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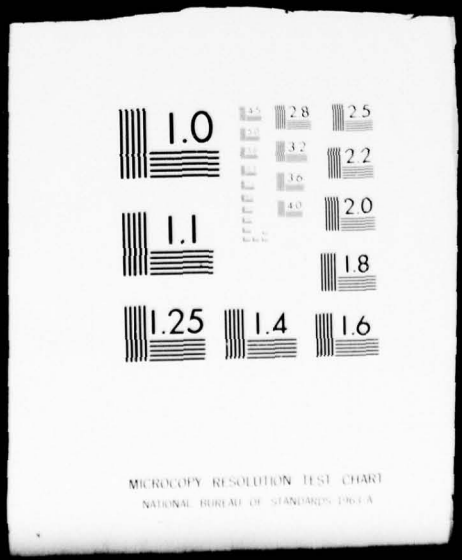

LEVEL II

CLINICAL INVESTIGATION SERVICE

Annual Research Progress Report

FISCAL YEAR 1978

Brooke Army Medical Center
Fort Sam Houston, Texas 78234

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER: MED-300	2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): ANNUAL RESEARCH PROGRESS REPORT Fiscal Year 1978	5. TYPE OF REPORT & PERIOD COVERED: ANNUAL - FY 78
6. PERFORMING ORG. REPORT NUMBER	
7. AUTHOR(s): THEODORE R. McNITT, M.D. Lieutenant Colonel, MC	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Clinical Investigation Service, Brooke Army Medical Center, Fort Sam Houston, Texas 78234	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: 12 279.1
11. CONTROLLING OFFICE NAME AND ADDRESS: Commander, Brooke Army Medical Center, Fort Sam Houston, Texas 78234	12. REPORT DATE: 1 October 1978
	13. NUMBER OF PAGES: 297 Pages
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): Office of The Surgeon General, Department of the Army, Washington, D.C. 20314	15. SECURITY CLASS. (of this report): Unclassified
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE: DISTRIBUTION UNLIMITED

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

N/A

18. SUPPLEMENTARY NOTES

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Clinical Investigations, all medical specialties
Investigational protocols
Publications, Presentations (at national, international, and regional science meetings)
Protocol Status (ongoing, completed, terminated, transferred) (continued)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Subject report identifies the research activities conducted by Brooke Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1978 and other known presentations and publications by the Brooke Army Medical Center professional staff. The research protocols described were conducted under the provisions of AR 40-38, as amended, Clinical Investigation Program; AR 40-7 Use of Investigational Drugs in Humans,
(continued on reverse side)

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

Block 19. Key Words

Group Studies (Southwest Oncology Group, Gynecology Oncology Group)
Protocol Registration
Technological Base (personnel, funding)

Block 20. Abstract.

USAMRDC 70-25, Use of Volunteers as Subjects of Research and BAMC Memo 40-98, Clinical Investigation Service, to insure the medical being, preservation of rights and dignity of human subjects who participated in these investigations.

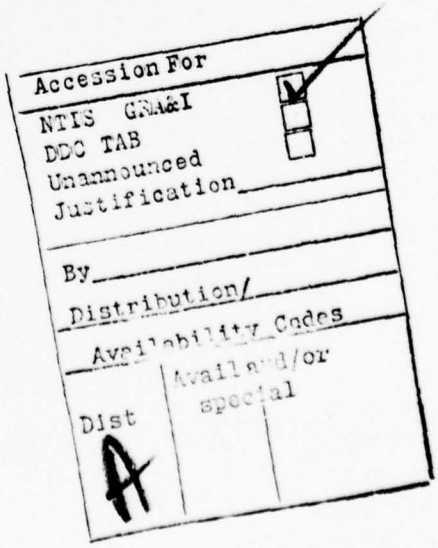
FOREWORD

The Clinical Investigation Service at Brooke Army Medical Center is dedicated to the continuation of clinical research. This report is evidence of the interest and support which the entire Medical Center staff has given to the Clinical Investigation Service. We are especially grateful for the assistance provided by both our former commander, BG Floyd W. Baker, and our current commander, BG Andre J. Ognibene. We are indebted to COL Norman W. Ream, Clinical Investigation Consultant, Health Services Command for his dedication to Army clinical investigation programs.

Over the past twelve months, this interest and support has resulted in the publication of 93 articles in major medical journals and the presentation of 123 papers at national and international meetings. We strongly believe that this reflects positively not only on Brooke Army Medical Center but also on the Army Medical Corps. In addition, we feel that it has provided a dynamic milieu for the training of medical corps officers and for the delivery of quality health care to our patients.

We express our most sincere appreciation for the tireless devotion of Mrs. Dodie Bratten who has significantly assisted in the management, administration and editorial aspects of the Clinical Investigation Service and without whom this report would not be possible.

THEODORE R. McNITT, M.D.
Lieutenant Colonel, MC
Chairman, Directorate for
Clinical Investigation Service



REPORT OF TOTAL ACTIVITIES OF CLINICAL INVESTIGATION SERVICE

FY 78

A. Objectives

The Clinical Investigation Service was established at Brooke Army Medical Center 9 August 1971 to coordinate clinical investigation activities throughout the hospital complex. It is an independent service directly under the Chief, Professional Services and operated under the guidance of the Directorate for Clinical Investigation Service, composed of three members from the Department of Medicine; and one each from Obstetrics-Gynecology, Pathology and Surgery; the Clinical Investigation Committee, composed of the chiefs of the various professional departments; and the Human Use Committee composed of lay personnel.

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

B. Technical Approach

Manpower

Name	Rank	Authorized		Title
	LTC			Chief
Parrish, Rob G.*	CPT	68C00	8Z	Laboratory Dir/Biochemist
Giolma, John P.	CPT	68Z00	8Z	Physiologist
Lieberman, Michael	CPT	68J00	8Z	Microbiologist
Greene, Joseph C.	SFC	92B3R		Sr Med Lab Sp, NCOIC
Sinegal, John H.	SSG	92B3R		Med Lab Sp
Plitt, James J.	SSG	92B2R		Med Lab Sp
Hunter, Deborah	SP5	01H2R		Biological Sci Asst
Wright, Gwendolyn	SP4	01H2R		Biological Sci Asst
McKissock, Donna	SP4	92B1R		Med Lab Sp
Bagwell, James	GS11	00334		Computer Sp
Strong, Geralyn	GS7	00404		Biological Lab Tech
Chapa, Isidoro	GS7	00645		Med Lab Tech
Bratten, Dodie	GS7	01087		Editorial Asst

*Served as Chief, October 1977-June 1978.

Directorate for Clinical Investigation Service

FY 78

Name	Rank	Organization	Title
McNitt, Theodore R.	LTC	Department of Medicine	Chairman
Parrish, Rob C.	CPT	Clinical Investigation Service	Recorder
Zeigler, Michael G.	COL	Department of Surgery	Member
Murgo, Joseph P.	LTC	Department of Medicine	Member
Steele, Russell W.	LTC	Department of Pediatrics	Member
Head, David R.	LTC	Department of Pathology and Area Lab Svcs	Member
Kennedy, Peter S.	MAJ	Department of Medicine	Member

FY 79

Name	Rank	Organization	Title
McNitt, Theodore R.	LTC	Department of Medicine	Chairman
Burleson, David	CPT	Clinical Investigation Service	Recorder
Shock, John P.	COL	Department of Surgery	Member
Murgo, Joseph P.	LTC	Department of Medicine	Member
Leman, Milton H.	LTC	Department of Obstetrics and Gynecology	Member
Head, David R.	LTC	Department of Pathology and Area Lab Svcs	Member
Kies, Merrill S.	MAJ	Department of Medicine	Member

Funding FY 78

MEDCASE	$ 12,613.00	2 Protocols
	$ 58,255.00	Laboratory
	$ 70,868.00	
Capital Equipment	$ 1,214.00	1 Protocol
Consumable Supplies	$ 32,400.80	18 Protocols
	$ 17,260.70	Laboratory
	$ 6,233.50	Contractual Services
	$ 55,895.00	
TOTAL	$128,977.00	

C. Progress

Protocol Disposition FY 78

	Completed	Terminated	Transferred	Ongoing to Fy 78
FY 72	2	-	-	-
FY 73	-	-	-	1
FY 74	5	-	-	1
FY 75	4	1	-	2
FY 76	8	1	1	4
FY 77	13	6	2	16
FY 78	2	2	2	34
	34	10	5	58

During FY 78, 93 manuscripts were accepted for publication in national and international journals. At the present time there are 31 manuscripts pending acceptance for publication. Thirty manuscripts were reviewed by members of the Directorate for fulfillment of residency requirement. One hundred and thirty-three presentations were made at netional and international meetings, and most of the material came from protocols registered in the Clinical Investigation Service.

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APPENDIX B

Southwest Oncology Group

***

Code:

Project Number - $C^{*}\text{-}1^{+}\text{-}78^{-}$

* - Clinical
\+ - Chronological Order of Registration
\- - Fiscal Year in Which Registered

C - Completed
O - Ongoing
T - Terminated
TR - Transferred

P - Published
SP - Submitted for Publication
PR - Presentation

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

PUBLICATIONS

Clinical Investigation Service

Lieberman, M.M. Pseudomonas ribosomal vaccines: Preparation, properties and immunology. Infect Immun 21,#1:76, 1978.

Allen, R.C. Chemiluminescence from eykaryotic and prokaryotic cells: The roles of reducing potential and oxygen. Photochem Photobiol (in press).

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Cardiology

Alter, B.R. et al. Echocardiographic detection of subannular aortic aneurysm. Amer J. Cardiol, (in press).

Westerhof, N. Arterial impedance, in Quantitative Cardiovascular Studies, Baltimore, University Park Press.

Dermatology

Rietschel, R.L., Madorsky, D.D. Male pattern alopecia regrowth following topical fluorouracil therapy. JAMA 238,#11, 12 Sep 77.

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Slay, R.D. Transient ST elevation associated with tension pneumothorax. JACEP (in press).

Wolcott, B.W., Pockey, P.H. The usefulness of x-ray examinations in the evaluation of patients with back pain. Ann Int Med (in press).

Infectious Disease

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Gangai, M.P. Pediatric abdominal masses. Hospital Medicine (in press).

Physical Medicine

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Cooke, A.J. Perspectives on test diets. J Amer Dietetic Asso, 1978 (in press).

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

PRESENTATIONS

Clinical Investigation Service

Allen, R.C. Chemiluminescence from eukaryotic and prokaryotic cells: The roles of reducing potential and oxygen. International Conference on Chemi- and Bioenergized Processes, Guaruja, Brazil, 8-10 August 1978.

Allen, R.C. Correlation of chemiluminescence to microbicial metabolic response from polymorphonuclear leukocytes: A study of in vitro aging. International Symposium on Analytical Applications of Bioluminescence and Chemiluminescence, Brussels Belgium, 6-8 September 1978.

Allen, R.C. The role of oxygen in chemoluminescence of phagocytosing leukocytes. Seminar presentation at Universite Catholique de Louvain, Faculté de Médecine, Brussels, Belgium, 11-16 September 1978.

Lieberman, M.M. Passive immunization of mice against Pseudomonas using a ribosomal vaccine. Exhibit, American Society of Microbiologists Meeting, Las Vegas, Nevada, 14-19 May 1978.

Department of Dentistry

Shelton, D.A. Outpatient general anesthesia. CME video tape. American Academy of Oral Surgery, Chicago, Illinois, September 1978.

Department of Medicine

Wolcott, B.W. A study of the usefulness of the chest x-ray in evaluating patients with acute cough. Association for Clinical Investigation, 1978.

Cardiology

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Murgo, J.P. Aortic input impedance. Toronto General Hospital, Toronto, Canada, November 1977.

Murgo, J.P. New techniques in cardiac catheterization. Toronto General Hospital, Toronto, Canada, November 1977.

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Giolma, J.P. Aortic input impedance in man during rest and exercise. 50th Scientific Sessions of the American Heart Association, Miami, Florida, November 1977.

Uhl, G.S. The hemodynamics of pulsus paradoxus in pericardial tamponade. 27th Annual Scientific Sessions of the American College of Cardiology, Anaheim, California, March 1978.

Murgo, J.P. Ejection dynamics of IHSS. University of Pennsylvania Cardiology Division, April 1978.

Murgo, J.P. New techniques in cardiac catheterization, multisensor catheters. University of Pennsylvania Cardiology Division, April 1978.

Murgo, J.P. High fidelity pressure relationships in myocardial and valvular heart disease. University of Pennsylvania Cardiology Division, April 1978.

Murgo, J.P. Ejection dynamics of hypertrophic cardiomyopathy. Southern Illinois School of Medicine, Springfield, Illinois, May 1978.

Murgo, J.P. Effects of respiration on right and left heart ejection dynamics: Correlates to splitting of the second heart sound. Southern Illinois School of Medicine, Springfield, Illinois, May 1978.

Uhl, G.S. Ventricular volume change dependency of EMD. Walter Reed Army Medical Center, Washington, D.C., May 1978.

Murgo, J.P. The clinical significance of the shape of the aortic pressure and flow wave form - insight into reflections. Walter Reed Army Medical Center, Washington, D.C., May 1978.

Murgo, J.P. Ejection dynamics in hypertrophic cardiomyopathy. Letterman Army Medical Center, Presidio of San Francisco, California, June 1978.

Murgo, J.P. Clinical research in an Army Medical Center. Letterman Army Medical Center, Presidio of San Francisco, California, June 1978.

Murgo, J.P. Ejection dynamics of hypertrophic cardiomyopathy. Eisenhower Army Medical Center, Augusta, Georgia, June 1978.

Murgo, J.P. Ejection dynamics of hypertrophic cardiomyopathy. Medical College of Georgia, Augusta, Georgia, June 1978.

Murgo, J.P. Ejection dynamics of hypertrophic cardiomyopathy. Medical College of South Carolina, Charleston, South Carolina, June 1978.

Murgo, J.P. The hemodynamics of second heart sound splitting. Research seminar, Medical College of South Carolina, Charleston, South Carolina, June 1978.

Murgo, J.P. Hemodynamics of myocardial and valvular heart disease. Medical College of South Carolina, Charleston, South Carolina, June 1978.

Murgo, J.P. Hemodynamic profile of the cardiomyopathies. Charleston Naval Hospital, Charleston, South Carolina, June 1978.

Murgo, J.P. Ischemic and myocardial heart disease: Basic review, recent advances and current controversies. Faculty member, American Heart Association sponsored course, July 1978.

Murgo, J.P. Mechanical effects of myocardial ischemia. American Heart Association, July 1978.

Murgo, J.P. Evaluation of global and regional left ventricular function. American Heart Association, July 1978.

Murgo, J.P. Hemodynamic profile of the cardiomyopathies. American Heart Association, July 1978.

Murgo, J.P. Flow dynamics in hypertrophic cardiomyopathy. World Congress of Cardiology, International Society on Cardiomyopathy, Tokyo, Japan, September 1978.

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Wheeling, J.R. Stabilization and transport. American Heart Association course "Advanced Cardiac Life Support," Brooke Army Medical Center, Fort Sam Houston, Texas, 2,3 June 1978.

Dermatology

Rietschel, R.L. Photocontact dermatitis to hydrocortisone. Hawaii Dermatology Seminar, Maui, Hawaii, 20-25 January 1978.

Rietschel, R.L. Contact urticaria from sorbic acid and synthetic cassia oil. Hawaii Dermatology Seminar, Maui, Hawaii, 20-25 January 1978.

Special Hematology

Rubin, R.N. Pure red cell aplasia complicating the connective tissue diseases. Eastern Division of the American College of Physicians, Philadelphia, Pennsylvania, 11-13 November 1977.

Infectious Disease

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Merrill R.H. Immune deficiency in dialyzed patients: A chronic model of acute trauma. Southeast Dialysis and Transplantation Meeting, Atlanta, Georgia, 10-13 August 1978.

Oncology

Kennedy P.S. Factors affecting size and distribution of platelet aggregates in blood. New methodical techniques. University of Arkansas, Little Rock, Arkansas, October 1977.

Kennedy, P.S. Management of patients with adenocarcinoma of unknown origin. University of Arkansas, Little Rock, Arkansas, October 1977.

Pulmonary Disease

Kelley, W.A. Diagnostic fiberoptic pleuroscopy. Exhibit, American College of Physicians, Boston, Massachusetts, 17-20 April 1978.

Brearley, C.B. Adjuncts for circulation. American Heart Association course "Advanced Cardiac Life Support," Brooke Army Medical Center, Fort Sam Houston, Texas, 2-3 June 1978.

Blumer, R. Acid-base balance. American Heart Association course "Advanced Cardiac Life Support," Brooke Army Medical Center, Fort Sam Houston, Texas, 2-3 June 1978.

Department of Obstetrics and Gynecology

Wallace, R.L. Inhibition of premature labor by Terbutaline. 26th Annual Meeting of the Armed Forces Seminar on Obstetrics and Gynecology and 16th Annual Meeting of the Armed Forces District of the American College of Obstetricians and Gynecologists, New Orleans, Louisiana, 10-13 October 1977.

Robards, J.S. Television as a media for patient and physician education. Exhibit, 26th Annual Meeting of the Armed Forces Seminar on Obstetrics and Gynecology and the 16th Annual Meeting of the Armed Forces District of the American College of Obstetricians and Gynecologists, New Orleans, Louisiana, 10-13 October 1977.

Department of Pathology and Area Laboratory Services

Taylor, R.G. Serology of amebiasis using the FIAX^{tm} system. 7th International Seminar on Amebiasis, Mexico City, Mexico, 3-5 November 1977.

Guentzel, M.N. Virulence factors affecting vibrio cholerae attachment. American Society for Microbiology Annual Meeting, Las Vegas, Nevada, 14-19 May 1978.

Madden, J.J. Clinical evaluation of an automated microbial detection and identification system. American Society for Microbiology Annual Meeting, Las Vegas, Nevada, 14-19 May 1978.

Madden J.M. Clinical evaluation of the McDonnel-Douglas Automicrobic system. American Society for Microbiology Texas Branch Meeting, Corpus Christi, Texas, 1977.

Koester, S. Diagnostic virology capability expanded by the use of electron microscopy at a major medical center. American Society of Electron Microscopy Texas Branch Meeting, San Antonio, Texas, 1978.

Kasai, G. Immunologic response of oncology patients to influenza immunization. American Society for Microbiology Texas Branch Meeting, San Antonio, Texas, 1977.

Jocz, R.J. Influenza A1 USSR among the military population at Brooke Army Medical Center - First isolation in Texas. Annual Southwest Conference on Diseases in Nature Transmissible to Man. San Antonio, Texas, 1978.

Head, D.R. Factor VIII, hemophilia A and von Willebrand's disease. Ohio State Universtidy Department of Pathology, Columbus, Ohio, 11-12 December 1977.

Head, D.R. Recent developments in the classification of hematopoietic malignancies. Army Medical Department Pathology Symposium, Fitzsimons Army Medical Center, Denver, Colorado, 18-20 April 1978.

Head, D.R. Genes affecting phenotypic (lab and clinical) expression of the Beta^{S} (Sickle) gene. Aerospace and Military Medicine Program, National Medical Association 83rd Annual Convention, 31 July 1978.

Head, D.R. Metastatic neuroblastoma in bone marrow aspirate smears. Tenth Triennial World Congress of Pathology, Rio de Janeiro, Brazil, 25-29 September 1978.

Department of Pediatrics

Steele, R.W. Transfer factor for the prevention of Varicella-Zoster infections in childhood leukemia. 17th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, 10-14 October 1977.

Steele, R.W. Transfer factor for the prevention of Varicella-Zoster infections in childhood leukemia. Society for Pediatric Research, San Francisco, California, 25-29 April 1978.

Wilson, F.P. Algorithm-directed triage in a large volume pediatric clinic. American Academy of Pediatrics, New York, New York, 5-10 November 1977.

Department of Psychiatry

Wakeman, R.J. 20th Annual Scientific Meeting of the American Society of Clinical Hypnosis, Atlanta Georgia, October 1977.

Worthington, E.R. Army psychology in the 1970's. Biennial DOD Psychology Symposium, USAF Academy, Colorado Springs, Colorado, April 1978.

Worthington, E.R. Sports Psychology consultation. Annual Southwestern Psychological Association Conference, New Orleans, Louisiana, April, 1978.

Worthington, E.R. Sports Psychology: The clinician and the modern pentathalon. American Psychological Association Conference, Toronto, Canada, August 1978.

Department of Surgery

Anesthesiology

Barrer, M.J. Anesthesia for the traumatized patient. University of Pennsylvania Medical Shool, Philadelphia, Pennsylvania. 1977.

Barrer, M.J. Clinical implications of platelet physiology. Salem Hospital, Boston, Massachusetts, 14 November 1977.

Barrer, M.J. Clinical implications of platelet physiology. Mount Auburn Hospital, Boston, Massachusetts, 15 November 1977.

Barrer, M.J. Clinical implications of platelet physiology. Providence Hospital, Springfield, Massachusetts, 16 November 1977.

Barrer, M.J. Clinical implications of platelet physiology. Fairfax Hospital, Fairfax, Virginia, 17 November 1977.

Barrer, M.J. Deep versus light halothane anesthesia during hypotension in rats - Effect on cerebral metabolism and survival. ASA Annual Meeting, New Orleans, Louisiana, October 1977.

Rayburn, R.L. CPRAM - Controlled partial rebreathing anesthesia method. Primary Childrens Medical Center, Salt Lake City, Utah, 10 October 1977.

Rayburn, R.L. CPRAM - Controlled partial rebreathing anesthesia method. Wilford Hall USAF Medical Center, Lackland Air Force Base, Texas, 21 January 1978.

Rayburn, R.L. CPRAM - Controlled partial rebreathing anesthesia method. Reynolds Army Hospital, Fort Sill, Oklahoma, 26 January 1978.

Rayburn, R.L. Local anesthetics - management of chronic pain. Reynolds Army Hospital, Fort Sill, Oklahoma, 25 January 1978.

Watson, R.L. CPRAM - Controlled partial rebreathing anesthesia methods. University of Illinois Medical School, Chicago, Illinois, 1977.

Watson, R.L. Myoglobinuria and anesthesia. Abraham Lincoln Medical Center, Chicago, Illinois, 1977.

Watson, R.L. Pharmacology of anticholinergics. U.S. Army Biomedical Laboratory, Aberdeen Proving Ground, Maryland, 10-14 October 1977.

Watson, R.L. A new concept in cardio-pulmonary resuscitation. A scientific exhibit for the Combined Federal Medical Services. American Hospital Association Meeting, Anaheim, California, 11-14 September 1978.

Zimmerman, B. The anesthesiologist role in the management of the burned patient. Wilford Hall Air Force Medical Center, Lackland Air Force Base, Texas, November 1977.

General Surgery

Jarstfer, B.S. Smoking, lipids and atherosclerosis. Southwestern Surgical Congress, Palm Springs, California, 17-20 August 1978.

Ortiz, J.E. Gastric carcinoma in the young. Southwestern Surgical Congress, Palm Springs, California, 17-20 August 1978.

Fanning, R.K. Anastomotic false aneurysms. Southwestern Surgical Congress, Palm Springs, California, 17-20 August 1978.

Finne, C.O. Trans-rectal drainage of pelvic abscesses. South Texas Chapter, American College of Surgeons, Houston, Texas, 3 February 1978.

Ophthalmology

Shock, J.P. American Academy of Opthalmology, Dallas, Texas, 2-7 October 1977.

Shock, J.P. Texas O&O, San Antonio, Texas, 12 November 1977.

Shock, J.P. St. Francis Lens Implant and Surgery Symposium, Miami, Florida, 11-15 December 1977.

