparations, as well as thin sections for electron microscopic analyses of injured cells. Because laser radiation injures by the generation of heat, both direct irradiations and heat-shock experiments have been designed. Intracellular mechanisms which lead to cell lethality or repair in tissues exposed to laser radiation probably are initiated immediately upon exposure. A knowledge of these mechanisms and of the nature of laser-induced injury is prerequisite for devising methods to facilitate repair, a matter of increasing significance in military medicine as the use of lasers increases. Experiments with heat shock are underway; injury and repair are being assessed by electron microscopy and by measurements of the transport of essential types of nutrients into the cell.

Though their priority has been reduced to a minimum, some measurements to elucidate changes in yeasts as a result of heat-shock have been made to round out earlier work with these cells. Heat exposures result in altered rates of glycolysis and sugar uptake. These effects appear to be linked to membrane alterations, a type of change important in many cellular responses. Measurements of the uptake of non-metabolized sugars have indicated an effect by added glucose upon membrane structure separate from the utilization of this sugar as an energy source. Clarification of the details of such a glucose effect would

help in understanding a number of responses to glucose by cells of various types.

Publications and/or Presentations:

Maxwell, W. A. and E. Spoerl. Ultrastructural changes in *Saccharomyces cerevisiae* treated with iodoacetic acid. Presented (by Maxwell) at the American Society for Cell Biology Meeting, San Diego, Calif., Nov 1970; J. Cell. Biol. 47: 132a, 1970.

Maxwell, W. A. and E. Spoerl. Mannitol uptake by *Saccharomyces cerevisiae*. J. Bacteriol. 105: 753-758, 1971; USAMRL Report No. 879, Jul 1970 (DDC AD No. 714187).

Maxwell, W. A. and E. Spoerl. Uranyl nitrate inhibition of transport systems in *Saccharomyces cerevisiae*. J. Bacteriol. 105: 1205-1206, 1971; USAMRL Report No. 883, Jul 1970 (DDC AD No. 715694).

Spoerl, E. Enhanced CO_2 production by yeast exposed to elevated temperatures. J. Gen. Microbiol. 62: 35, 1970.

Spoerl, E. Disruption of yeast membranes by methylphenidate. J. Bacteriol, 105: 1168-1174, 1971.

Selected Bibliography:

Bessis, M. Micro-irradiation of cells. In: Recent Progress in Photobiology. E. J. Bowen (Ed.), New York: Academic Press, pp. 291-309, 1965.

Photophysiology. A. C. Giese (Ed.), Vols. I and II. New York: Academic Press, 1964.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 08 6081	71 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 04 09	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	06	056
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Procede with Security Classification Code)

(U) Diseases of Laboratory Animals Used in Support of Military Medical Research (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

001700 Animal Husbandry; 002600 Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY		16. PERFORMANCE METHOD
70 06	CONT	DA		C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	.2	6
	CURRENT 72	.2	.2

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

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20. PERFORMING ORGANIZATION

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SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Shelton, W. H., CPT

NAME: Burns, M. G., CPT DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Provide EACH with Security Classification Code) (U) Animals; (U) Animals, Laboratory; (U) Diseases of Animals; (U) Parasitic Diseases; (U) Primates; (U) Military

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

23. (U) To identify, characterize, and treat the sporadically occurring diseases encountered in laboratory animals used by the investigator; particular attention will be directed to those diseases that may be communicable to man, and to those diseases arising in animals from geographic areas where our military forces may be deployed (e.g., Africa, South America).

24. (U) Surveillance of the animal colonies of the laboratory (nonhuman primate, dogs, cats, rabbits, mice, goats) for the presence of disease agents or processes will be carried out on a continuous basis. The pathogenesis of the disease state, when recognized, will be investigated and possible control measures studied and instituted.

25. (U) 71 01 01 - 71 06 30 Five confirmed cases of tuberculosis were diagnosed in one shipment of 30 monkeys destined for military laser research program. To prevent spread of this disease the animals were quarantined for an extended period, until three negative consecutive TB tests were obtained. Routine diagnostic radiography has been established to aid in the detection of advanced tuberculosis in which a false negative tuberculin test is demonstrated frequently, in an attempt to prevent the spread of this disease to other valuable military research primates. A study to determine the extent of bacteriological flora in the animal holding facilities is still in progress. This study is an attempt to ascertain both the efficiency of cleaning and disinfecting schedules and to determine the possible contaminating sources both for valuable research animals and animal caretakers. A laboratory breeding colony of beagle dogs for research support has been established to provide healthy animals with known histories on demand. The initial breeding colony was obtained from WRAIR, Washington, DC.

*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 66 AND 1498-1, 1 MAR 66 (FOR ARMY USE) ARE OBSOLETE.

B71P 06 056 (cont)

Detail Sheet #1

Publications and/or Presentations:

Morrissey, R. L., D K. Hysell, and W. L. Janik. Transferrin polymorphism of *Cercocebus torquatus atys* (sooty mangabey). USAMRL Report No 901, Oct 1970 (DDC AD No 716353).

Selected Bibliography:

None.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6084	71 07 01	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. DISP'N INSTR'S	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 22	D. CHANGE	U	U	NA	NL	[X] YES [ ] NO	A. WORK UNIT

10. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	08	085
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Military Performance: Psychophysiology of Vision (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

012000 Optics; 005900 Environmental Biology; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
63 09	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	1.9	149
FISCAL YEAR CURRENT 72	1.9	165

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

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TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

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TELEPHONE: 502-6242025

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Lewis, G. W., CPT

NAME: Schjelderup, J. R. DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Vision; (U) Neurophysiological; (U) Color; (U) Discrimination; (U) Duties; (U) Binocular; (U) Night; (U) Military; (U) Volunteer

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

23. (U) Enhanced visual performance during continuous military operations depends upon appropriate use of the mechanisms underlying vision. Knowledge of the mechanisms of binocular vision and the neurophysiological processes of visual resolution and suppression is necessary to secure maximal visual information under the conditions of night (highly directional or non-directional) illumination. The interaction of ocular muscle balance and visual disorders, with the variety of military optical instruments directly affects the soldier's ability to execute his assigned duties.

24. (U) Studies will be conducted, predominantly in monkeys, but also using humans, exploring the electrophysiological correlates--ERG and cortical evoked potentials--of form vision. In addition, using cortical and depth electrodes, the effects of central stimulation will be studied. Primate behavioral preparations will be used as a model for human strabismus by severing the lateral rectus muscle of one eye during early infancy. The visual decrement and changes in electrophysiology will be studied.

25. (U) 71 01 01 - 71 06 30 Final hardware interfacing and calibration for computer reduction and analysis of vision electrophysiological data has been completed. Extended refinement of the computer program for this data analysis is underway. A setup for stereoscopic presentation of moving stimuli has been completed. Preliminary data is being taken. The initial objective shall be to evaluate with quantitative measures the depth displacements produced by a single moving stimulus above or below the fixation point. Behar, I. The effect of differential overtraining of the positive and negative stimulus on the aversiveness of the negative stimulus. USAMRL Rep. No. 923, Mar71; Adams, C. K. and I. Behar. Spectral sensitivity in the neonate monkey; Harker, G. S. The Mach-Dvorak phenomenon and binocular fusion of moving stimuli. Presented at the Ann Mtg of the Assoc for Res in Vis and Ophthalmology, Sarasota, FL, Apr71.

*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 68 AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE.

B71P 08 085 (cont)

Detail Sheet #1

Progress:

A computer program (software) has been developed which will allow digitized electrophysiological vision data to be loaded into a large computer buffer, or core area, from digital magnetic tape. The program follows a system approach incorporating load, digital tape to disc (core) conversion, power spectral analysis, and analysis of variance subroutines. All system control may be made remotely, via a local teletype terminal.

Compatibility between the local digital magnetic tape unit hardware and the large contracted computer facility has been established. The software system necessitated designing-in the capability to convert basic digitized data on the magnetic tape into a format which the computer could accept. Data handling is checked by inputing calibration data before and after the experimental data. Compensatory factors are being included in the software in such a way that two preamplifiers, with differential output may be utilized. The pre-amplifier discrepancies will be accepted or rejected by pre-established criteria for variability. The compensated data is scaled to a calibration record and voltage parameters. Transformation of the scaled data is obtained using a Fast Fourier Transformation (FFT) algorithm. Print-out of the data before and after calibration, before and after scaling, and before and after transformation can be obtained. Transformed data may then be statistically analyzed by calling a completely factorialized, analysis of variance subroutine. Use of analysis of variance allows interpretation of the transformed data (power spectral analysis) in the much more powerful realm of statistics.

In the future, coherence and regression analysis may be incorporated in the software system. In addition to frequency information, carrier frequency and phase information will be incorporated into the computer analysis of the electrophysiological data.

Several specific problems with hardware have been encountered. The digital magnetic tape unit did not accept data to an acceptable tolerance due to skewing of the write and read magnetic tape heads. Parity, the internal check made for correct data input, was also inaccurate, due to the excessive skewing. Acceptable tolerance with the current computer processing of the digital data is much tighter than previously. To achieve the higher tolerance levels the digital tape transport, data electronics, and control unit were returned to a manufacturer's service center for examination and repair. Currently, the interfacing between the local averaging computer-analog-to-digital converter is undergoing a similar upgrading.

B71P 08 085 (cont)

Detail Sheet #2

This reduction and analysis system for visual electrophysiology data has been assembled to handle extremely varied types and amounts of analog data. The investigation of target detection and acquisition, comparing periodic and aperiodic visual stimulation, is now underway. In the future, potential clinical usage of this system will be examined. Such usage would include computerized pattern recognition of visual records under biomedical stress, ophthalmic fatigue, and ophthalmic disease conditions. Three papers describing this hardware and software system are in preparation.

Two studies on visual discrimination learning in non-human primates were completed. In one, the effect of differential overtraining of the positive and negative stimulus on the aversiveness of the negative stimulus was compared. It was found that differential overtraining significantly altered the relative aversiveness of the negative stimuli. In the second study, the effects of two types of pretraining were compared on subsequent learning-set formation. Neither win-stay nor lose-shift pretraining when given alone facilitate such learning although the effects of each are quite different.

The initial study of the Mach-Dvorak phenomenon has been completed. Data taking was finished early in the year. Analysis and writeup progressed slowly with recent completion of the manuscript titled "The Mach-Dvorak phenomenon and binocular fusion of moving stimuli." The major conclusions of this research are: 1) Manipulation of exposure duration demonstrated an equivalence of the relative depth perceived due to eye sequence with that predicted by the rule, 'the short exposure precedes the long exposure in perception time.' Conceivably, the neural characteristics operative in determining the effective eye sequence of short and long exposures are also effective in eye sequencing when the exposures are equal; 2) The simultaneous and alternate neutral points, much as their occurrence is concomitant to the cyclic nature of the stimulation, are not conjugate in their response to experimental manipulations. Both neutral points are responsive to exposure duration though to a different degree and in a manner suggestive of the operation of multiple processes; 3) Manipulation of the luminance level viewed by the referent eye, to reverse the direction of the concomitant interocular illumination difference, produced changes both consistent and inconsistent with the conduction latency explanation offered for the Pulfrich phenomenon. The physical upper limit of perceived depth with manipulation of exposure duration was consistent with that obtained with Δ log I differences alone and evidence no discontinuity as the limit of intermittence was approached; 4) Evidence for a time-locked fusion contour was not obtained. Rather, the data indicate a complex

Detail Sheet #3

interrelation of several possible experimental manipulations though interocular delay, the primary experimental manipulation, requires a zero referent or "fusion contour" for the generation of positive and negative disparity, the presumed mechanism of its functioning; 5) Nasal-temporal conduction-time differences seem to be clearly evident in the divergent-convergent categorization of the obtained data; 6) Simple additivity of the disparities from interocular illumination difference and intermittence was not demonstrated Rather, the manipulation of intermittence and luminance produced interactive effects. Thus, the latency explanation of Pulfrich is not directly generalizable to Mach-Dvorak; however, no barrier is offered by the obtained data to the generalization of an explanation of the Mach-Dvorak to the Pulfrich phenomenon.

A new experimental setup providing for electronic control of stereoscopically presented stimuli has been completed Pilot work has verified the equivalence of this situation to that used in the initial study.

Publications and or Presentations:

Adams, C. K and I Behar Spectral sensitivity in the neonate monkey. Presented (by Adams) at the annual meeting of the Association for Research in Vision and Ophthalmology, Sarasota, Fla., Apr 1971.

Behar, I The effect of differential overtraining of the positive and negative stimulus on the aversiveness of the negative stimulus. USAMRL Report No 723, Mar 1971 (DDC AD No. 724143)

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Detail Sheet #4

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6083	71 07 01	OD-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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	08	088
b. CONTRIBUTING				
c. ~~CONTRIBUTING~~	CDOG 1412A(2)			

11. TITLE (Procede with Security Classification Code)

(U) Military Performance: Biomechanical Aspects (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

007500 Human Factors Engineering

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
56 01	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

c. TYPE: d. AMOUNT:

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

18. RESOURCES ESTIMATE	PRECEDING/CURRENT	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	71	2.8	206
	72	2.8	199

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Experimental Psychology Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)

NAME: Lloyd, A. J., CPT

TELEPHONE: 502-6243345

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Herbert, M. J.

NAME: Caldwell, L. S. DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Efficiency; (U) Performance; (U) Military; (U) Decrement; (U) Effectiveness; (U) Fatigue; (U) Stress; (U) Motor Unit; (U) Volunteer

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

23. (U) The soldier's mode of response to stressful situations affects his efficiency and the accomplishment of the military mission. With the increased complexity of performance demanded of the individual soldier, a research program has been pursued to study fatigue and its influence on performance. The areas considered include skill development and degradation of basic and complex tasks through fine motor unit training and military related tasks; and the electromyographic assessment of muscle efficiency as a means of allaying the onset of fatigue.

24. (U) A study is being made of the effect of auditory feedback on the efficiency of gross muscle activity. Single motor unit research is concerned with acquisition and maintenance of control of single and multiple units. Effort is continuing to identifying basic abilities in complex skills, and changes in skill composition as a function of acquisition (practice), fatigue, and stress.

25. (U) 71 01 01 - 71 06 30 Studies are also being made of possible sources of interference in learning to acquire and maintain control of multiple motor units. Surface electromyographic studies have revealed progressive changes in the amplitude and frequency of potentials related to differences in load and contraction time. Two papers on complex skills are in the first draft stage of preparation. One paper reports support for the regression theory of skill fatigue. A second paper reports that different skill components are transferred from one task to another dependent upon the level of skill attained in the initial task. Caldwell, L.S. Serial isometric fatigue functions with variable intertrial intervals. J. Mot. Behav. 3:17, 1971; Caldwell, L.S. Decrement and recovery in repetitive maximal work sessions. Human Factors, 12:547, 1970; Lloyd, A.J. and E.B. McClaskey. Subjective assessment of effort in dynamic work. J. Mot. Behav. 3:49, 1971; Lloyd, A.J., et al. Subjective and electromyographic assessment of duration during an isometric muscle contraction. Ergonomics, 13:685, 1970.

*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.

Detail Sheet #1

Progress:

The electromyographic analysis of muscle activity during continuous isometric exercises has indicated that this measure has the potential to provide information regarding the normal development of a fatigue state in a muscle as well as influences from various parameters related to the subject's attitude toward the specific task at hand. The development of fatigue results in a pattern change of muscle activity from a normal random pattern to one of motor unit synchronization. The onset of synchronized signals correlated with the onset of muscle tremors which further interferes with skilled responses. Normal synchronization results during later stages of fatigue. The introduction of some stressors has been demonstrated previously to produce an early onset of the synchronization phenomenon.

Physical performance has been proposed to be an aversive condition to a large number of ambulatory psychiatric patients with the hyperventilation syndrome. This condition was studied as a potential stressor which would produce a decrement in physical performance as a result of inefficient muscle utilization produced by early synchronization. The results indicated that hyperventilators respond aversively to physical activity, yet are more efficient in the isometric exercise than control subjects. A new treatment for immediate symptom alleviation was proposed as a potential means to reduce their military ineffectiveness.

If synchronization could be allayed, sustained performance should improve. Subjects who were provided with immediate feedback of their muscle activity did not increase in the endurance of an isometric contraction but demonstrated that the same performance could be conducted with significantly less muscle activity. It was proposed that this reduced activity would result in an efficiency which would be significant in a long performance series.

Studies have been conducted to relate the synchronization of the muscle activity to central origins. The analysis will consist of the relationship of the neuromuscular signals to EEG signals of the cortical motor area in an attempt to obtain more information regarding central and peripheral contributions to the muscle response.

A further analysis is being made on data where men were required to perform a strenuous task for a predetermined period of time. Preliminary results indicate that men voluntarily suppress the synchronization phenomenon and pace their performance in order to successfully complete the task.

B71P 08 088 (cont)

Detail Sheet #2

Electromyographic analysis of dynamic work represented by treadmill walking has demonstrated a significant difference in muscle activity when compared to a sustained isometric contraction. The men demonstrated a consistent reduction in muscle activity as they approached a maximum voluntary state of fatigue. Further analyses are required before any definitive statements can be made. Similar preliminary findings were obtained when a phasic isometric task was introduced.

Research on the general question of the similarities and differences in training or transfer phenomena existing when complex psychomotor tasks are compared to the well-documented data on verbal tasks was suspended during the third quarter, FY 1971, due to breakdown of the Modified Mashburn Apparatus. This work will resume when the contact plates can be rebuilt. Work is progressing on three papers: Performance decrement produced by nine hours of driving, a study of the regression hypothesis of skill fatigue involving shifts in ability patterns, and transfer of training as revealed by changes in ability measures from the training to the transfer task. The transfer study which employed the Modified Mashburn Apparatus (SAM Complex Coordinator) is closest to completion.

The investigation of fine motor skills had advanced in a continuing series of studies on single motor unit training. The basic technique monitors bioelectric activity of motor units by means of fine-wire intramuscular electrodes and has considerable potential in the area of myoelectrically controlled prosthetic devices. Recent efforts have focused on concurrent control of multiple units. Results indicate that with direct auditory feedback of motor unit activity subjects find learning to control a second motor unit considerably more difficult than learning to control the first. In order to determine the reason for this, followup experiments are in progress to examine transfer and retention of training. The results of these experiments should illuminate possible sources of interference encountered when training two or more units concurrently.

Data taken during constant speed walking at two preset mile per hour values has demonstrated that data taken on the original short treadmill were in some way contaminated. The present data provided the expected relationship that tall men take long strides and short men take short strides, where the previous data had shown that tall men take short numerous strides and short men take long albeit fewer strides. The basic problem apparently was the length of the treadmill and control of drive motor noise. The new treadmill is of the longer version. With completion of noise control, the study will be reinitiated.

B71P 08 088 (cont)

Detail Sheet #3

Publications and/or Presentations:

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Caldwell, L. S. Serial isometric fatigue functions with variable intertrial intervals. USAMRL Report No. 886, Aug 1970 (DDC AD No. 714190); J. Mot. Behav. 3(1): 17-30, 1971.

Caldwell, L. S. Review of scaling of pain and effort in strenuous physical performance. Presented in a colloquium series for USARIEM, Natick, Mass., May 1971.

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Lloyd, A. J. Surface electromyography during endurance of isometric contractions. USAMRL Report No. 906, Oct 1970 (DDC AD No. 715746); J. Appl. Physiol. 30(5): 713-719, 1971.

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6085	71 07 01	DD DR&E(AR)636

3. DATE PREV SUMRY	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 01 22	D. CHAN.	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. MD CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	08	089
b. CONTRIBUTING				
c. ///////////	CDOG 1412A(2)			

11. TITLE (Provide with Security Classification Code)

(U) Military Performance: Auditory Perception and Psychophysics (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

013400 Psychology (individual and group behavior); 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
55 01	CONT	DA	C. In-House

17. CONTRACT/GRANT

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

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 71	2.1	103
FISCAL YEAR CURRENT 72	2.1	116

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory
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RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Experimental Psychology Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Cronholm, J. N.
TELEPHONE: 502-6242025
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Moske, J. D.
NAME: Schjelderup, J. R. DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Provide each with Security Classification Code)

(U) Vigilance; (U) Perception; (U) Military; (U) Hearing Conservation; (U) Volunteer; (U) Communication

23. TECHNICAL OBJECTIVE

24. APPROACH

25. PROGRESS (Furnish individual paragraphs identified by number. Provide text of each with Security Classification Code.)

23. (U) The sounds of combat, radio "static," vehicular, and engine noise are typical backgrounds which degrade the soldier's ability to give and receive necessary commands by voice and electronic means. This research is designed to assess the effects of these sounds on the soldier's performance of military tasks, to evaluate and improve the predictive value of models of processes involved in the communication of auditory messages and to promote hearing conservation in military personnel.

24. (U) Factors influencing attention are being studied using simple signals. The listener acts as an information relay detecting and retransmitting signals. Comparisons between the transmitted and retransmitted signal trains yield readily quantifiable measures of performance. Independent variables include stress induced by competition and instructions, signal-masker parameters, and response bias. Auditory perception is being studied with vocal and voice-like signals and maskers. Emphasis is on the identification of complex signal parameters and their relation to auditory communication and binaural unmasking. Response related factors such as reaction and decision times are regularly monitored.

25. (U) 71 01 01 - 71 06 30 Data collection is complete on a study of the effects of mean signal rate, signal to noise ratio, and intersignal interval distribution on the detection of randomly occurring signals; analysis of the data is underway. Studies of binaural unmasking of discrete frequency signals with pulsed and continuous maskers continue. Mosko, J. D. and A. S. House. Binaural unmasking of vocalic signals. J. Acoust. Soc. Amer., 49, No. 4 (Part 2): 1203-1212, 1971.

* Applicable to contractors upon congressional disclosure

DD FORM 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

B71P 08 089 (cont)

Detail Sheet #1

Progress:

Work in the area of attentional processes has resulted in the completion of computer hardware and software comprising a signal generation, experimental control, and data acquisition system. Once calibrated, this system was used to conduct a parametric study of auditory signal detection with random intersignal intervals. The experiment was designed to determine the effects of three variables on detection performance: 1) mean signal rate (two levels), 2) signal to noise ratio (four levels), and 3) intersignal interval probability distribution (two levels: exponential and gamma). The data collected under these 16 treatments are in the form of temporal histograms which in turn are estimates of certain conditional probability distributions related to hits, misses, correct negatives, and false alarms. Analysis is underway. A model of the processes underlying signal detection with random intersignal intervals is under development and is an outgrowth of earlier work (Cronholm, 1968). A paper by Cronholm, "Probability gate statistics," describing some general properties of probability gates used in several models (Luce, 1970; Cronholm, 1968) has been published.

Continued effort in the area of perceptual processes has been devoted to the acquisition and development of equipment because of certain interesting inconsistencies discovered in the binaural unmasking data gathered during the previous year. However, a paper with A. S. House from Dr. Mosko's dissertation on the "Binaural unmasking of vocalic signals" has been published. In addition, Dr. Mosko has produced two USAMRL reports evaluating earplugs, one of which has been published in the open literature. In this study it was shown that the Gundefender earplug offers both improved speech intelligibility and protection from temporary threshold shift equivalent to the standard issue Army plug. Work continues on other problems of speech intelligibility. These studies are concerned with the acoustic parameters of speech signals which govern intelligibility in the presence of unwanted noise.

Work in the third area, response processes involved in auditory communication, is exemplified by pilot studies by Dr. Cronholm of response patterning in the signal detection setting without signals. This work was undertaken to explore how false alarm responses are produced as a function of noise level alone. Mean false alarm rates have been obtained at one noise level. In future experiments interresponse time histograms will be obtained at several noise levels.

Publications and/or Presentations:

B71P 08 089 (cont)

Detail Sheet #2

Cronholm, J. N. Probability gate statistics. Behav. Res. Methods & Instrumentation, 2(4): 160-161, 1970.

Mosko, J. D. Real-ear evaluation of earplugs using one-third octave bands of noise. USAMRL Report No. 907, Oct 1970 (DDC AD No. 715748).

Mosko, J. D. and A. S. House. Binaural unmasking of vocalic signals. J. Acoust. Soc. Amer. 49, No. 4 (Part 2): 1203-1212, 1971.

Selected Bibliography:

Cronholm, J. N. A stochastic model of signal detection under conditions of temporal uncertainty. USAMRL Report No. 782, 1968 (DDC AD No. 693868).

Green, D. M. and J. A. Swets. Signal Detection and Psychophysics. New York: Wiley, 1966.

Grice, G. R. Stimulus intensity and response evocation. Psychol. Rev. 75: 359-373, 1968.

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Luce, R. D. and D. M. Green. Detection of auditory signals presented at random times, II. Percept. & Psychophys. 7(1): 1-13, 1970.

Nickerson, R. S. and D. W. Burnham. Response times with nonaging foreperiods. J. Exp. Psychol. 79: 452-457, 1969.

Project No. 3A061102B71R	Research in Biomedical Sciences
Task No. 01	Surgery
Work Unit No. 102	Effects of Laser Radiation on Immune Mechanisms
Work Unit No. 103	Cutaneous Burns Induced by Laser Radiation
Work Unit No. 280	Laser Effects Upon Visual Performance
Task No. 03	Psychiatry
Work Unit No. 126	Military Performance: Traumatic Origins of Hearing Loss
Work Unit No. 127	Military Performance: Psychophysics of Visual Perception
Work Unit No. 128	Military Performance: Physical Decrement and Endurance

Investigators

WU No. 102	Anthony J. Luzzio, Ph.D.
WU No. 103	Arnold S. Brownell, Ph.D. Wordie H. Parr, Ph.D. David K. Hysell, MAJ, VC
WU No. 280	David I. Randolph, Ph.D. Wordie H. Parr, Ph.D. John T. Ervin, MAJ, VC
WU No. 126	George A. Luz, CPT, MSC James H. Patterson, CPT, MSC James D. Mosko, Ph.D. John R. Schjelderup, B.E.E.
WU No. 127	Isaac Behar, Ph.D. Frederick N. Dyer, Ph.D. George S. Harker, Ph.D. John R. Schjelderup, B.E.E.

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Lee S. Caldwell, Ph.D.
Samuel C. Shiflett, CPT, MSC
Andree J. Lloyd, CPT, MSC
John R. Schjelderup, B.E.E.
E. Booker McClaskey, M.S.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6075	71 01 22	DD-DR&E(AR)636

3. DATE PREV SUMRY	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
70 10 20	H. TERMINATION	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71R	01	102
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Effects of Laser Radiation on Immune Mechanisms (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002600 Biology; 009600 Masers and Lasers

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
59 10	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 70	.9	60
FISCAL YEAR CURRENT 71	.9	94

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Biophysics Division
US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic participation)
NAME: Luzzio, A. J.
TELEPHONE: 502-6246630
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME:
NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede each with Security Classification Code)

(U) Laser, Injury, Biological; (U) Antibody; (U) Antigen; (U) Immunity

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

23. (U) To investigate, by immunological techniques, the mechanisms that are involved in the production of opacities in the lens of the eye induced by laser radiation. Information in this area will permit a more accurate prediction of the amount of laser energy necessary to cause lens damage, thereby providing better standards for the safety of military personnel employing laser systems.

24. (U) Normal proteins of the cornea and lens will be characterized by standard immunochemical techniques. Changes in the antigenic structure of these tissues following laser irradiation will be sought and the relationship of these changes to cataractogenesis will be determined.

25. (U) 70 10 01 - 70 12 31 Column chromatographic and electrophoretic studies to compare protein fractions separated from normal and laser-induced cataractous lenses have been terminated; the decreasing emphasis in laser biology research has prompted this action. The data from these studies are being analyzed for a final report.

*Available to contractors upon originator's approval

DD, FORM 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.

B71R 01 102 (cont)

Detail Sheet #1

Progress:

Ocular exposure to high levels of unfocused, pulsed ruby laser radiation results in cataract formation in rabbits. Soluble lens extracts from laser induced cataractous and normal rabbit lenses were studied by electrophoresis, column chromatography, and immunological, and carbohydrate analytical methods. The electrophoretic, immunological, and chromatography data provided no evidence for the occurrence of additional or altered specificity of proteins in laser induced cataractous lenses. However, it was shown that proteins from cataracts behave antigenically the same as heat denatured lens protein. The increase in reactivity is probably due to the increase in antigen combining sites brought about by the aggregation of protein molecules. Hexose and polyol concentrations did not differ significantly between normal and cataractous lenses.

The clinical resemblance of laser induced cataracts to the so-called "glassblower's cataract" along with the aforementioned findings strengthens the contention that laser induced cataractogenesis results from heat alone.

A final report is in preparation.

Publications and/or Presentations:

None.

Selected Bibliography:

Francois, J., M. Rabaey and L. Stockmans. Gel filtration of the soluble proteins from normal and cataractous humans lens. Exp. Eye Res. 4: 312-318, 1965.

Kabat, E. E. and M. M. Mayer. Experimental Immunochemistry. Springfield, Illinois: Charles C. Thomas, 2d Edition, 1961.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6103	71 07 01	DD DR&E AR(A)1A

3. CATEGORY	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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. MODIFS	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A061102B71P	01	103
b. CONTRIBUTING				
11111111	CDOG 1412A(3)			

11. TITLE (Include Security Classification Code)

(U) Cutaneous Burns Induced by Laser Radiation (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002600 Biology; 009600 Masers and Lasers

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
66 07	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. NUMBER: NA
b. TYPE
c. KIND OF AWARD
d. EFFECTIVE DATE
e. EXPIRATION
f. CUM. AMT.
g. AMOUNT

18. RESOURCES ESTIMATE	PROFESSIONAL MAN YRS	FUNDS (In Thousands)
FISCAL YEAR PRECEDING: 71	1.5	85
FISCAL YEAR CURRENT: 72	1.5	60

19. RESPONSIBLE DOD ORGANIZATION

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TELEPHONE: 502-6245749
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Parr, W. H.
NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Laser; (U) Skin Lesions; (U) Safety; (U) Infection; (U) Military

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

23. (U) To investigate the potential of high intensity laser radiation of a given frequency to induce skin lesions as a function of power density and exposure time; to provide pertinent data for safety standards in military laser systems application; to study laser induced skin burns in animals with respect to susceptibility to systemic bacterial infection.

24. (U) Thermal damage produced in porcine skin by carbon dioxide laser radiation with millisecond and nanosecond exposure times will be determined. Injuries resulting from rapid sequential pulsing of subthreshold exposures will also be investigated. Threshold values in pigmented porcine skin for other laser radiation will be determined.

25. (U) 71 01 01 - 71 06 30 Two detector systems for scanning the high intensity carbon dioxide laser beam have been completed and tested. The skin of seven pigs has been exposed to 6 millisecond pulses of carbon dioxide laser radiation. The damage ranged from erythema to steam blebs. The data are now being processed to determine threshold doses for the various levels of injury.

*Available to contractors upon originator's approval

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

Detail Sheet #1

Progress:

The skin of darkly pigmented pigs was exposed to Q-switched ruby laser radiation with an exposure time of 20 nanoseconds. The resulting damage was evaluated by gross visual observation as well as histological techniques. Depigmentation of the skin at the site of impact of the laser beam was used for visual assessment of damage. Histological evaluation of tissue damage has now been completed by MAJ David K. Hysell, VC, presently on duty at the US Army Research Institute of Environmental Medicine. The measured absorption of visible and near infrared radiation by this porcine skin closely resembles that of darkly pigmented American Negroes. The measured threshold values for damage induced by ruby laser radiation in dark porcine skin can be considered a "worse case" for military personnel.

Progress in the study of skin damage by CO_2 laser radiation was delayed for several months because of an inoperable laser. Upon the repair and return of the laser by the manufacturer, work was initiated to stabilize both the total power output and beam geometry of the laser. Careful control of the temperature environment of the laser head produced reasonable stability of the laser beam.

Two detectors for scanning the high intensity CO_2 laser beam have been completed and tested. Absolute calibration of the devices has presented some problems. However, work is continuing and calibration is expected to be completed shortly.

The skin of seven white pigs has been exposed to 6 millisecond pulses of high intensity laser radiation. The gross damage ranged from erythema to explosive steam blebs. The histological evaluation of the lesions is nearly complete. Final analysis of the data to determine the threshold doses for various levels of injury cannot be completed until the absolute calibration of the scanning devices is complete.

Publications and/or Presentations:

None.

Selected Bibliography:

Brownell, A. S., W. H. Parr, D. K. Hysell, and R. S. Dedrick. Threshold lesions induced in porcine skin by CO_2 laser radiation. USAMRL Report No. 732, 1967 (DDC AD No. 659347).

Detail Sheet #2

Davies, J. M. The effect of intense radiation on animal skin. A comparison of calculated and observed burns. Quartermaster Research and Engineering Command Report T-24, 1959 (DDC AD No. 456794).

Derksen, W. L., J. Bracciavanti and G. Mixter, Jr. Burns to skin by millisecond light pulses. NAVAPLSCIENLAB Project 9400-12, Report 1, 1964.

Fine, S., W. P. Hansen, G. R. Peacock, E. Klein and Y. Laor. Biophysical studies with the CO_2 laser. NEREM Record, p. 166, 1966.

Helevig, E. G., W. A. Jones, J. R. Hayes, and E. H. Zeitler. Anatomic and histochemical changes in skin after laser irradiation. First Annual Conference on Biological Effects of Laser Radiation. Fed. Amer. Soc. Exp. Biol. Proc., Suppl. 14, 1965.

Henriques, F. C., Jr. and A. R. Moritz. Studies of thermal injury. I. The conduction of heat to and through skin and the temperature attained therein. A theoretical and an experimental investigation. Amer. J. Pathol. 23: 531, 1947.

Lyon, J. L., T. P. David, and H. E. Pearse. Studies on flash burns. The relation of thermal energy applied and exposure time to burn severity. Univer. of Rochester Atomic Energy Report UR-394, 1955.

Moritz, A. R. Studies of thermal injury. III. The pathology and pathogenesis of cutaneous burns. An experimental study. Amer. J. Pathol. 23: 915, 1947.

Moritz, A. R. and F. C. Henriques, Jr. Studies of thermal injury. II. The relative importance of time and surface temperature in the causation of cutaneous burns. Amer. J. Pathol. 23: 695, 1947.

Perkins, J. B., H. E. Pearse, and H. D. Kingsley. Studies on flash burns: the relation of the time and intensity of applied thermal energy to the severity of burns. Univer. of Rochester Atomic Energy Report UR-217, 1952.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0B 6070	71 07 01	DD DR&E (AR)636

3. DATE PREV SUMY	4. SUMMARY SCTY	5. WORK SECURITY	6. REGRADING	6A. DOD'D INSTR'N	6B. SPECIFIC DATA-CONTRACTOR ACCESS	7. LEVEL OF SUM
71 01 01		U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62720A	3A061102B71R	01	280
b. CONTRIBUTING				
c. REMARKS				

11. (U) Laser Effects Upon Visual Performance (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
002600 Biology; 009600 Masers and Lasers

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
68 07	CONT	DA	C. In-House

17. CONTRACT/GRANT
a. DATE/EFFECTIVE — EXPIRATION
b. NUMBER: NA
c. TYPE — d. AMOUNT
e. KIND OF AWARD — f. CUM. AMT.

18. RESOURCES ESTIMATE	g. PROFESSIONAL MAN YRS	h. FUNDS (In Thousands)
FISCAL YEAR PRECEDING 71	1.9	45
FISCAL YEAR CURRENT 72	1.9	47

19. RESPONSIBLE DOD ORGANIZATION
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GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

20. PERFORMING ORGANIZATION
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SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Parr, W. H.
NAME: Ervin, J. T., MAJ DA

21. KEYWORDS (Provide EACH with Security Classification Code): (U) Laser; (U) Visual; (U) Electrophysiological; (U) Electroretinographic; (U) Acuity; (U) Flashblindness; (U) Military

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

23. (U) To measure and evaluate the effects of exposure to laser radiation upon the visual and electrophysiological functions of the eye. Knowledge in this area will contribute to a better understanding of the effects, if any, of low dosage laser exposure on the visual function in the absence of visible damage as it applies to military laser systems.