Shock, J.P. California Medical Association Meeting, San Francisco, California, 19 March 1978.

Shock, J.P. Phacofragmentation Course, San Francisco, California, 17-18 March 1978.

Shock, J.P. Walter Reed Ophthalmology Meeting, Washington, D.C., 10-13 April 1978.

Flynn, H.W., Jr. The Society of Air Force Clinical Surgeons, San Antonio, Texas, 1977.

Flynn, H. W., Jr. The American Medical Association Meeting, San Francisco, California, 1977.

Flynn, H.W., Jr. The Virginia Society of Ophthalmology and Otolaryngology, Williamsburg, Virginia, 5 May 1978.

Flynn, H.W., Jr. The University of Virginia, Charlottesville, Virginia, 8-9 May 1978.

Paglen, P. The aeromedical disposition of the aphakic flyer. South Texas Chapter, American College of Surgeons, Houston, Texas, 3 February 1978.

Orthopedics

Shaver, G.B. Finger tip amputations and avulsions. Society of Military Orthopedic Surgeons, Wilford Hall Air Force Medical Center, Lackland Air Force Base, Texas, 28 November - 1 December 1977.

Jackson, J.P. Reexamination of the green flexor carpiulnaris tendon transfer in cerebral palsy. Society of Military Orthopaedic Surgeons, Lackland Air Force Base, Texas, 28 November - 1 December 1977.

Shook, J.B. Results of reconstructive procedures for the hip in patients with myelomeningocele. Society of Military Orthopaedic Surgeons, Lackland Air Force Base, Texas, 28 November - 1 December 1977.

McIlwain, W.A. The Bi-polar low friction hip prosthesis of Gilberty. Society of Military Orthopaedic Surgeons, Lackland Air Force Base, Texas, 28 November - 1 December 1977.

Shaver, G.B. The Hiss bunionectomy. North American Orthopaedic Traveling Fellows, University of Texas Medical School at San Antonio, 3 April 1978.

Peters, V.T. Treatment by open reduction and internal fixation of fractures of the feet. U.S. Air Force Podiatry Seminar, Brooks Air Force Base, Texas, October 1977.

Shaver, G.B. Fingertip and nail injuries. Tri-Service Hand Symposium on the Management of the Injured Hand, Brooks Air Force Base, Texas, 16 May 1978.

Shaver, G.B. Compression neuropathies in the upper extremity. Tri-Service Hand Symposium on the Management of the Injured Hand, Brooks Air Force Based, Texas 16 May 1978.

Thoracic Surgery

Treasure, R.L. Thoracic chest trauma. 17th Annual John R. Durrance Chest Conference, Aspen, Colorado, 15-18 February 1978.

Traugott, R.C. Latent pericardial tamponade following open heart surgery. Association of Army Cardiology, Walter Reed Army Medical Center, Washington, D.C., 4-6 May 1978.

Cavanaugh, D.G. Experience with cardioplegia at Brooke Army Medical Center. Association of Army Cardiology, Walter Reed Army Medical Center, Washington, D.C., 4-6 May 1978.

Urology

Fairchild, W.V. The incidence of bladder cancer following cyclophosphamide therapy. South Central Section Meeting of the American Urological Association, Tulsa Oklahoma, October 1977.

Fairchild, W.F. The incidence of bladder cancer following cyclophosphamide therapy. Kimbrough Urological Seminar, Denver, Colorado, November 1977.

Wells, W.G. The role of bone marrow acid phosphatase in the staging of adenocarcinoma of the prostate. South Central Section Meeting of the American Urological Association, Tulsa, Oklahoma, October 1977.

Wells, W.G. The role of bone marrow acid phosphatase in the staging of adenocarcinoma of the prostate. Kimbrough Urological Seminar, Denver, Colorado, November 1977.

Gangai, M.P. Unusual aspects of transitional cell carcinoma of the ureter. Kimbrough Urological Seminar, Denver, Colorado, November 1977.

Spence, C.R. Treatment of varicocele. Kimbrough Urological Seminar, Denver, Colorado, November 1977.

Spence, C.R. Urologic emergencies. Central Texas Association of Military Physician Assistants, San Antonio, Texas, October 1977.

Gangai, M.P. The use of full thickness free skin grafts in the treatment of urethral strictures in the male. Panamanian Urological Society, August 1978.

Gangai, M.P. The use of full thickness free skin grafts in the treatment of urethral strictures in the male. Urology Residents and Staff, Gorgas Army Hospital, Canal Zone, August 1978.

Gangai, M.P. Transitional cell carcinoma of the ureter. Panamanian Urological Society, August 1978.

Gangai, M.P. Pediatric abdominal masses. Isthmanian Medical Society, Panama, August 1978.

Gangai, M.P. Clinical significance of hematuria. Medical Staff at Coco Soho Hospital, Panama, August 1978.

Gangai, M.P. Clinical significance of hematuria. Professional Staff Conference, Gorgas Army Hospital, Canal Zone, August 1978.

Gangai, M.P. The use of full thickness free skin grafts in the treatment of urethral strictures in the male. Displayed at American Urological Association Meeting, Washington, D.C., May 1978.

Occupational Therapy

Palm, L. Chaired discussion group, Texas Occupational Therapy Association Min-Conference, Houston, Texas, 23 April 1978.

Physical Therapy

Greathouse, D.G. Electroresponsive behavior of sural nerve as a function of limb temperature in man. American Physical Therapy Association National Conference, Las Vegas, Nevada, 16-22 June 1978.

Greathouse, D.G. Rationale and interpretation of clinical electromyography for selected orthopaedic problems. American Physical Therapy Association National Conference, Las Vegas, Nevada, 16-22 June 1978.

Morris, L. Thoracic surgery: Pre and post-op P.T. treatment. Physical Therapy Comprehensive Chest Program via Teleconference Network of Texas, 25 April 1978.

Social Work Service

Strauss, L.I. The effect of an ongoing bereavement group program in support of independent living. Statewide National Association of Social Workers Conference. 22 October 1978.

Kelley, H.A. Child advocacy resources expansion. Third National Conference on child abuse and neglect, New York, New York, April 1978.

El-Beheri, B.B. Dietetic audit - A giant step for nutritional care. American Dietetic Association, Los Angeles, California, 10-14 October 1977.

Cooke, A.J. Perspectives on test diets. American Dietetic Association, Los Angeles, California, 10-14 October 1977.

Baggan, M.V. American Dietetic Association, New Orleans, Louisiana, 25-29 September 1978.

Dougherty, K. American Dietetic Association, New Orleans, Louisiana, 25-29 September 1978.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
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CLINICAL INVESTIGATION SERVICE

MANUSCRIPTS SUBMITTED FOR PUBLICATION

Clinical Investigation Service

Lieberman, M.M., McKissock, D.C., Wright, G.L. Passive immunization against Pseudomonas with a ribosomal vaccine induced immune serum and immunoglobulin fractions. Infection and Immunity.

Department of Medicine

Cardiology

Murgo, J.P., et al. Aortic input impedance in normal man: Relationship to pressure waveshapes and reflections. Circulation Research.

Dermatology

Jucas, J.J., Rietschel, R.L., Lewis C.W. Unilateral nevoid telangiectasia syndrome in a prepubertal male. Archives of Dermatology.

Endocrinology

Van Cleave, S.J., Corrigan, D.F. Anterior pituitary necrosis in Korean hemorrhagic fever. Journal of the American Medical Association.

General Medicine

Wehrle, P.A. The immune thrombocytopenic purpuras. Southern Medical Journal.

Barrett, J.R. Renal sodium regulation and salt wasting nephropathy. Texas Medical Journal.

Dwyer, J.P. Effect of propranolol on ischemic myocardium. Osteopathic Annals.

Special Hematology

Rubin, R.N. Recurrence of hemolysis in hereditary spherocytosis due to leukemic infiltration of an accessory spleen. Annals of Internal Medicine.

Infectious Disease

McNitt, T.R., Everett, E.D., Duplantis, A.J. Pulmonary function abnormalities in adult patients with rubeola. Annals of Internal Medicine.

Stevens, D.L. Everett, E.D., Spebar, M.J. Coccidioidal pericarditis: Report of a case and a review of the literature. Resubmitted to Quarterly Journal of Medicine.

Stevens, D.L., Taylor, R.G., Everett, E.D., Owensby, O., McNitt, T.R. Amebic liver abscess: Report of a case presenting with nonreactive serologic tests for Entamoeba histolytica. American Journal of Gastroenterology.

Haburchak, D.R. Current concepts: Gram negative sepsis and septic shock. Military Medicine.

Nephrology

Wright, L.F., Leverton, R.S., Whitman, W.H. Severe diabetic ketoacidosis with a normal anion gap. Archives of Internal Medicine.

Oncology

Luedke, D.W., Kennedy, P.S., Rietschel, R.L. Adriamycin induced skin necrosis. Journal of Plastic and Reconstructive Surgery.

Shildt, R.A., Luedke, D.W., Kasai, G., El-Beheri, S., Laham, M. Antibody response to influenza immunization in adult patients with malignant disease. Cancer.

Kennedy, P.S. Neuroblastoma rosette formation in bone marrow aspirates - report of 3 cases. Cancer.

Kennedy, P.S. Factors affecting size distribution of platelet aggregates in blood. Biochemistry Biophysics Acta.

Kennedy, P.A. Effects of acute changes in arterial blood gases on platelet aggregation. Biochemistry Biophysics Acta.

Pulmonary

Kelley, W.A., Dewey, G.C. Tracheal bronchus presenting with obstrction. Chest.

Department of Pathology and Area Laboratory Services

Head, D.R., Kennedy, P.S., Goyette, R.E. Metastatic neuroblastoma in bone marrow aspirate smears. Cancer.

Herrera, G.A. Neurosecretory granule-like structures in lymphomas. Human Pathology.

Archer, S.B., McCue, M.J., Shirley, I.G. Autoanti-U in a patient on chemotherapy. Transfusion.

Department of Radiology

Limbacher, J.P. CT findings of caroticocavernous fistula. American Journal of Roentgenology.

Schnicker, S.C., Goldberger, L.E. Acute endobronchial histoplasmosis. Radiology.

Levy, L.B. A study of retakes in diagnostic radiology in an Army Medical Center. Radiology.

McCauley, R.K. Combined liver-stomach imaging for evaluating epigastric masses. Journal of Nuclear Medicine.

Department of Surgery

Anderton, B.J., Watson, R.L., Parrish, R.G., Lieberman, M.M. Naloxone: Human placental passage. Anesthesiology.

Pruett, C., Baird, R. Laryngotracheal transillumination as a means for blind orotracheal intubation - light wand intubation. Anesthesiology.

Paglen, P.G. Fibrous histiocytoma of the conjunctia. Annals of Ophthalmology.

Cavanaugh, D.G., Walker, O.M., Treasure, R.L. Cardiomegaly? Chest.

Traugott, R.C., Will, R.J., Cavanaugh, D.G., Oddi, M.A., Treasure, R.L. Late pericardial tamponade following open heart surgery. Journal of Thoracic and Cardiovascular Surgery.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Some Common Dietary Constituents on the Solubility of Cholesterol in Lipid Bilayer Membranes.

WORK UNIT NO.: C-24-76

PRINCIPAL INVESTIGATOR: Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: John H. Sinegal, SSG

OBJECTIVES

To determine if xanthine oxidase, polyunsaturated fatty acids, or other lipophilic or lipo-active dietary constituents might affect cholesterol solubility in lipid bilayer membranes and thus play a role in the etiology of atherosclerosis.

TECHNICAL APPROACH

The original plan, as outlined in the protocol itself, calls for construction of a heating block suitable for mounting on a microscope stage and intended to contain a glass microscope slide and coverslip. A phase contrast microscope would then be used to view phase changes in a phospholipid cholesterol mixture held between slide and coverslip. This plan encountered difficulties in that accurately measuring temperatures between a glass microscope slide and coverslip is extremely difficult, if not impossible, and secondly, space limitations between available phase contrast microscope objectives and stages is limiting in construction of a suitable heating block.

An ESR spectrophotometer is sensitive to free radicals; molecules containing an unpaired electron. Some nitroxides are stable free radicals and nitroxide analogs of biochemical compounds are commercially available. The nitroxide analog of cholestane (4',4'-Dimethylspiro[5α cholestane-3',3' oxazolidin]-3-yloxyl) resembles cholesterol in structure. The re-revised technical approach of this protocol is to use the spin labelled cholestane to observe formation of cholesterol or cholesterol analog clusters in the plane of a lipid bilayer membrane. Using the spin label technique, aggregates of two or more molecules can be detected. Thus, with ESR spectroscopy, temperature dependent phase changes can be detected in phospholipid bilayer membranes with accurate temperature determinations.

C-24-76 (Continued)

Personnel: 1 SSG (9 months)
1 SSG (4 months)

Funding:

	Consumable Supplies
FY 78	$ 2,966.70
FY 77	$ 2,483.12
FY 7T	$ 1,444.03
FY 76	$ 1,817.77

PROGRESS

Lipids for this protocol were extracted, sealed in ampules, and stored at -70°C. Experiments using the cholestane spin label in phosphatidyl serine lipid bilayer membranes showed that cholestane does form clusters between 1 and 10 mole% cholestane in a mixture of phosphatidyl serine and cholesterol, the spin label detected a phase transition in the phosphatidyl serine cholesterol system occurring at about 30°C. This is 20-25°C higher than the corresponding phase transition in the absence of cholesterol.

Since the principal investigator has departed this duty station and there are no other investigators interested in lipid experimentation, this study is considered completed.

Status: Completed.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of the Effect of CNS Active Drugs on Membrane Bound Cations

WORK UNIT NO.: C-28-76

PRINCIPAL INVESTIGATOR: Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: Robert L. Watson, Jr., M.D., LTC, MC; James J. Plitt, M.S., SSG

OBJECTIVES

To better understand the effect of CNS depressants and narcotic antagonists on sodium and calcium bound to nerve membranes, and to develop a safe and efficient *in vitro* method of evaluating the potency of narcotics and narcotic antagonists.

TECHNICAL APPROACH

Calcium and sodium are both known to bind to phosphatidyl serine, a major constituent of neural tissue. Cephalin fraction, which contains PS, has been extracted from bovine brain and several grams of pure phosphatidyl serine have been separated from the cephalin fraction. The second phase of the research is to measure the binding of sodium and calcium to lipid bilayer membranes. Sodium-22 and calcium-44 have been purchased in order to observe their binding to phospholipid bilayer membranes.

Personnel: 1 SSG (10 months)

Funding:

	Consumable Supplies
FY 78	-
FY 77	$ 808.78
FY 7T	$ 195.00
FY 76	

C-28-76 (Continued)

PROGRESS

Experiments were used to refine techniques of handling small amounts of lipids and sodium 22 which is a gamma emitter. It was found that 1 to 4 sodiums per phosphate bind to phosphatidyl serine lipid bilayer membranes. Attempts to determine the details of sodium and calium binding to phospholipid bilayer membranes were inconclusive.

Since the principal investigator has departed this duty station and there are no other investigators interested in lipid experimentation, this study is considered completed.

Status: Completed.

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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of the Molecular Conformation of Erythromycin 2'Esters and Bioactivity.

WORK UNIT NO.: C-34-76

PRINCIPAL INVESTIGATORS: Dennis L. Stevens, M.D., MAJ, MC;
Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the nuclear magnetic resonance of various erythromycin 2'esters in order to predict the feasibility of developing better drugs for clinical use.

TECHNICAL APPROACH

Erythromycin is administered as the ester of a variety of fatty acids covalently bound to the 2' position. The biological activity and toxicity of these esters has been established; however, the subtlety of the substitutions does not suggest the wide range of response obtained from administering the different esters.

Nuclear magnetic resonance techniques will be used to determine the conformation of several esters of erythromycin as a function of pH. Specifically, we will measure the Spin Lattice relaxation times (T_1's) of different functional groups in the molecule. We will correlate the conformational changes with intestinal absorption, antibiotic potency, and hepatic toxicity reported in the literature. Ideally, the in vitro data we collect, coupled with the physiological data found in the literature will enable us to choose an ester which will yield an intermediate conformational change and will retain the qualities necessary for effective clinical use.

Personnel: None

Funding: None

C-34-76 (Continued)

PROGRESS

Due to the release from active duty of Dr. Parrish before the protocol was completed, we are presently negotiating with Southwest Research Foundation for their assistance in analyzing the erythromycin compounds by nuclear magnetic resonance.

Status: Ongoing.

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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Physiological Origins and Clinical Applications of Cardiac Related Electrical Impedance Waveforms.

WORK UNIT NO.: C-4-77

PRINCIPAL INVESTIGATOR: John Paul Giolma, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: Joseph P. Murgo, M.D., LTC, MC

OBJECTIVES

To better understand the origins of cardiac related thoracic impedance waveforms in man and to develop a basis of clinical applications of impedance techniques.

TECHNICAL APPROACH

Part I - Noninvasive Studies. Electrical impedance measurements are taken on the thorax of 20 normals and of patients with a variety of disease classifications along with systolic time interval information. Measurements are taken in the noninvasive laboratory of the Cardiology Service, BAMC, and include electrocardiogram, carotid pulse tracing, the electrical impedance baseline, electrical impedance changes, and the derivative of electrical impedance signal. Additionally, in some patients ultrasound echocardiograms are obtained simultaneously with the impedance measurement. The intent is to look for variations of timing and features of impedance signals between normals and the various patient groups.

Part II - Invasive Studies. Thoracic electrical impedance measurements are taken during the catheterization procedure on adult normals using physiologic maneuvers and injections of saline and contrast material to provide information concerning the contributions of the pulmonary and systemic circulation to the cardiac related impedance signal.

Personnel: None.

Funding:	Consumable Supplies
FY 77	$ 73.50
FY 7T	$ 150.00

C-4-77 (Continued)

PROGRESS

Noninvasive Studies. These studies suggest that timing and amplitude features of the impedance derivative signal are affected as much by anatomical variations among subjects as they are by pathology.

Invasive Studies: A second patient was studied in the cardiac catheterization laboratory with equipment suitable for use in sensitive patient areas. The new sine wave flow meters still interact with the impedance measurement both in salt water tank tests and with the patient studied to the extent that measurements are not possible using these two kinds of equipment during our complicated catheterization procedures.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: The Development of a Gram-Negative Bacterial Vaccine for Laboratory Animals.

WORK UNIT NO.: C-7-77

PRINCIPAL INVESTIGATOR: Michael M. Lieberman, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: Donna DeSoto, SP4; Gwendolyn Wright, SP4

OBJECTIVES

To develop a safe and effective, broad-spectrum, gram-negative bacterial vaccine for laboratory animals.

TECHNICAL APPROACH

The initial phase of the project encompasses the development of a ribosomal vaccine for several serotypes of Pseudomonas aeruginosa. The bacteria are grown in broth culture, harvested and washed by centrifugation, and subjected to ultrasonic disruption for preparation of crude extracts. The ribosomes are isolated from the extracts by ammonium sulfate fractionation and ultracentrifugation. The isolated ribosomes are chemically analyzed for protein and RNA content and tested for immunogenicity in mice. Mice are given two vaccinations seven days apart and directly challenged by inoculation of live virulent organisms ten days after the second vaccination. Control (non-vaccinated) mice are also challenged. The percentage of mice that survive 48 hours post challenge are scored to determine the extent of protection afforded by the vaccine.

In addition, the vaccine is used to immunize rabbits and the rabbits bled to obtain immune serum. The immune serum is then tested by injecting it into mice which are subsequently challenged by inoculation with live bacteria. Mice that are injected with pre-immune rabbit serum are also included in the challenge as controls. The challenged mice are then scored for survival as above in order to determine the ability of the immune serum to confer passive protection against Pseudomonas to the mice.

Personnel: 1 SP4 (12 months)
1 SP4 (3 months)

C-7-77

Funding:	FY 78	FY 77
Capital Equipment	$1,214.00	
Consumable Supplies	$3,557.70	$2,177.90

PROGRESS

The results obtained so far demonstrated that vaccines prepared from a majority of serotypes used were immunogenic, i.e., afforded 60 to 100% mouse protection against a challenge inoculum containing 8 to 50 50% lethal doses. In some cases vaccine doses as low as 1 μg of RNA provided 100% mouse protection. Molecular sieve chromatography of a highly immunogenic ribosomal preparation on Sepharose 4B demonstrated the presence of two molecular weight fractions: (1) peak A, an excluded peak (thus having a molecular weight of at least 2×10^7), and 2) peak B, considerably retarded, with an elution position corresponding to a molecular weight of about 2.2×10^6, approximating that of typical 70S ribosomes. Both peaks A and B were immunogenic; however, the immunogenicity of peak A was greater (i.e., a smaller immunizing dose was required) than that of peak B. Peak A was shown to contain components of lipopolysaccharide in addition to protein and RNA (which comprised 80% of the dry weight of peak A). On the other hand, peak B was shown to be free of lipopolysaccharide, and 100% of its dry weight consisted of protein and RNA.

Furthermore, the results of the passive immunizing experiments demonstrate that protection by the ribosomal vaccine against challenge with live organisms is serum-mediated. As described above, the vaccine can be separated into two components on the basis of molecular weight and that both the higher (peak A) and lower (peak B) molecular weight fractions were capable of inducing active immunity in mice. Both fractions are also capable of eliciting the production of mouse protection antibody in rabbits. Agar gel diffusion (AGD) with antisera to peaks A, B, or unfractionated vaccine indicated a common antigenic component among them in addition to an extra antigen in unfractionated vaccine not present in peak B. Passive hemagglutination (PHA) with antisera to peaks A and B demonstrated high titer agglutinating antibody only with antiserum to peak A when a method of erythrocyte sensitization for lipopolysaccharide (LPS) antigens was used. Also, PHA was greatly inhibited by small amounts of LPS prepared from the same organism from which the vaccine was made. Both antisera to peaks A and B fix complement with either A or B antigens. Antisera to peaks A and B, when reacted with peak B antigen, have about the same complement fixation (CF) titer (as determined by a quantitative CF test). However, when peak A antigen is used, antiserum to peak A has about twice the CF titer that antiserum to peak B has. These results are consistent with chemical observations which suggest that the ribosomal vaccine contains LPS in addition to an unidentified immunogenic principle endogenous to ribosomes. Furthermore, this immunogen is present in both peaks A and B, but detectable amounts of LPS are present only in peak A.

C-7-77

The relative importance of the IgG and IgM classes of antibodies was also compared. The results indicated that both IgG and IgM isolated from immune rabbit serum are protecitve in mice. Only IgG precipitated with the vaccine in AGD, but both IgG and IgM were active in PHA and in CF. The PHA titer of the IgM was higher than that of the IgG, but the CF titer of the IgG was higher than that of the IgM. The mouse protective capability of the IgG and IgM was about the same.

Status: Ongoing.

Lieberman, M.M., McKissock, D.C. and Wright, G.L. Passive immunization against Pseudomonas with a ribosomal vaccine induced immune serum and immunoglobulin fractions. Submitted to Infection and Immunity for publication.

Lieberman, M.M. Pseudomonas ribosomal vaccines: preparation, properties and immunogenicity. Infect Immun 21:76-86, 1978.

Lieberman, M.D. Passive immunization of mice against Pseudomonas using a ribosomal vaccine. Exhibit at American Society of Microbiologist Meeting, 14-19 May 1978, Las Vegas, Nevada.

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

INVESTIGATION PROJECT RESUME

TITLE: In Vitro Studies of Amphotericin B.

WORK UNIT NO.: C-16-78

PRINCIPAL INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC: Dennis L. Stevens, M.D., Ph.D., MAJ, MC: Michael M. Lieberman, Ph.D., CPT, MSC

ASSOCIATE INVESTICATORS: Geralyn Strong, DAC

OBJECTIVES

To study the mechanism of polyene antibiotic action and to develop in vitro biological and physical techniques that will be useful in determining species specific efficacy and concentrations of selected polyene antibiotics.

TECHNICAL APPROACH

The two aspects of this protocol are 1) development of an electron spin resonance assay technique for Amphotericin B and 2) studies of factors affecting the in vitro efficacy of Amphotericin B.

Personnel: 1 GS 7 (3 months)

Funding:

PROGRESS

The effect of various sterols on the growth inhibition of Candida albicans by Amphotericin B was studied in vitro. Cultures of C. albicans were grown in the presence or absence of Amphotericin B and various sterols and growth monitored by measurement of the increase in culture

C-16-78 (Continued)

turbidity (which was correlated with culture viability determinations). The results demonstrated the following:

a. Amphotericin B alone, at a final concentration of 0.24 μg/ml, completely inhibited the growth of C. albicans.

b. Ergosterol, at a molar ratio of 3:1, ergosterol:Amphotericin B, was able to prevent this growth inhibition yielding 70% of the maximal (uninhibited) growth rate;

c. Other sterols could also prevent this growth inhibition by Amphotericin B, but to a lesser extent than ergosterol, the order of decreasing effectiveness for these sterols was ergosterol > dehydrocholesterol > cholesterol > β-sitosterol > stigmasterol > dihydrocholesterol, α-cholestane.

From these results, attempts are being made to correlate the structural features of the sterols to their functional capability relative to prevention of Amphotericin B activity. Based on such considerations, the understanding of the mechanism of action of Amphotericin B will be clarified in terms of the interaction of the antibiotic with sterol components of the membranes of living cells.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: The Molecular Pathology of Alpha Toxin from Clostridium Perfringens upon Polymorphonuclear Leukocyte (PMNL) Function.

WORK UNIT NO.: C-35-78

PRINCIPAL INVESTIGATORS: Dennis L. Stevens, M.D., Ph.D., MAJ, MC;
Robert C. Allen, M.D., Ph.D., CPT, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Michael M. Lieberman, Ph.D., CPT, MSC; John H. Sinegal, SSG; Geralyn Strong, DAC; John Posch, DAC

OBJECTIVES

To study membrane alterations of PMNL resulting from the action of α-toxin C. perfringens, the etiologic agent of gas gangrene.

TECHNICAL APPROACH

Research techniques to be employed will include:

a) Purification of PLC from C. perfringens and B. cereus.

b) Comparison of PLC activity from various sources.

c) PMNL microbicidal metabolism

d) Chemotaxis of PMNL and the effect of exposure to PLC will be studied using modified Boyden Chamger and agarose gel technique.

Personnel: 1 GS7 (1 month)

Funding:	Consumable Suplies
Fy 78	$790.93

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Oral Transplants of Freeze-Dried Allografts.

WORK UNIT NO.: C-12-75

PRINCIPAL INVESTIGATOR: Donald H. Newell, D.D., COL, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether freeze-dried bone allografts can be used in one, two, and combined one and two wall oral bony defects with predictable results.

TECHNICAL APPROACH

The surgical site is exposed via a buccal and lingual full or partial thickness mucoperiosteal flap. Intraosseous defects are recontoured and one wall or two wall bony defects are prepared by removing the cortical plate within the defect. The freeze-dried allograft material is mixed with sterile saline to a paste-like consistency and packed in and around the existing bony defect. The patients will be recalled one year post-grafting to re-open the operative site for evaluation and additional surgical intervention as indicated.

Personnel: None.

Funding: None.

PROGRESS

This study of oral transplants of freeze-dried allografts which was started by COL James Lane and continued by LTC John Moyer has been discontinued for the following reasons:

1. The study is completely under the control of the Periodontic Service, Bethesda Naval Hospital. The clinical material submitted from BAMC

C-12-75 (Continued)

is only a small sample of the total number of cases being used in this study since many military and civilian periodontists are participating.

2. Many patients are reluctant to have a second surgical reentry procedure performed one year after the original grafting procedure which is what the Bethesda protocol calls for.

3. The Bethesda study is not as well designed to gather reliable data as I feel it should be. Instead of taking measurements of the bone defects at the time of grafting and again at the time of reentry, they are relying on visual evaluations and clinical photographs (2" x 2" Kodachromes) to estimate the percentage of new bone formation within the defect. These methods are subject to a great deal of error through personal bias, photographic technique and individual visual variations.

For these reasons primarily, I have elected not to continue participation in the study.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: An Evaluation of Enflurane Combined with Nitrous Oxide as an Amnesic Agent for Outpatient Oral Surgery.

WORK UNIT NO.: C-20-76

PRINCIPAL INVESTIGATOR: John E. Buhler, Jr., MAJ, DC

ASSOCIATE INVESTIGATORS: Richard A. Kraut, LTC, DC; David W. Shelton, COL, DC; David Mangelsdorff, B.A., M.A., Ph.D.; Robert L. Watson, Jr., COL, MC

OBJECTIVES

Nitrous Oxide added to the amnesia technique described by Kraut et al. (see Annual Report FY 77) to allow reduction in the concentration of ethrane used in the mixture.

TECHNICAL APPROACH

Thirty consecutive ASA I patients requesting general anesthesia participated in the study. Two days prior to surgery patients underwent complete workpup; i.e., medical history and physical examination; CBC; PT; PTT; urinalysis; and chest x-ray. All patients remained NPO a minimum of 8 hours prior to surgery. Cardiac and blood pressure monitors were attached, and IV infusion of D_5RL was begun. Nitrous oxide-enflurane mixture was administered via nasal mask, and surgery was performed. The questionnaire was completed postoperatively by patient according to Kraut, et al. (See Annual Report FY 77).

Personnel: None

Funding:

	MEDCASE
FY 78	-
FY 77	-
FY 7T	-
FY 76	$10,200.00

PROGRESS

Among the 30 anesthetics administered in this manner, there were no complications. Heart rate and rhythm remained stable, as did respiratory rate and depth.

The mean percent inspired Enflurane ranged from 0.45 to 0.50 and the percent nitrous oxide from 40% to 50%.

Five patients successfully underwent the surgical procedure and amnesia technique, but answered more than two of the discriminator questions incorrectly on the amnesia test and were excluded from the amnesia analysis.

The remaining 25 patients' responses were analyzed with the aid of a computer and verified with analysis of variance and sign test. Five questions were selected as being most indicative of amnesia during the surgical procedures. Nineteen of 25 patients were manesic for all five questions, three patients recalled only one event, two patients recalled two events, and one patient recalled three events. The amnesic effect of Enflurane/nitrous oxide was significant to the $p = .05$ level.

All 25 patients felt that their extractions were not an unpleasant experience, that they would desire this type of anesthetic technique for future extractions and that they would recommend it to their friends.

Twenty-seven of 30 patients completed their 30 minute psychomotor function test faster than their preoperative test, and all patients left the clinic within 20 minutes of completion of this test.

Conclusions: The addition of 40-50% nitrous oxide to the anesthetic technique described by Kraut, et al. allows the use of one-third the concentration of Enflurane while retaining the ability to create a state of cooperative amnesia. The technique is simple, safe, has rapid recovery, and is readily accepted by the patient. It has been found to be a beneficial adjunct to local anesthesia when general oroendotracheal anesthesia is not deemed necessary.

Status: Completed.

Kraut, R.A.; Buhler, J.E.; Shelton, D.W.; and Watson, R.L. An evaluation of Enflurane as an amnesic agent for outpatient oral surgery. J Oral Surg 36:278, April 1978.

Buhler, J.E.; Kraut, R.A.; Shelton, D.W.; Mangelsdorff, D.; and Watson, R.L. An evaluation of Enflurane combined with nitrous oxide as an amnesic agent for outpatient oral surgery. Submitted to J Oral Surg.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: G-44-72

PRINCIPAL INVESTIGATORS: Larry D. Hudson, CPT, MC; Charles W. Lewis, COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

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

TECHNICAL APPROACH

Frozen and fixed specimens received from military hospitals worldwide continue to be processed for immunofluorescence.

Personnel: None

Funding:

	MEDCASE	Consumable Supplies
FY 78		$ 34.50
FY 77	-	$ 842.50
FY 7T	-	-
FY 76	$1,734.00	-
FY 75	-	-
FY 74	-	$ 277.90
FY 73	-	$ 200.00

PROGRESS

This fluroescent antibody technique to investigate various dermatoses is now a routine procedure. An indirect immunofluroescent technique has been developed for the detection of double stranded native DNA antibodies.

C-44-72 (Continued)

This has proven to be extremely helpful in the evaluation of patients with systemic lupus erythemosus.

Status: Completed.

Presented at the New Advances in Immunofluroescence meeting May 1978.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-28-73

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

ASSOCIATE INVESTIGATORS: John Paul Giolma, Ph.D., CPT, MSC; Barry Alter, M.D., MAJ, MC; James F. Dorethy, M.D., MAJ, MC; Harold Felter, M.D., MAJ, MC; John Logsdon, M.D., MAJ, MC; Gregory Uhl, M.D., MAJ, MC; R. Eugene Bowers, M.D., MAJ, MC; Richard Davis, M.D., Ph.D., MAJ, MC; Timothy Webb, Ph.D., CPT, MSC; George M. McGranahan, Jr., M.C., COL, MC

OBJECTIVES

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

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

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

4. To quantitate left ventricular hydraulic output power.

5. To measure aortic and pulmonary artery input impedance by Fourier analysis and to determine the effect of changing physiologic states upon the impedance.

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

TECHNICAL APPROACH

All adult patients for routine right and left heart catheterization are evaluated in the usual manner by a cardiac fellow prior to catheterization. This evaluation includes strip chart echocardiography to

C-28-73 (Continued)

determine the patient's suitability for certain aspects of the protocol. During catheterization, special, custom-designed, right and left heart catheters are introduced into the right and left heart such that simultaneous high fidelity pressures are measured from the pulmonary artery, right ventricle, right atrium, left ventricle, and aorta. In addition, electromagnetically derived aortic and pulmonary flow velocities are recorded from the same sites that high fidelity pulmonary artery and aortic pressures are obtained. Patients are studied during both rest, supine exercise, and depending upon the patient's disease during a variety of other stresses or pharmacologic interventions. Some patients also undergo simultaneous external echocardiography during catheterization. The study is terminated after bi-plane ventricular angiography and coronary arteriography if indicated.

Patients undergoing catheterization with the flow catheters also have aortic root and/or pulmonary angiography for purposes of determining the diameters of these great vessels. These parameters are necessary to calculate flow velocity from volumetric flow itself.

Major changes have taken place in the way the Honeywell 316 computer can be employed in the research effort in cardiac catheterization. A significant programming effort has gone into improving the automated fashion in which the computer defines timing and amplitude measurements from the signals generated during the catheterization procedure. The ease of using the Fourier analysis programs has been increased making the acquisition of input impedance data simpler and quicker. Major changes in the technique by which cursors and measurements are corrected have taken place permitting recalculations of stroke volume after the movement of flow cursors. These and other changes greatly facilitate the use of the catheterization laboratory computer as it was originally configured; however, the ability to generate new data is not matched by an ability to analyze it on the catheterization laboratory computer. Hence, a new and greatly improved signal processing system has been planned for use in future years.

Major improvements in the analog electronics of both laboratories have been implemented, greatly facilitating the use of the equipment during catheterization procedures and during tape playback for research and other purposes. The acquisition of new echocardiographic equipment, including an external doppler and two-dimensional capabilities, greatly facilitates the derivation of noninvasive signals and images for clinical and for research purposes. The 9830 programmable calculator system continues to provide measurements from signals and images. In addition, the new proposed system will greatly facilitate processing the enormous amount of data generated from two-dimensional ultrasound.

Personnel: 1 CPT (12 months)
1 GS11 (12 months)
1 SP4 (10 months)

C-28-73 (Continued)

Funding:	MEDCASE	CONSUMABLE SUPPLY FUNDS		
		Consumable Supplies	Contractural Services	Reprints
FY 78	$ 7,399.04			
FY 77	$53,813	$ 115.00		
FY 7T		$ 85.00		
FY 76	$48,902.82			$ 245.00
FY 75	$33,653.44	$ 129.76		
FY 74	$29,354.25		$43,573.00	
FY 73	$43,000.00			

PROGRESS

Growing familiarity of technician personnel with projects in Cardiology and the arrival of a new computer specialist have greatly enhanced the ability of Cardiology to accept and process beat by beat cardiovascular and physiologic data.

Fluid input impedance measurements in the pulmonary artery and the ascending aorta coupled with a study in the descending aorta have now provided more detailed information concerning the nature of pressure and flow transmission in these vessels. These measurements form a data base involving those with no known organic heart disease and provide a foundation for a new ongoing study of those with atherosclerotic heart and vessel disease. Other aspects of the impedance study involve better definition of the applications of the Fourier analysis to such studies, including specialized averaging techniques for better defining spectral information.

Extensive use of the catheterization laboratories' ability to store signals and to do beat by beat analysis of cardiovascular signals using the 9830 calculators has provided the ability to perform detailed analysis of the effects of respiration on pressure and flow and the relationships of changes in parameters derived from these signals to the splitting of the second heart sound. This study on a group of normals is now completed. Similar techniques were also used in furthering the study on cardiac tamponade begun last year adding two more patients as they have become available into this study which is providing information on paradoxical pulse during tamponade. A study has begun using four patients with constrictive pericarditis, examining the relative effects of the disease on amplitude and timing information in the cardiovascular system.

The ongoing study on idiopathic hypertrophic subaortic stenosis (IHSS) continues, examining the effects of Propranolol on ejection dynamics in patients with this unusual and interesting disease.

C-28-73 (Continued)

The arrival of new instrumentation, namely the doppler and two-dimensional echo equipment, along with additional personnel will now provide the Cardiology Non-Invasive Laboratories with a strong footing for clinical research similar to that presently underway in the catheterization laboratories. An initial study using non-invasive measurements in patients with IHSS is now underway.

Status: Ongoing.

Murgo, J.P., Alter, B.R., Dorethy, J.D., McGranahan, G.M.: The ejection dynamics of hypertrophic cardiomyopathy during the presence and absence of intraventricular gradients. Submitted to Journal of Clinical Investigation.

Murgo, J.P., Giolma, J.P., Westerhof, N.: The contribution of systemic input impedance measurements to an analysis of wave reflections in normal man. Submitted to Circulation Research.

Murgo, J.P., Giolma, J.P., Altobelli, S.A., Westerhof, N.: Systemic input impedance in normal man during rest and dynamic exercise. Submitted to Circulation Research.

Murgo, J.P.: Multisensor catheterization - Five years experience. Submitted to Catheterization and Cardiovascular Diagnosis.

Murgo, J.P., Dorethy, J.D., Alter, B.A.: Normal right and left ventricular ejection dynamics in man during rest and exercise. Submitted to Circulation.

Logsdon, J.D., Murgo, J.P., McGranahan, G.M.: Right and left heart ejection dynamics during the Valsalva maneuver. Submitted to Circulation.

Murgo, J.P. - Visiting consultant to Toronto General Hospital, Toronto, Canada: Presented three research seminars on (1) Hypertrophic Cardiomyopathy, (2) Aortic Input Impedance, and (3) New Techniques in Cardiac Catheterization. November 1977.

Murgo, J.P. - Aortic Flow Dynamics in Hypertrophic Cardiomyopathy with and without Left Ventricular Pressure Gradients. 50th Scientific Sessions of the American Heart Association, Miami, Florida. November 1977.

Felter, H.G. - Effects of Respiration on Right and Left Heart Ejection Dynamics: Correlates to the Second Heart Sound. 50th Scientific Sessions of the American Heart Association, Miami, Florida. November 1977.

Giolma, J.P. - Aortic Input Impedance in Man During Rest and Exercise 50th Scientific Sessions of the American Heart Association, Miami, Florida. November 1977.

C-28-73 (Continued)

Uhl, G.S. - The Hemodynamics of Pulsus Paradoxus in Pericardial Tamponade. 27th Annual Scientific Sessions of the American College of Cardiology, Anaheim, California. March 1978

Murgo, J.P. - Visiting Consultant to University of Pennsylvania Cardiology Division. Presented three seminars on: (1) Ejection Dynamics of IHSS, (2) New Techniques in Cardiac Catheterization, Multisensor Catheters, (3) High Fidelity Pressure Relationships in Myocardial and Valvular Heart Disease. April 1978.

Murgo, J.P. - Visiting Consultant to Southern Illinois School of Medicine, Springfield, Illinois. Presented two lectures on: (1) Ejection Dynamics of Hypertrophic Cardiomyopathy, (2) Effects of Respiration on Right and Left Heart Ejection Dynamics: Correlates to Splitting of the Second Heart Sound. May 1978.

Uhl, G.S. - Walter Reed Army Medical Center, "Ventricular Volume Change Dependency of EMD." May 1978.

Murgo, J.P. - The Clinical Significance of the Shape of the Aortic Pressure and Flow Wave Form - Insight into Reflections. Walter Reed Army Medical Center, Washington, D.C. May 1978.

Murgo, J.P. - Visiting Consultant, Letterman Army Medical Center, Presidio of San Francisco, California. Presentations: (1) Ejection Dynamics in Hypertrophic Cardiomyopathy, (2) Clinical Research in an Army Medical Center. June 1978.

Murgo, J.P. - Visiting Consultant, Eisenhower Army Medical Center and the Medical College of Georgia, Augusta, Georgia. Grand Rounds presentation: Ejection Dynamics of Hypertrophic Cardiomyopathy. June 1978.

Murgo, J.P. - Visiting Consultant, Medical College of South Carolina, Charleston, South Carolina. Grand Rounds presentation: Ejection Dynamics of Hypertrophic Cardiomyopathy. Research seminar: The Hemodynamics of Second Heart Sound Splitting. Presentation to Fellows: Hemodynamics of Myocardial and Valvular Heart Disease. June 1978.

Murgo, J.P. - Visiting Consultant, Charleston Naval Hospital. Presentation: Hemodynamic Profile of the Cardiomyopathies. Junes 1978.

Murgo, J.P. - Faculty member, American Heart Association sponsored course entitled "Ischemic and Myocardial Heart Disease: Basic Review, Recent Advances and Current Controversies. Three presentations: (1) Mechanical Effects of Myocardial Ischemia, (2) Evaluation of Global and Regional Left Ventricular Function, (3) Hemodynamic Profile of the Cardiomyopathies. July 1978.

C-28-73 (Continued)

Murgo, J.P. - World Congress of Cardiology, invited speaker for the International Society on Cardiomyopathy, "Flow Dynamics in Hypertrophic Cardiomyopathy," Tokyo, Japan. September 1978.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO. C-16-74

PRINCIPAL INVESTIGATORS: Peter S. Kennedy, MAJ, MC; Daniel Marmer, M.S., M.T. (ASCP)

ASSOCIATE INVESTIGATORS:

OBJECTIVES

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

TECHNICAL APPROACH

Patients with multiple platelet transfusions are evluated for the presence of antibodies. Multiple antibody procedures such as complement fixation, serotonin release assay and platelet aggregation assay are employed. The platelets identified as having iso-antibodies are further studied to see if sensitivity is selective to isolated random donor platelets. A method of freezing platelets for the serotonin release assay to give a standard assay approach utilizing a multiple donor pool has been established.

Personnel: None

Funding:

	Consumable Supplies
FY 78	-
FY 77	$ 532.00
FY 7T	$ 159.15
FY 76	$ 301.10
FY 75	$ 345.15

PROGRESS

The [^{3}H] platelet serotonin release assay is a sensitive means for detecting antiplatelet antibodies. We have found that by using prelabelled

C-16-74 (Continued)

frozen platelets which have been treated with the cryoprotective agent dimethyl sulfoxide (DMSO), the performance of this assay can be facilitated without interfering with its sensitivity. There was 100% correlation between the standard [^{3}H] platelet serotonin release assay using fresh platelets and the modified assay using prelabelled, frozen, cryopreserved platelets when sera from 12 patients with known antiplatelet antibodies were tested. When normal serum samples (n = 111) were tested against 10 platelet donors, a false positive rate of 3.9% was observed. This modification provides a simple means for quickly screening large numbers of potential platelet donors at one time.

Status: Completed.

Marmer, D.J., Bowman, R.P., and Kennedy, P.S. A simplified [^{3}H] serotonin release assay for the detection of platelet antibodies. Accepted for publication in the American Journal of Hematology.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-23-74

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

ASSOCIATE INVESTIGATORS: David R. Head, M.D., LTC, MC;
Richard E. Goyette, M.D., MAJ, MC

OBJECTIVES

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

TECHNICAL APPROACH

To establish the function of an individual platelet after platelet antibodies are identified. Platelet antibody studies have been established and are functional. A new technique has been developed for looking at low platelet function. To date this has been a significant problem in that many patients with platelet antibodies have very low platelet counts and the actual function is difficult to determine.

Personnel: None.

Funding:

	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	-
FY 75	-
FY 74	$ 196.00

C-23-74

PROGRESS

A method of looking at platelet function with low platelet counts has been established by using a collagen stimulation and counting platelet aggregates both before and after stimulation. A pilot study has been done which shows this procedure to be very efficacious and has shown no hindrance to platelet function in the presence of platelet antibodies.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Clinical Outpatient Algorithm Validation - A Pilot Study.

WORK UNIT NO.: C-9-75

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if clinical outpatient algorithms originally used to treat civilian outpatient populations can be validated and improved in a military outpatient environment - a phase I study.

TECHNICAL APPROACH

Using the standardized data base collections of algorithm-directed AMOSIST's coupled with a standardized outcome analysis at a fixed point following the index visit, data on large numbers of patients presenting to the BAMC Emergency Room/AMIC with a variety of common chief complaints are examined. In some instances randomly selected patients are reevaluated by staff physicians using this same data base in order to be able to compare the process of care of algorithm-directed AMOSIST's and traditionally directed physicians. Investigations to this point have concentrated on patients presenting with upper respiratory illness, back pain, headache, and extremity trauma.

Personnel: None

Funding:

	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	-
FY 75	$3,125.00

C-9-75 (Continued)

PROGRESS

The ability of non-physician providers to collect the data required by an algorithm for upper respiratory illness (URI) management, and the appropriateness of resulting key management decisions, were studied by comparing non-physician data and management decisions on 426 patients to those of internists. The internists, blinded to Amosists' findings and plans, evaluated the same patients and indicated management without using the algorithm (AM-MD Study). To control for variability of internists' data collecting and illness management, 171 additional patients were evaluated and managed consecutively by two internists each also kept unaware of the other's findings and plans (MD-MD Study).

Overall AM-MD agreement on history and physical findings (90% and 81%) and on the need for tests (84%) and treatment (87%) was as high as MD-MD agreement (91%, 80%, 88%, and 75%, respectively). In both studies, there was significantly more agreement on history data than on physical findings, evaluation, and therapy.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Measurement of Transepidermal Water Loss in Anhidrotic Ectodermal Dysplasia and Erythroderma.

WORK UNIT NO.: C-29-75

PRINCIPAL INVESTIGATOR: Robert L. Rietschel, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To measure total body evaporative water loss in skin conditions of excessive and insufficient transepidermal water loss and compare these values with measurements of water loss from small areas of skin.

2. To study the effect of various topical compounds in common dermatologic use on transepidermal water loss in individuals with excess or insufficient water loss.

TECHNICAL APPROACH

A stream of dry nitrogen gas is blown across the skin surface and then into an electrolytic moisture analyzer. The amount of moisture present is detected and expressed in $mg/cm^2/hr$.

Personnel: None.