24. (U) Monkeys will be trained by operant conditioning techniques to respond positively to the various visual stimuli required for tests of acuity, dark adaptation, monochromatic and achromatic difference thresholds and critical flicker frequency thresholds. The ability to discriminate in these various tests will be retested, after exposure of the eye to laser and other high energy light sources, to measure changes produced. Electroretinographic and evoked cortical potentials will be used to evaluate the relatively rapid recovery of the eye to flashblinding stimuli as well as to provide correlative data for retinal exposures of more intense, structurally damaging light.

25. (U) 71 01 01 - 71 06 30 The right eyes of seven monkeys have been exposed to laser radiation. Three animals received approximately 1 millijoule per square centimeter. Subsequent analysis showed an immediate loss of visual acuity to 18 percent of preexposure levels. Seven weeks after exposure the animals returned to a stable level of 45 to 50 percent of the preexposure acuity. Three other animals received a "minimal" dose of approximately 164 microjoules per square centimeter. Each showed foveal lesions; however, visual acuity did not change. In the seventh animal a dose of 720 microjoules produced an immediate decrement in acuity which returned to normal within 7 weeks. Subsequently, the left eyes of three of the original test animals have been exposed. The data are consistent with the above results. Flashblindness research has been initiated with the exposure of rhesus monkeys to various wavelengths of light. Recovery time data have not been analyzed to date.

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

B71R 01 280 (cont)

Detail Sheet #1

Progress:

The study of the effects of Q-switched ruby laser radiation on the visual acuity of the rhesus monkey has continued. In addition, studies have been initiated to determine the effects of the wavelength of a flashblinding source upon the recovery time of rhesus monkeys.

a. Visual acuity - Seven rhesus monkeys were trained to discriminate a Landolt "C" from an "O" of the same size. The task required the animal to depress a lever at the beginning of a trial, characterized by the onset of a light and tone in the test module. The lever activated a projector shutter system which flashed either a "C" or an "O" onto a screen located approximately 50 cm in front of the animal. If a "C" was presented, the animal was trained to release the lever immediately. If an "O" was presented, the animal continued to hold the lever down until the light and noise were shut off. Various sized Landolt rings were presented to each animal. Acuity thresholds were determined by computing the Landolt gap size which yielded a correct response 75% of the time. After initial training periods, binocular and monocular acuity measures were obtained for approximately 4 months or until the visual acuity values for each animal had stabilized. During July and August (1970) three trained animals (RM 46, RM 65, and RM 49) were given single Q-switched laser exposures of 1.11, 0.72, and 0.170 mj in the right eye (1.0 mj represents the energy level at which there is a 100% probability of producing a visible retinal lesion, while 0.72 mj and 0.170 mj represent the 75 and 50% probability points, respectively). Irradiations were made at the USAMRDC-AMC Laser Safety Team laboratories, Frankford Arsenal. Two other animals (RM 99 and RM 100) were similarly exposed to 1.0 mj and 0.170 mj, respectively, in January 1971. Two additional animals trained at the Frankford Arsenal facility (RM 13 and RM 16) were given laser exposures in November 1970 and May 1971.

The effects of these laser exposures upon the visual acuity of the animals varied as a function of the dose levels used. RM 46, RM 100, and RM 13 received approximately 1 mj of energy incident at the corneal surface. All three animals showed immediate acuity losses. For 1 (RM 13) to 3 weeks (RM 46), acuity was not measurable in the exposed eyes, while the left, or control eyes showed normal acuity. Each of the three animals showed gradual improvement in acuity of the exposed eye during the following 6 to 8 weeks. At this time, the acuity in the right eye stabilized at between 40 to 60% of preexposure

acuity levels and remained at this level for 6 to 8 months. Ophthalmoscopic examination showed large uniform lesions in each eye completely encompassing the fovea and central macular area.

Animals receiving approximately 0.170 mj of energy (RM 16 and RM 49) showed no changes in the exposed eye 1 hour later. Ophthalmoscopic examination revealed lesions in each eye completely encompassing the fovea, but of less severity than in animals receiving the highest dose.

An eccentric lesion developed in the right eye of one animal (RM 65). The dose was calculated at 0.720 mj at the cornea and encompassed an estimated 80% of the fovea. An immediate loss of acuity to 33% of the preexposure level was followed by a rapid improvement to a normal level of acuity within 4 weeks.

Animals RM 46, 65, and 49 were exposed again in February 1971, this time in their left eyes. RM 46 received approximately 0.170 mj, and RM 65 and RM 49, approximately 1.0 mj. RM 46 showed an immediate decrement in visual acuity in the exposed eye, followed by an apparent return to normality within 2 weeks. The left eye of RM 65 also showed an immediate decrease in acuity followed by a return to its preexposed acuity within 3 weeks. RM 49 (1 mj exposure) showed a slight decrease in acuity in a return to normal values within 1 week.

A seventh animal, RM 99, died 2 weeks after receiving a 1.0 mj exposure and the data were not considered sufficient to include in the analysis.

Three rhesus monkeys are in the first stages of acuity training and will be exposed to the Q-switched laser within 1 month. The three animals already exposed in one eye will receive a second exposure in the other eye within 2 months. The three animals previously exposed in both eyes will be sacrificed soon and, in cooperation with the Joint Laser Safety Team, electron and light microscopic studies will be made to evaluate the observed pathological changes and relate these to the observed changes in visual acuity. Eventually, all of the animals involved in visual acuity tests will undergo this latter examination.

b. Flashblindness - Research has been initiated to determine the factors influencing the recovery of the visual system following exposure to high intensity flashes of light. Previous research (Randolph, J. Opt. Soc. Amer. 58: 424, 1968) has shown that recovery from flashblindness is closely related to both the wavelength of the

flashblinding stimulus and the wavelength of the target used to measure recovery. In the present research design one of six wavelengths, each equated for equal power at 1.0×10^{-3} w/cm^2, will be flashed into the eye of a rhesus monkey. Recovery of visual response to one of the six different wavelengths applied at 1.0×10^{-5} w/cm^2 will then be evaluated by measuring the time required for insilateral and contralateral occipital evoked potentials and the electroretinogram to return to their preflashblinding amplitudes and latencies. Monochromatic light, generated by a krypton laser system, at 468, 520, 530, 570, 647, and 676 nm will be used both for flashblinding and for recovery measurements at each of these wavelengths. Evoked cortical potentials from a number of rabbits and two monkeys at several of these wavelengths have been averaged and are currently being evaluated for variability and relative amplitude and latency differences. When these data have been analyzed, daily fluctuations in both evoked occipital potentials and ergs can be controlled to insure independence of the effects of each wavelength upon the recovery from flashblindness.

While the electroretinogram and the evoked cortical potentials are reliable measures of flashblindness recovery, direct measures of the temporary effects of flashblindness would be more directly related to military problems. To accomplish this, rhesus monkeys are being trained to discriminate between various wavelengths of light generated by the Krypton laser. Following this training, each animal will have electrodes implanted in the occipital cortex. Flashblindness effects upon the perception of color and the relationship of this perception to the evoked cortical potentials will then be directly evaluated. Recommendations for flashblindness protective devices can then be made based upon perceptual and electrophysiological criteria.

Publications and/or Presentations:

Randolph, D. L., J. L. Campbell, H. S. Zwick, and E. Beatrice. The effect of foveal laser exposures on the visual acuity of rhesus monkeys. Paper presented (by Randolph) at the Association for Research in Vision and Ophthalmology meeting, Sarasota, Fla., Apr 1971.

Selected Bibliography:

Jones, A. E. and A. J. McCartney. Ruby laser effects on the monkey eye. Invest. Ophthal. 5: 474, 1966.

Randolph, D. L. Recovery time of cats following high illuminance stimulation. J. Opt. Soc. Amer. 58: 424, 1968.

Detail Sheet #4

Randolph, D. I. Electroretinographic and behavioral recovery time of cats to high intensity photic stimulation. In: Davies and Randolph (Eds.), Natick Flashblindness Symposium, NAS-NRC Armed Forces Vision Committee, Washington, D. C., Nov 1969.

Vassiliades, A., et al. Investigations of laser damage to ocular tissues. Final Report, USAF, Aerospace Medical Division, Brooks AFB, Tex., Mar 1968.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6082	71 07 01	DD-DR&E(AR)636

3. DATE PREV SUMRY	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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3A06116 B71R	03	126
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Military Performance: Traumatic Origins of Hearing Loss (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

007500 Human Factors and Engineering; 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
55 01	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	2.2	86
CURRENT FISCAL YEAR 72	2.2	87

19. RESPONSIBLE DOD ORGANIZATION

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20. PERFORMING ORGANIZATION

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SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Patterson, J. H., CPT

NAME: Mosko, J. D. DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Noise Damage; (U) Hearing Loss; (U) Auditory System; (U) Combat Effectiveness; (U) Susceptibility; (U) Protective Devices; (U) Volunteer

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

23. (U) Reclassification of highly trained and experienced personnel due to service connected, noise induced, hearing loss critically reduces combat effectiveness. In addition, increased incidence of hearing loss among inductees requires prior selection to assure military benefit from specialized training. This research relates the physical parameters of military noise to the psychophysical and physiological behavior of the human auditory system. These data, with other medical and engineering data, will be used to evaluate and improve hearing protection for military personnel.

24. (U) The relation between physical characteristics of the ear, physical characteristics of noise, and susceptibility of ears to noise damage will be studied in human and animal ears. Human studies will explore the hazards of the auditory environments projected through the Army 1985 Follow-On Study. Studies will be made of any protective devices made available to this laboratory.

25. (U) 71 01 01 - 71 06 30 The analysis of the data obtained from monkeys exposed to impulsive noises has been completed. A computer-controlled program for the detection of novel sound patterns in chinchillas exposed to noise is running and preliminary data are being initiated. A computer-controlled device which will enable a systematic investigation of the parameters of impulse noise and their effects on auditory performance has been established and the initial data are being obtained. Instrumentation has been constructed to study directional hearing in humans exposed to noise environments and audiokinetic nystagmus. Mosko, J.D. Non-titled paper presented to FASEB Ad Hoc Group Mtg on "A review of the adverse biomedical effects of sound in the military environment, Bethesda, MD, Jun71; Luz, G.A., et al. The relationship between temporary threshold shift and permanent threshold shift in rhesus monkeys exposed to impulse noise. USAMRL Rep. No. 928, Apr71; Luz, G.A. and J.D. Mosko. The susceptibility of the chinchilla ear to damage from impulse noise. USAMRL Rep. No. 921, Mar71.

*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.

B71R 03 126 (cont)

Detail Sheet #1

Progress:

In one study (also mentioned in last year's report), no relationship could be found between TTS and PTS in a group of monkeys exposed to impulse noise (USAMRL Report No. 928, Apr 1971). Other relationships did emerge. This study suggested--but did not prove--that a small amount of PTS at one audio frequency may produce an increased sensitive and increased resistance to TTS at some other frequency. Thus, this study confirmed a similar observation for tank crew men, whose low frequency hearing appeared to improve during the course of 20 years service, a period during which their high frequency hearing drops by 40 dB (Paparella and Melnick). The study also supported the clinical concept that high frequency PTS is a more sensitive index of damage to hearing than is low frequency PTS.

At the end of the study, the monkeys were turned over to Drs. Jordan, Pinheiro, Jiminez, and Chiba of the Inner Ear Research Program at Case-Western Reserve University Medical School. These investigators provided USAMRL with cochleograms of the monkey ears. (A cochleogram is a graph of the percentage of sensory cells present in the cochlea as a function of distance within the cochlea.) The results of the eleven analyses were so impressive that it was decided to build the potential for the same type of histology (i.e., the "surface preparation") within the Experimental Psychology Division. The necessary equipment is being purchased and Mr. Carl Guthrie was trained in this technique by Dr. David Lipscomb, Director of the University of Tennessee Noise Study Laboratory.

The surface preparation of histology allows one to make a comparison between the patterns of hair cell damage induced by different types of noise. Thus, it can provide one kind of index of hazardous noise. Although it is a relatively new technique, it is already being used to index the hazard of different kinds of impulse noise. For example, Hamernik et al (1971) have shown how the extent of hair cell damage changes as the number of impulse exposures is increased and how the pattern of damage differs between two different shapes of impulse. A parameter not yet explored which is within the immediate research capacity of USAMRL is the effect of impulse width on the pattern of damage, an experiment which is easily programmed with the variable width impulse generator, developed several years ago through an SGO contract to R. Benson and Associates.

The development of a still more versatile impulse generator was begun in the past year. From the digital to analog converter of the

Detail Sheet #2

PDP-8 computer, a short transient voltage is fed into a powerful amplifier. The amplifier drives a public address system driver which is closely coupled to the ear. In initial tests, this system produced impulses with peak levels of greater than 150 dB SPL. Although the level of these impulses cannot match those produced by the variable width impulse generator, they can be shaped in rather precise ways, a feature not present in the other system. For example, one can change the shape of the impulse while keeping the total energy of the impulse constant.

Although the development of the capacity for inner ear histology is important, it would be naive to suppose that an adequate index of hazardous noise could be produced from this technique. There are many cases in which hearing loss does not correlate with the loss of hair cells. An obvious example is any hearing loss connected with changes in the ossicles of the middle ear. Even within the category of what is conventionally termed "sensorineural loss", there is often a lack of correlation between audiometric and histological measures. For example, Bredberg, in an important study of the surface preparation histology of human ears, found cases of histological loss without comparable audiometric loss and cases of audiometric loss without comparable histological loss. Assuming that neither the histologist nor the audiologist made a mistake, such cases would suggest that there are more factors underlying sensorineural loss than the loss of hair cells. During the past year, the research program at USAMRL has obtained data that would suggest this is so. When the patterns of PTS in the noise-damaged monkeys were compared with the respective cochleograms, it was apparent that large amounts of hair cell loss can be sustained with only small shifts in thresho'd sensitivity. More than 90% of the outer hair cells had to be destroyed at some point in the cochlea before the monkeys showed a corresponding dip in their pure tone audiogram. These results corresponded to those of a similar study carried out with chinchillas at the Central Institute for the Deaf in St. Louis. On the other side of the coin, a study in which chinchillas were exposed to the same impulses as the monkeys (USAMRL Report No. 921, Mar 1971) yielded small but consistent losses of pure tone sensitivity with insignificant losses of hair cells. This analysis was provided by Dr. Lipscomb and also by our own laboratory.

Conceivably, the chinchillas suffered a displacement of the ossicular chain. On the other hand, there could have been permanent changes in the input impedance of the inner ear. Such changes of impedance within the inner ear have been suggested by several investigators (Beagley, Khanna, and Tonndorf). The possibility of a

B71P 03 126 (cont)

Detail Sheet #3

reversible change in inner ear impedance was also underscored in the model of impulse noise induced TTS published this year in collaboration with Dr. David Hodge of BEL, Aberdeen Proving Grounds.

Since the model is speculative (as is the concept of reversible changes in inner ear impedance), effort has been devoted this year to exploring the "S-type" of TTS postulated in the model. Two questions were asked: (1) Can the S-type of TTS be demonstrated in species other than man and monkey? (2) Is the S-type TTS merely an artifact of behavioral audiometry or does it show up in physiological measures of the auditory system? To answer these questions, evoked potential audiometry was carried out on chinchillas. Most of the year has been devoted to the development of a suitable system for evoked response audiometry. As yet, there is too little data available for any conclusion.

Faced with the lack of correlation between hair cell loss and PTS, many auditory researchers have begun to search for more sensitive measures of auditory sensitivity. During the past year, efforts have been made to find auditory discriminations that are more sensitive to noise than is the detection of pure tones. A program that tests the ability of human ears to discriminate between transients having identical energy spectra (but differing shapes in time) has been adapted for use with the PDP-8. This program runs three subjects simultaneously and performs preliminary analyses of the data. The PDP-8 has also been programmed to test auditory discrimination in the chinchilla. In this program, sounds are presented at regular intervals (e.g., once every 15 seconds). Whenever there is a change in a parameter of the sound, the subject is required to respond. Although this program will eventually be used to study noise damage in the chinchilla, the initial experiments have been directed to answer some basic questions about the nature of this paradigm.

Another problem common to noisy environments is the effect of noise on other sense modalities. Instrumentation is being constructed to study directional hearing in humans exposed to noise environments and audio-kinetic nystagmus.

Publications and/or Presentations:

Jacobson, E. J., M. P. Downs, and J. L. Fletcher. Clinical findings in high frequency thresholds during ototoxic drug usage. J. Aud. Res. 9: 379-385, 1969.

B71R 03 126 (cont)

Detail Sheet #4

Luz, G. A. Current studies of hearing at USAMRL. Presented at AMEDD Annual Conference in Psychology, Fitzsimons General Hospital, Denver, Colo., Dec 197[illegible]

Luz, G. A., J. L. Fletcher, [illegible]. [illegible] Frawel, and J. D. Mosko. The relationship between temporary threshold shift and permanent threshold shift in rhesus monkeys exposed to impulse noise. USAMRL Report No. 922, Apr 1971.

Luz, G. A. and [illegible]. Hodge. Recovery from impulse-noise induced TTS in monkeys and men: A descriptive model. J. Acoust. Soc. Amer. 49: 1770-1777, 1971.

Luz, G. A. and J. D. Mosko. The susceptibility of the chinchilla ear to damage from impulse noise. USAMRL Report No. 921, Mar 1971; presented (by Luz) at the Spring Meeting of the Acoustical Society of America, Washington, D. C., Apr 1971

Mosko, J. D. A review of the adverse biomedical effects of sound in the military environment. Presented to Federation of the American Society for Exper. Biology Ad Hoc Group Meeting, Bethesda, Md., Jun 1971.