Funding:	Consumable Supplies	MEDCASE	Rental
FY 78			$24.00
FY 77	-	-	$21.00
FY 7T	-	-	$ 5.25
FY 76	-	-	$21.00
FY 75	$ 255.95	$ 1,250.00	

PROGRESS

Only one patient with erythroderma was available for study. She responded to therapy so rapidly that test results could not be standardized.

C-29-75 (Continued)

Status: Ongoing.

Rietschel, R.L. A method to evaluate skin moisturizers in vivo. J Invest Derm 70:152-155, 1978.

Rietschel, T.L. and Wilmore, D.W. Heat loss in anhidrotic ectodermal dysplasia. J Invest Derm (in press).

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

INVESTIGATION PROJECT RESUME

TITLE: Quantitative Studies of Phagocytosis - the Use of Acridine Orange (AO) as an Indicator of Phagocytic Ingestion and Bactericidal Effects.

WORK UNIT NO.: C-9-76

PRINCIPAL INVESTIGATOR: Dennis L. Stevens, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To study the phagocytosis of polymorphonuclear leukocytes of acridine orange stained bacteria.

2. To develop a simple reliable assay of this process which will be amenable to clinical laboratory utilization.

TECHNICAL APPROACH

Acridine orange stained E. coli were fed to human granulocyte suspensions and the fluorescence spectra recorded at different incubation times. A new Aminco Bowman R136 photomultiplier tube was utilized.

Personnel: None

Funding:	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	$ 549.46

PROGRESS

Acridine orange fluorescence of bacteria ingested by human PMN_1 is dependent upon a) the pH of the phagolysosome, b) the concentration of the dye within the phagolysosome, and c) incubation time.

Since acridine orange, like gentamicin, is a basic anion, it is concentrated within acidic phagolysosomes at a rate proportional to the

C-9-76 (Continued)

(hydrogen ion) concentration difference between cytoplasmic and phagolysosome contents. The pH of the phagolysosome is dependent upon a) lactic acid accumulation, b) hydrogen pump (the inner layer of phagolysosome membrane is in fact derived from the outer aspect of the cell cytoplasmic membrane), and c) other hydrogen ion yielding reactions related to granulocytic-phagolysosome metabolism.

Thus, the change in visible fluorescence of ingested bacteria from green to orange cannot be construed as a loss of viability of the organism. Nevertheless, measurement of qualitative shifts in fluorescence (green to red) may well be a useful indicator of phagocytosis induced intracellular granulocytic microbicidal activity.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Glycerol Lysis Time as a Rapid Screening Measure for Red Cell Membrane Effects.

WORK UNIT NO.: C-15-76

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

ASSOCIATE INVESTIGATORS: John Posch, DAC

OBJECTIVES

1. To determine normal values of glycerol lysis time.

2. To determine if red cell membrane defects such as thalassemia and spherocytic anemias can be detected out of the range of normal.

3. To statistically evaluate the lysis curve and delineate the best and simplest points for correlating hemolysis to cellular defect.

4. To determine whether this test can be used as a rapid screening measure in a busy hematology clinic.

TECHNICAL APPROACH

Glycerol lysis time is being performed on a large number of patients to establish a number range of abnormalities.

Personnel: None.

Funding:

	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	$ 213.15

PROGRESS

It has been suggested that this test be utilized as a rapid screening test to differentiate patients with abnormal hemoglobinopathies and

C-15-76 (Continued)

thalassemia's from normals and those with iron deficiencies. A sizeable number of patients with these disorders have been identified in the Clinic and glycerol lysis time (GLT) curves have been determined on each as well as on a large series of normal controls. Our present results, although at variance with a previous report on similar patients, indicate that certain hemoglobinopathies (i.e., beta-thalassemia, sickle cell anemia, SC disease) demonstrate unusually high glycol lysis times. However, other milder hemoglobinopathies, such as sickle cell trait, alpha thallassemia, and Hgb AC trait, give variable results overlapping with normal and iron deficiency values. Other parameters including slopes, other times (i.e., GLT 25%, 75%, 90%, etc.), use of slightly different reagents, and comparison with CBC parameters were determined to select possible more helpful parameters in differentiating between these anemias. It has been determined that abnormal values do indicate the presence of one of the above disorders, and in some cases the specific abnormality can be differentiated by means of the glycerol lysis time and CBC results. In too many cases, however, these results are borderline or normal, and the usual laboratory work-ups utilized for diagnosis of hemoglobinopathies and iron deficiencies must be performed to detect and differentiate these anemias. This test, although an intersting test to augment other studies in the evaluation of red cell anemias, is not recommended as a routine screening tool as the results are not conclusive nor sufficient for diagnosis of such abnormalities.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Demonstration of a Testosterone Binding Protein in Semen.

WORK UNIT NO.: C-23-76

PRINCIPAL INVESTIGATOR: Albert Thomason, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate a testosterone binding protein in semen.

TECHNICAL APPROACH

Attempts are being made to demonstrate a specific binding protein by using polyacrylamide gel electrophoresis and radioactive testosterone. Two approaches have been used so far: 1. To add the radioactive testosterone to the semen before the electrophoresis and then to count consecutive sections of the gel to see if any of the sections contained high counts; and 2. To place the testosterone directly into the gel and subsequent to the electrophoresis to section the gel into consecutive equal segments.

Personnel: None.

Funding: None.

PROGRESS

Efforts to locate a specific protein band binding testosterone have been unsuccessful. The problem is thought to be mainly technical. It is planned to use some of the newer techniques of polyacrylamide electrophoresis in an attempt to isolate a testosterone binding peptide.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Heavy Metal Metabolism and Its Effect on Leukemias.

WORK UNIT NO.: C-1-77

PRINCIPAL INVESTIGATOR: Jerry Phillips, M.D.

ASSOCIATE INVESTIGATORS: Dan Marmer, M.S., M.T. (ASCP)

OBJECTIVES

To clearly define the cellular actions of zinc at a molecular level. Of particular interest are: 1) identification of the intracellular systems associated with zinc; 2) characterization of the mechanisms by which such systems are affected by zinc; and 3) both identification and characterization of systems in which zinc metabolism is abnormal, such as appears to be the case with leukemia lymphocytes.

TECHNICAL APPROACH

Human peripheral blood was obtained by venipuncture from healthy donors and from donors with chronic lymphocytic leukemia. Purified lymphocyte populations were assessed for viability by exclusion of trypan blue, for thymus-dependent (t) lymphocytes by the ability to form rosettes with sheep erythrocytes, and for thymus-independent (b) lymphocytes by the ability to form rosettes from sheep erythrocytes coated with antibody and complement.

To assay zinc uptake, 1.5×10^6 lymphocytes were suspneded in 1 ml. serum-free RPMI-1640 in culture tubes. Each culture received 10 g. (^{65}ZN)zinc transferrin. Finally, varying concentrations of either PHA or poly-L-ornithine were added. Cultures were incubated overnight at 37°C in a humidified atmosphere of 5% CO_2 in air. Incubations were terminated by addition of 2 ml. ice-cold PBS followed by centrifugation at 160xg for 10 minutes. The cell pellet was resuspended in 2 ml. ice-cold PBS and again centrifuged. This process was repeated one additional time. The final washed cell pellet was suspended in 2 ml. cold PBS and the cells collected by vacuum filtration. Radioactivity associated with the lymphocytes was then assessed. All cultures were run in duplicate.

Personnel: None.

Funding: None.

C-1-77 (Continued)

PROGRESS

The relative effects of PHA and poly-L-ornithine on zinc uptake differed between normal and CLL lymphocytes. The ratio, i.e. zinc uptake in poly-L-ornithine cultures/zinc uptake in PHA culture, appears to be characteristic for each of the lymphocyte populations used. For the normal donors this ratio is 1.9 ± 0.2, while the ratio is only 0.9 ± 0.3 for the CLL donors. Using Student's t-test, it was determined that the difference between these two ratios is statistically significant ($P < .001$). Additionally, lymphocytes from one donor with lymphoma and one donor with Hodgkin's disease were tested and the ratios of 3.4 and 2.8, respectively, were obtained.

It is proposed that this technique may be useful in the diagnosis of chronic lymphocytic leukemia as well as in the assessment of the efficacy of chemotherapeutic regimes.

Status: Completed at BAMC; Ongoing at University of Texas Health Science Center.

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

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Hemodynamic Effects of Angiographic Contrast Material with Dynamic and Static Exercise.

WORK UNIT NO.: C-3-77

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

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the usefulness of postangiographic hemodynamic data in assessing left ventricular function by comparison with the effects of standard forms of left ventricular stress in the cardiac catheterization laboratory.

TECHNICAL APPROACH

Following left ventriculography performed at the time of cardiac catheterization, serial measurement of the following parameters was made: pulmonary capillary wedge, pulmonary arterial, right ventricular, right atrial, left ventricular, and aortic pressures; serial thermal dilution cardiac outputs; pulmonary artery and aortic flow velocity signals. These parameters were then compared to those obtained in the resting and steady exercise states. In order to carry out the project, a special high fidelity left ventricular injection catheter has been designed.

Personnel: None.

Funding: None

PROGRESS

At this point, the project has been delayed because of design and performance problems with the special high fidelity injection catheter.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Modified Time-Motion Study of Outpatient Flow at BAMC AMIC

WORK UNIT NO.: C-5-77

PRINCIPAL INVESTIGATOR: Richard A. Call, II, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Barry W. Wolcott, M.D., LTC, MC

OBJECTIVES

1. To determine the various processing linkages, service times, waiting times, routes, patient types, and staffing for treating patients in the general, adult, non-appointment AMIC at BAMC.

2. To provide analysis of operations of the AMIC utilizing a modified time and motion study and data reduction procedures developed by the Indian Health Service.

3. To suggest modifications in ER/AMIC medical process to provide more medically effective care with current resources.

4. To compare these process aspects at BAMC with those of other civilian and governmental clinics with similar missions but differing structure.

TECHNICAL APPROACH

Using a protocol developed by the Indian Health Service, time clocks were placed at all patient care stations within the ER/AMIC. Data were collected on 1800 patients presenting to the ER/AMIC during a one week period. The method of data collection allowed calculation of both cueing time and service time at each station throughout the ER/AMIC system. The data are entered into a computer; the program allows for search by time of patient arrival, day of patient arrival, complaint at time of arrival, initial care provide, and a variety of other variables.

Personnel: None

Funding None

C-5-77 (Continued)

PROGRESS

After collection of the initial time-motion data and its analysis, it was decided to terminate the study. In view of this, the simulation computer programs were not used.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: The Mechanism of the Modulation of Lymphocyte Functions by Complement.

WORK UNIT NO.: C-6-77

PRINCIPAL INVESTIGATOR: Michel Laham, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Joseph C. Greene, SFC

OBJECTIVES

Previous work done in collaboration with Drs Richard Panush and Jacques Caldwell at the University of Florida has demonstrated that in vitro responses of human peripheral blood lymphocytes (PBL) to mitogens, as measured by the uptake of labelled thymidine (3HTdR), were significantly decreased in the presence of human Complement (C) components C_1, C_4, and C_2. The purpose of this project is to study the mechanism of this inhibition of lymphocyte functions by C.

TECHNICAL APPROACH

During my first year of research here at BAMC, SSG Hartley Selfridge was designated to help me in my research endeavors. After many delays, we got in at most 2-3 months of good research, during which we confirmed some of the data I had obtained earlier at the University of Florida. We were also able to perfect the technique of T and B cell separation by differential rosette formation and Ficoll-Hypaque sedimentation. There were some glaring problems, however, with the mitogen stimulation data.

First, when comparing the dose responses of cells cultured in the presence and absence of complement, we were forced to plate both together on the same microtiter plate, because we were having poor reproducibility from one plate to another. Secondly, we had very little internal consistency with quadruplicate cultures showing standard deviations of 30-40%.

When SFC Joseph Greene arrived to replace SSG Selfridge, no provisions were made for any overlap. Although a proficient and experienced technician, SFC Greene had had no previous exposure to the techniques of cellular immunology. So, we had to start "from scratch". That it took us only 6 months to begin putting out meaningful data is a tribute to SFC Greene's abilities, since it normally takes at least a year.

C-6-77 (Continued)

In the process, we achieved good plate-to-plate reproducibility. That has allowed us to plate dose-responses for comparison in identical positions on two different plates. That, in turn, has eliminated the built-in column-to-column variability as one moves from one side of the plate to the other with the cell harvester.

We also achieved good internal consistency with standard deviations for each quadruplicate culture in the range of 10-15%. This was done mainly by switching to a newer model harvester, the M-12 Victor by Brandel. This new harvester, unlike the older model, delivers the saline wash to each individual well, through a manifold under pressure from a solenoid-activated water-pump.

Personnel: 1 SFC (12 mos)

Funding:	Consumable Supplies
FY 78	$1,257.30
FY 77	$1,275.10
FY 7T	$ 447.00

PROGRESS

The results we have since obtained are solid, with differences between complement-free cultures and C_{142}-treated cultures significant in the order of $P < .001$. We have shown conclusively that at high-close mitogen, C_{142} together enhance lymphocyte responses and delay high-dose tolerance. This effect is dependent upon the enzymatic activity of the complement since heat-inactivated C_{142} do not affect the lymphocytes' responses.

At low doses of mitogen, the effect of complement becomes less apparent and it does not affect the lymphocytes' spontaneous unstimulated uptake of labelled thymidine. Some of our experiments actually show inhibition of responses at low-dose mitogen. This implies a steady-state modulation of the lymphocytes' activity and a marked potentiation of their responses when stimulated. Our results fit in with earlier reports by Good and Azar that depletion of the terminal components of complement with cobra venom increases the lymphocytes' responses to mitogens and antigens.

Our present purpose is to systematically investigate the observed phenomenon. This will be done as follows:

1. Determine whether this effect of C_{142} persists when the cells are washed after incubation with complement, then exposed to mitogen.

C-6-77 (Continued)

2. Determine the critical concentration of C_{142} required by dose-responses for all three together and for each one separately.

3. Study the kinetics of the reaction by harvesting cells at 24, 48, 72, 96 and 120 hours of incubation, respectively.

4. Finally, observe the effect of complement on separated populations of T and B cells.

It is anticipated that we can achieve all of the above within 6-8 months.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: The Use of Lyophilized Homografts for Creation of AV Fistula in Dialyzed Patients.

WORK UNIT NO.: C-10-77

PRINCIPAL INVESTIGATORS: Richard H. Merrill, M.D., LTC, MC;
Bruce S. Jarstfer, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether a more effective and less expensive dialysis access procedure can be developed.

TECHNICAL APPROACH

Lyophilized homografts are to be compared against the standard bovine xenograft for creation of A-V fistula in patients requiring chronic hemodialysis. The patients are randomized and the physicians caring for the patient are blinded as to the exact appliance used. All fistula undergo weekly evaluation for dysfunction.

Personnel: None.

Funding:	Consumable Supplies
FY 78	-
FY 77	$ 133.70

PROGRESS

Twenty-three patients with end-stage renal failure were entered into a single blind study utilizing the bovine (B) xenograft (12 pts.) or a saphenous (S) vein (11 pts.) harvested from cadaveric sources and lyophilized. In group B, the longest follow-up to date is 139 weeks with an average graft function of 57 weeks (range 27-139 weeks). In group S,

C-10-77 (Continued)

the longest follow-up is 95 weeks with an average of 46 weeks (range 11-95 weeks) graft function.

There were eight complications in seven patients in the B group (seven thromboses and one aneurysm); five of the eight were surgically corrected, seven complications (seven thromboses) in five patients occurred in the S group; three of the seven were surgically corrected. The average time from insertion to first complication in group B was 24 weeks (range 3-50 weeks); 43 weeks (range 11-95) in group S. The interval between first use for vascular access the first complication was 20 weeks (range 3-50 weeks) in group B and 33 weeks (6-94 weeks) in group S. Two grafts in group B and two in group S have not yet been used for hemodialysis. One patient in group S was lost to follow-up.

These results indicate that the readily available lyophilized cadaveric graft is an acceptible substitute for current commercial products.

Status: Completed.

Presented at the Southeastern Dialysis and Transplantation Association meeting.

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

INVESTIGATION PROJECT RESUME

TITLE: Antibody Titer Response to Swine Influenza Immunization in an Oncology Population.

WORK UNIT NO.: C-11-77

PRINCIPAL INVESTIGATOR: Richard A. Shildt, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Dan W. Luedke, M.D., MAJ, MC; Michel N. Laham, M.D., MAJ, MC: George Kasai, Ph.D., DAC

OBJECTIVES

1. To compare antibody titer response of a population of oncology patients who receive swine influenza immunization with that of normal controls and immunosuppressed patients without malignant disease.

2. To correlate the antibody titer response with immunoglobulin levels and lymphocyte counts.

3. To compare the morbidity of influenza immunized oncology patietns with normal controls and immunosuppressed patients without malignant disease.

4. To record the incidence of respiratory tract and swine influenza illnesses in our immunized population.

TECHNICAL APPROACH

At the time of immunization, 10 cc of blood were collected and the sera analyzed for swine influenza antibody titers. Twenty initial samples were sent to the Virology Lab for complement fixation and hemagglutination titer determinations. Three and nine weeks after inoculation a second and third sample was collected and evaluated for the factors mentioned above.

The participants were given typewritten instructions on how to report the side effects of the inoculation and were asked to report any viral illnesses they develop during the "flu" season (from inoculation to April). Viral illness was defined as any respiratory symptom complex. The participant was examined and interviewed by one of the investigators and a throat culture for virus obtained. A serum sample was drawn three weeks after the illness and examined for a rise in swine influenza antibodies.

Personnel: None.

Funding: None.

C-11-77 (Continued)

PROGRESS

Eighty-two patients with solid tumors and lymphomas were immunized with New Jersey, Hong Kong and Victoria influenza vaccines. Patients were divided into groups according to treatment: chemotherapy, radiotherapy or no treatment. Four parameters were examined to assess the response to immunization: sero-conversion, protective titer level, geometric mean titer, and response to multiple vaccines. Patients with lymphoma showed the lowest antibody response. Patients with solid tumors had antibody responses which were not significantly different from controls but were superior to lymphoma patients ($p < .01$). Timing of chemotherapy, immunoglobulin levels, and lymphocyte counts did not appear to play a major role in determining the antibody response. Patients with neoplastic diseases should be immunized against the prevailing influenza virus. Patients with lymphoma should also receive antiviral prophylactic therapy during influenza epidemics.

Conclusions: Influenza immunzation of patients with malignant disease is recommended. Protective antibody titers would be expected in 80-90% of solid tumor patients and in patients receiving radiation therapy, but only in 30-40% of lymphoma patients. The side-effects are not prohibitive and should not prevent immunization of patients with low sero-conversion rates. However, one should consider additional antiviral prophylactic therapy, such as amantadine, in patients with lymphoma.

Status: Completed.

Shildt, R.A., Luedke, D.W., Kasai, G., El-Beheri, S., and Laham, M.: Antibody response to influenza immunization in adult patients with malignant disease. Submitted to Cancer.

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

INVESTIGATION PROJECT RESUME

TITLE: A Prospective Study of the Usefulness of the Chest X-ray in Evaluating Patients with Acute Cough.

WORK UNIT NO.: C-19-77

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Staff, General Medicine Service

OBJECTIVES

To determine if the use of the chest x-ray is cost-effective in the evaluation of ambulatory patients presenting with an acute cough at BAMC; to determine the value of clinical signs and symptoms and the clinician's judgment, in predicting the presence of infiltrate on chest x-ray; and to compare cough patients evaluated with a chest x-ray with cough patients evaluated without a chest x-ray, in terms of clinical outcome and the cost of care.

TECHNICAL APPROACH

Patients presenting to the ER/AMIC whose reasons for seeking evaluation include a cough are candidates for the study. After obtaining informed consent, these patients are examined by a research assistant who uses a check sheet to establish a uniform history of the present illness and past medical history. They are then evaluated by a staff physician who performs a standardized and defined physical examination and makes judgments concerning the necessity for a chest x-ray at the time of this visit. All patients are x-rayed and the x-rays are randomly shown or not shown to the staff physician. Patients are discharged home on the medical care prescribed by the staff physician and in a pre-defined period following the index visit the patients are contacted to obtain outcome and satisfaction data. All data are entered into a computer.

Personnel: None

Funding: None

PROGRESS

To date 1,750 patients have been entered into the study. Analysis of early data indicate that the chest x-ray results do not alter the care process of the attending physician.

C-19-77 (Continued)

Status: Ongoing.

Wolcott, B.W. A Study of the Usefulness of the Chest X-ray in Evaluating Patients with Acute Cough. Presented at the Association for Clinical Investigation meeting, 1978.

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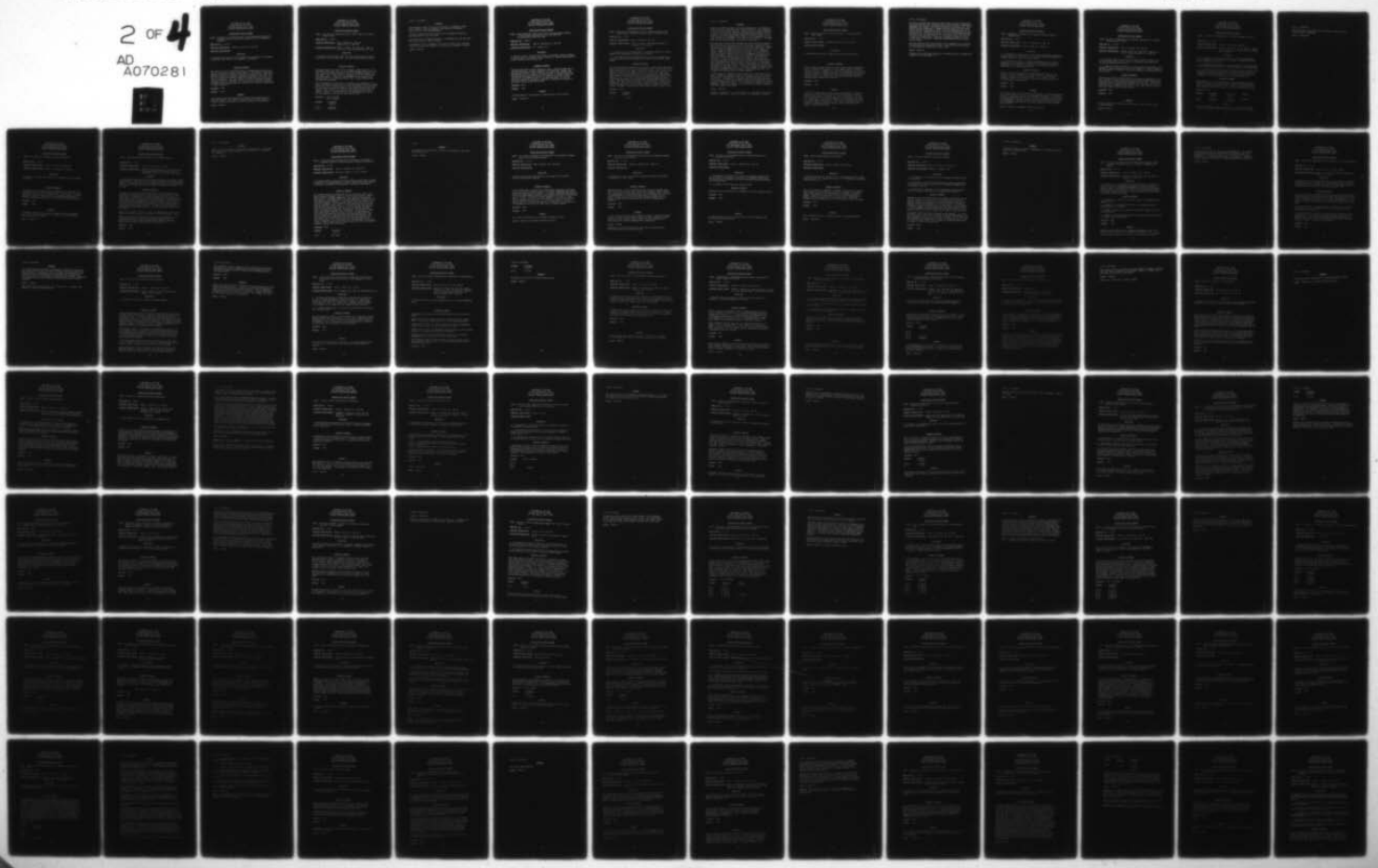

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of the Effectiveness of Oral Methoxsalen Followed by Longwave Ultraviolet Light (UVA 320-400 nm) in the Treatment of Psoriasis.

WORK UNIT NO.: C-23-77

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of 8-methoxypsoralen (methoxsalen) and longwave ultraviolet light (PUVA) in the treatment of psoriasis.

TECHNICAL APPROACH

The patient is given a prescribed dosage of 8-methoxypsoralen two hours prior to long-wave ultraviolet light exposure. The amount of light energy applied to the skin is gradually increased to obtain clinical clearing of the skin disease and to promote pigmentation (tanning) of the skin. The eyes are protected by special ultraviolet glasses that block out penetration of ultraviolet. The light dosage is carefully regulated to prevent a sunburn reaction of the skin. All patients receive initial laboratory screening studies and ophthalmologic evaluation and follow-up examinations at regular intervals.

Personnel: None.

Funding: None.

PROGRESS

Forty patients have been treated by this method with generally good to excellent results. New patients are entered into the study based on clinical condition and extent of disease as outlined in the protocol.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: The Toxicity of Aminoglycosides to Kidney Tumor Cell Lines in Tissue Culture.

WORK UNIT NO.: C-26-77

PRINCIPAL INVESTIGATOR: Dan W. Luedke, M.D., MAJ, MC
James Boyd, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC: James J. Plitt, M.S., SSG, Deborah Hunter, B.S., SP5

OBJECTIVES

To establish various kidney tumor cell lines *in vitro* and to test the efficiency of kill of these tumor lines with various aminoglycosides.

TECHNICAL APPROACH

Four kidney tumor cell lines will be obtained. These lines are: 1) an autonomous kidney tumor line, 2) an estrogen-dependent kidney tumor cell line, 3) the estalished line BHK-21, and 4) an epithelial kidney cell line (HAK). All of these lines are malignant and all are derived from the Syrian hamster. They will be established in our laboratory and characterized as to population doubling times, cloning efficiencies, and saturation densities.

We will determine the cytotoxicity of gentamicin and paromomicin in log phase cells and in resting cells. Toxicity measurements will be performed by the usual colony counting method. After incubating cells with antibiotics, viable colonies are fixed and stained with crystal violet and counted. These in turn are compared to untreated controls to give a survival fraction. Concentration and time dependenceof the toxicity will be examined for each drug in each line of cells.

Personnel: 1 SSG (9 months)
1 SP5 (4 months)

Funding:

	Consumable Supplies
FY 78	$3,801.69
FY 77	$1,414.00

C-26-77 (Continued)

PROGRESS

The synergistic effect of urea on the toxicity of Gentamicin, using K.B.E. (kidney) cells, was studied. The toxicity of Gentamicin alone on K.B.E. cells was established.

By itself, Gentamicin in the concentration of 1500μg/ml reduced the cell population to 52% in 72 hours.

The toxicity of urea alone was studied. At 1000 mg% urea, the cell population was reduced to 49% in 72 hours.

A synergistic effect of Gentamicin and urea is noted for all concentrations of urea, when the Gentamicin concentration is 500μg/ml or greater.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Tumor Immunology - Multi-test Device with Standardized Antigens to Assay Delayed Hypersensitivity Via the Skin Test. (Collaboratorive Study with UTSA)

WORK UNIT NO.: C-28-77

PRINCIPAL INVESTIGATOR: James R. McDonald, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: W. T. Kniker, M.D.

OBJECTIVES

To carry out initial clinical skin testing of individual "Recall" antigens on healthy adults to establish safety and degree of delayed hypersensitivity using a new multi-test delivery unit.

TECHNICAL APPROACH

The multi-test device contains eight test sites. Antigens being used include Streptokinase, Tetanus, Diphtheria, Old Tuberculin, Candida, and glycerinated controls. These substances are used in two concentrations. The complete set of antigens at low concentration is applied to the right forearm, and the higher concentration is applied to the left forearm. The patient is evaluated at four to six hours and again at 24 and 48 hours for evidence of erythema or induration. Induration is measured in millimeters in two planes and recorded.

Personnel: None

Funding: None

PROGRESS

Following change of investigators, no work was done on this project.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: Histologic Characterization of Early Adriamycin-induced Soft Tissue Injury - Possible Therapeutic Role of Glucocorticoids.

WORK UNIT NO.: C-29-77

PRINCIPAL INVESTIGATOR: Dan W. Luedke, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Robert W. Rietschel, M.D., MAJ, MC

OBJECTIVES

1. To characterize the histopathology of Adriamycin-induced soft tissue damage after subcutaneous extravasation in rabbits.

2. To determine whether the adminisatration of local or systemic glucocorticoids concurrent with Adriamycin will modify resultant soft tissue damage.

TECHNICAL APPROACH

Two adult male rabbits were used for the study. After shaving the animals' backs, each rabbit was injected intradermally with 0.1 ml of freshly prepared Adriamycin solution (Adria Laboratories, Milan, Italy, final concentration 1.0 mg/ml). The animals received a total of nine injections, spaced at 3 cm. intervals and a saline control injection. Subsequently, full thickness 4 mm. punch biopsies of the Adriamycin injected site were taken at 2, 6, 12, 24, 48, 72, 96, and 168 hours following injection. A final biopsy was taken at three weeks when ulceration was clinically apparent. The saline control injection site was biopsied two hours after application. Each injection site was biopsied only once. Specimens were transferred immediately to 10% formalin fixative, embedded in paraffin blocks, sectioned, and stained with hematoxylin-eosin in routine fashion.

Personnel: None

Funding:	Consumable Supplies
FY 78	$ 32.00

C-29-77 (Continued)

PROGRESS

Grossly, the lesions evolved slowly and undramatically. The characteristic red color of Adriamycin was visible through the intact epidermis for up to 96 hours after injection. Within 24 hours, a papule developed at the site of injection, persisting throughout the duration of the experiment. The overlying epidermis remained essentially normal for the first 96 hours with subsequent development of dry desquamation and ulceration evident at three weeks. At no time was there evidence of inflammation, nor was there evidence of infection in any lesion.

Microscopically, the earliest findings were vasodilation and sludging of red blood cells noted at two hours after injection. Between 48 and 72 hours, the vascular endothelium began to show early degenerative changes, and there were extravasated red blood cells in the deeper dermal structures. During this same interval, early necrobiosis of collagen was evident, without concomitant cellular infiltrate. At no time did we observe a leukocytoclastic vasculitis or inflammatory infiltration of dermal structures. Between four and seven days after Adriamycin injection, the epidermis became necrotic and ulcerated. Hair follicles atrophied. A crust of polymorphonuclear leukocytes had formed over the surface epithelium and the superficial dermal vessels were dilated with polymorphonuclear leukocytes and red blood cells. No inflammatory cells were seen in the reticular dermis. Extravasated red blood cells were common in the upper dermis. The reticular dermis was acellular and contained no normal blood vessels. The area resembled an ischemic necrosis with no inflammation and virtually no blood vessels present. The collagen was acellular and had a spongy appearance.

At three weeks, the epidermis, where present, was covered with a thick crust. Acanthosis, spongiosis and areas of necrosis were still evident. The vessels of the papillary dermis were engorged and filled with red blood cells. Fibroblasts were commonly seen in the superficial dermis. In the reticular dermis the fibroblastic response was diminished; unlined vascular channels were present. The collagen had a thickened, sclerotic appearance. While extravasated red blood cells were common, inflammatory cells were conspicuously absent.

Status: Completed.

Luedke, D.W., Kennedy, P.S. and Rietschel, R.L. Adriamycin induced skin necrosis. Submitted to Journal of Plastic and Reconstructive Surgery.

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

INVESTIGATION PROJECT RESUME

TITLE: Immune Deficiency in Dialyzed Patients: A Chronic Model of Acute Trauma

WORK UNIT NO.: C-32-77

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

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the etiology of immune depression in renal failure.

TECHNICAL APPROACH

Patients with end-stage renal failure were monitored using immunologic tests to determine the integrity of their immune system. The tests included T and B cell enumeration, chemotaxis, immunoglobulin determinations, skin-window, lymphokine production, blastogenesis, ingestion and killing of bacteria. These results were correlated with the length of time on dialysis, and compared with patients with various degrees of end-stage renal failure not on dialysis.

Personnel: None

Funding: None.

PROGRESS

It has been assumed that the depressed cellular immunity in patients with chronic renal failure is due to some "uremic toxin". However, there are many groups of patients and clinical situations that result in a depression of cell mediated immunity but with normal renal function; among them protein-calorie malnutrition and phosphate depletion. If a uremic toxin is responsible, rather than a deficiency state, the presence of depressed cellular immunity should correlate with the degree of renal insufficiency.

C-32-77 (Continued)

Forty-three patients with end-stage renal disease on chronic hemodialysis and fifteen patients with varying degrees of renal failure on conservative management were studied. Neutrophile chemotaxis was assayed, and T and B lymphocytes were enumerated. B lymphocytes were similar in both groups and not different from normals, while T cells were depressed only in the dialysis group. Chemotaxis was normal in the non-dialysis group, but was depressed in the patients on dialysis. There was no correlation between serum creatinine and chemotaxis in the non-dialysis group, but there was a tendency for chemotaxis to become more abnormal as length of time on chronic dialysis increased. Complement and immunoglobulins were normal in both groups.

This data indicates that the depressed cellular immunity seen in patients with end-stage renal disease may be due to protein-calorie malnutrition or other deficiency rather than a uremic toxin.

Status: Completed.

Presented at the 10th Annual Meeting of the American Society of Nephrology November 1978 in Washington, D.C.

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

INVESTIGATION PROJECT RESUME

TITLE: Management of Patients with a Metastatic Adenocarcinoma of Unknown Origin.

WORK UNIT NO.: C-34-77

PRINCIPAL INVESTIGATOR: Peter S. Kennedy, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine the individual yield of various diagnostic procedures in finding the site of tumor origin in patients who present with metastatic adenocarcinoma with no obvious primary source.

2. To assess the efficacy of combination chemotherapy in palliative management of this disease as demonstrated by the percent of patients showing objective response to treatment, and by survival duration of responding vs. non-responding patients.

TECHNICAL APPROACH

Patients with adenocarcinoma from an unknown primary source are put through a series of diagnostic screening studies in an attempt to establish a diagnosis of the primary tumor. If no primary is found, treatment is begun using a 3-drug regimen which includes fluorouracil, cyclophosphamide, and adriamycin.

Personnel: None

Funding: None

PROGRESS

Eight patients have been treated with this regimen. Five have demonstrated an objective response. Five of six responding patients are alive; median survival for this group has not been reached at six months. All patients have demonstrated vomiting, alopecia and marrow suppression requiring drug dose adjustments. This protocol has been accepted for group-wide study by the Southwest Oncology Group, and further progress will be reported under SWOG 7717.

Status: Ongoing as a Southwest Oncology Group study.

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

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Radiotherapy on Regional Lung Function in Patients with Bronchogenic Cancer.

WORK UNIT NO.: C-36-77

PRINCIPAL INVESTIGATOR: Peter S. Kennedy, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Stephen Sorgen, M.D., MAJ, MC; A. Baker, M.D., LTC, MC; Charles Brearley, M.D., MAJ, MC

OBJECTIVES

1. To evaluate regional lung function in patients with localized, unresectable bronchogenic cancer by means of radionuclide lung scans, plus selected pulmonary function tests.

2. To compare regional lung function in patients before and serially after therapeutic super voltage irradiation in an attempt to correlate changes in RLF with response to treatment, respiratory symptoms, local disease control, and survival.

TECHNICAL APPROACH

Patients with unresectable bronchogenic cancer who are candidates for primary treatment by cobalt irradiation undergo Xenon-Technesium Ventilation-Perfusion lung scans and selected pulmonary function tests. These studies along with clinical evaluation and standard P.A. chest x-ray will be repeated serially. Changes in the results of these tests will be correlated with tumor response and recurrence patterns.

Personnel: None

Funding: None

PROGRESS

Patients continue to be entered into this study. Data on early entries is being analyzed.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Electronic Size Measurements of Platelet Aggregates in Blood.

WORK UNIT NO.: C-37-77

PRINCIPAL INVESTIGATOR: Peter S. Kennedy, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: David R. Head, M.D., LTC, MC; Robert P. Bowman, M.D., LTC, MC; A. O. Brossoit, SP5; Dan Marmer, M.S., MT (ASCP)

OBJECTIVES

1. To establish a normal range of values for the size distribution of platelet aggregates formed in vitro in response to aggregating agents ADP, epinephrine and collagen.

2. To investigate the usefulness of Coulter methods in evaluating platelet function in patients who have a platelet count less than $100,000/mm^3$.

3. To determine the effects of selected cytotoxic agents including nitrogen mustard, Adriamycin, vincristine, actinomycin-D, vinblastine and mitomycin-C on platelet function in man as they may relate to the development of local venous thrombosis at the drug infusion site.

TECHNICAL APPROACH

Measurements of the size distribution of platelet aggregates formed in vitro in response to various aggregating agents using an electronic particle counter are determined. This represents a rapid, high resolution, quantitative whole blood assay for evaluating platelet function.

Personnel: None

Funding:	Consumable Supplies	Contractual Services	MEDCASE
FY 78	$1,225.62	$ 974.50	$3,900.50
FY 77	$ 216.60	$ 2,375.00	

PROGRESS

With the acquisition of the calculator with the interface compatible with the Z-1H Coulter counter we were quite successful in evaluating

C-37-77 (Continued)

platelet function. The study will be continued in private practice by the principal investigator.

Status: Transferred.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Eosinophilia in Dialysis Patients.

WORK UNIT NO.: C-42-77

PRINCIPAL INVESTIGATOR: Richard A. Stor, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Paraic J. Mulgrew, M.D., LTC, MC

OBJECTIVES

To attempt to elucidate the incidence of eosinophilia in the dialysis population.

TECHNICAL APPROACH

All patients in the dialysis unit were evaluated for the presence of eosiniophilia using latest eosinophil count. Various causes of eosinophilia were looked for and an immunologic screen was done. An attempt was made to correlate the presence of eosinophilia with different machines, equipment, medications, disease process and time on dialysis.

Personnel: None.

Funding: None.

PROGRESS

Eosinophilia continues to be present intermittently in approximately 60% to 70% of dialysis patients here at BAMC. No etiologic factors have been found to this date.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Algorithm Directed Troop Medical Care (ADTMC) Project.

WORK UNIT NO.: C-46-77

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: William H. Bell, MAJ, MSC; 1st Cavalry Division Surgeon and Staff, Fort Hood, TX; Staffs of Troop Medical Clinics 5, 7, and 8, Fort Hood, TX

OBJECTIVES

To take existing algorithm directed triage and health care delivery systems, adapt them to a combat arms troop environment, and test the hypothesis that medical treatment/return to duty of soldiers who need to be seen at military sick call can be expedited with no decrease in the quality of medical care provided.

TECHNICAL APPROACH

In Phase 1 of the project, Brooke Army Medical Center-validated triage algorithms will be modified for use in one of the two divisions at Fort Hood, Texas. Following the collection of background data on the sick call process in both the test and control divisions, an algorithm directed triage system will be implemented in the test division. The effects of this system will be measured through the use of time clocks and comparison with the previous system as it existed in the test division and as it still exists in the control division. The total sick call time will be measured using methodology modified to fit the two-division structure at Fort Hood.

Phase 2 of the project involves the use of validated acute care clinical algorithms by military physician extenders in the Troop Medical Clinics.

Phase 3 of the project involves the preparation and implementation of algorithmic protocols for periodic review and evaluation of active duty military personnel with documented chronic medical conditions (hypertension, diabetes, pseudofolliculitis barbae, etc.)

Personnel: None.

Funding: None.

C-46-77 (Continued)

PROGRESS

Many difficulties have been encountered with this project. At the present time, we are trying to determine the feasibility of continuation vs. termination.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Tetracycline-induced Ultraviolet Fluorescence of Pathologic Pulmonary Tissues as Viewed Through the Fiberoptic Bronchoscope.

WORK UNIT NO.: C-1-78

PRINCIPAL INVESTIGATOR: Alvin J. Schonfeld, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: William W. Burgin, Jr., M.D., COL. MC

OBJECTIVES

To establish whether *in vivo* tetracycline labeling can be used to aid the endoscopist in locating pathologic pulmonary tissues when viewed through a fiberoptic bronchoscope incorporating an ultraviolet light source.

TECHNICAL APPROACH

The standard fiberoptic bronchoscope with an ultraviolet light source passed through the biopsy channel of the scope will be used. Areas of the lung will be examined segmentally, first using the incandescent light source. If abnormal areas are noted, these will be biopsied using the standard biopsy technique. If no abnormal areas are noted in any particular segement. The incandescent light source will be turned off and the ultraviolet light source will be turned on and the area again examined with the new light source. should an abnormal area then appear, then the ultraviolet light source will be removed, and under direct visualization through the bronchoscope, the area will be biopsied, again using a standard biopsy technique. Following biopsy of the lesion which previously fluoresced, the ultraviolet light source will be reinserted to insurethe proper area has been biopsied. The patients will be pre-treated for four days with 250 mg tetracycline four times a day, and the medication will be discontinued one day prior to endoscopy. It is anticipated that discontinuance of the medication at least 24 hours prior to the procedure will allow only abnormal tissues to retain their fluorescence.

Personnel: None.

Funding:	Contractual Service
FY 78	$11,578.00

C-1-78

PROGRESS

No progress has been made due to delays in fabrication of the ultraviolet light source.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Are Cirrhotic Patients at Increased Risk for Bacteremia Following Upper Gastrointestinal Endoscopy?

WORK UNIT NO.: C-4-78

PRINCIPAL INVESTIGATOR: Hugh P. McElwee, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To define the frequency and duration of bacteremia in the cirrhotic patient following oral endoscopy.

TECHNICAL APPROACH

Fifty patients with a clinical and/or histological diagnosis of cirrhosis of the liver and 50 patients without liver disease undergoing upper gastrointestinal endoscopy will be studied. A complete esophagogastroduodenoscopy will be performed whenever possible and performance and site of any biopsies will be recorded. Blood will be drawn immediately (1-5 min.), 10 min., 30 min., 2 hrs., and 4 hrs. after the procedure. Blood will be injected into an anaerobic blood culture. At 24 hours and on days 7 and 21, a sample from each bottle will be subcultured aerobically and anaerobically. All organisms recovered will be identified by standard methods.

Personnel: None.

Funding: None.

PROGRESS

This study was transferred to Fitzsimons Army Medical Center.

Status: Ongoing at Fitzsimons Army Medical Center.

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

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Sodium Nitroprusside Infusion on Hemoglobin Oxygen Carrying Patterns in Man.

WORK UNIT NO.: C-5-78

PRINCIPAL INVESTIGATOR: Stephen H. Humphrey, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the effect of sodium nitroprusside infusion on the ability of hemoglobin to carry oxygen.

TECHNICAL APPROACH

Immediately prior to and at intervals during sodium nitroprusside infusion, 7 milliliter arterial blood samples were obtained. These aliquots were then assayed for total hemoglobin by the cyanmethomoglobin technique, for methemoglobin by standard spectrophotometric technique, and for oxygen carrying capacity after 20 minutes tonometry against room air. Oxygen carrying capacity is measured with the Van Slyke manometric apparatus.

Personnel: None.

Funding: None.

PROGRESS

To date, three patients have been completely studied. Decrease in oxygen carrying capacity has been observed in each patient ranging from 10-21%. Changes in oxygen carrying capacity appear related to infusion rate. There has been no change in methemoglobin concentration.

Status: Ongoing

Presented at the 7th Annual Association of Army Cardiology Meeting, Walter Reed Army Medical Center, May 1978.

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

INVESTIGATION PROJECT RESUME

TITLE: Minoxidil as an Anti-Hypertensive in Patients Refractory to Available Medications.

WORK UNIT NO.: C-6-78

PRINCIPAL INVESTIGATOR: Paraic J. Mulgree, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if minoxidil is an effective alternative treatment for patients whose blood pressure is refractory to available drugs or who have experienced unacceptable side effects from them and whose situation is life-threatening.

2. To document clinical experience with this drug.

TECHNICAL APPROACH

Minoxidil will be administered as recommended by the drug company protocol.

Personnel: None.

Funding: None.

PROGRESS

One patient with refractory hypertension was placed on Minoxidil with excellent hypertensive control.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Systolic Hypertension in the Elderly.

WORK UNIT NO.: C-7-78

PRINCIPAL INVESTIGATOR: Lucius F. Wright, M.D., CPT, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the benefits and the risks of treating pure systolic hypertension (systolic BP > 160 mm Hg; diastolic BP < 90 mm Hg) in an elderly population aged 65 to 74.

TECHNICAL APPROACH

This is a prospective, randomized, unblinded clinical trial of hypotensive therapy. Subjects will be stratified on the basis of existing target organ damage and then randomized into treatment and control groups. Controls will be matched to insure an even distribution of smokers and obesity relative to the treatment group. Fifty-five patients will be included in each area for a total of 220 in the study.

Personnel: None.

Funding: None.

PROGRESS

Study terminated because of inadequate numbers of eligible patients.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: Serum ACTH Levels in Lung Cancer Patients.

WORK UNIT NO.: C-10-78

PRINCIPAL INVESTIGATOR Merrill S. Kies, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Sherwyn L. Schwartz, M.D.

OBJECTIVES

1. To determine if serum ACTH levels are abnormally elevated in lung cancer patients.

2. To determine if elevated serum ACTH levels correlate with disease recurrence in lung cancer patients who have undergone attempted curative surgical resection.

3. To determine if serum ACTH levels correspond to clinical disease activity in patients with oat cell carcinoma treated medically.

TECHNICAL APPROACH

ACTH levels in two groups of lung cancer patients and controls will be studied. Group A will consist of 20 consenting patients with histologically proven oat cell carcinoma of the lung. Group B will be composed of 20 patients considered for definitive surgical treatment of suspected or proven primary non-oat cell lung cancer. If no malignancy is found at surgery, the patient will enter the control group. Group C will be composed of patients undergoing exploratory thoracotomy for suspected lung cancer who at surgery are not found to have lung cancer.

Pretreatment ACTH levels will be obtained on all patients. In Group A patients, a second assay will be obtained if the patient achieves a complete remission of all clinical evidence of disease. Serial ACTH levels will thereafter be obtained every 2 months until relapse occurs. Group B patients will have ACTH levels performed at 4 weeks postoperatively and, again if clinical relapse occurs.

Personnel: None.

Funding: None.

C-10-78 (Continued)

PROGRESS

The study will begin as soon as arrangements are finalized for determination of the ACTH levels.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Bacterial Antibiotic Resistance Mediated by Plasmids - Demonstration and Characterization of Plasmids as Epidemiologic Markers.