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B71R 03 126 (cont)

Detail Sheet #5

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Selected Bibliography:

Beagley, H. A. Acoustic trauma in the guinea pig. I. Electrophysiology and histology. Acta Otolaryng. 60: 437-451, 1965.

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA OA 6 | 71 07 01

71 01 22 | D. CHANGE | | U | NA | NL

61102A | 3A061102B71R | 03 | 127

CODE 141

(U) Military Performance: Psychophysics of Visual Perception (18)

013400 Psychology (individual and group behavior)

50 08 | CONT | DA | C. In-house

NA

71	1.4	69
72	1.4	75

Hq, US Army Medical Research Laboratory
Fort Knox, KY 40121

Conte, Nicholas F., COL
502-6241759

FOREIGN INTELLIGENCE CONSIDERED

Experimental Psychology Division
US Army Medical Research Laboratory
Fort Knox, KY 40121

Behar, I.
502-6242025

Dyer, F. N.
Harker, G. S.

DA

(U) Visual Skill; (U) Criteria; (U) Soldiers; (U) Night Vision; (U) Target Detection

23. (U) Continuous military operations require that targets be detected and identified under illumination conditions which severely tax the visual capability. Individual differences in visual skill are studied to enhance unaided vision and to optimize the utilization of optical devices. The monkey is used as an experimental model of man for assessing potentially hazardous conditions. Perceptual processing is studied as the ultimate determiner of effective visual functioning. Such knowledge will provide for selection criteria to identify soldiers with superior night vision.

24. (U) Experimental set-ups are being developed for the study of static and dynamic visual resolution for a wide variety of conditions including a broad range of luminances, target contrasts, spectral composition of target and/or surround, and modulation depth and frequency. Results will be expressed in terms of contrast transfer functions to facilitate the determination of individual differences and to develop selection criteria for superior visual skills. Parallel experiments will be conducted using infrahuman primates as subjects.

25. (U) 71 01 01 - 71 06 30 Optical and electronic systems are continuing to be developed for the evaluation of wavelength effects in visual latency and for the determination of visual resolution for dynamic targets at photopic and scotopic levels, for foveal and peripheral sites, and at varying contrast levels. Data collection is in progress on studies of central variables in visual information processing, including computer generated stimuli. The time between the presentation of the response stimulus and interfering stimuli is a potent variable in Stroop-like paradigms. Dyer, F. N. Latencies for matching of word-color pairs with "irrelevant" words or colors. USAMRL Rep. No. 920, Feb 71; Dyer, F. N. A comparison of chromatic and achromatic versions of the Stroop color-word test. Psychon. Sci. 22(4): 235, 1971.

DD FORM 1498

B71R 03 127 (cont)

Detail Sheet #1

Progress:

Largely through the Stroop paradigm, i.e., combination of word and color stimuli with resultant difficulty for color naming, the central processing of visual stimuli was studied. Bilingual performance with interfering words in one language and naming in another indicated that the site of this interference is at a cognitive or perceptual level rather than an overt response level. Manipulation of the relative processing rates of color and word information indicated that precise arrival of the processed word and color stimuli is necessary for high color naming interference. Even by manipulating these timing relationships, however, no appreciable interference could be generated in an analog of the Stroop paradigm where movement direction and direction names were combined. This implies that basic differences exist between the central processing of color and movement. This appears to be the first demonstration of central processing differences in contrast to well-known peripheral processing for different visual dimensions.

Since the human eye has considerable axial chromatic aberration, it is necessary when studying the sensitivity or resolution of small chromatic stimuli to correct this aberration with the use of an "achromatizing" lens. This lens, when moved laterally in front of the eye while viewing an intricate multicolored pattern, produces an interesting visual effect which has been termed the "dancing arabesque." This consists of a relative change in the spatial position of areas of different color. An explanation of this effect is based on the measured refractive power of the lens as a function of wavelength; below 500 nm the lens is progressively negative while above 500 nm it is progressively positive. Secondary visual effects are an illusion of depth, and the production of a border in the absence of one, or the exaggeration and minimization of borders when present.

Instrumentation, both optical and electronic, has been completed for the study of wavelength effects in visual latency. Whereas prior studies addressed to this question have confounded a luminance change with the onset of the chromatic stimulus, and since there is good electrophysiological evidence that luminance information is carried by separate fiber systems and has precedence at the cortex, the present research system was designed to effect a change from a maximally desaturated stimulus to one of maximum saturation with no change in total luminance.

A pilot study run with a tachistoscope utilizing a same and difference task demonstrated the possibility of differentiating colossal

B71R 03 127 (cont)

Detail Sheet #2

transfer between the two hemispheres of the brain. This work was modeled after existing studies in the literature to look at the possibility of using this technique for [illegible] brain function with respect to linguistic, cognitive, and perceptual functions. The technique is confounded by the necessity to [illegible] control in order to attribute the findings to the [illegible] characteristics.

Publications and/or Presentations:

Schaer, J. The dancing araboscope: an unusual visual effect. USAMRL Report No. 913, Nov 1970 (DDC AD No. 718027).

Dyer, F. N. Word reading, color naming and Stroop interference as a function of background luminance. USAMRL Report No. 889, Aug 1970 (DDC AD No. 716351).

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Bedford, R. E. and G. Wyszecki. Axial chromatic aberration of the human eye. J. Opt. Soc. Amer. 47: 564-565, 1957.

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B71P 03 127 (cont)

Detail Sheet #3

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

			A 03 6071	71 07 01			
71 01 22	D. CONT		6.1	PE			
	61102A	3A061102B74	03	124			

(U) Military Performance Physical Decrement and Enhancement (18)

013400 Psychology (individual and group behavior)

68 07	CONT	6A	C. In-house

	PREVIOUS		
FISCAL YEAR	71	2.1	88
	PROJECTED		
	72	2.1	90

Hq, US Army Medical Research Laboratory
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FOREIGN INTELLIGENCE CONSIDERED

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Caldwell, L. S.
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Lloyd, [illegible] J., CPT
Shiflett, [illegible] C., CPT 6A

(U) Military Operations; (U) Effectiveness; (U) Work; (U) Personality; (U) Decrement; (U) Differences; (U) Endurance; (U) Fatigue; (U) Volunteer

23. (U) Planning for continuous and sustained military operations requires knowledge of the performance capabilities of man and of the observed differences in his response to work stress. Studies are of performance changes resulting from strenuous physical work with repeated work-rest cycles and inadequate opportunity for recovery from fatigue. Individual patterns and degrees of decrement are examined in their relationship to personality variables to better understand the basis for individual differences in response to physically demanding work.
24. (U) Successive strength decrement functions for maximal work loading with varied rest intervals are being studied to derive a general formula to predict output levels for various combinations of work and rest. Also, investigations are aimed at isolating factors which influence the courses of fatigue and recovery. Research on dynamic work (treadmill walking) is concerned with the effects on performance of such social variables as competition, cooperation, co-action, and supervision. Individual differences in work output are related to personality structure.
25. (U) 71 01 01 - 71 06 30 A series of strength and endurance tests were made on a group of ten subjects at 4 hour intervals during a 6 day period including one 36-hour period of continuous work. Between the strength and endurance tests the subjects worked on a battery of performance tests involving light physical activities. No appreciable decline in physical output was obtained during the period of continuous performance but there was some evidence that the subjects tended to work at less than a maximal level in the initial work periods in preparation for the period of high demand. A second treadmill has been installed and calibration and preliminary testing is underway. Shiflett, S.C. The effect of two variables on treadmill walking speed. USAMRL Rep. No. 917, Jan71; Caldwell, L.S. Review of scaling of pain and effort in strenuous physical performance. Presented in a colloquium series for USARIEM, Natick, MA, May71.

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

B71R 03 128 (cont.)

Detail Sheet #1

Progress:

Studies of muscular output in serial isometric contractions have shown that with a wide variety of work-rest ratios the shape of the fatigue function tended to remain constant. The effect of shortening the work period or lengthening the rest period was simply to increase the mean level of output. Also, successive fatigue functions tended to be quite similar and the primary effect of repeating the performance with inadequate rest periods was to reduce the mean output. For all conditions of work and rest the adjustment to the work schedule occurred early in the series of trials with the principal decrement evident by the second trial. The results of these studies suggest that with a short sample of performance under a given condition of work and rest times one can predict the decrement which would be produced by lengthy performance at that specific work-rest ratio since the rate of reduction in output tends to remain constant after one or two sessions.

Several investigators have reported that strong subjects incur more fatigue than do weaker ones performing under the same conditions. Recent studies in this laboratory have shown that there is an appreciable correlation between the strength of an individual and the absolute reduction in output produced by a period of maximal muscular output but that the relative (percentage-of-maximum) loss is unrelated to strength. Thus, we have not found, as some contend, that strong muscles are less efficient than weak ones. Also, in a study of the fatigue functions of strong and weak muscle groups in the same subjects the relative decrements were found to be quite similar. It has been repeatedly observed that the relative decrement produced by a sustained contraction is principally determined by the relative starting point. That is, those subjects who begin near their previously determined maximum output levels have a greater absolute and relative decrement than those who start at lower levels, and the relative starting points are unrelated to strength.

In a recent study muscular strength and endurance were measured at 4-hour intervals during two 12-hour working days followed by a 36-hour period of continuous activity and then two final 12-hour working days. Except when being tested for strength and endurance, the subjects were engaged in primarily sedentary tasks. There was no appreciable reduction in output during the sustained performance phase of the study but this was apparently caused by a reduction in output level in anticipation of the period of maximum stress. The results of this study suggest that even with instructions to work as hard as possible at all times

there is a general tendency to maintain a performance reserve in anticipation of future requirements. If this is true, the decrement functions for lengthy work session should not show the initial rapid reduction in output typical of brief work sessions, and the starting points for long sessions should be lower than for brief ones. This interpretation is not supported by the work-rest ratio data, but there was a limited range of trial durations employed in these studies. Data are now being collected to answer the question of whether trial duration influences the form of the decrement function. In this study durations ranging from 30 to 120 seconds are being employed.

Studies of the influence of social factors on physical performance have shown that prior performance produces strong context effects which may obscure the subtle influences of social variables on performance. In one study audience effects, treadmill speed, and the effects of previous experience on treadmill performance were examined. Audience effects were not significant thus suggesting that this effect is more subtle than presumed by some investigators. The significant sequence effect indicates that one must use repeated measurements designs with caution when manipulating social variables. In the same study it was found that variables may operate in an interactive manner either simultaneously or sequentially and that few, if any, variables are effective under all conditions.

Publications and/or Presentations:

Shiflett, S. C. Physical performance assessment: physical decrement and enhancement. Presented at AMEND Annual Conference in Psychology, Denver, Colo., Dec 1970.

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Humphreys, P. W. and A. R. [illegible] the blood flow through active and inactive muscles of the forearm during sustained hand-grip contractions. J. Physiol. 166: 120-135, 1963.

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McGlynn, G. H. The relationship between maximum strength and endurance of individuals with different levels of strength. Res. Quart. 40: 529-535, 1969

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Project No. 3A062110A821	Combat Surgery
Task No. 00	Combat Surgery
Work Unit No. 155	Military Blood Banking: Preservation Methods and Logistics
Work Unit No. 156	Immunologic Effects of Biologics on Donor Blood; Antibody Characterization in Human Tissue Transplants
Work Unit No. 157	Study of Logistic Problems of Stored Blood and Components in the Military
Work Unit No. 158	Military Blood Banking: Automated Methodology
Work Unit No. 161	Military Blood Banking: Biochemical Alterations of Human Red Blood Cells in Cold Storage
Work Unit No. 162	Military Blood Banking: Effect of Protective Additives on Essential Components of Stored Red Blood Cells
Work Unit No. 164	Military Blood Banking: Evaluation of Changes in Blood During Storage
Work Unit No. 170	Biochemistry of Hormones, Proteins, and Nucleic Acids in Military Stressful Conditions
Work Unit No. 171	Military Blood Banking: Biochemical Basis of Human RBC Survival
Work Unit No. 172	Military Blood Transfusion Reactions
Work Unit No. 174	Military Blood Banking: The Mechanism of Erythrocyte Catabolism During Storage
Work Unit No. 175	Military Blood Banking. Evaluation of Resuscitation by Transfusion of Blood and Other Substances
Work Unit No. 176	Evaluation of Blood Banking Methods and Transfusion Practices
Work Unit No. 177	Blood Antibodies and Their Identification and Selection of Human Histocompatibility Antigenic Systems

Investigators:

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WU No. 156	Frank R. Camp, Jr., LTC, MSC Clarence E. Bell, Jr., MAJ, MC
WU No. 157	Charles E. Shields, LTC, MC Frank R. Camp, Jr., LTC, MSC Clarence E. Bell, Jr., MAJ, MC Dailey W. McPeak, B.S.
WU No. 158	Frank R. Camp, Jr., LTC, MSC Clarence E. Bell, Jr., MAJ, MC
WU No. 161	Frank DeVenuto, Ph.D. Sarah M. Wilson, B.A. Mildred C. Edinger, B.S.
WU No. 162	Walter F. Kocholaty, Ph.D. John L. Gray, B.S. M. Edith Ledford, A.B. Thomas A. Billings, B.S.
WU No. 164	R. Ben Dawson, Jr., MAJ, MC Harry Lopas, LTC, MC Norman I. Birndorf, MAJ, MC Charles E. Shields, LTC, MC
WU No. 170	Frank DeVenuto, Ph.D.
WU No. 171	Walter F. Kocholaty, Ph.D. John L. Gray, B.S. M. Edith Ledford, A.B. Thomas A. Billings, B.S.
WU No. 172	Frank R. Camp, Jr., LTC, MSC Charles E. Shields, LTC, MC
WU No. 174	Gerald L. Moore, Ph.D. John L. Gray, B.S.

WU No. 175	Harry Lopas, LTC, MC Norman I. Birndorf, MAJ, MC R. Ben Dawson, Jr., MAJ, MC Charles E. Shields, LTC, MC
WU No. 176	Charles E. Shields, LTC, MC Frank R. Camp, Jr., LTC, MSC
WU No. 177	Frank R. Camp, Jr., LTC, MSC Clarence E. Bell, Jr., MAJ, MC

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6095	71 07 01	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8. DISP'N INSTR'N	8b. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	155
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Military Blood Banking: Preservation Methods and Logistics (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
65 11	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	.4	99
FISCAL YEAR CURRENT 72	.4	103

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Blood Transfusion Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)

NAME: Camp, F. R., Jr., LTC

TELEPHONE: 502-6241251

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Birndorf, N. I., MAJ

NAME: Bell, C. E., Jr., MAJ DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede each with Security Classification Code)

(U) Blood; (U) Military; (U) Additives; (U) Storage; (U) Preservation; (U) Components; (U) Logistics; (U) Donor

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

23. (U) To determine the best additive or combination of additives that will extend the shelf life of blood beyond the present period of 21 days and, in addition, will support adequate oxygen transport. The effects of storage are included to determine the optimum procedures for handling and transfusing whole blood and blood components.

24. (U) Programs will, initially, be concerned with in vitro studies to evaluate the efficiency of various additives to support oxygen transport. Both acid-citrate-dextrose (ACD) and citrate-phosphate-dextrose (CPD) anticoagulants will be used. Filtration studies will include both whole blood, with and without additives and blood components.

25. (U) 71 01 01 - 71 06 30 Fresh blood collected into various anticoagulants is being filtered through glass beads in 4 and 6 mm plastic tubing in order to reduce the white blood cell count so that red cells only may be collected from the donor, thus eliminating incompatible antigens of the HLA and Four antigens that are carried on the white cells. The effects of certain salts and glutathione on hemoglobin function have been restudied and the results prepared for publication. This paper, which was presented in part in abstract form in Blood, 34: 29, 1969, is being submitted to Vox Sanguinis for publication.

*Available in contractor's own defense's proposal

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

A821 00 155 (cont)

Detail Sheet #1

Progress:

The effect of storage on the oxygen transport system of the red cell has been under study (also see Work Unit No. 164, A821).

The ability of adenine to maintain good red cell posttransfusion survival after 35-42 days of storage has not been accompanied by improved oxygen transport capability. In contrast, inosine is associated with improved oxygen transport function. Combinations of these additives are under evaluation.

Fresh blood collected into various anticoagulants was filtered through 4 and 6 mm plastic tubing containing glass beads, with a 90% reduction in platelet count. Reductions in white blood cell counts have also been observed but this finding is inconsistent and requires confirmation. Work in this area continues.

The effects of various salts on the function of human hemoglobin were studied and first reported in abstract form in Clinical Research, 18: 402, 1970. The tentative conclusion was that the salt effects might be explained by either the chloride ion or the pH in the red cell.

Blood CO levels were significantly lowered prior to donation by exercise or oxygen breathing (hyperventilation).

Publications and/or Presentations:

Craycroft, Mary J., F. B. Camp, Jr., F. P. Ellis, N. F. Conte, Margaret E. McPeak, and Ima C. Shipley. The forensic testing laboratory, 1971--problems, progress and people. USAMRL Report No. 937, Jun 1971.

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A821 00 155 (cont)

Detail Sheet #2

Shields, C. E. Studies on stored whole blood. IV. Effects of temperature and mechanical agitation on blood with and without plasma. Transfusion, 10(4): 155, 1970; USAMRL Report No 882, Jul 1970 (DDC AD No. 714188).

Shields, C. E., M. Lonas, and N. I. Birndorf. Investigation of nephrotoxic effects of adenine and its metabolic product, 2,8-dioxyadenine, on primates (*Macaca fas*). J. Clin. Pharmacol. 10(5): 316, Sep-Oct 1970.

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Selected Bibliography:

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Bartlett, G. R. and H. N. Barnet. Changes in the phosphate compounds of the human red blood cell during blood bank storage. J. Clin. Invest. 39: 56, 1960.

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A821 00 155 (cont)

Detail Sheet #3

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Horejsi, J. and A. Komarkova. The effect of SH-groups on the affinity of haemoglobin to oxygen. Clin. Chim. Acta, 3: 131, 1957.

Horejsi, J. and A. Komarkova. The influence of some factors of the red blood cells on the oxygen-binding capacity of haemoglobin. Clin. Chim. Acta, 5: 383, 1960.

Luque, J., D. Diederich, and S. Grisolia. Binding of 2,3-diphosphoglycerate to oxyhemoglobin. Biochem. Biophys. Res. Commun. 36: 1019, 1969.

Rossi-Fanelli, A., E. Antonini, and A. Caputo. Studies on the relations between molecular and functional properties of hemoglobin. II. The effect of salts on the oxygen equilibrium of human hemoglobin. J. Biol. Chem. 236: 397, 1961.

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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6096	71 07 01	DD-DR&E(AR)636

3. DATE PRE. SUMM'Y	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8. DISP'N INSTR'N	9. SPECIFIC DATA-CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	156
b. CONTRIB'G	72XX777	CDOG T412A(2)		

11. TITLE (Precede with Security Classification Code)
(U) Immunologic Effects of Biologics on Donor Blood; Antibody Characterization in Human Tissue Transplants (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
003800 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
65 04	CONT	DA	C. In-House

17. CONTRACT/GRANT
a. DATE/EFFECTIVE — EXPIRATION:
b. NUMBER: NA
c. TYPE — d. AMOUNT:
e. END OF AGRMT — f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
PRECEDING FISCAL YEAR 71	.5	50
CURRENT FISCAL YEAR 72	.5	110

19. RESPONSIBLE DOD ORGANIZATION
NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION
NAME: Blood Transfusion Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Provide Name if U.S. Academic Institution)
NAME: Camp, F. R., Jr., LTC
TELEPHONE: 502-6241251
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Bell, C. E., Jr., MAJ
NAME:

21. GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede each with Security Classification Code)
(U) Therapy; (U) Histocompatibility; (U) Transplantation
(U) Donor; (U) Blood; (U) Military;

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

23. (U) To more accurately identify the group O (universal) donor whose blood can be transfused safely during military operations or other emergency situations; to establish a histocompatibility testing capability which can potentially be used for blood component therapy or other tissue transplantation.

24. (U) Group O human blood containing anti-A and anti-B hemolysins will be fractionated into IgM and IgG immunoglobulin fractions; the hemolytic activity of the native serum and of these fractions will be accurately measured in vitro, compared, and correlated with routine serological tests available to a blood processing center. Identical studies will be performed with subhuman primate (Macaca irus) blood containing potent hemolysins with the addition of in vivo assay in other Macaca irus monkeys. The technique of lymphocyte typing has been set up; a panel of lymphocyte typing antisera will be gradually accumulated from commercial sources (limited) and from screening postpartum women at US Ireland Army Hospital, Fort Knox (limited). The feasibility of producing such sera in animals will be investigated.

25. (U) 71 01 01 - 71 06 30 In the area of hemolytic transfusion reactions in monkeys (Macaca irus), we have prepared and assayed several monkey IgG fractions containing hemolytic antibodies. Infusing these IgG fractions into monkeys we have shown that a direct correlation exists between the hemolysin content of the IgG fraction infused and the amount of hemolysis and severity of disseminated intravascular coagulation (DIC) produced. Preliminary evidence has been obtained that vigorous preheparinization can reduce the associated DIC; however, the net benefit to the recipient monkey is unknown. The kallikrein (and empirically the kinin) system appears to be involved. With reference to lymphocyte typing, considerable evidence has been obtained that a rabbit anti-human lymphocyte serum contains antibodies to a human species antigen and that the human HLA antigens are combined in, or located close to, the human species antigen.

DD FORM 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

A821 00 156 (cont)

Detail Sheet #1

Progress:

Studies with saliva agglutinins were completed, indicating that the salivary anti-A and anti-B immunoglobulin system is more or less distinct from that responsible for serum anti-A and anti-B. With respect to hemolytic transfusion reactions (HTR) in monkeys (*Macaca irus*), technics were developed in preparing and assaying monkey IgM and IgG fractions from immune plasmas containing hemolytic antibodies. Virtually all hemolytic activity appears to reside in the IgG fraction, its infusion into monkeys produces HTR's with associated disseminated intravascular coagulation (DIC), renal damage, and death--the severity of these reactions being directly proportional to the hemolytic content of the IgG. Preliminary evidence has been obtained that vigorous preheparinization can block the associated DIC; however, the net benefit to the recipient monkey is unknown. The kallikrein (and empirically the kinin) system appears to be involved. In the area of lymphocyte typing several postpartum sera have been screened for valuable lymphocyte isoantibodies. Considerable evidence has been obtained that a rabbit anti-human lymphocyte serum contains antibodies to a human species antigen and that the human HL-A antigens are contained in, or located close to, the human species antigen.

Publications and/or Presentations:

Bell, C. E., Jr. and H. P. Fortwendler. The salivary anti-A and anti-B isoantibody system in group O males. USAMRL Report No. 927, Apr 1971.

Camp, F. P., Jr., H. S. Kaplan, F. R. Ellis, C. M. Zmijewski, and N. F. Conte. Tissue transplantation--the universal donor and blood group antibodies. USAMRL Report No. 860, Jul 1970 (DDC AD No. 715696); J. Forensic Sci. 15: 500, 1970.

Selected Bibliography:

Jakobowicz, Rachel, Mira Ehrlich, and I. J. Grayson. Crossreacting antibody and saliva agglutinins. Vox Sang. 12: 340-353, 1967.

Jakobowicz, Rachel, J. J. Grayson, and P. T. Simmons. Observations on saliva agglutinins. Med. J. Australia, 1: 301-431, 1966.

Jandl, James H. Mechanisms of antibody-induced red cell destruction. Haematologia, 2: 35-[illegible] 1965.

Detail Sheet

Dandl, [illegible] Richardson Jones, and William B. Castle. The destruction of red cells by antibodies in man. I. Observations on the sequestration and lysis of red cells altered by immune mechanisms [illegible] 36: 1423-1459, 1957

[illegible], and N Veall. Removal of incompatible red cells, the spleen. Brit J Haemat 3: 125-133, 195[illegible]

[illegible] and F Falkowski. The specificity of the antibody in paroxysmal hemoglobinuria (P.C.H.). Transfusion, 3: 27[illegible]239, 1963

Morrison, P. L. Blood-group antibodies and red-cell destruction. Brit Med [illegible] 2:[illegible] 1385-1388, 1953

Morrison, P. L. Blood-group antibodies and red-cell destruction. Brit Med [illegible] 2:5161) 1123-1129, 1953

Sears, David G., Robert T. Mead, and Scott N. Swisher. Differences in the mechanism of [illegible] immune hemolysis related to antibody specificity. J Clin Invest 43(6): 975-986, 1964.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. Agency Accession: DA OA 6097
2. Date of Summary: 70 09 01
Report Control Symbol: DD DR&E AR 636

3. Date Prev Sum'ry: 70 07 01
4. Kind of Summary: H. TERMINATION
5. Summary Scty: U
6. Work Security: U
7. Regrading: NA
8a. Dissem Instr'n: NL
8b. Specific Data Contractor Access: [X] Yes [ ] No
9. Level of Sum: A. Work Unit

10. No./Codes	Program Element	Project Number	Task Area Number	Work Unit Number
a. Primary	62110A	3A062110A821	00	157
b. Contributing	//////	CDOG 1412A(2)		

11. Title: (U) Study of Logistic Problems of Stored Blood and Components in the Military (18)

12. Scientific and Technological Areas: 003500 Clinical Medicine

13. Start Date: 66 04
14. Estimated Completion Date: CONT
15. Funding Agency: DA
16. Performance Method: C. In-House

17. Contract/Grant
a. Dates/Effective: Expiration:
b. Number: NA
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	70	3	8
Current	71	.3	9

19. Responsible DOD Organization
Name: Hq, US Army Medical Research Laboratory
Address: Fort Knox, KY 40121
Responsible Individual
Name: Conte, Nicnolas F., COL
Telephone: 502-6241759

20. Performing Organization
Name: Blood Transfusion Division
Address: US Army Medical Research Laboratory
Fort Knox, KY 40121
Principal Investigator
Name: Shields, C. E., LTC
Telephone: 502-6246750
Social Security Account Number:
Associate Investigators
Name: Camp, F. R., Jr., LTC
Name: [illegible] DA

21. General Use: FOREIGN INTELLIGENCE CONSIDERED

22. Keywords: (U) Blood; (U) Blood Banks; (U) Blood Donors; (U) Equipment and Supplies; (U) Transportation; (U) Human Volunteer

23. (U) To develop--and recommend for implementation--improvements in the logistics for handling and supply of blood and blood products to military field units and CONUS military hospitals.

24. (U) Effects of transportation and temperature on blood are being evaluated in conjunction with the overseas blood program. Studies are being prepared to develop an associated automatic data processing system to use along with the automated mass blood grouping system presently being integrated into the Army Blood Program for the purposes of closer coordination of overseas demand and national supply.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated and combined with existing work units which have related areas of research.

*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.

A821 00 157 (cont)

Detail Sheet #1

Progress:

Technics and materials designed to provide greater mechanical and temperature protection for whole blood and blood products have been studied. The use of air cap for packaging fresh frozen plasma and cryoprecipitate has proven to be an efficient means of preventing breakage in CONUS and overseas shipment to S.E. Asia (see USAMRL Report No. 918, Feb 1971 - Cargo coding developments in military blood bank logistics, by D. W. McPeak, F. R. Camp, Jr., G. Seeger, and N. F. Conte; paper has been accepted for publication in Military Medicine and is in press). The use of a practical, reliable, and inexpensive temperature monitor has been recommended for development.

Publications and/or Presentations:

None.

Selected Bibliography:

Orlina, A. R., L. N. Button, and B. J. Taylor. Effect of transportation on the posttransfusion survival of blood stored in CPD. Transfusion, 8: 165-171, 1968.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

71 01 22

(U) Military Blood Banking

003500 Medical Medicine

66 04

NA

25

Hq, US Army Medical Research Laboratory
Fort Knox, KY 40121

Conte, Nicholas
502-5241759

FOREIGN INTELLIGENCE CONSIDERATION

(U) Sickle Cell; (U) Hepatitis Associated Antigen

23. (U) To find the best method and equipment for blood procedures in the military and to determine effective methods for sickle cell trait and hepatitis in prospective blood donors. Evaluation of a practical frozen blood program for [illegible] continually required to work toward blood bank [illegible]

24. (U) Various programs will involve research and development in screening for ABO blood group and Rh type of military recruits for routine processing of whole blood prior to [illegible] trait on an AutoAnalyzer designed to provide count for [illegible], as well as Vietnam returnees [illegible]

25. (U) 71 01 21 [illegible] sickle cell hemoglobin employing the Addy [illegible] with a reducing agent--sodium dithionite [illegible] agent--saponin. The cost of the reagents [illegible] testing recruit soldiers arriving at [illegible] will be published as a [illegible] in developing suitable methods [illegible] antigen (HAA).

DD FORM 1498

A821 OC 158 (cont)

Detail Sheet #1

Progress:

Four major problem areas have been studied to improve military blood bank methodology These areas include: sickle cell screening, Australian antigen-HAA testing, an automated military blood grouping and typing system, and a frozen blood bank for military exigencies.

An automated screening test for the detection of hemoglobin S has been developed and field tested on 8,000 military personnel at Fort Kno The test costs .03 per sample and 100% reliability has been demonstrated by electrophoresis.

Collaborative studies concerning detection methodology for Australian antigen are continuing with the National Research Council and the laboratories of Dr. Baruch S. Blumberg. Technics under study include agar gel diffusion, immuno-osmo-electrophoresis and complement-fixation Search continues for better antigenic and antibody sources. A study just concluded reveals a significant increase of Au(1) and anti-Au(1) in Vietnam returnees.

Study during the past year has resulted in resolution of the various requirements necessary to achieve a fully automated military blood grouping and typing system that would interface with the currently available AutoAnalyzer blood grouping system. This system would provide sample identification, automatic interpretation, and collation of results. Field testing will be accomplished in early 1972 at USAMRL, Fort Knox.

Progress on establishing a frozen blood bank for military exigencies, research, and related areas of development include the decision, resulting from several years of system comparisons, that the Linde liquid nitrogen-low glycerol system is most feasible and economical. One 24 unit refrigerator is planned for installation in late 1971.

Publications and/or Presentations:

Allen, T. E , F. P. Camp, Jr., and C. E. Shields. Newly designed equipment for the blood banks. Exhibit at the 23rd Annual Meeting, American Association of Blood Banks, San Francisco, Calif., Oct 1970.

Camp, F P , Jr and N F Conte. Possible impact of Au/SH antigen detection on blood banking and transfusion services. Vox Sang. 19: 178, 1970

A821 00 158 (cont)

Detail Sheet #2

Camp, F. R., Jr., H. P. Fortwengler, and B. F. Meney, Jr. Automated quantitation of A and B blood group substances. Presented (by Fortwengler) at the meeting of Technicon International Congress, New York, N. Y., Nov 1970

Camp, F. R., Jr., [illegible] Kaplan, [illegible] E. Shields, N. F. Conte, Mary J. Craycroft, and B. F. Meney, Jr. [illegible] saliva agglutinins and automated methods for universal donor screening. USAMRL Report No. 891, Aug 1970 (DDC AD No. 7[illegible])

Craycroft, Mary J., F. R. Camp, Jr., Margaret E. McPeak, and Ima G. Shirley. Forensic testing [illegible] a reference and blood grouping laboratory. Presented (by Craycroft) at the 23rd Annual Meeting, American Association of Blood Banks, San Francisco, Calif., Oct 1970.

Henry, R. L., R. M. Nalbandian, B. M. Nichols, P. L. Wolf, and F. R. Camp, Jr. Modified sickledex tube test: A specific test for S hemoglobin. USAMRL Report No. 897, Sep 1970 (DDC AD No. 715743)

Henry, R. L., R. M. Nalbandian, B. M. Nichols, P. L. Wolf, and F. R. Camp, Jr. An automated screening method for the specific detection of homozygous and heterozygous S hemoglobin. USAMRL Report No. 898, Sep 1970 (DDC AD No. 715744)

Nalbandian, R. M., R. L. Henry, P. L. Kessler, P. L. Wolf, and F. R. Camp, Jr. [illegible] gelation test. New Eng. J. Med. 284: 502, 1971

Nalbandian, R. M., R. L. Henry, B. M. Nichols, F. R. Camp, Jr., and P. L. Wolf. The Mo[illegible] test. Part [illegible]. Evidence for the modified Murayama hypothesis for the sickling mechanism of sickling. USAMRL Report No. 893, Sep 1970 (DDC AD No. 715245)

Nalbandian, R. M., R. L. Henry, B. M. Nichols, F. R. Camp, Jr., and P. L. Wolf. The Mo[illegible] test. Part 2. Principles, technique, interpretation, [illegible] data. USAMRL Report No. 894, Sep 1970 (DDC AD No. 715249)

Nalbandian, R. M., R. L. Henry, M. [illegible]eenhart, B. M. Nichols, and F. R. Camp, Jr. [illegible] reversible inhibition by urea in invert sugar: optical and electrophoretic [illegible] evidence. USAMRL Report No. 895, Sep 1970 (DDC AD No. 715[illegible])

/E

A821 00 158 (cont)

Detail Sheet #3

Nalbandian, R. M., R. L. Henry, G. Shultz, F. R. Camp, Jr., and P. L. Wolf. Sickle cell crisis terminated by use of urea in invert sugar in two cases. USAMRL Report No. 896, Sep 1970 (DDC AD No. 721005)

Nalbandian, R. M., R. L. Henry, T. Evans, F. R. Camp, Jr., P. L. Wolf, and N. F. Conte. Embryonic, fetal, and neonatal hemoglobin synthesis: relationship to abortion and thalassemia. USAMRL Report No. 910, Nov 1970 (DDC AD No. 717231).

Nalbandian, R. M., R. L. Henry, F. R. Camp, Jr., and D. L. Kessler. Consumption coagulopathy: practical principles of diagnosis and management. USAMRL Report No. 912, Nov 1970 (DDC AD No. 719700)

Nalbandian, R. M., B. M. Nichols, F. R. Camp, Jr., N. F. Conte, Jeanne M. Lusher, and R. L. Henry. The detection of sickle cell disease in large human populations by an automated technique. USAMRL Report No. 936, Jun 1971

Radcliffe, J. H., C. E. Shields, F. R. Camp, Jr., and N. F. Conte. Comparison of blood collected by vacuum methods and gravity flow. USAMRL Report No. 934, May 1971

Selected Bibliography:

Atchley, W. A., N. V. Bhagavan, and S. P. Masouredis. Influence of ionic strength on the reaction between anti-D and D positive red cells. J. Immun. 93: 701, 1964

Hirszfeld, L. and S. Dubiski. Untersuchungen über die Struktur der inkompleten Anti-körper. Schweiz. Z. Path. Bact. 17: 73, 1954.

Huggins, C. E. Reversible agglomeration used to remove dimethylsulfoxide from large volumes of frozen blood. Science, 139: 504, 1963.

Hughes-Jones, N. C., B. Gardner, and R. Telford. The effect of pH and ionic strength on the reaction between anti-D and erythrocytes. Immunology, 7: 72, 1964

Lalezari, P. A polybrene method for the detection of red cell antibodies. Fed. Proc. 26: 756, 1967

A821 00 158 (cont)

Detail Sheet #4

Lalezari, P. A new red cell method for the simultaneous detection of hemagglutinins and leukoagglutinins. In: Histocompatibility Testing 1967. Copenhagen: Munksgaard, p. 419, 1967.

Lalezari, P. A new method for the detection of red cell antibodies. In: Automation in Analytical Chemistry. Technicon Symposia, pp. 192-196, 1967.

Lalezari, P. and T. H. Spaet. Antiheparin and hemagglutinating activities of polybrene. J. Lab. Clin. Med. 57: 868, 1961.