WORK UNIT NO.: C-13-78

PRINCIPAL INVESTIGATOR: Francis O'Donnell, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., MAJ, MC

OBJECTIVES

To document the role of plasmids in mediating antibiotic resistance in clinical isolates of Klebsiella pneumoniae and other gram negative bacteria, and to characterize the plasmids in terms of molecular weight using agarose gel electrophoresis, with a view to using such information in the epidemiologic study of serious nosocomial infections caused by antibiotic resistant bacteria.

TECHNICAL APPROACH

1. Verification of antibiotic resistance patterns of Klebsiella pneumoniae isolates.

2. Attempt to "cure" Klebsiella isolates of the plasmids thought to mediate antibiotic resistance.

3. Attempt to transfer the plasmids via bacterial conjugation with recipient bacteria.

4. Attempt to demonstrate plasmid DNA and characterize molecular weights via agarose gel electrophoresis.

Personnel: None.

Funding: None.

PROGRESS

Antibiotic resistance patterns of Klebsiella pneumoniae isolates have been verified. "Curing" was attempted via incubation at 44°C. Replica plating technique was used to detect bacteria which had lost their

C-13-78 (Completed)

resistance to antibiotics. No curing was demonstrated. Use of other curing techniques was not begun based upon a decision to move on to methods of "3". Secured a string of E. coli (C600) from Dr. Moody, University of Texas Health Science Center at San Antonio. This strain is well suited as a recipient of plasmids transferred by conjugation.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Amantadine in the Prophylaxis of Influenza A/USSR/77

WORK UNIT NO.: C-14-78

PRINCIPAL INVESTIGATOR: David W. Potts, M.D., MAJ, USAF MC

ASSOCIATE INVESTIGATORS: Dennis L. Stevens, M.D., MAJ, MC; Theodore R. McNitt, M.D., LTC, MC

OBJECTIVES

To document the clinical and epidemiologic characteristics of influenza A/USSR/77 infection in a young adult population and evaluate the effect of amantadine on the incidence, duration and clinical manifestations of influenza infection, and on the subclinical infection rate.

TECHNICAL APPROACH

A group of young adult soldiers (age 18-24 years) living in two separate dormitories/barracks were randomly divided into two groups, one of which received amantadine, 100 mg BID for thee weeks, following initial occurrence of influenza-like illness in association with A/USSR/77 virus isolations. A second group of equal size was given a placebo BID for three weeks.

In order to document the possible presence of A/Texas/- or A/Victoria-like viruses, as well as A/USSR/77 viruses, nose and throat cultures were taken from all subjects.

A 10 ml blood sample was taken at the start of the study from all participants, and a post-epidemic serum was collected 2-3 weeks after the epidemic ended. Serologic testing documented which strains of virus infected the subjects and what the clinical and subclinical infection rate was in treated and untreated individuals.

Personnel: None.

Funding: None.

C-14-78 (Continued)

PROGRESS

The study established the safety of amantadine; difficulty concentrating and insomnia were the only side effects observed significantly more often among recipients of amantadine. The small number of participants in the study and the low overall incidence of infection with influenza virus precluded a definitive conclusion that amantadine was effective in reducing the incidence and severity of disease in those infected with influenza A/USSR/77.

Status: Ongoing.

Potts, D.W.; Kantro, R.J.; McNitt, T.R.; and Jocz, R.J. Influenza 1978. Submitted to Southern Medical Journal.

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

INVESTIGATION PROJECT RESUME

TITLE: The Etiology of Postpericardiotomy Syndrome.

WORK UNIT NO.: C-17-78

PRINCIPAL INVESTIGATOR: Dennis L. Stevens, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Larry D. Hudson, M.D., CPT, MC; Richard C. Traugott, M.D., LTC, MC

OBJECTIVES

To determine the etiology of postpericardiotomy syndrome.

TECHNICAL APPROACH

Patients undergoing open heart procedures on the Thoracic Surgery Service will have the following tests in addition to whatever routine tests are currently obtained. Sera will be obtained pre-op, during episodes of pericarditis, and at 1, 2, and 3 weeks post surgery for CMV titers, adenovirus, Coxsackie B(1-6) and antiheart antibodies. Pericardial fluid and pleural fluid will be submitted for glucose, proteins, complement, aerobic, anaerobic, fungal, TB and viral cultures. During the episode of pericarditis, urine will be submitted for CMV studies.

At the time of surgery, it is usual and customary here, as well as at other medical centers, to amputate the right atrial appendage when bypass plumbing is being attached. We propose to obtain a small portion of this specimen which would be frozen at $-70^{o}C$ and stored for later fluorescent antibody assays, i.e. when pre-op, acute and convalescent serum collection is complete.

As the pericardium must be entered for such surgery, we propose that a small 1-2 mm x 5 mm sliver of pericardium be obtined at that time and frozen at $-70^{o}C$ for later assays, as with the atrial appendage.

Thin sections of the biopsy specimen will be obtained using the Dermatology Cryostat. If sera containing anti pericardial antibody is present in acute and convalescent sera, then such immunoglobulins

C-17-78 (Continued)

will be bound to the thin sections of that tissue even after washing with appropriate buffer. Demonstration of this antibody may be accomplished by adding fluorescein labelled goat-antihuman globulin to the tissue sections.

Personnel: None.

Funding: None.

PROGRESS

Paired serum specimens from 45 consecutive patients undergoing open heart surgery have been collected. In addition, pericardial and myocardial tissue from 40 patients have also been obtained. Clinical summaries of these patients are being evaluated and tabulated. Indirect fluorescence antibody assays have not yet been performed. All specimens are frozen at -70°C until analyses can be completed.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Controlled Study of the Effects of High Dose Corticosteroids Versus Medium Dose Corticosteroids in the Management of Acute Asthma.

WORK UNIT NO.: C-19-78

PRINCIPAL INVESTIGATOR: Glenn L. Bugay, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Roy S. Adaniya, M.D., MAJ, MC; Susan Marshall, M.D.

OBJECTIVES

1. To compare the efficacy of high dose corticosteroids (loading dose of 1 gm. of methylprednisolone followed by 500 mg. I.V. q6h) versus medium dose corticosteroids (loading dose of 60 mg. of methylprednisolone followed by 20 mg. I.V. q6h) on acute asthmatic attacks. Objective parameters to be compared include changes in PFT's and ABG's.

2. To compare complications of high dose corticosteroids versus medium dose corticosteroids.

TECHNICAL APPROACH

The study group will consist of adult patients with asthma whose symptoms remain unchanged while on therapeutic dose of methyl xanthines and sympathomimetics. The dosage of corticosteroids will be double blinded by the pharmacy service - 10 patients receiving medium dose, as defined in the objectives, and 10 patients receiving high dose.

Personnel: None.

Funding: None.

PROGRESS

One patient has been admitted to the study. The primary asthma season is in the fall in this area and additional patient participation is expected.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Effects of Aspirin Administration on Mortality in Infected Rats.

WORK UNIT NO.: C-20-78

PRINCIPAL INVESTIGATOR: David W. Potts, M.D., MAJ, USAF MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., MAJ, MC; Michael M. Lieberman, Ph.D., CPT, MSC; Bryon Wilson, MAJ, VC; Francis O'Donnell, M.D., LTC, MC

OBJECTIVES

To study the effects of aspirin administration on an infected mammalian model.

TECHNICAL APPROCH

Four groups of 20 rats will be prepared and treated in the following manner.

Group I will be the controls and receive neither aspirin nor Pseudomonas. They will be inoculated with 1 cc of TSB intraperitoneally.

Group II will receive 1 cc of TSB containing the dose of Pseudomonas, $2.5x10^6$, then $2.5x10^7$, and then $2.5x10^8$, and no aspirin.

Group III will receive the Pseudomonas and then aspirin, either 30 mg/kg, 60 mg/kg, or 75 mg/kg, on an every four hour basis.

Group IV will receive the intraperitoneal injection of TSB without Pseudomonas and the aspirin on an every 4 hours basis.

For the entire group, the temperature will be taken rectally with an IVAC thermometer every 2 hours. The dose of aspirin and the time of death will be recorded.

Personnel: None.

C-20-78 (Continued)

Funding:	Consumable Supplies
FY 78	$ 513.30

PROGRESS

The design of the study is currently being revised.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Benzoyl Peroxide in the Treatment of Superficial Mycoses.

WORK UNIT NO.: C-24-78

PRINCIPAL INVESTIGATOR: John J. Jucas, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Robert L. Rietschel, M.D., MAJ, MC; Charles W. Lewis, M.D., COL, MC

OBJECTIVES

To evaluate the efficacy of benzoyl peroxide in a double blind study comparing the active agent against its vehicle in the treatment of various superficial fungal infections. These will include tinea versicolor, tinea corporis, tinea pedis, tinea cruris, and tinea unguinum.

TECHNICAL APPROACH

A double blind compared study for the efficacy of benzoyl peroxide in the treatment of the above fungal infections will be carried out. A commercial benzoyl peroxide will be paired against its vehicle. Patients will be cultured for fungi before and during the study.

Personnel: None.

Funding: None.

PROGRESS

Investigational drug #14303 was received in May 1978. At present, we are awaiting the arrival of the bnzoyl peroxide and its vehicle.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Determination of Opsonizing Antibody in People Receiving Polyvalent Pneumococcal Vaccine

WORK UNIT NO.: C-25-78

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

ASSOCIATE INVESTIGATORS Dennis L. Stevens, M.D., MAJ, MC; David W. Potts, M.D., MAJ, USAF MC; Robert C. Allen, M.D., CPT, MC

OBJECTIVES

To determine the serum opsonizing activity in selected patients in response to a polyvalent pneumococcal vaccine.

TECHNICAL APPROACH

Patients, who are determined by their attending physicians to be at risk for pneumococcal disease, will be vaccinated using a polyvalent pneumococcal vaccine. 15 cc. of blood will be drawn immediately prior to vaccination and again at 3-4 weeks following vaccination. These blood samples will be allowed to clot at room temperature following which serum will be removed and stored at $-70^{o}C$ until studied.

After incubation with the test sera, the organism suspension will be added to a vial containing PMN's. These vials will be counted in a Beckman LS 133 scintillation counter operated in the out-of-coincidence mode. The increase in counts and the rate of increase will be used as a measurement of opsonic activity.

Personnel: None

Funding: None.

PROGRESS

Twenty-five pre- and post vaccine sera have been obtained for evaluation. These represent samples from patients with a) chronic obstructive pulmonary disease, b) neoplasia, c) splenectomy, and d) sickle cell disease. We plan to obtain an additional 25 patients for study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Antibody Response to Pneumococcal Vaccine in Adult Patients with Malignant Disease.

WORK UNIT NO.: C-26-78

PRINCIPAL INVESTIGATOR: Richard A. Shildt, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: James Boyd, M.D., MAJ, MC; Ronald Rubin, M.D., MAJ, MC; J. Dean McCracken, M.D., LTC, MC

OBJECTIVES

1. To compare antibody responses in a population of oncology patients immunized with pneumococcal vaccine with that of normal controls.

2. To further clarify the optimum time to immunize patients receiving cytotoxic agents.

3. To obtain baseline data regarding efficacy of pneumococcal vaccine in selected patient populations.

TECHNICAL APPROACH

Patients in the Oncology Clinic and normal controls were immunized with Pneomovax vaccine. Serum was obtained at immunization and four weeks later and frozen. The serum will be analyzed for antibody determination.

Personnel: None.

Funding: None.

PROGRESS

About 100 patients have been immunized and sera collected and frozen. The remaining 50 patients will be vaccinated in August and September.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: The Relationships of Vaginal and Cervical Flora in Pregnancy and Premature Rupture of Membranes.

WORK UNIT NO.: C-11-75

PRINCIPAL INVESTIGATOR: James E. Connerth, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Willie J. Lett, M.D., MAJ, MC; Warren N. Otterson, M.D., COL, MC: Rudi Ansbacher, M.D., COL, MC; Barry L. Davison, M.S., CPT, MSC

OBJECTIVES

To assess the possible degree of correlation between vaginal and cervical flora in pregnancy and premature rupture of membranes.

TECHNICAL APPROACH

Serial aerobic and anaerobic cultures (1st and 3rd trimester) of the vagina and cervix were taken on approximately 900 gravidas. Seventy patients with spontaneous rupture of membranes were also cultured (vagina and amniotic fluid if present).

Personnel: None

Funding:

	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	$2,200.00
FY 75	$4,099.81

PROGRESS

Data gathering have been completed. A wide range of anaerobic and aerobic organisms were recovered. No definite correlation between Microflora and spontaneous rupture of membranes was demonstrated on statistical analysis.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: The Decision to Obtain Voluntary Sterilization.

WORK UNIT NO. C-1-76

PRINCIPAL INVESTIGATOR: Margaret Clark

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

OBJECTIVES

To study the determinants of choice of male versus female sterilization procedures. To evaluate postoperative satisfaction with the operation of choice in terms of these factors.

TECHNICAL APPROACH

A self-completion questionnaire has been given to individuals who come to the Department of Obstetrics and Gynecology and to the Department of Urology seeking information and counseling regarding voluntary sterilization. A follow-up questionnaire has been mailed to consenting individuals approximately six months after a sterilization procedure.

Personnel: None

Funding: None

PROGRESS

The study of 188 couples showed that when the husband had little interest in the choice of procedure, the wife was more likely to be sterilized. Eighty-six men chose vasectomies while 102 women chose either laparoscopic tubal ligations or vaginal hysterectomies. 61% of husbands who said contraceptives and coitus-related reasons were of major importance received a vasectomy, but when the husband considered these as minor resons, only 32.3% received vasectomies. When the husband showed interest, there was no evidence of a particular procedure being more prevalent than another.

C-1-76 (Continued)

Other factors affecting a couple's decision included (a) number of children the couple had; (b) opinion of the physician, family, or friends; and (c) the nature of the couple's relationship.

Status: Completed.

Submitted for publication, (journal unknown).

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

INVESTIGATION PROJECT RESUME

TITLE: Spinal Cord Injuries: Sperm Antibodies.

WORK UNIT NO.: C-3-76

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., COL, MC

ASSOCIATE INVESTIGATOR: Mauro P. Gangai, M.D., COL, MC

OBJECTIVES

To determine the incidence of sperm-agglutinating and sperm-immobilizing antibodies in the sera of 25 men after spinal cord injuries.

TECHNICAL APPROACH

Men hospitalized with spinal cord injuries or those seen in the Urology Clinic, BAMC, have a sexual history taken to determine the frequency of erections, seminal emissions, and sexual history prior to and subsequent to their injury. Ten milliliters of blood are drawn from each man, the serum is removed from the clotted blood by centrifugation, complement is destroyed by heating the serum for 30 minutes at 58° Celsius, and the serum samples are stored at below -25° Celsius until and between testing days.

The macroscopic gelatin sperm-agglutination and the sperm-immobilization test are utilized to determine the presence of circulating sperm antibodies, using pooled rabbit serum as the complement source and normal semen samples obtained from donors with at least 60 million spermatozoa per milliliter and motility above 70 percent as the antigen.

Results will be correlated with each man's history and compared to previously obtained data from men studied before and after bilateral vas ligations.

Personnel: None

Funding: None

C-3-76 (Continued)

PROGRESS

This study has been transferred to Letterman Army Medical Center.

Status: Transferred to Letterman Army Medical Center.

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

INVESTIGATION PROJECT RESUME

TITLE: Maternal Cellular Immunity During Pregnancy.

WORK UNIT NO.: C-21-77

PRINCIPAL INVESTIGATOR: Roger L. Wallace, D.O., CPT, MC

ASSOCIATE INVESTIGATORS: Frank P. Wilson, D.O., CPT, MC; Robert P. Bowman, M.D., LTC, MC; Rudi Ansbacher, M.D., COL, MC; Russell W. Steele, M.D., LTC, MC; John Posch, M.S.

Dan Marmer, M.S.; I. Chapa OB.

To determine if cell mediated immunity is altered during pregnancy as determined by in vitro lymphocyte function studies. An attempt will be made to outline immune parameters in normal pregnant women.

Newborn infants will also be assessed clinically to establish if there is any relationship between maternal immune mechanisms during pregnancy and problems during early infancy.

TECHNICAL APPROACH

Patients from the OB clinic will be studied during their gestations and blood specimens will be collected once every two months during pregnancy for the appropriate studies. Lymphocyte function studies will include surface immunoglobulins, quantitative immunoglobulin, EAC rosettes, E rosettes, mitogen stimulation, mixed lymphocyte cultures. Comparisons will be made with previously published data and establish normal immune parameter.

Personnel: None

Funding: None

PROGRESS

After initial research it was found that excessive time consumption and laboratory support needed to complete the project made it prohibitive at this time.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: Inhibition of Premature Labor with Terbutaline.

WORK UNIT NO.: C-39-77

PRINCIPAL INVESTICATOR: Roger L. Wallace, D.O., CPT, MC

ASSOCIATE INVESTIGATORS: David L. Caldwell, M.D., CPT, MC; Rudi Ansbacher, M.D., COL, MC: Warren N. Otterson, M.D., COL, MC

OBJECTIVES

To study inhititory effects of terbutaline on premature labor.

TECHNICAL APPROACH

Patients of less than 36 weeks gestation admitted to the Obstetric Service in premature labor will be initially treated with terbutaline. Terbutaline will be administered by an initial intravenous loading dose, followed by a subcutaneous dose for 24 hours, followed by a p.o. maintenance dose. During the p.o. maintenance one-half of the patients will receive an oral placebo and one-half of the patient will receive oral terbutaline.

Personnel: None

Funding: None

PROGRESS

Thirty-nine patients, all diagnosed as being in labor prior to 36 weeks gestation, have been treated with Terbutaline. With successful treatment arbitrarily defined as prolongation of gestation by 72 hours or more, 37 patients (95%) were successfully treated. In all 39 patients, uterine activity was initially arrested with intravenous therapy, however, in two patients, uterine relaxation was not able to be maintained after cessation of intravenous administration. The infusion rate has

C-39-77 (Continued)

been found to vary from 10 mcg. to 80 mcg. per minute. An initial intravenous bolus of 0.25 mg. given with the start of the infusion has been found to rapidly obliterate uterine activity.

Not a single infant has died of respiratory distress syndrome. Pediatric follow-up examinations of the infants have shown all infants to be developed mentally and neurologically comparable to their peers.

Side effects have been mild and extremely well tolerated, and no untoward or serious side effects have occurred. The most common side effect has been maternal tachycardia with the mean pulse rate increased from 89 beats per minute to 126 beats per minute during intravenous infusion. Hypotension or hypertension has not been encountered during the study. Fetal tachycardia has often accompanied maternal tachycardia during infusion, and in 80% of the cases fetal heart rate reached or exceeded 150 beats per minute. In no case did the fetal heart rate exceed 180 beats per minute. Other side effects have included dizziness, palpitations and tremor during intravenous infusion, but these were mild and well tolerated. While on oral maintenance therapy, several patients noted slight tremors, but these were mild and usually resolved after one to two weeks.

The average prolongation of gestation was 3.7 weeks. Gestation has been prolonged beyond 36 weeks in 25 patients.

Conclusions: These preliminary results have shown Terbutaline to be a safe, well tolerated and effective inhibitor in premature labor.

Status: Ongoing.

Wallace, R.L., et al.: Inhibition of premature labor with terbutaline. Obstet. Gynec. 51:387, 1978.

Wallace, R.L. Inhibition of Premature Labor by Terbutaline. Presented at Armed Forces District, American College of Obstetricians and Gynecologists, New Orleans, La., 9-13 October 1977.

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

INVESTIGATION PROJECT RESUME

TITLE: Prolactin Levels in Hypertensive Pregnancies.

WORK UNIT NO.: C-8-78

PRINCIPAL INVESTIGATOR: Joseph C. Webster, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Alexander G. Juden, Jr., M.D., COL, MC; Residents, Department of Obstetrics and Gynecology

OBJECTIVES

To determine whether hypertension occurring after onset of pregnancy is associated with elevated prolactin levels as compared with normotensive pregnancies.

TECHNICAL APPROACH

Serum prolactins are being drawn at certain stages in gestation prior to 1030 hours to avoid diurnal changes. The values present in those eventually becoming pre-eclamptic will be compared with values from normotensive patients.

Personnel: None.

Funding: None.

PROGRESS

Approximately one-half the number of patients needed for the study have been enrolled. Due to an increase in requests for prolactin levels and a lack of personnel, the Area Lab Facility has been unable to process the study samples. Arrangements are being made for the studies to be done commercially.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Comparison Study of Cesarean Section.

WORK UNIT NO.: C-39-78

PRINCIPAL INVESTIGATOR: Danny R. Barnhill, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: David L. Caldwell, M.D., CPT, MC; Roger L. Wallace, M.D., CPT, MC; Alexander G. Juden, Jr., M.D., COL, MC

OBJECTIVES

To determine if postoperative Cesarean section febrile morbidity can be reduced by operative technique or prophylactic antibiotics.

TECHNICAL APPROACH

One hundred patients undergoing primary low cervical transverse (LCT) Cesarean section will be included for study and divided into three groups.

Group 1: Transperitoneal primary LCT Cesarean section.
Group 2: Transperitoneal primary LCT Cesarean section with prophylactic antibiotics.
Group 3: Extraperitoneal primary LCT Cesarean section.

Each patient will be assigned to one of the three groups according to previously defined risk factors. This will be done in an effort to assure that the patients in the three groups are similar.

Personnel: None.

Funding: None.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Microbiologic Comparison of Therapeutic and Disc Antibody Activity Against Selected Enteric Bacteria.

WORK UNIT NO.: C-16-75

PRINCIPAL INVESTIGATOR: Cleste N. Guerra

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the sensitivity patterns of therapeutic antibiotics and antibiotic-impregnated discs.

2. To develop and perform antibiotic sensitivity tests designed to compare the effectiveness of both laboratory methods in relation to proper patient care.

3. To provide better laboratory indices by which physicians may more accurately assess the drug of choice in treatment of patient infections.

TECHNICAL APPROACH

A comparison of results of various antibiotics (diagnostic and therapeutic) against various enteric organisms from infected patients is performed by using the plate sensitivity method (with recorded disc concentrations) and serial tube dilutions sensitivity tests (aqueous solution of drugs equivalent to the disc concentration).

Personnel: None.

Funding:

	Capital Equipment
FY 78	-
FY 77	-
FY 7T	-
FY 76	$930.00

C-16-75 (Continued)

PROGRESS

This study continues to confirm the experimental design; i.e., it offers more definitive sensitivity results and provides physicians with laboratory data of practical clinical value.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Diagnosis and Management of Hemostatic Changes in Cardiac By-Pass Surgery.

WORK UNIT NO. C-17-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard C. Traugott, M.D., LTC, MC; Special Hematology Staff

OBJECTIVES

To determine the specific hemostatic changes occurring during cardiac by-pass surgery.

TECHNICAL APPROACH

A battery of hemostatic tests will be performed on all scheduled cardiac by-pass surgery patients within three days before surgery. These include: Protime (PT), activated partial thromboplastin time (APTT), bleeding time (BT), platelet count (PC), split products (FSPs), thrombin time (TT), fibrinogen (I), factor IX assay, factor VIII assay, reptilase time (RT) if the TT is abnormal), platelet aggregation, and platelet adhesivity (Wright).

Coagulation results for each patient will be correlated with the patient's clinical status and interpreted by standard techniques. When abnormalities are delineated, appropriate corrective action will be undertaken. Abnormalities noted will be tabulated for the entire series and correlated with patient's age, status, operation, operation time, pump time, heparin dose, protamine dose, blood loss, blood product replacement and unusual operative complications.