Litwin, S. D. and F. P. Camp, Jr. Gm typing: Studies on an automated method. Technicon Internat. Congr. 1: 275, 1969.

Litwin, S. D. and F. P. Camp, Jr. Automated detection of Gm factors of human γG globulin. USAMRL Report No. 803, Nov 1968 (DDC AD No. 690271); Vox Sang. 17: 194, 1969.

Galbandian, R. M., R. L. Henry, B. M. Nichols, F. R. Camp, Jr., and P. L. Wolf. Molecular basis for a simple, specific test for S hemoglobin: The Murayama test. Clin. Chem. 16: 945, 1970.

Pollack, W. Some physicochemical aspects of hemagglutination. Ann. N. Y. Acad. Sci. 127: 892, 1965.

Pollack, W., H. J. Hager, P. Reckel, D. A. Toren, and H. P. Singher. A study of the forces involved in the second stage of hemagglutination. Transfusion, 5: 158, 1965.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6107	71 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'RY
71 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	161
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with security classification code): (U) Military Blood Banking: Biochemical Alterations of Human Red Blood Cells in Cold Storage (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 003500 Clinical Medicine; 002300 Biochemistry

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
67 03	CONT	DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER: NA
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	71	2.5	77
CURRENT	72	2.5	53

19. RESPONSIBLE DOD ORGANIZATION
NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION
NAME: Biochemistry Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)
NAME: DeVenuto, F.
TELEPHONE: 502-6242053
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Wilson, S. M.
NAME: Edinger, M. C. DA

21. GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede each with security classification code): (U) Red Blood Cells; (U) Hormones; (U) Donors; (U) Blood Preservation; (U) Military; (U) Treatment

23. TECHNICAL OBJECTIVE. 24. APPROACH. 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with security classification code.)

23. (U) To acquire knowledge concerning the biochemical alterations occurring in human whole blood and red blood cells during cold storage, including a study of the effects of hormones and other additives in preventing or limiting these undesirable changes. The goal is to extend the useful period blood can be stored and used effectively in the treatment of military casualties and other illnesses.

24. (U) Units of blood are obtained from healthy male and female donors and stored under blood banking conditions. At designated intervals during storage, aliquots of blood are withdrawn; red blood cells are prepared and membrane preparations are obtained using available procedures. Aliquots of whole membranes or separated components of the membrane are used for interaction studies with labeled progesterone or related hormones. Other aliquots of stored blood obtained from male and female donors are withdrawn at various times of storage for analysis of biochemical parameters such as ATP, hemoglobin, pH, in vitro spontaneous hemolysis, osmotic fragility, and several different enzymes in order to correlate the preservation of blood with endocrine activity of the donor.

25. (U) 71 01 01 - 71 06 30 Biochemical changes occurring during storage of human blood are being investigated. The influence of blood components (platelets and plasma proteins) as well as other additives such as vitamins, thyroid and other hormones are being studied in assessing their role in extending the shelf life of human blood. Young and old red cells from fresh blood have been separated and differences in biochemical parameters have been assayed. A report on the fractionation, chemical analysis, and electron microscopic observations of red cell membranes is in preparation.

*Available to contractors upon originator's approval

DD, FORM 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.

A821 00 161 (cont)

Detail Sheet #1

Progress:

In the investigation of cells of different age groups in human blood it has been found that young (low density) and old (high density) cells, prepared from fresh blood, demonstrate differences in osmotic fragility, spontaneous hemolysis, activity of enzymes, and levels of ATP. When membrane preparations obtained from young and old cells are subjected to fractionation by disc electrophoresis they present electrophoretic patterns which are qualitatively and quantitatively different for the cells in the two age groups; this suggests the possibility that specific membrane proteins are related to particular structural and functional aspects of the red cells. A correlation has been established between the increase in specific gravity and the decrease in osmotic resistance of human red blood cells under blood banking conditions when storage is extended to 42 days.

In the evaluation of the effect of various additives, units of blood have been stored for 42 days under different conditions: 1) packed red cells with addition of progesterone, testosterone, or androsterone, 2) erythrocytes suspended in buffer with addition of adenine or progesterone plus adenine, 3) whole male blood with addition of progesterone. By the criteria of *in vitro* determinations, progesterone, in physiological concentrations, is effective in protecting the red cells during storage by minimizing the spontaneous lysis, changes in osmotic resistance, and loss of ATP. The greatest effect in this respect was obtained by addition of progesterone plus adenine to erythrocytes suspended in buffer.

The investigation of the biochemical and biophysical parameters involved in the structural integrity of the red cell membrane has shown that some of these parameters, such as blood relative viscosity, seem to be directly correlated to cell deformability; that is, the ability of the red cell to change configuration and survive repeated passages through the microcirculation. From the results obtained it is becoming evident that some of the additives to the blood act as ligands and interact with components of the red cell membrane minimizing the deterioration of the cell permeability during storage of blood under blood banking conditions.

The new procedure, electrophocusing, has been established for the isolation of protein fractions of the cell membrane in quantities necessary for several biochemical analyses.

The influence of blood components (platelets and plasma proteins) on red cells preservation has been studied; the results have shown that

Detail Sheet #2

whereas platelets may have a positive effect, several plasma protein fractions are detrimental to the survival of cells after prolonged storage. The implication of these findings is to be explored.

Publications and/or Presentations:

DeVenuto, F., H. L. Wilson, Sarah M. Wilson, and Dorothy F. Ligon. Biochemical alterations during storage of human blood from male and female donors. Proc. Soc. Exp. Biol. Med. 136: 183, 1971.

DeVenuto, F. and Sarah M. Wilson. Steroid hormones in the preservation of human blood. USAMRL Report No. 909, Nov 1970 (DDC AD No. 715749)

DeVenuto, F. and D. Santella. Bioparameters of human blood cells of two different age groups. USAMRL Report No. 922, Mar 1971 (DDC AD No. 724142)

Selected Bibliography:

Benbassat, J. Effect of packing and resuspension on the osmotic fragility and rate of autohemolysis of incubated red blood cells. Clin. Sci. 37: 99, 1969.

DeVenuto, F. Interaction of progesterone and aldosterone with red blood cells of the rat. Proc. Soc. Exp. Biol. Med. 124: 478, 1967.

DeVenuto, F. Swelling of human red blood cells, preserved with addition of progesterone, as determined by spectrophotometric measurements. Proc. Soc. Exp. Biol. Med. 129: 106, 1968.

Haradin, A. R., R. I. Weed, and C. F. Reed. Changes in physical properties of stored erythrocytes: relation to *in vivo* survival. Blood, 30: 876, 1967.

Marchesi, V. T. and E. Steers. Selective solubilization of a protein component of red cell membrane. Science, 159: 203, 1968.

Marks, P. A., A. B. Johnson, and E. Hirschberg. Effect of age on the enzyme activity in erythrocytes. Proc. Nat. Acad. Sci. (USA), 44: 529, 1958.

A821 00 161 (cont)

Detail Sheet #3

Nakao, M., T. Nakao, S. Yamazoe, and H. Yoshikawa. Adenosine triphosphate and shape of erythrocytes. J. Biochem. 45: 487, 1961.

Prankerd, T. A. J. The aging of red cells. J. Physiol. 143: 325, 1958.

Shields, C. E. Comparison studies of whole blood stored in ACD and CPD and with adenine. Transfusion, 8: 1, 1968.

Wilmer, E. N. Steroids and cell surfaces. Biol. Rev. 36: 368, 1961.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6108	71 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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	162
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Procede with Security Classification Code) (U) Military Blood Banking: Effect of Protective Additives on Essential Components of Stored Red Blood Cells (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
002300 Biochemistry; 003500 Clinical Medicine; 016200 Stress Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
67 03	CONT	DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: NA — 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 71	2.1	82
FISCAL YEAR CURRENT 72	2.1	64

19. RESPONSIBLE DOD ORGANIZATION
NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION
NAME: Biochemistry Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Kocholaty, W. F.
TELEPHONE: 502-6244350
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Gray, J. L.
NAME: Ledford, M. E. DA

21. GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code) (U) Cell Constituents; (U) Hemolysis; (U) Donors; (U) Additives; (U) Blood Preservation; (U) Therapeutic; (U) Military

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

23. (U) To investigate the composition of human red blood cells stored under blood banking conditions. To quantify and characterize the essential components involved in the energetics of the red cell during prolonged storage. To study the influence of potentially protective additives in extending the viability of human red blood cells in storage. Knowledge in this area will permit whole blood to be maintained in a useful therapeutic state for longer periods than is now possible, thus obviating the need for frequent replenishment in military combat areas and hospitals, and providing for greater utility of the available supply.

24. (U) Intact red cells will be investigated with respect to reactive groups and "sensitive" sites possibly involved in the control of membrane permeability. The binding of various dyes will be utilized to provide identification of significant changes in the composition and possibly viability of the red cell. Modification of blood storage conditions, such as pH variation and chemical composition of anticoagulants, will be investigated.

25. (U) 71 01 01 - 71 06 30 Studies on the effect of pH on osmotic fragility of the red cell during storage in the presence of adenine in ACD anticoagulant were completed. Investigations of varying phosphate concentrations in CPD anticoagulant in the presence and absence of adenine on the viability of the red cell were completed and a report is being prepared. An experiment utilizing methylene blue and a wide range of anticoagulant pH has been initiated.

*Available to contractors upon official request

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.

A821 00 162

Detail Sheet #1

Progress:

Investigations designed to prolong the lifespan of the human red cell under blood banking conditions were continued in CPD blood using individual additives such as methylene blue, adenine, and inosine. Studies of 2,3-DPG, ATP, osmotic fragility, and oxygen-carrying capacity levels disclosed that the optimum concentration of inosine resulted in very high levels of 2,3-DPG and of hemoglobin function after 6 weeks of storage when compared to controls. However, ATP levels could not be increased significantly above control values using various concentrations of inosine and adenine in combination. Several possible approaches to improve ATP levels are, at present, in various stages of completion; these include dependency of added methylene blue, the possible mode of action of CPD versus ACD anticoagulant, and concentration of inorganic phosphate in the preservation medium.

Publications and/or Presentations:

Billings, T. A., D. J. Lenzi, and W. F. Kocholaty. Construction of a vessel for cleaning glassware to be used for fluorometric assays. USAMRL Report No. 885, Aug 1970 (DDC AD No. 715693).

Kocholaty, W. F., R. B. Dawson, Jr., Edith B. Ledford, J. L. Gray, T. A. Billings, and T. J. Ellis. Human blood stored in CPD-methylene blue with addition of adenine and inosine: The effect on hemoglobin function, 2,3-DPG and ATP. USAMRL Report No. 884, Jul 1970 (DDC AD No. 714189).

Selected Bibliography:

Brin, M. and R. H. Yonemoto. Stimulation of the glucose oxidative pathway in human erythrocytes by methylene blue. J. Biol. Chem. 230: 307, 1958.

Bunn, H. F., Mary H. May, W. F. Kocholaty, and C. E. Shields. Hemoglobin function of stored blood. USAMRL Report No. 790, 1968 (DDC AD No. 690802); J. Clin. Invest. 48: 311, 1969.

Chanutin, A. The effect of addition of adenine and nucleosides at the beginning of storage on the concentrations of phosphates of human erythrocytes during storage in acid-citrate-dextrose and citrate-phosphate-dextrose. Transfusion, 7: 120, 1967.

Detail Sheet #2

Dawson, R. B., Jr. The hemoglobin function of blood stored at 4°C. USAMRL Report No. 836, 1969 (DDC AD No. 701884); In: Red Cell Metabolism and Function, G. J. Brewer (Ed.), New York: Plenum Press, pp. 305-317, 1970.

Sass, M. D., C. J. Caruso, and D. R. Axelrod. Accumulation of methylene blue by metabolizing erythrocytes. J. Lab. Clin. Med. 69: 447, 1967.

Sass, M. D., C. J. Caruso, and D. R. Axelrod. Evaluation of stored blood by methylene blue reduction. J. Lab. Clin. Med. 73: 744, 1969.

Seeman, P. M. Membrane stabilization by drugs: tranquilizers, steroids, and anesthetics. Int. Rev. Neurobiol. 9: 145, 1966.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6110	71 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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	164
b. CONTRIBUTING				
c. ~~CONTRIBUTING~~	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Military Blood Banking: Evaluation of Changes in Blood During Storage (18)

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
67 04	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

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 71	1.2	92
FISCAL YEAR CURRENT 72	1.2	100

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Blood Transfusion Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)

NAME: Dawson, R. B., Jr., MAJ

TELEPHONE: 502-6243040

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Lopas, H., LTC

NAME: Birndorf, N. I., MAJ DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Blood Transfusions; (U) Additives; (U) Military; (U) Storage; (U) Therapy

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

23. (U) To prolong the storage time of whole blood to be used for transfusion purposes and to assume that the blood will be normally functional.

24. (U) Metabolic additives, including adenine and inosine, will be added at various times and in various concentrations.

25. (U) 71 01 01 - 71 06 30 Work continues on determining the optimal pH of a citrate-dextrose solution for maintaining 2,3-DPG for hemoglobin function and ATP for red cell viability. Previous work had indicated that CPD at pH 5.5 was better than ACD at pH 5.0. More recent studies indicate that pH 6.0 may be even superior. A second extensive study, applying automated analytic technics and computer data analysis in which adenine was added to citrate-dextrose preservative, has confirmed the impression that a pH of 6.0 may be desirable. This work is continuing with similar studies with added inosine and, finally, in a joint effort with the biochemists the optimal phosphate concentration is being determined in similar experiments.

*Available to contractors with originator's approval

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A821 00 164 (cont)

Detail Sheet #1

Progress:

Preliminary studies using automated analysis of ten units, including computer analysis of data, suggest that a pH higher than that of ACD (5.5) is optimal.

Phosphate concentrations studied in the range 0 to 20 mM indicate that 2 mM phosphate was clearly the best for maintaining 2,3-DPG; 5 mM was nearly as good. There was very little difference between 2 and 5 mM phosphate with respect to maintaining ATP. The highest phosphate concentration was least effective.

Blood collected into CPD containing adenine, inosine, and methylene blue maintained normal p_{50} and 2,3-DPG values (measures of hemoglobin function) through 6 weeks of storage at 4 C.

Publications and/or Presentations:

Dawson, R. B., Jr. The function of human hemoglobin: salt effects. USAMRL Report No. 914, Dec 1970 (DDC AD No. 719701); presented at the Annual Meeting of the Blood Research Institute, Boston, Mass., Dec 1970.

Dawson, R. B., Jr. Hemoglobin function in stored blood: VII. Effects of salts and glutathione. USAMRL Report No. 924, Mar 1971.

Dawson, R. B., Jr. Blood preservation solutions: A review. USAMRL Report No. 926, Apr 1971.

Dawson, R. B., Jr. Rapid adaptation to hypoxia. New Eng. J. Med. 283: 265, 1970 (Letter).

Dawson, R. B., Jr. and T. J. Ellis. Hemoglobin function of blood stored at 4 C in ACD and CPD with adenine and inosine. Transfusion, 10(3): 113, 1970.

Dawson, R. B., Jr., Mildred C. Edinger, and T. J. Ellis. Hemoglobin function in stored blood: IV. Red cell ATP and 2,3-DPG in ACD and CPD with adenine and inosine. J. Lab. Clin. Med. 77: 46, 1971.

Dawson, R. B., Jr., M. R. Loken, and D. H. Crater. Hemoglobin function in stored blood: IX. A modified preservative with optimal pH to maintain red cell 2,3-DPG (function) and ATP (viability). USAMRL Report No. 932, May 1971; Clin. Res. 19: 416, 1971 (Abstract).

A821 00 164 (cont)

Detail Sheet #2

Dawson, R. B., Jr. and W. F. Kocholaty. Hemoglobin function: Effects of methylene blue and inosine on p_{50} and 2,3-DPG in CPD-stored blood. Blood, 36: 847, 1970.

Dawson, R. B., Jr. and W. F. Kocholaty. Hemoglobin function in stored blood: VI. The effect of phosphate on red cell ATP and 2,3-DPG. USAMRL Report No. 915, Dec 1970 (DDC AD No. 719702).

Dawson, R. B., Jr. and W. F. Kocholaty. Hemoglobin function in stored blood: VIII. Further effects of phosphate on red cell ATP and 2,3-DPG. USAMRL Report No. 925, Mar 1971.

Dawson, R. B., Jr., W. F. Kocholaty, and J. L. Gray. The hemoglobin function and 2,3-DPG of blood stored at 4°C in ACD and CPD: pH effect. Transfusion, 10: 299, 1970.

Shields, C. E., H. S. Kaplan, and R. B. Dawson, Jr. Biological alterations occurring during red cell preservation. USAMRL Report No. 881, Jul 1970 (DDC AD No. 715702).

Selected Bibliography:

Benesch, R. and R. E. Benesch. The effect of organic phosphates from the human erythrocyte on the allosteric properties of hemoglobin. Biochem. Biophys. Res. Commun. 26: 162, 1967.

Beutler, E., A. Meul, and L. A. Wood. Depletion and regeneration of 2,3-diphosphoglyceric acid in stored red blood cells. Transfusion, 9: 109, 1969.

Chanutin, A. and R. R. Curnish. Effect of organic and inorganic phosphates on the oxygen equilibrium of human erythrocytes. Arch. Biochem. 121: 96, 1967.

Strumia, M. M., P. V. Strumia, and A. J. Eusebi. The preservation of blood for transfusion. VII. Effect of adenine and inosine on the adenosine triphosphate and viability of red cells when added to blood stored from zero to seventy days. J. Lab. Clin. Med. 75: 244, 1970.