Personnel: None

Funding: None

PROGRESS

Two hundred and eighty-seven patients have been studied. Pertinent findings are: prolonged PT postoperatively which is thought to be

C-17-77 (Continued)

partially due to an unexplained postoperative decrease in factor VII; postoperative thrombocytopenia; occasional residual heparin postoperatively; and occasional residual postoperative transfusional depletion of factors V and VIII.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Laser Nephelometric Assay of Factor VIII Antigen and Anti-Thrombin III (AT-III).

WORK UNIT NO.: C-25-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Agnes Rohan, DAC, Brenda Harris, DAC, Madelyn Stewart, DAC; Dan Marmer, DAC: John Posch, DAC

OBJECTIVES

To establish a rapid immunologic assay of factor VIII Antigen and AT-III using a laser nephelometer.

TECHNICAL APPROACH

When a satisfactory system is developed, AT-III will be determined in a series of normal and abnormal patients by the nephelometric procedure and by radioimmunodiffusion. Resulsts of the two methods will be compared by linear regression analysis.

Factor VIII determinations will be performed by nephelometry and by electroimmunodiffusion for a series of normal and deficient patients. Nephelometric results will be compared with EID results by linear regression analysis.

Personnel: None.

Funding:

	Consumable Supplies
FY 78	$ 395.00
FY 77	$ 374.00

PROGRESS

Approximately 40 samples of $VIII_{Ag}$ have been assayed, using our current system, and results compared very favorably with results obtained by an EID assay.

C-25-77 (Continued)

The AT-III study has not yet started due to lack of personnel to pursue the study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Hemoglobinopathy Testing of United States Army Inductees - Analysis of Two Systems.

WORK UNIT NO.: C-44-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: V. Coley, MAJ, MSC; Agnes Rohan, DAC, Madelyn Stewart, DAC; Brenda Harris, DAC; John Posch, DAC; Dan Marmer, DAC

OBJECTIVES

To analyze the cost per subject, error rate, feasibility for mass screening and rate of detection of abnormal hemoglobin variants with two screening systems, one based on a semiautomated dithionate screen for sickle hemoglobin and the second based on a Coulter S CBC and cellulose acetate hemoglobin electrophoresis.

TECHNICAL APPROACH

A pilot study will be conducted testing 5,000 student volunteers at the Academy of Health Sciences using two testing systems:

a. Semiautomated dithionate testing, with confirmation of abnormals by cellulose acetate hemoglobin electrophoresis.

b. Coulter S CBC with reticulocyte count and cellulose acetate hemoglobin electrophoresis with densitometric A_2 quantitation, alkali denaturation hemoglobin F determine, and clarification of borderline A_2 values by column chromatography. Abnormal results will be investigated and confirmed by standard laboratory methods.

Personnel: None

Funding: None

PROGRESS

One hundred and twenty-six volunteers were studied in a pilot study. Four cases of AS were identified by both systems, and two cases of AC by the latter system. No other abnormalities were found.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: a. Compilation of Atlas of Electron Micrographs of Known Viruses.
b. Electron Microscopic Examination of Selected Viral Cultures for Detection of Mixed Viral Infections.

WORK UNIT NO.: C-45-77

PRINCIPAL INVESTIGATOR: George J. Kasai, Ph.D.

ASSOCIATE INVESTIGATORS: Dermott Acton, SFC; Alan Weckerling, DAC; Steven K. Koester, DAC; Lucy Olalde, DAC

OBJECTIVES

a. An atlas of the ultrastructural characteristics of known viral agents in tissue culture, confirmed by antibody neutralization, will be compiled. The cellular location and ultrastructural characteristics of each identified virus will be noted, and electron micrographs of representative forms will be prepared of each virus.

b. The recognition of mixed viral infections by ultrastructural detection of more than one viral agent, and identification of the agents involved by their ultrastructure, will be attempted on unknown viral cultures that are not identifiable by present laboratory methods. Since this will be done on all ambiguous viral cultures during the period of the study, an estimate of the incidence of dual viral infections will be possible.

TECHNICAL APPROACH

Cultures giving ambiguous neutralization results will be studied by electron microscopy for the detection of viral particles. This procedure can be applied to viral agents possessing different ultra structuraly morphologies or those that are reporduced in the two different areas of the cell proper (i.e. cytoplasm or the nucleus).

Cultures will be derived from patients' specimens submitted by various medical facilities requesting our services. These will be processed in accordance with our standard operating procedures. The portion of work in electron microscopy will be handled by that section with the aid of our personnel in identifying and clarifying the particular fields of interest.

Personnel: None.

C-45-77 (Continued)

Funding:	Consumable Supplies
FY 78	$759.06

PROGRESS

All of the tissue controls have been processed and photographed for reference to normal cellular appearances. Numerous viral agents have been processed and photographed, and others are being readied for furhter work. The progress of this portion of the investigation is dependent upon time that can be spared for these studies in the Electron Microscopy Service. As unidentifiable specimes are encountered they will be turned over to Electron Microscopy for processing and photographing.

Status: Ongoing.

Koester, S.K. Diagnostic Virology Capabilities Expanded by the Use of Electron Microscopy at a Major Medical Center. Presented at the Seventh Annual Joint Symposium of the Texas and Louisiana Societies for Electron Microscopy, San Antonio, Texas, 10 February 1978.

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

INVESTIGATION PROJECT RESUME

TITLE: Hemoglobinopathy Testing of United States Army Inductees - Natural History of Hemoglobinopathies in the Army

WORK UNIT NO.: C-48-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richert Goyette, M.D., MAJ, MC; M. McCue, Ph.D., MAJ, MSC

OBJECTIVES

To prospectively identify and follow individuals with hemoglobinopathies and matched controls for morbidity in an Army Environment.

TECHNICAL APPROACH

Individuals with hemoglobinopathies identified in Part a. (C-44-77) of this project will be informed of genetic implications and possible morbidity of their hemoglobinopathy and/or hematologic abnormality. They will be paired with normal (AA) individuals, and after assignment will be followed for a minimum of two years with CBC and reticulocyte count every six months. Participants will remain in the study until discharged from the Army, or termination of the study.

Personnel: None.

Funding: None.

PROGRESS

This project has not yet commenced because we have been unable to obtain personnel to perform C-44-77, on which this study is dependent.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Comparative Survey of Ruba-Cell and Ruba-Tec Procedures on Submitted Specimens. Evaluation of the ELISA Method for Rubella Screening in a Clinical Diagnostic Laboratory.

WORK UNIT NO.: C-3-78

PRINCIPAL INVESTIGATOR: George J. Kasai, Ph.D.

ASSOCIATE INVESTIGATOR: Helen Wilson, DAC; Winnie Ruth Callahan, DAC; Steven K. Koester, DAC; Dermott Acton, E-7; Patricia Casey, E-5

OBJECTIVES

To compare the various tests available for rubella screening and to evaluate each with respect to cost, efficiency and accuracy.

TECHNICAL APPROACH

The Ruba-Cell and Ruba-Tec kits were performed on a comparative basis using several hundred clinical specimens with hi-pos, lo-pos and negative controls. The Elisa kits were tested simultaneously with the above on three different kits received, while the FIAX test was performed on selected specimens from the above series and finally including 50+ specimens in the entire runs.

Personnel: None.

Funding: None.

PROGRESS

Initially the Ruba-Cell and Ruba-Tec were compared indicating the qualitative Ruba-Cell technique as acceptable for screening purposes provided specimens were diluted 1:2 before running the test for Ruba-Cell. When comparisons were made with the Elisa method, this method

C-3-78 (Continued)

proved to be inappropriate because the three kits received demonstrated appreciable inactivations of the enzyme conjugates used in the tests. Direct testing of the enzyme conjugates with specific substrates did give a reaction which was less than what the manufacturer had claimed. (This was confirmed by telephonic communications with the company).

The final results pointed out the fact that the IDT kit (FIAX method), which is a fluorescent technique, was the most efficient in terms of time required for running the test, the technician's time, cost per specimen, and stability of reagents used on the test sample. The results were also of an advantage in that they could be expressed in definite quantitative terms. These were all read by a spectrophotometer thus eliminating the guess work introduced by the technician as in the Ruba-Cell and Ruba-Tec procedures.

It is recommended that the ELISA method not be used for other immunological procedures unless the reagent can be conjugated and prepared in the laboratory if the enzyme Alkaline phosphatase is to be used. Perhaps horse raddish veroxidase would be a better enzyme to use in the conjugation to immunoglobulin and use in the ELISA procedure. Further investiation has been accepted by the OB-GYN section for rubella screening.

Status: Ongoing

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

INVESTIGATION PROJECT RESUME

TITLE: AKR-J Mouse Lymphoma - A Model for Childhood and Adolescent Convoluted "T"-cell Lymphoma.

WORK UNIT NO.: C-15-78

PRINCIPAL INVESTIGATOR: Thomas W. Panke, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: David R. Head, M.D., LTC, MC; Dan J. Marmer, MS, MT (ASCP); Agnes E. Rohan, MT (ASCP

OBJECTIVES

To develop standards for evaluation of neoplastic lymphoid proliferations and to study the convoluted "T"-cell lymphoma of childhood through an animal model.

TECHNICAL APPROACH

AKR-J receipient mice will be anesthetized, and the skin shaved and prepared with 70% alcohol. Transplant recipients will be divided into two groups. Sham-transplanted mice will have a transplant of 0.1 cc of sterile Hank's balanced salt solution (no tumor) placed subcutaneously in teh 4 mm incision. Tumor-transplanted mice will receive a single 2 mm^3 piece of tumor placed subcutaneously as above. The incision will be closed with a single metallic clip.

Lymphocyte function studies will be performed to evaluate the nature of the neoplastic lymphocytes and to determine the number of T and B lymphocytes in the peripheral blood before and following tumor transplant.

Personnel: None.

Funding: None.

PROGRESS

Preliminary studies were conducted in mice and confirmed the T-cell nature of the neoplasm. The study was not completed because of limited technical support and the departure of the two principal investigators.

C-15-78 (Continued)

Status: Terminated.

Panke, T., Langlinais, P., Marmer, D. and Head, D.: An animal model for childhood convoluted T-cell lymphoma. Anat Rec (in press).

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

INVESTIGATION PROJECT RESUME

TITLE: Oxauracil Typing of *Herpesvirus simplex* Type I and II Clinical Isolates

WORK UNIT NO.: C-33-78

PRINCIPAL INVESTIGATOR: Lawton A. Seal, 1LT, MSC

ASSOCIATE INVESTIGATORS: Steven K. Koester, DAC; Richard M. Jamison, Ph.D.

OBJECTIVES

1. To evaluate the efficacy of Oxauracil in the differentiation of HSV clinical isolates (wild strains) using tissue culture cell lines currently available in the Virology Laboratory.

2. To establish a new and rapid procedure for typing HSV wild strains, thereby reducing the time required to obtain reliable results.

TECHNICAL APPROACH

This study proposes to evaluate the efficacy of Oxauracil in typing wild strains of HSV isolated in this laboratory and the Virology Laboratory of Louisiana State University School of Medicine, using primary tissue culture cell lines readily available. Currently in this laboratory there are approximately 20 clinical isolates which have been confirmed as HSV and preserved. Dr. Jamison can supply approximately 15 additional isolates. Additional isolates will be obtained if required to assure approximately equal numbers of each type of HSV. Following initial passage of each isolate HSV typing will be performed by the method of specific antiserum neutralization. Specimens will be coded and submitted in a blind manner for Oxauracil typing.

Personnel: None.

Funding:	Consumable Supplies
FY 78	$ 312.92

PROGRESS

At this time initial passage and specific antisera neutralization of each isolate is under way with approximately 60% of the isolates typed.

C-33-78 (Continued

Preliminary studies indicate cell lines available in the laboratory may not support Oxauracil typing of HSV isolates. This observation has not been confirmed. Upon completion of the tissue culture laboratory, other cell lines will be readily available for further study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-14-74

PRINCIPAL INVESTICATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., COL., MC; I Chapa, DAC

OBJECTIVES

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

TECHNICAL APPROACH

Assays of Varicella-Zoster induced lymphocyte blastogenesis were accomplished with methods similar to those employed for a one way mixed lymphocyte culture. Stimulating cells include tissue culture cells persistently infected with Varicella-Zoster virus and uninfected culture cells. Counts per minute for lymphocytes incubated with the infected cells divided by counts per minute following incubation with uninfected cells determined the blastogenic index and a value of 3 or greater is considered positive in most assays. This assay has been extended to include other infectious agents including herpes virus, cytomegalic virus, influenza virus, and Sporothrix schenckii.

Personnel: 1 GS-7 (9 months)

Funding:	Consumable Supplies	Capital Equipment
FY 78	$3,127.07	-
FY 77	$3,654.13	-
FY 7T	$ 506.75	-
FY 76	$2,617.10	-
FY 75	$1,112.50	$ 695.00
FY 74	$ 165.00	

C-14-77 (Continued)

PROGRESS

These assays have been demonstrated to be both sensitive and specific and have been successfully used in the clinical setting.

Techniques learned in this study were applied to developing blastogenic assays with various antigens. These have included sporothrix schenkii, herpes simplex type 1, herpes simplex type 2, cytomegalovirus, and coccidiomycosis. In addition, the ontogenesis of varicella-zoster infection in both the normal and compromised host was examined. This assay was also employed to examine cell immune responses to varicella-zoster during treatment with adenine arabinoside.

Fourteen publications have eminated from this study along with five presentations one of which won the Eighth Ogden Bruton Award at the 11th Annual Services Pediatric Seminar in 1976.

Status: Completed at Brooke Army Medical Center.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-15-74

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

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., COL, MC; I. Chapa, DAC

OBJECTIVES

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

TECHNICAL APPROACH

A ^{51}Cr lymphocytotoxicity microassay to cell lines persistently infected with HSV-1, HSV-2 or V-Z is being used in the study. Briefly, this technique examines lymphocyte-target cell interaction employing the infected cell lines as target cells. The quantitative release of ^{51}Cr from the target cells is used as an index of lymphocyte mediated reactivity against the infected cells. Uninfected tissue cultures serve as controls to quantitate ^{51}Cr release not attributed to virus itself. Specific immune release of 8% or greater is considered positive in these assays.

Personnel: 1 GS-7 (9 months)

Funding:

	Consumable Supplies
FY 78	$1,368.00
FY 77	$3,855.67
FY 7T	$1,176.80
FY 76	$2,141.50
FY 75	$ 504.00
FY 74	$1,296.78

C-15-74 (Continued)

PROGRESS

Following initial efforts to standardize this assay of cytotoxicity to herpes group virus infected cell lines, the assay was employed in the clinical setting to investigate various aspects of medial disease. Patients with primary immune deficiency, malignancy and herpes virus infection, subacute sclerosing panencephalitis, and experimental primate animals infected with herpes virus were investigated. Two areas of greatest interest concern changes in this assay during treatment with adenine arabinoside and examination of transfer factor to prevent herpes virus infection in non-human primates. This assay was used to monitor methods of immunotherapy and disease progress and treatment.

Status: Completed at Brooke Army Medical Center.
Ongoing at University of Arkansas for Medical Sciences.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-42-74

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

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., COL, MC; I. Chapa, DAC

OBJECTIVES

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

TECHNICAL APPROACH

Dialyzable transfer factor (TF_d) was prepared and purified from donors by the methods of Lawrence and Al-Askari. In most cases, leukocytes have been obtained by leukapheresis using a continuous-flow celltrifuge, (American Instrument Co.). Lymphocytes are separated from the cell pack using a Hypaque-Ficoll gradient, freeze thawed in the presence of DNase 10 times and TF was then dialyzed and concentrated by lyophilization. All recipients of human transfer factor are first tested for skin test and blastogenic responses to the antigens under investigation at which time, transfer factor is injected subcutaneously in the dose equivalent to $1x10^9$ lymphocytes. Three days after injection skin tests are usually repeated and blood is again drawn for in vitro study.

Personnel: 1 GS-7 (9 months)

Funding:

	Consumable Supplies
FY 78	$1,776.70
FY 77	$3,141.45
FY 7T	$ 452.50
FY 76	$2,818.30
FY 75	$1,331.00
FY 74	$1,092.41

C-42-74 (Continued)

PROGRESS

Patients with disseminated coccidioidomycosis and primary immune deficiency have been treated with good results. In addition, experimental animals infected with herpes simplex virus have been treated with transfer factor. Prevention of overwhelming infection with this virus has been achieved.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Immunologic Parameters in Three Nonhuman Primates.

WORK UNIT NO.: C-19-75

PRINCIPAL INVESTICATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: I. Chapa, DAC

OBJECTIVES

To undertake a derailed analysis of host herpes virus interaction in nonhuman primates in an effort to find factors in each of three species of norhuman primates which are most critical to defense against infections and oncogenic agents.

TECHNICAL APPROACH

Multiple parameters of cell-mediated immunity, humoral immunity, and phagocytic function in three species of non-human primates, i.e. baboon, cebus and marmoset, were evaluated. These species of primates were also treated with human dialyzable transfer factor and protection from fulminant infection was evaluated.

Personnel: 1 GS-7 (9 months)

Funding:

	Consumable Supplies
FY 78	$2,769.83
FY 77	$ 890.28
FY 7T	$ 302.05
FY 76	$1,215.87
FY 75	$2,750.11

PROGRESS

It was demonstrated that there is a phylogenetic difference in the immune responses of primates with the parameters of cellular immunity best demonstrating such differences.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Red Cell Affinity in Newborn Rabbits After Acute and Chronic Intrauterine Hypoxia.

WORK UNIT NO.: C-13-77

PRINCIPAL INVESTIGATOR: Werner N. Keidel, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Robert P. Bowman, M.D., LTC, MC; John Posch, DAC

OBJECTIVES

To determine the clinical and chemical correlates of experimental intrauterine hypoxia on the red cell 2,3 DPG levels in newborn rabbits.

TECHNICAL APPROACH

Pregnant New Zealand white rabbits are placed in a high altitude chamber and the atmospheric pressure slowly lowered over 48 hours to 470 mm Hg. The rabbits are maintained at this pressure for 7 to 10 days or until term. The animals are then removed and the fetal rabbits delivered via cesarean section under pentobarbital anesthesia. Blood is collected from the umbilical vessels and/or the thoracic aorta for hemoglobin, hematocrit, red cell 2,3 DPG and intraerythrocytic pH.

Personnel: None

Funding:	Consumable Supplies
FY 77	$2,101.00

PROGRESS

This principal investigator has departed this duty station and is continuing the study at a civilian institution.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: The Influence of Intrauterine Hypoxia on Neonatal Red Cell pH, 2,3 DPG and P_{50}.

WORK UNIT NO.: C-18-77

PRINCIPAL INVESTIGATOR: Werner N. Keidel, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Robert P. Bowman, M.D., LTC, MC:
Melvin Baden, M.D., COL, MC

OBJECTIVES

To determine if intrauterine hypoxia decreased neonatal red blood cell affinity for oxygen thus improving oxygen delivery to the tissues.

TECHNICAL APPROACH

Cord blood is collected at delivery for measurement of hemoglobin, hematocrit, blood gases, red cell 2,3 DPG and intraerythrocytic pH. Blood is also collected for determination of fetal hemoglobin concentration. The effective 2,3 DPG fraction is calculated by the equation:

$$DPG \times (HgbA\ \% + 0.4 \times HgbF\ \%)$$

Personnel: None

Funding: None

PROGRESS

Analysis of three different methods for determining fetal hemoglobin concentration were carried out and compared with results from column separation. The method of Chaplin et al. was most accurate for the concentration of HgbF usually found in the premature and term infant. Since the start of the study, the number of infants delivered with intra-uterine growth retardation has been quite small so that no statement can be made regarding the effects of intra-uterine hypoxia on erythrocyte 2,3 DPG.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Urinary LDH Activity and Isoenzyme Patterns in Normal, Premature, and Term Infants.

WORK UNIT NO.: C-20-77

PRINCIPAL INVESTIGATOR: Werner N. Keidel, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: William A. Rouse, M.D., MAJ, MC

OBJECTIVES

To develop normal values for urinary lactic dehydrogenase activity and isoenzyme patterns in the premature and term infant.

TECHNICAL APPROACH

Urine is collected in Hollister urine bags on newborns during their 3 day hospitalization. An aliquot of urine is analyzed for LDH activity on a DuPont ACA Autoanalyzer and the remainder is sent to the Chemistrry Section of the Dept. of Pathology for determination of the LDH isoenzyme pattern using Beckman LDH Isoenzyme kits. Part of the urine is sent for a routine urinalysis.

Personnel: None

Funding: None

PROGRESS

Forty urinary LDH assays have been determined on 27 infants. The average urinary LDH activity was 66.20 with a range of 14-370. Because of the low urinary LDH activity, it has been difficult to visualize the isoenzyme patterns on electrophoresis without first concentrating the urine.

The initial phase of this study has been completed at this institution. Further studies are being conducted at a civilian facility.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Effects of Asphyxia on Intestinal Enzymes in Newborn Rats.

WORK UNIT NO.: C-24-77

PRINCIPAL INVESTIGATOR: Werner N. Keidel, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Elliott Weser, M.D., UTSA; William B. Winborn, UTSA

OBJECTIVES

To study the effects of asphyxia on intestinal disaccharidase activity in the newborn rat model of necrotizing enterocolitis.

TECHNICAL APPROACH

Newborn rat pups will be asphyxiated by daily enclosure in an air-tight plastic bag until they are limp, cyanotic and gasping (usually 3-5 minutes). The rat pups will be resuscitated and returned to their cages. Split litters of rat pups will be inoculated with Klebsiella by administering a saline suspension of bacteria. After daily asphyxia the pups will be sacrificed sequentially. The bowel will be weighed and dissacharidase activity will be measured in the duodenum, jejunum and ileum. The succus intericus will be analyzed in each segment for pH, K^+, reducing substances and bacterial counts.

Personnel: None

Funding: None

PROGRESS

A suitable animal model was not found, and therefore, the study was terminated.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: Pediatric Clinical Algorithm Validation, Cost Analysis, and PAMOSIST Reliability.

WORK UNIT NO.: C-2-78

PRINCIPAL INVESTIGATOR: Ana A. Ortiz, M.D., MAJ, MC

ASSOCIATE INVESTIGATOR: Barry Wolcott, M.D., LTC, MC; Frank P. Wilson, D.O., MAJ, MC

OBJECTIVES

1. To determine if a pediatric clinical algorithm utilized by physician extenders can be validated in a pediatric outpatient population.

2. To compare the process and outcome data obtained by PAMOSIST's and pediatricians utilizing a standardized data base in the evaluation and treatment of children with acute URI compltinas.

3. To utilize the process and outcome data generated by PAMOSIST's and pediatricians to generate clinical algorithms of measurable cost and outcome.

TECHNICAL APPROACH

Complete medical history and physical examination data are collected on a checklist which is transcribed and programmed into computer terminals at Seattle, Wahsington (USPHS). Data compiled is then analyzed as to PAMOSIST error in both algorithm usage and treatment protocols received.

Personnel: None.

Funding: None.

PROGRESS

Approximately 1500 patient's charts have now been collected and analyzed. We are now planning to compare PAMOSIST data collection with M.D. data collection.

Status: Ongoing.

Wilson, F.P.: Algorithm-Directed Triage in a Large Volume Pediatric Clinic. Presented to the American Academy of Pediatrics, 5-10 November 1977, New York, New York

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

INVESTIGATION PROJECT RESUME

TITLE: Effects of the Antiviral Agent BW 248U on Cellular Immune Mechanisms *in vitro*.

WORK UNIT NO.: C-9-78

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

ASSOCIATE INVESTIGATOR: Isidor Chapa, DAC

OBJECTIVES

To evaluate possible toxicity *in vitro* on cellular immune mechanisms by the new antiviral agent BW 248U.