Strumia, M. M., P. V. Strumia, and A. J. Eusebi. Effect of multiple additions of adenine and inosine on the function of stored erythrocytes. Proc. Soc. Exp. Biol. Med. 135: 443, 1970.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0A 6070	71 07 01	DD DR&E(AR)636

3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8A. ORD'G HIST'N	8B. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
71 01 22	C. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A82T	00	170
b. CONTRIBUTING				
c. ADDITIONAL	CDOG 1412A(2)			

11. TITLE (Project with Security Classification Code) (U) Biochemistry of Hormones, Proteins, and Nucleic Acids in Military Stressful Conditions (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
302300 Biochemistry

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
63 11	CONT	DA	C. In-House

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

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
FISCAL YEAR — PRECEDING 71	.5	38
FISCAL YEAR — CURRENT 72	.5	32

19. RESPONSIBLE DOD ORGANIZATION
NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION
NAME: Biochemistry Division
US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Provide last name, first name, middle initial)
NAME: DeVenuto, F.
TELEPHONE: 502-6242053
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME
NAME DA

21. GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Provide each with Security Classification Code)
(U) Stress; (U) Hormones; (U) Treatment; (U) Soldier

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

23. (U) To investigate the mechanisms by which proteins are synthesized within the cell and the manner in which body hormones exercise their influence on the process. Knowledge in this area will be invaluable in the treatment of the sick and wounded soldier and will provide a basis for favorably influencing the manner in which damaged tissue is repaired.

24. (U) Preparation and isolation of cell constituents. Separation of the genetic material, which is represented by the nucleic acid DNA, separation of various nuclear proteins such as nucleohistones and isolation of cytoplasmic components such as ribosomes, polysomes, and various enzymes involved in protein biosynthesis. It is possible that nuclear proteins, by interacting with active sites of the DNA, act as repressors. Hormones could prevent this blocking action by a strong interaction with nuclear proteins, therefore acting as derepressor. The effect of hormones on the aggregation and disaggregation of the polyribosome chains will be investigated in an in vitro system using procedures developed in our laboratory.

25. (U) 71 01 01 - 71 06 30 An increased protein synthesis and an increase amount of enzymes are required in wounds, burns, fatigue, and other stressful conditions to which the soldier is exposed in the performance of his duties. The determining factors for the protein synthetic activity of the living cells has been investigated. When ribosomes are dissociated no protein synthesis occurs. When the biosynthesis of a specific protein or enzyme is required by the organism, several ribosomes associate with messenger ribonucleic acid to form polysome chains and protein synthesis takes place. This association is regulated by complex mediators in the cell and our investigations have shown that hormones play an important role in the functional activity of the cell.

* Complete applicable items with an asterisk (*).

DD FORM 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

A821 00 170 (cont)

Detail Sheet #1

Progress:

Data from this laboratory indicate that the action of these hormones is expressed not only in the nucleus of the cell by an interaction with nuclear proteins such as histones, but also in the cytoplasm by an effect on the aggregation of ribosomes in polysome chains. The ribosomes, which represent the factory for protein synthesis in the cell, can be associated in groups of six or more forming polyribosomes which are active in the biosynthesis of proteins. When this activity of the cell is at a steady state the profile shows that the ribosomes are in singles (monosomes), in pairs (duosomes), or in groups of three (trisomes) which are not active in the biosynthesis of proteins or enzymes. Our studies indicate that the association or dissociation of the ribosomes appears to be regulated by the level of adrenocorticosteroid hormones and by the diet which determines the amount of amino acids in the cell. This mechanism is very important in conditions of stress and our efforts are directed to elucidate, at the molecular level, the various factors involved.

Publications and/or Presentations:

DeVenuto, F. RNA - dependent DNA polymerose. Presented at the Medical Faculty Seminar, University of Louisville, Louisville, Ky., Apr 1971.

DeVenuto, F. Challenge to the central dogma of molecular biology. Presented at the Conference Seminar, USAMRL, Fort Knox, Ky., May 1971.

Selected Bibliography:

Crick, F. H. C. The origin of the genetic code. J. Mol. Biol. 38: 367, 1968.

DeVenuto, F. and T. Muldoon. Interactions between corticosteroids and fractions of mitochondria and nuclei from normal rat liver cells. Exper. Cell Res. 50: 338, 1968.

Florini, J. R. and C. B. Brewer. Amino acid incorporation into protein by cell-free preparations from rat skeletal muscle. III. Comparison of activity of muscle and liver ribosomes. Biochemistry, 4: 253, 1965.

White, A., M. Blecher, and L. Jediskin. Mechanism of Action of Steroid Hormones. New York: Pergamon Press, 1961.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1 AGENCY ACCESSION	2 DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0B 6074	71 07 01	DD-DR&E(AR)636

3 PREV. SUMMARY	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 01 22	D. CHANGE	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10 NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	171
b. CONTRIBUTING				
[illegible]	CDOG [illegible]12A(2)			

11 TITLE (Include with Security Classification Code)

(U) Military Blood Banking: Biochemical Basis of Human RBC Survival (18)

12 SCIENTIFIC AND TECHNOLOGICAL AREAS

002300 Biochemistry

13 START DATE	14 ESTIMATED COMPLETION DATE	15 FUNDING AGENCY	16 PERFORMANCE METHOD
68 10	CONT	DA	C. In-House

17 CONTRACT/GRANT

a. DATES EFFECTIVE: EXPIRATION:
b. NUMBER: NA
c. TYPE: d. AMOUNT:
e. NO. OF AWARDS: f. CUM. AMT.

18 RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (in thousands)
FISCAL YEAR PRECEDING 71	1.7	70
FISCAL YEAR CURRENT 72	1.7	66

19 RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20 PERFORMING ORGANIZATION

NAME: Biochemistry Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)
NAME: Kocholaty, W. F.
TELEPHONE: 502-6244350
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Gray, J. L.
NAME: DA

21 GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22 KEYWORDS (Provide Each with Security Classification Code)

(U) Blood Cell; (U) Membrane; (U) Enzymes; (U) Storage

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

23. (U) To devise and evaluate biochemical and physicochemical tests that can be used reliably to determine the metabolic state of stored red blood cells. To identify key metabolic events that are responsible for the aging process of red blood cells in order to develop simple methods for extending the life-expectancy of the red blood cell (whole blood) in storage.

24. (U) Intact red cells will be investigated with respect to reactive groups and "sensitive" sites possibly involved in the control of membrane permeability. The binding of various dyes will be utilized to provide identification of significant changes in the composition and possibly viability of the red cell. The possibility of a membrane lesion occurring during storage of the red cell by spontaneous activation of enzymes within the membrane or the red cell internal structure will be studied.

25. (U) 71 01 01 - 71 06 30 Examination in the ultracentrifuge of the proteolytic enzyme extracted from the red cell stroma indicated a potential dissociation in the presence of Triton X-100. This solubilizing agent was shown to have no deleterious effect on the enzyme activity. More highly purified preparations free of hemoglobin were obtained by ammonium sulfate fractionation and subjected to Sephadex chromatography in the presence of Triton X-100. This technique, however, did not indicate dissociation of the proteinase into subunits and failed to improve separation of the enzyme from other stromal proteins.

* applicable to contractual effort identified as a project

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

A821 00 171 (cont)

Detail Sheet #1

Progress:

With the establishment of optimum sodium chloride requirements for maximum proteolytic activity on Azocoll as a substrate for assay and employment of the recently described substrate fluorescein-tagged human hemoglobin, activation and inhibition studies were continued employing these procedures as well as casein and BIEE on proteolytic activity associated with the human red blood cell membrane. Assay using Azocoll demonstrated complete inhibition of this activity with a low concentration of Co^{++}, but much higher concentrations were required to approach the same degree of inhibition when fluorescein-tagged hemoglobin was used as substrate. However Zn^{++} appeared to give a greater inhibition using tagged hemoglobin as substrate than with Azocoll.

Comparison of inhibition or activation by cysteine and a variety of metal ions on extracts of membrane preparations obtained by slightly different procedures produced ratios of proteolytic to esterolytic activities that indicated the possible presence of more than one proteinase in the membrane extracts. Chromatography on DEAE-cellulose effected some further purification of the proteolytic activity, but did not remove entirely the contaminating hemoglobin nor did it appear to give any separation of the possible two or more proteinases.

Ultracentrifuge studies on stroma protein preparations and on proteinase extracts subjected to solubilization by sodium dodecyl sulfate or Triton X-100 indicated a potential dissociation, at least in the presence of Triton X-100, a surfactant which showed no significant effect on the proteolytic activity using Azocoll as the substrate.

Membrane extracts almost completely free of hemoglobin were produced by incorporating fractionation by ammonium sulfate precipitation and were employed in sephadex chromatography procedures in the presence of Triton X-100. However, to date no separation of the proteinase or their possible subunits has been achieved by this technique. Portions of the recent investigation studies mentioned were included in the USAMRL Report No. 930 of Dr. Moore et al.

Publications and/or Presentations:

None.

Selected Bibliography:

A821 00 171 (cont)

Detail Sheet #2

Bernacki, R. J. and H. B. Bosman. Properties of a protease of human erythrocyte plasma membranes. Fed. Proc. 30: 1184, 1971.

DeLumen, B. O. and A. L. Tappel. Fluorescein-hemoglobin as a substrate for cathepsin D and other proteases. Anal. Biochem. 36: 22, 1970.

Dodge, J. T., C. Mitchell and D. J. Hanahan. The preparation and chemical characteristics of hemoglobin-free ghosts of human erythrocytes. Arch. Biochem. Biophys. 100: 119, 1963.

Morrison, W. L. and H. Neurath. Proteolytic enzymes of the formed elements of human blood. J. Biol. Chem. 200: 39, 1953.

Nelson, W. L., E. I. Ciaccio, and G. P. Hess. A rapid method for the quantitative assay of proteolytic enzymes. Anal. Biochem. 2: 39, 1961.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1 AGENCY ACCESSION	2 DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 08 6073	70 09 01	DD DR&E(AR)636

3 DATE PREV SUM'RY	4 KIND OF SUMMARY	5 SUMMARY SCTY	6 DOWN GRADING	7 SECURITY	8a DISP'N INSTR'N	8b SPECIFIC DATA - CONTRACTOR ACCESS	9 LEVEL OF SUM
70 07 01	R. TERMINA-	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10 NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	172
b. CONTRIBUTING				
c. [illegible]	CDOG T4T2A(2)			

11. TITLE (Precede with Security Classification Code)

(U) Military Blood Transfusion Reactions (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

003500 Clinical Medicine

13 START DATE	14 ESTIMATED COMPLETION DATE	15 FUNDING AGENCY	16 PERFORMANCE METHOD
68 07	CONT	DA	C. In-House

17. CONTRACT GRANT

a. DATES/EFFECTIVE — EXPIRATION

b. NUMBER: NA

c. TYPE — d. AMOUNT

e. KIND OF AWARD — f. CUM AMT

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PREVIOUS 70	1	1
	CURRENT 71	1	1

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-6[illegible]1759

20. PERFORMING ORGANIZATION

NAME: Blood Transfusion Division

ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

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

NAME: Camp, F. R., Jr., LTC

TELEPHONE: 502-6241251

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME: Shields, C. E., LTC

NAME: DA

21. GENERAL USE

FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code)

(U) Transfusion Reactions; (U) Human Volunteer; (U) Blood Transfusion; (U) Blood Group Compatibility.

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

23. (U) To develop a system for the collection and analysis of data relative to transfusion reactions occurring in the military service. To devise and recommend for implementation, a fail-safe procedure for the prevention and treatment of blood transfusion reactions occurring within our military hospitals.

24. (U) A feasibility study will be initiated involving the hospitals in the 1st Army area and Walter Reed General Hospital. Transfusion data for the hospital, as well as clinical and laboratory reports of transfusion reactions, will be requested. Confirmation and supplemental laboratory investigation of such reactions will be accomplished and reported to the referring hospital.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated and combined with existing work units which have related areas of research

*Available to contractors upon [illegible]

DD FORM 1 MAR 66 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1 1 MAR 70 (FOR ARMY USE) ARE OBSOLETE

Detail Sheet #1

Progress:

Since June 1968 data have been collected concerning the numbers of blood transfusions and transfusion reactions occurring in Army military hospitals in the First US Army area.

Analysis of the data reveals that in excess of 20,000 units of whole blood and blood components were transfused to patients in these medical facilities.

There were 254 reactions reported in three classifications: a) - Febrile reactions - 72; b) Urticarial reactions - 178; c) Hemolytic reactions - 3. No deaths from blood transfusion reaction were reported.

One unit of blood was transfused for every four units crossmatched in the blood banks of the various hospital pathology services, representing 20,000 transfusions actually used of the 80,000 units crossmatched for serologic compatibility. Remaining time of the 21-day shelf life of whole blood allowed many of the blood units to be recrossmatched for other patients. On the other hand, blood continually committed to patients by crossmatch and not used resulted in outdating and loss of the blood.

The use of blood components has sharply increased, especially in the larger hospitals and this upward trend continues. The increased use of blood component therapy is the result of newer, more established medical treatment practices. With the shift in emphasis away from whole blood, the result is the extension of one unit of whole blood into two, three, and four useful products. Blood wastage from outdating will eventually be eliminated entirely.

The use of RhoGam has been administered in proportion to the number of Rh negative (eligible) females delivering Rh positive infants. The sharp decrease in hemolytic disease of the newborn is a direct result of RhoGam therapy.

Publications and/or presentations:

Camp, F. R., Jr., V. F. Conte, F. R. Ellis, R. M. Nalbandian, and D. L. Kessler. Standardization of blood transfusion reaction studies in the military. Delegation of responsibility for a medical team concept. Role of the hospital transfusion board. Milit. Med. 135: 967, 1970.

A821 00 172 (cont)

Detail Sheet #2

Nalbandian, R. M., F. R. Camp, Jr., N. F. Conte, and D. L. Kessler. A fail-safe approach to incompatible blood transfusions. Lab. Med. 1: 33, 1970; Exhibit at the Medical Society of the State of North Carolina, Pinehurst, N.C., May 1971.

Nalbandian, R. M., R. L. Henry, F. R. Camp, Jr., P. L. Wolf, and N. F. Conte. A practical synopsis of consumption coagulopathy. USAMRL Report No. 892, Aug 1970 (DDC AD No. 715701); Milit. Med. 136: 349, 1971.

Selected Bibliography:

Camp, F. R., Jr., N. F. Conte, F. R. Ellis, R. M. Nalbandian, and . Kessler. Standardization of blood transfusion reaction studies the military. Delegation of responsibility for a medical team concept. Role of the hospital transfusion board. USAMRL Report No. 867, Apr 1970 (DDC AD No. 707395); Milit. Med. 135: 967, 1970.

Nalbandian, R. M., I. J. Mader, R. R. Margulis, and F. R. Camp, Jr. Preventing death from incompatible transfusions. Post Grad. Med. 45: 84, 1969.

RESEARCH AND [illegible] WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 6118	71 07 01	DD DR&E(AR)636

3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8A. DOD'N INSTR'N	8B. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
71 07 22	[illegible]	[illegible]	[illegible]	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	6[illegible]A	3A[illegible] DA82T	00	174
b. CONTRIBUTING				
c. COMPATIBLE				

11. TITLE (Provide with security classification code): Military Blood Banking: The Mechanism of Erythrocyte Catabolism during Storage (U)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 002300 Biochemistry

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
67 11	CONT	DA	C. In-House

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER: NA
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 71	1.2	17
CURRENT FISCAL YEAR 72	1.2	33

19. RESPONSIBLE DOD ORGANIZATION

NAME: rg, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

PERSON(S) IN INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION

NAME: Biochemistry Division
US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. academic institution)
NAME: Moore, G. L.
TELEPHONE: 502-6242931
SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS
NAME: Gray, J. L. DA
NAME:

21. GENERAL USE: FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Provide each with Security Classification Code): (U) Red Blood Cells; (U) Storage; (U) Preservation; (U) Utilization; (U) Military

23. TECHNICAL OBJECTIVE: (U) To increase our knowledge concerning the factors involved in maintaining the functional integrity of red blood cells during cold storage through a study of the mechanisms that lead to red cell disruption. This information will lead to development of preservation methods for extending the utilization of blood beyond the present 21 day limit.

24. APPROACH: (U) To study by chemical, physicochemical, and biological means, red cells and red cell membranes from fresh and stored bloods. To measure storage-induced changes in the biochemical and physicochemical properties, and stabilities of red cell membrane. To study the properties, reactivity, and control mechanisms of a membrane proteinase, and the effects of platelets on red cell storage properties.

25. PROGRESS (Furnish individual paragraphs identified by number. Precede text with Security Classification Code.): (U) 71 01 01 - 71 06 30: Cold storage of red cells causes the cell membranes to decrease in their stability and their structural flexibility as measured by their decreased ability to undergo secondary structural changes and interact with florescent structural probes. Evidence was gathered in favor of the protective binding of progesterone on the red cell surface, and the interrelationship between membrane structure changes and [illegible] function changes in the presence of adenine-inosine was elucidated. Initial studies were done on the effects of platelets on red cell storage, and on platelet contamination of red cell membrane preparations.

DD FORM 1498 [illegible] DD FORM 1498A 1 NOV 68

A821 00 174 (cont)

Detail Sheet #1

Progress:

Several techniques were developed to measure the catabolic stress of cold storage on red cell membranes. These include fluorescent probe and turbidity techniques as well as several specific assay procedures. Membrane changes in stored red cells were analyzed in three situations:

a. The storage of whole blood reveals that during storage the membrane is reduced in hydrophobicity and undergoes changes in shape at a molecular level. In addition, lipid, sialic acid, and free nelp-hydryl groups are lost, as well as the ability of the proteins to maintain a state of molecular flexibility.

b. An examination of progesterone-treated red cells indicated that the progesterone does stabilize the red cell membrane for at least 28 days after causing an initial change in the membrane analogous to "locking it in" a modified conformation. By 42 days of storage the progesterone effect seems to "wear off". This study also indicated the high sensitivity of the techniques being used.

c. Red cells were stored with multiple additions of adenine-inosine to maintain hemoglobin function as reflected by high levels of 2,3-DPG. Membrane studies of these cells indicate that catabolism continues at a rate analogous to controls indicating that preservation of the membrane is independent from maintenance of hemoglobin function, and with the advent of the adenine-inosine procedure may be the limiting factor in the length of red cell storage time.

Initial studies were carried out on the effect of platelets and platelet breakdown products on the storage properties of red cells.

Publications and/or Presentations:

Moore, G. L. and R. S. Antonoff. Two dimensional paper separation of dansyl amino acids. Anal. Biochem. 39: 260, 1971.

Moore, G. L., R. S. Antonoff, and D. C. Rau. Changes in erythrocyte membranes during cold storage II. USAMRL Report No. 935, May 1971.

Moore, G. L., R. S. Antonoff, and D. C. Rau. Physicochemical changes in erythrocyte membranes during cold storage in the presence of progesterone. USAMRL Report No. 938, Jun 1971

A821 00 174 (cont)

Detail Sheet #2

Moore, G. L., W. F. Kocholaty, D. A. Cooper, J. L. Gray, and S. L. Robinson. A proteinase from human erythrocyte membranes. Biochem. Biophys. Acta, 212: 126, 1970.

Moore, G. L. and C. D. Purpura. A modified polyacrylamide gel slicer. Anal. Biochem. 39: 258, 1971.

Moore, G. L., D. C. Rau, and J. L. Gray. Turbidity measurements of solubilized human erythrocyte membranes. USAMRL Report No. 930, Apr 1971.

Moore, G. L., D. C. Rau, and Ann S. Wredman. Platelet contamination of erythrocyte membrane preparations. USAMRL Report No. 916, Dec 1970 (DDC AD No. 718626).

Selected Bibliography:

Bakerman, S. and G. Wasemiller. Studies on structural units of human erythrocyte membrane. Biochemistry, 6: 1100, 1967.

Blumenfeld, O. The proteins of the erythrocyte membrane obtained by solubilization with aqueous pyridine solution. Biochem. Biophys. Res. Commun. 30: 200, 1968.

Morrison, W. L. and H. Neurath. Proteolytic enzymes of the formed elements of human blood. J. Biol. Chem. 200: 39, 1953.

Rosenberg, S. A. and G. Guidotti. The protein of human erythrocyte membranes. J. Biol. Chem. 243: 1985, 1968.

Rubalcava, B., D. M. deMunoz, and C. Gitler. Interaction of fluorescent probes with membranes. Biochemistry, 8: 2742, 1969.

Weed, R. I. and C. F. Reed. Membrane alterations leading to red cell destruction. Amer. J. Med. 41: 681, 1966.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	DA OB 6076	2. DATE OF SUMMARY	71 07 01	REPORT CONTROL SYMBOL
3. DATE PREV SUMRY	71 01 22	4. KIND OF SUMMARY		
5. SUMMARY SCTY	U	6. WORK SECURITY	U	
7. REGRADING	NA	8a. DISB'N INSTR'N	NL	9. LEVEL OF SUM: A. WORK UNIT

10. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62	3A062110A8	03	175
b. CONTRIBUTING				
c.	CDOG 1412A			

11. TITLE (Precede with Security Classification Code): (U) Military Blood Banking: Evaluation of Resuscitation by Transfusion of Blood and Other Substances (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 002300 Clinical Medicine

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

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER: NA

c. TYPE: d. AMOUNT:

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

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	71	2	188
CURRENT	72	2	144

19. RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory

ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL

NAME: Conte, Nicholas F., COL

TELEPHONE: 502-624-?753

20. PERFORMING ORGANIZATION

NAME: Blood Transfusion Division

ADDRESS: US Army Medical Research Laboratory, Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR

NAME: Lopas, H., LTC

TELEPHONE: 502-6243519

SOCIAL SECURITY ACCOUNT NUMBER:

ASSOCIATE INVESTIGATORS

NAME: Birndorf, N. I., MAJ

NAME: Dawson, R. B., MAJ, DA

21. GENERAL USE: FOREIGN INTELLIGENCE CONSIDERED

22. KEYWORDS (Precede EACH with Security Classification Code): (U) Blood; (U) Transfusion; (U) Military; (U) Resuscitation; (U) Therapy

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS

23. (U) The use of blood and blood substitute therapy for blood loss in the treatment of the military combat casualty and other medico-surgical conditions.

24. (U) To evaluate the use of blood and to seek and evaluate blood substitutes in the treatment of blood loss in the military combat casualty and other medico-surgical conditions.

25. (U) 71 01 01 - 71 06 30 An experimental transfusion reaction model has been established in primates using hyperimmune plasma fractions. Infusions of antibody directed against recipient red cells produce dose related intravascular hemolysis and disseminated intravascular coagulation (DIC). Autopsy studies show fibrin thrombi in glomerular tufts. This work has characterized and greatly enhanced knowledge of the transfusion reaction with respect to pathophysiology and antibody species responsible. It has also made a model available which has a predictable outcome and can be used to evaluate hemolytic potential of pooled plasma products and fractions used commercially. Pretreatment of experimental animals with heparin has not been wholly effective in preventing DIC; other specific therapy should be studied, such as mannitol--to augment urinary blood flow, hexadimethrine--to inhibit Hageman factor activation, and dipyridamole--to inhibit platelet aggregation.

DD FORM 1498

A821 00 175 (cont)

Detail Sheet #1

Progress:

An experimental transfusion reaction model has been established in primates using hyperimmune plasma fractions Infusions of IgG directed against recipient red cells produce dose related intravascular hemolysis and disseminated intravascular coagulation (DIC). Autopsy studies show fibrin thombi in glomerular tufts.

This work has characterized and greatly refined knowledge of the transfusion reaction with respect to antibody species responsible and pathophysiology. It has also made available a model which has a predictable outcome and can be used to evaluate the hemolytic potential of pooled plasma products and fractions used commercially.

Pre-treatment of experimental animals with heparin has not been wholly effective in preventing DIC; other specific therapy should be studied, such as mannitol, to augment urinary blood flow, hexadimethrine to inhibit Hageman factor activation, and dipyridamole to inhibit platelet aggregation.

Publications and/or Presentations:

Birndorf, N. I. and H. Lopas. Effects of red cell stroma-free hemoglobin solution on renal function in monkeys. J. Appl. Physiol. 29: 570, 1970.

Birndorf, N. I. and H. Lopas. Disseminated intravascular coagulation and renal failure: Production in the monkey with autologous red cell stroma. USAMRL Report No. 902, Oct 1970 (DDC AD No. 716354); presented (by Birndorf) at the 23rd Annual Meeting, American Association of Blood Banks, San Francisco, Calif , Oct 1970.

Birndorf, N. I., H. Lopas, S. J. Robboy, W E. Biddison, M. Ann Wredman, and R. L. Zimmerman. Plasma transfusion reactions in isoimmunized monkeys. USAMRL Report No. 929, Apr 1971.

Birndorf, N. I., J. D. Pearson, and M Ann Wredman The clotting system of monkeys: A comparison of coagulation factors and tests between cynomolgus monkeys (*Macaca fasc.*) and humans Comp. Biochem. Physiol. 38A: 157-161, 1971.

Camp, F. R., Jr. and N. F. Conte. Military blood banking (civil disasters). USAMRL Report No. 931, May 1971.

A821 00 175 (cont)

Detail Sheet #2

Camp, F. R., Jr., N. F. Conte, N. I. German, R. M. Nalbandian, H. S. Kaplan, and K. I. Tobias. Progress notes in military blood banking. A systematic approach to early recognition and treatment of incompatible blood transfusion injury. USAMRL Report No. 919, Feb 1971 (DDC AD No. 721006).

Camp, F. R., Jr., R. M. Nalbandian, N. F. Conte, and F. R. Ellis. Forensic aspects of transfusion reactions. USAMRL Report No. 933, May 1971; presented (by Camp) at the 23rd Annual Meeting, American Academy of Forensic Sciences, Phoenix, Ariz., Feb 1971.

Lopas, H. and N. I. Birndorf. Hemolysis and intravascular coagulation due to incompatible red cell transfusion in isoimmunized monkeys. USAMRL Report No. 900, Sep 1970 (DDC AD No. 716352); presented (by Lopas) at the 23rd Annual Meeting, American Association of Blood Banks, San Francisco, Calif., Oct 1970.

Rosenfield, R. E., E. M. Berkman, and F. R. Camp, Jr. Transfusion reactions: Method of. In: H. F. Conn (Ed.), Current Therapy, Philadelphia: W. B. Saunders Co., pp. 270-274, 1971.

Selected Bibliography:

Bender, M. A. Blood volume of the rhesus monkey. Science, 122: 156, 1955.

Brandt, J. L., N. R. Frank, and H. C. Eichelman. The effects of hemoglobin solutions on renal functions in man. Blood, 6: 1152-1158, 1951.

Breen, F. A. and J. L. Tullis. Ethanol gelation: A rapid screening test for intravascular coagulation. Ann. Intern. Med. 69: 1197-1206, 1968.

Brun, C. A rapid method for the determination of paraaminohippuric acid in kidney function tests. J. Lab. [illegible] 37: 455-466, 1951.

DeNava [illegible]. [illegible] erence to the [illegible].

Hamilton, [illegible]. [illegible] Preparation [illegible] Med 86: 455-4[illegible]

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1 AGENCY ACCESSION	2 DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0B 6077	70 09 01	DD DR&E(AR)636

3 DATE PREV SUM	4 KIND OF SUMMARY	5 SUMMARY SCTY	6 RSRCH SECURITY	7 REGRADING	8B DISP'N INSTR'N	8b SPECIFIC DATA-CONTRACTOR ACCESS	9 LEVEL OF SUM
70 07 01	[illegible]	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10 NO. OBS	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	176
b. CONTRIBUTING	//////////	CDOG 1412A(2)		

11. TITLE (Precede with Security Classification Code)

(U) Evaluation of Blood Banking Methods and Transfusion Practices (18)

12 SCIENTIFIC AND TECHNOLOGICAL AREAS

003500 Clinical Medicine

13 START (Yr Qtr)	14 ESTIMATED COMPLETION DATE	15 FUNDING AGENCY	16 PERFORMANCE METHOD
69 01	CONT	DA	C. In-House

17 CONTRACT/GRANT

a. DATE/EFFECTIVE: NA — EXPIRATION:
b. NUMBER:
c. TYPE: — d. AMOUNT:
e. KIND OF AGCY: — f. CUM. AMT.:

18 RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 70	.6	35
FISCAL YEAR CURRENT 71	.6	59

19 RESPONSIBLE DOD ORGANIZATION

NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

22 GENERAL SF

FOREIGN INTELLIGENCE CONSIDERED

20 PERFORMING ORGANIZATION

NAME: Blood Transfusion Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U S Academic Institution)
NAME: Shields, C. E., LTC
TELEPHONE: 502-6246750
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Camp, F. R., Jr., LTC
NAME: DA

23 KEYWORDS (Provide Key Words with Security Classification Code)

(U) Transfusion; (U) Blood Components; (U) Blood Therapy; (U) Transfusion Reactions; (U) Human Volunteer

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

23. (U) To evaluate whole blood and blood components in the treatment of the military combat casualty with particular emphasis on improving the quality and efficacy of the transfused product.

24. (U) One phase will consist of collecting data on the usage of blood and components and their outcome. The second phase will consist of simulating transfusion practices in an animal model.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated and combined with existing work units which have related areas of research.

DD FORM 1498 [illegible] OF THIS FORM ARE OBSOLETE. DD FORM 1498A 1 NOV 68 [illegible] FOR ARMY USE) ARE OBSOLETE

A821 00 176 (cont)

Detail Sheet #1

Progress:

Results of a transfusion reaction survey in military hospitals is reported in Work Unit No. 172 (A821).

A model for the study of plasma transfusion reactions in subhuman primates was developed in *Macaca irus* monkeys. Plasma transfusion reactions in this species resulted in hemolysis, disseminated intravascular coagulation, and with evidence of intravascular fibrin deposition at autopsy. These reactions appeared very similar to those observed human cases.

Publications and/or Presentations:

Camp, F. R., Jr. and C. E. Shields. The role of automated blood grouping as an information retrieval system. Milit. Med. 135: 636, 1970.

Forrester, R. H., C. E. Shields, F. R. Camp, Jr., and T. P. Harville. Evaluation of an automated method for blood grouping in the military service--A system analysis. Milit. Med. 135: 740, 1970.

Shields, C. E. Quality control approach to improved donor care. Transfusion, 10: 272, 1970.

Shields, C. E., A. H. Schipul, Jr., and J. Williams. Elevated carboxymonoxide levels from smoking in blood donors. Presented (by LTC Camp) at the 13th International Society of Hematology Congress, Munich, Germany, Aug 1970; Transfusion, 11: 89, 1971 (Abstract).

Selected Bibliography:

Barnes, A. and T. E. Allen. Transfusions subsequent to administration of universal donor blood in Vietnam. JAMA, 204: 695, 1968.

Birndorf, N. I., H. Lopas, S. J. Robboy, W. E. Biddison, M. Ann Wredman, and R. L. Zimmerman. Plasma transfusion reactions in isoimmunized monkeys. USAMRL Report No. 929, Apr 1971.

Dauber, L. G., L. J. Reed, H. P. Fortwengler, and F. R. Camp, Jr. The occurrence of blood group substances A and B in proprietary gamma globulin of placental origin. USAMRL Report No. 807, Dec 1968 (DDC AD No. 686269).

A821 00 176 (cont)

Detail Sheet #2

Grove-Rasmussen, M., R. S. Shaw, and E. Marceau. Hemolytic transfusion reaction in a group-A patient receiving group O blood containing immune anti-A antibodies in high titer. Amer. J. Clin. Path. 23: 828, 1953.

Springer, G. F. and R. Schuster. Stimulation of isohemolysins and isoagglutinins by influenza virus vaccines. Vox Sang. 9: 589, 1964.

Stevens, A. R. and C. A. Finch. A dangerous universal donor. Acute renal failure following transfusion of group O blood. Amer. J. Clin. Path. 24: 612, 1954.

Zettner, A. and J. R. Bove. Hemolytic transfusion reaction due to interdonor incompatibility. Transfusion, 3: 48, 1963.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA 0B 6078	70 09 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 CONTRA. FOR ACCESS	9. LEVEL OF SUM
70 07 01	H. TERMINATION	U	U	NA	NL	☒ YES ☐ NO	A. WORK UNIT

10. NO. CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62110A	3A062110A821	00	177
b. CONTRIBUTING				
c. [illegible]	CDOG 1412A(2)			

11. TITLE (Precede with Security Classification Code)
(U) Blood Antibodies and Their Identification and Selection of Human Histocompatibility Antigenic System (18)

12. SCIENTIFIC AND TECHNOLOGICAL AREAS
003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
69 01	CONT	DA	C. In-House

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER: NA
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 70	.5	22
	CURRENT 71	.4	35

19. RESPONSIBLE DOD ORGANIZATION
NAME: Hq, US Army Medical Research Laboratory
ADDRESS: Fort Knox, KY 40121

RESPONSIBLE INDIVIDUAL
NAME: Conte, Nicholas F., COL
TELEPHONE: 502-6241759

20. PERFORMING ORGANIZATION
NAME: Blood Transfusion Division
ADDRESS: US Army Medical Research Laboratory
Fort Knox, KY 40121

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: Camp, F. R., Jr., LTC
TELEPHONE: 502-6241251
SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS
NAME: Bell, C. E., Jr., MAJ
NAME: DA

21. GENERAL USE
FOREIGN INTELLIGENCE CONSIDERED

22. KEY WORDS (Precede EACH with Security Classification Code)
(U) Tissue Antibodies; (U) Blood Antigens; (U) Blood Antibodies; (U) Histocompatibility; (U) Human Volunteer

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

23. (U) To explore the role of blood group and leucocyte antigens and antibodies as they affect the compatibility status of donor and recipient in organ transplantation, particularly as it applies to the treatment of the military combat casualty and related conditions.

24. (U) Blood banking technics will be expanded to investigate lymphocyte/leucocyte antigens along with the appropriate antisera. These will then be applied to study donor and recipient antigenic systems and degree of histocompatibility.

25. (U) 70 07 01 - 70 08 31 This work unit was terminated and combined with existing work units which have related areas of research.

*Available to contractors upon requestor'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

A821 00 177 (cont)

Detail Sheet #1

Progress:

A laboratory has been developed with a capability of typing lymphocytes. This laboratory can now support research concerning the antigenic systems of red cells, white cells, and eventually platelets.

Publications and/or Presentations:

Camp, F. R., Jr., V. F. Conte, and F. R. Ellis. The significance of early 20th century Germanic and other European scientific contributions in the advancement of present-day research in organ transplant hematology. Presented (by Camp) at the 13th International Society of Hematology Congress, Munich, Germany, Aug 1970.

Selected Bibliography:

Rapaport, F. P., J. Dausset, L. Legrand, A. Barge, H. S. Lawrence, and J. M. Converse. Erythrocytes in human transplantation: effects of pre-treatment with ABO group-specific antigens. J. Clin. Invest. 47: 2206-2216, 1968.

Walford, R. L. The isoantigenic systems of human leukocytes. Medical and biological significance. Haematologica, 2: 2, 1969.

Walford, R. L., R. Gallagher, and G. M. Troup. Human lymphocyte typing with isologous antisera; technical considerations and a preliminary study of the cytotoxic reaction system. Transplantation, 3(3): 387-401, 1965.

ADDITIONAL PUBLICATIONS*

Kocholaty, W. F., Edith Bowles-Ledford, Joyce G. Daly, and T. A. Billings. Preparation of a coral snake antivenin from goat serum. USAMRL Report No. 899, Sep 1970 (DDC AD No. 715699).

Kocholaty, W. F., Edith Bowles-Ledford, Joyce G. Daly, and T. A. Billings. Toxicity and some enzymatic properties and activities in the venoms of crotalidae, elapidae, and viperidae. Toxicon, 9: 131, 1971.

*Research was performed under Work Unit No. 149, Project No. 3A061101A91C 00; the Work Unit was terminated as of 30 June 1967 and the papers were published during FY 1971