TECHNICAL APPROACH

Assay of lymphocyte blastogenesis, cytotoxicity, and LIF production were completed *in vitro* using herpes group viruses as antigens and target cells for cytotoxicity. It was demonstrated that these assays were useful in monitoring toxicity of antiviral agents.

Personnel: 1 GS7 (6 months)

Funding:	Consumable Supplies
FY 78	$ 1,260.00

PROGRESS

Inhibition of the cellular immune parameters were noted with concentrations of the drug greater than 100 micrograms.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Transfer Factor for the Prevention of Varicella-Zoster Infections in Childhood Leukemia.

WORK UNIT NO.: C-12-78

PRINCIPAL INVESTICATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., COL, MC; Isidor Chapa, DAC

OBJECTIVES

To evaluate the clinical efficacy of specific human dialyzable transfer factor in preventing or attenuating varicella-zoster (VZ) infection, usually chicken pox, in children with acute lymphoblastic leukemia. This study will also examine the development of both cellular and humoral immunity to VZ virus following administration of TF_d in these patients.

TECHNICAL APPROACH

Human dialyzable transfer factor was prepared from patients recovering from chicken pox by leukapheresis. A production protocol was completed with careful monitoring of contamination in final production. Transfer factor was administered to 15 patients with leukemia and multiple parameters of cellular immunity were evaluated.

Personnel: 1 GS7 (9 months)

Funding:	Consumable Supplies
FY 78	$ 5,845.16

PROGRESS

Preliminary study was completed demonstrating that the transfer factor could elicit positive immune responses in leukemic recipients.

Status: Transferred to University of Arkansas for Medical Sciences.

Steele, R.W.: Transfer Factor for the Prevention of Varicella-Zoster Infections in Childhood Leukemia. Presented at the 17th Interscience Conference on Antimicrobial Agents and Chemotherapy, 10-14 October 1977, New York, New York.

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

INVESTIGATION PROJECT RESUME

TITLE: Cerebrospinal Fluid Calcium Levels in Newborn Infants.

WORK UNIT NO.: C-23-78

PRINCIPAL INVESTIGATOR: Paul H. Ratner, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Melvin Baden, M.D., COL, MC; Calvin Kennedy, DAC

OBJECTIVES

1. To determine to what extent cerebrospinal fluid calcium is correlated with serum ionic calcium concentration.

2. To determine what portion of cerebrospinal fluid is ionic calcium.

3. To attempt to ascertain positive correlations between cerebrospinal fluid calcium concentration and other possibly significant parameters; (i.e., total serum calcium, ionic calcium, phosphorus, carbon dioxide concentration, total serum protein and serum albumin) that may affect the level of cerebrospinal fluid calcium.

4. To demonstrate the practical clinical applicability of determining the ionic calcium concentration from direct measurement of the cerebrospinal fluid calcium concentration.

TECHNICAL APPROACH

At the time of lumbar puncture, 1 cc of cerebrospinal fluid will be set aside for total and ionic calcium determinations. In addition, 2 cc. of whole blood will be obtained, centrifuged, the serum decanted and frozen immediately (for total and ionic calcium and phosphorus, carbon dioxide, total protein and albumin (SMA 20 profile)).

Personnel: None.

Funding: None

PROGRESS

This study demonstrated significantly that it is not feasible or practical to determine the ionic calcium concentration directly from measurement of the CSF calcium concentration.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-35-74

PRINCIPAL INVESTIGATOR: Alton W. Baker, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

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

TECHNICAL APPROACH

Routine studies are performed utilizing 1-2 millicuries Indium 111 DTPA injected intrathecally with subsequent scanning performed at 2 hours, 6 hours, 24 and 48 hours as needed.

Personnel: None.

Funding: None.

PROGRESS

The study is still under evaluation with 36 patients having been studied to date with satisfactory images and findings in all patients being obtained without evidence of untoward side effects being noted.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: NEN ^{99M}Tc Stannous Glucoheptonate for Intravenous Administration.

WORK UNIT NO.: C-6-76

PRINCIPAL INVESTIGATOR: Alton W. Baker, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Broad clinical evaluation of the NEN Stannous Glucoheptonate Kit after reconstitution with ^{99M}Tc-sodium pertechnetate as a diagnostic agent for studying the kidney.

TECHNICAL APPROACH

Routine studies are performed after the injection of 2-4 millicuries Technetrium 99m labeled to glucoheptonate with pinhole images being obtained in multiple views posteriorly.

Personnel: None.

Funding: None.

PROGRESS

To date we have studied 20 patients with this agent, and all patients have obtained satisfactory images without untoward side effects.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: MPI ^{99M}Tc-dimercaptosuccinic Acid for Intravenous Administration.

WORK UNIT NO.: C-14-76

PRINCIPAL INVESTIGATOR: Alton W. Baker, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Broad clinical evaluation (Phase III) of MPI kidney scintigraphin reagent after reconstitution with ^{99M}Tc-sodium pertechnetate as a diagnostic agent for studying the kidney.

TECHNICAL APPROACH

1-2 millicuries of ^{99M}Tc-dimercaptosuccinic acid is administered intravenously for high resolution kidney imaging studies.

Personnel: None.

Funding: None.

PROGRESS

Ten studies on patients have been performed with good results.

This drug has received approval by the Federal Drug Administration and therefore, the study is completed.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Intravenous Administration of ^{131}I-6-B-Indomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging.

WORK UNIT NO.: C-12-77

PRINCIPAL INVESTIGATOR: Alton W. Baker, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenal-cortical disorders and as a potential scanning agent for detecting structural abnormalities of the adrenal medulla.

TECHNICAL APPROACH

After the IV administration of approximately 1 to 2 millicuries of I-131 labeled 6-B-Iodomethylnorcholesterol (NP-59) over a 2 to 5 minute time interval, the patient is returned in approximately 4 to 6 days for an initial scan of the body. A subsequent scan is performed at approximately 6 to 8 days and depending upon the magnitude of uptake in the adrenal glands, scanning is carried from the 8th to 10th day. At this time, when clinical judgment indicates that the scan appears to be adequate for evaluating whether the adrenals are within normal limits or abnormal, a subsequent renal scanning agent is injected IV (Tc Glucoheptonate or TC DTPA) for visualizing kidneys and noted the relationships of the kidneys to the adrenal glands.

Personnel: None

Funding: None

PROGRESS

Only one patient was studied during the past year with good results being obtained with the patient being identified as having bilateral Cushing's disease.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Technetium-99m-pyridoxylideneglutamate (99m-Tc-PG) for Diagnosis of Hepatobiliary Disease.

WORK UNIT NO.: C-22-78

PRINCIPAL INVESTIGATOR: Alton W. Baker, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the clinical efficacy of Tc-99m-PG as a diagnostic hepatobiliary and gallbladder agent.

TECHNICAL APPROACH

Utilization is made of approximately 2-5 millicuries of Technetium 99m PG injected IV with subsequent flow study and views being obtained at 10 minutes, 20 minutes, 30 minutes up to six hours as needed.

Personnel: None.

Funding: None.

PROGRESS

Two patients have been studied with satisfactoty results. No untoward side effects have been identified.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

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

WORK UNIT NO.: C-6-72

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

ASSOCIATE INVESTIGATORS: Olyn M. Walker, M.D., LTC, MC; George M. McGranahan, M.D., COL, MC

OBJECTIVES

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

TECHNICAL APPROACH

We continue to utilize the intra-aortic balloon, primarily as an assist device in treating patients with low output syndrome following complicated open heart surgery.

Personnel: None

Funding: None

PROGRESS

The effectiveness of this device has been demonstrated, and the current mortality rate in patients in whom this device is necessary is at a very acceptable level.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Biodegradable Cuffs, an Adjunct to Peripheral Nerve Repair in Dogs.

WORK UNIT NO.: C-23-75

PRINCIPAL INVESTIGATOR: Robert L. Reid, M.D., COL, MC

ASSOCIATE INVESTIGATORS: Stephen C. Boone, M.D., LTC, MC; Duane E. Cutright, D.D., COL, DC, WRAIR

OBJECTIVES

To determine the efficacy of biodegradable cuffs at the suture site of sectioned peripheral nerves.

TECHNICAL APPROACH

Ten adult mongrel dogs were used in the study. The ulnar nerves in the forelimb and perceneal nerves in the hindlimbs were surgically exposed, transected, and repaired with 9-0 nylon epineural sutures using magnification. One side was repaired in the standard fashion and used as a control. The other side was repaired in the same fashion but in addition the anastomotic site was covered with a standard copolymer cuff whose cross-section diameters were $2\frac{1}{2}$ times that of the repaired nerve. Nerve conduction and electromyographs were conducted on all limbs at monthly intervals and at time of sacrifice. After the anastomotic site was resected, light and electromicroscopic studies were performed at the Walter Reed Army Institute for Research to determine the amount of local invasiveness of scar tissue and/or reaction in the nerve to the copolymer biodegradation.

Personnel: None.

Funding:

	Consumable Supplies
FY 78	-
FY 77	-
FY 7T	-
FY 76	-
FY 75	$ 1,630.18

PROGRESS

The early reaction to the biodegradable copolymer was generally one of hydrolysis and phagocytosis with occasional giant cells and with few typical inflammatory cells such as polymorphonuclear leukocytes, plasma cells and lymphocytes.

The eight week samples showed partial breakdown of the cuff into small particles. These particles were surrounded by many phagocytic cells which dispersed slowly as the material hydrolyzed and disappeared in the later time samples. The final degradation varied over a period of 3 weeks when all samples were consided. However, by 8 weeks it was essentially degraded to where tissue proliferated through it, and it no longer served as a barrier to the ingrowth of perineural connective tissue.

The proliferation of fibrous connective tissue between the nerve and the inside of the cuff was in a parallel fashion. This connective tissue was most likely epineural in origin and had not proliferated from perineural sources outside the cuff.

The distance of the nerve itself from the area of degradation of the copolymer in most cases appeared to be greater than necessary for optimum nerve repair or indeed to prevent an overgrowth of connective tissue around the nerve inside the cuff.

The nerve alignment in both control nerves and experimental nerves was inconstant.

The nerve conduction studies first showed evidence of motor return in both the test and control nerves at approximately the 9th week after section and repair. In subsequent weeks there was a tendency for the motor latency time to decrease and for the compound muscle action potential to increase in amplitude and decrease in temporal dispersion. There was a wide variation in the postoperative response from animal to animal. Because of the small number of animals, no statistical significance could be placed on the results.

Electromyography of the appropriate muscles revealed positive sharp waves and fibrillation potentials from the 8th through the 24th postoperative weeks. The positive sharp waves and fibrillations decreased in quantity after the 16th week. Again, no definite difference could be documented between the test nerves and the controls although there was a general impression of earlier response in the experimental nerves by the electromyographer.

This study on repair of peripheral nerves has demonstrated the following:

C-23-75 (Continued)

a. The biodegradable cuff is readily placed with conventional surgical armamentarium.

b. Tissue tolerance to the cuff is high.

c. Fibrosis around the nerve is less with the use of the cuff.

d. Exact microscopic nerve alignment is difficult to achieve even with magnification and nerve conductive techniques.

e. No increase in conductivity could be demonstrated utilizing the cuff.

f. The inside cuff diameter to nerve diameter does not appear to be optimally 2 to 1 utilizing these biodegradable cuffs.

g. The development of better methods of evaluating peripheral nerve responses is needed.

Status: Completed

Reid, R.L., Cutright, D.E., and Garrison, J.S.: Biodegradable cuff an adjunct to peripheral nerve repair: a study in dogs. British Hand Journal, "The Hand", (in press).

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

INVESTIGATION PROJECT RESUME

TITLE: Laparoscopy Under Subarachnoid Block.

WORK UNIT NO.: C-13-76

PRINCIPAL INVESTIGATOR: Robert McPherson, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Residents and Staff, Department of Ob-Gyn

OBJECTIVES

To evaluate the effectiveness of subarachnoid block as the anesthesia of choice in laparoscopy.

TECHNICAL APPROACH

Female volunteers scheduled for laparoscopic tubal ligation under subarachnoid anesthesia will be tested at regular intervals (pre- and post-subarachnoid block to the T-6 level with pontocaine) to determine vital capacity and peak expiratory flow rates.

Pulmonary function (volumes and flow rates) will be recorded on a Donti pulmonary function analyzer during distension of the peritoneal cavity created by the usual pneumoperitoneum technique.

Personnel: None

Funding: None

PROGRESS

Following the departure of the principal investigator, it was decided to terminate the study.

Status: Terminated

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

INVESTIGATION PROJECT RESUME

TITLE: Comprehensive Rehabilitation of the Laryngectomee. (Collaborative Study with the University of Texas at San Antonio)

WORK UNIT NO.: C-21-76

PRINCIPAL INVESTIGATOR: Sonley R. LeMay, Jr., M.D., COL, MC

ASSOCIATE INVESTIGATORS: George A. Gates, M.D.; Edmund Lauder, M.S.; J. C. Cooper, Ph.D.

OBJECTIVES

To acquire normative data about the biological, psychological, social and employment aspects of laryngectomee rehabilitation; to demonstrate a comprehensive program of rehabilitation is more efficient than current methods; and to statistically validate the indices of successful and unsuccessful rehabilitation.

TECHNICAL APPROACH

Preoperatively, written informed patient consent is secured. Biological, biographical, psychological, social, employment and financial data are obtained. Speech data and a brief interview are recorded on videotape. Each patient is presented with standardized educational material and a criterion based test.

Postoperatively, a second auditory evaluation is made. A treatment plan is developed based on the patient's physical condition and psychological and speech evaluations. One to two hour individual and/or group speech therapy sessions are conducted weekly. Progress is assessed monthly. Three and six month follow-up evaluations are performed with respect to esophageal speech fluency and technical proficiency, psychological and social adjustment, and employment and financial status. Manometric data are again obtained at the end of six months.

Retrospective control patients undergo comparable assessment procedures as detailed in the grant proposal.

Personnel: None

Funding: None

C-21-76 (Continued)

PROGRESS

The data is being evaluated.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Determination of Preventive Keflin Delivered to the Site of Total Joint Replacement.

WORK UNIT NO.: C-22-77

PRINCIPAL INVESTIGATOR: Thomas J. Parr, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Neal A. Jewell, M.D., Henry A. Mayer, M.D., M.D. LTC, MC

OBJECTIVES

To determine the levels of cephalosporin delivered to the site of total joint replacement procedures: 1) To determine an exact dose/route regimen in total joint replacement; 2) to thereby devise a standardized protocol for preoperative, intraoperative and postoperative administration of preventive antibiotic in total joint replacements.

TECHNICAL APPROACH

Patients in this study have been divided into three groups based on the route of delivery and the frequency of delivery of their antibiotics. During surgery, samples of venous blood, joint fluid, and approximately one square centimeter of muscle will be taken from the patient and submitted to the clinical investigation division of Lilly for Keflin assay. Their clinical response of the patient will also be followed.

Personnel: None.

Funding: None.

PROGRESS

To date, we have completed four patients out of the anticipated thirty-six. Part of the difficulty has been as a result of forwarding of the specimen to the Lilly Lab, as well as scheduling of total hip patients.

Status: Ongoing.

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

INVESTIGATION PROJECT REUME

TITLE: Human Placental Transfer of Naloxone.

WORK UNIT NO.: C-33-77

PRINCIPAL INVESTIGATOR: Barry J. Anderton, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Robert L. Watson, M.D., LTC, MC; Melvin Baden, M.D., COL, MC; Rob G. Parrish, Ph.D., CPT, MSC, Michael M. Lieberman, Ph.D., CPT, MSC

OBJECTIVES

To assess the degree and time course of placental transfer of Naloxone (Narcan) during normal vaginal deliveries using a new sensitive and specific radioimmune assay.

TECHNICAL APPROACH

Selected female volunteers at term who have received narcotics prior to their delivery will be given Naloxone (40 mg/kg body weight) 15 minutes prior to their delivery. Fetal cord blood will then be analyzed with a radioimmuno assay (RIA) technique for maternal-fetal transmission of Naloxone.

Personnel: None.

Funding: None.

PROGRESS

Naloxone rapidly crossed the placenta in significant levels. Peak newborn levels (18-23 ng/ml) were detected 2-3 minutes after maternal injection. Neonatal naloxone levels declined with an increasing interval between maternal injection and neonatal arterial sampling, but significant levels were still present (6.6 ng/ml) at 25 minutes. Maternal levels of naloxone peaked more slowly. The highest maternal level

C-33-77 (Continued)

(17.8 ng/ml) was measured at 4 minutes after injection. Maternal levels declined with an increasing interval between injection and sampling with 6.7 ng/ml measured at 26 minutes. Generally, naloxone levels exceeded maternal levels during the first 5 minutes after naloxone injection; while maternal levels exceeded neonatal levels from 10-26 minutes after injection.

Conclusions: Maternal administration of 20 ug/kg of naloxone intravenously 2-25 minutes prior to delivery will produce clinically significant umbilical artery naloxone levels in the newborn. The delay in reversal of narcotic depression in the newborn sometimes encountered with other routes of naloxone administration is avoided when naloxone is given to the parturient.

Status: Completed.

Anderton, B.J., Watson, R.L., Parrish, R.G. and Lieberman, M.M.: Naloxone: Human placental passage. Submitted to Anesthesiology for publication.

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

INVESTIGATION PROJECT RESUME

TITLE: The Aerobic Microbiologic Flora of the Contact Lens Carrying Case.

WORK UNIT NO.: C-40-77

PRINCIPAL INVESTIGATOR: Patrick G. Paglen, M.D., CPT, USAF MC

ASSOCIATE INVESTIGATORS: Michelle Bright; Roy Kincaid; Robert Ferguson; Joseph Madden, CPT, MSC

OBJECTIVES

To determine the aerobic microbiologic flora present in the contact lens carrying case of 100 consecutive patients seen in the BAMC Eye Clinic.

TECHNICAL APPROACH

Each patient who reports to the Eye Clinic will be questioned as to whether or not they wear contact lenses. If they wear lenses we will ask them if we may culture their lens case. If they agree, cultures will be obtained in a sterile fashion. Initially the capsule within the culturette will be burst and the damp swab will be removed by holding the culturette cap around its stem. The lens case will be swabbed once from side to side.

Personnel: None

Funding: None

PROGRESS

It was found that most patients who wear contact lenses do not carry their cases with them. Consequently, individuals were being selectively sampled.

Status: Terminated.

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

INVESTIGATION PROJECT RESUME

TITLE: Measurement of CO_2 Production and Humidification during Anesthesia with the Bain and Watson Circuits.

WORK UNIT NO.: C-41-77

PRINCIPAL INVESTIGATOR: Robert Rayburn, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To measure CO_2 production and humidification in children using the Mapleson D type circuit (Bain or Watson circuit).

TECHNICAL APPROACH

The Bain co-axial anesthetic circuit was studied as a semi-open or partial rebreathing system during spontaneous respiration in 20 adult patients. Premedication consisted of glycopyrrolate (.004) mg/kg) intramuscularly and induction of anesthesia was accomplished with nitrous oxide and oxygen (1:1) and halothane, or an intravenous dose of thiopental (2-4 mg/kg). Following intravenous succinylcholine (1.5 mg/kg), the trachea of each patient was sprayed with 4% lidocaine and intubation performed. The patients were allowed to breathe spontaneously after full recovery from the muscle relaxant, while anesthesia was maintained with nitrous oxide and oxygen (1:1) and halothane (0.7 per cent or less). Fresh gas flow rates initially were set at a high flow, usually 15,000 $ml/m^2/min$ and, after one hour, tidal volume, respiratory rate, and the fractional concentration of mixed expired carbon dioxide ($F_E\bar{C}O_2$) were recorded. At the same time, an arterial blood gas sample was drawn to measure PCO_2, PO_2 and pH. Patients with an initial arterial PCO_2 value greater than 44 torr were eliminated from the study. After these initial readings, those patients retained in the study had their fresh gas flow rates varied over the range of 15,000 $ml/m^2/min$ to 2000 $ml/m^2/min$ at 30 minutes intervals. Tidal volume, respiratory rate, $F_E\bar{C}O_2$, and arterial blood gas values were recorded at each setting.

Personnel: None

C-41-77 (Continued)

Funding:	Capital Equipment	Consumable Supplies
FY 78		$2,550.00
FY 77	$ 885.35	$ 390.00

PROGRESS

The results indicate that fresh gas flow rates in excess of those required for controlled ventilation are necessary during spontaneous respiration. A fresh gas flow index of 3500 to 4000 $ml/m^2/min$ produced no significant change in $PaCO_2$ from control values, and cause only a moderate increase in respiratory minute volume. When ventilation exceeds fresh gas flow, $P_E\bar{C}O_2$ followed the same general slope as $PaCO_2$ at various flow rates.

Status: Completed.

Rayburn, R.L. CPRAM - Controlled Partial Rebreathing Anesthesia Method. presented at the Primary Childrens Medical Center, Salt Lake City, Utah, 10 October 1977; Wilford Hall USAF Medical Center, Lackland Air Force Base, Texas, 21 January 1978; Reynolds Army Hospital, Fort Sill, Oklahoma, 26 January 1978.

Watson, R.L. CPRAM - Controlled Partial Rebreathing Anesthesia Methods. Visiting Professor, University of Illinois Medical School, 1977.

Rayburn, R.L. Measurement of CO_2 Production and Humidification During Anesthesia with the Bain and Watson Circuits. Submitted to Anesthesiology.

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

INVESTIGATION PROJECT RESUME

TITLE: Contrast and Spatial Frequency Sensitivity as a Screening Test for Retinal Disease.

WORK UNIT NO.: C-10-78

PRINCIPAL INVESTIGATOR: Antonio San Martin, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: John P. Shock, M.D., COL, MC

OBJECTIVES

To determine the usefulness of a new test, in which patients are asked to view printed sinusoidal gratings of varying contrast, as an indicator of retinal disease.

TECHNICAL APPROACH

Arden's test will be administered to patients with documented retinal pathology and to a comparable set of age-matched controls. The test involves looking at a series of five sheets of paper and indicating if and when a pattern is seen on the paper. Results will be catagorized whena sufficient number of patients have been seen to give statistical significance.

Personnel: None.

Funding: None.

PROGRESS

This study will begin upon completion of internship by principal investigator.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Oxytrode Sensor and the Clinical Utility of Concurrent Continuous Measurement of Arterial and Central Venous PO_2.

WORK UNIT NO.: C-18-78

PRINCIPAL INVESTIGATOR: Richard C. Traugott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Robert L. Treasure, M.D., COL, MC; Robert L. Watson, M.D., COL, MC; Raymond J. Will, M.D., MAJ, MC; Mr. Aubrey O. Bailey

OBJECTIVES

To evaluate accuracy, safety, feasibility, and clinical utility of the OXYTRODE Sensor for continuous measurement of arterial and mixed venous PO_2 during cardiopulmonary bypass by measurement and/or observation of:

a, Accuracy - by statistically valid comparison with conventional intermittent sampling.

b. Safety - by observation of the lack of occurrence of any adverse effects unforeseen in preclinical testing.

c. Feasibility - by Observation of such practical considerations as requirements for operational space, setup time, calibration, records storage, packaging, etc.

d. Clinical utility - by obtaining investigators evaluation of the OXYTRODE Sensor relative to current methodology.

To evaluate clinical utility of concurrent continuous measurement of arterial and mixed venous PO_2 difference.

TECHNICAL APPROACH

Patients undergoing non-emergency surgery using cardiopulmonary bypass via a pump-oxygenator in which bypass time is expected to equal or exceed one hour will be entered into the study. A written record will be kept of oxygen concentration being added to oxygenator, the flow rate of the pump, and clock times of all changes in these values.

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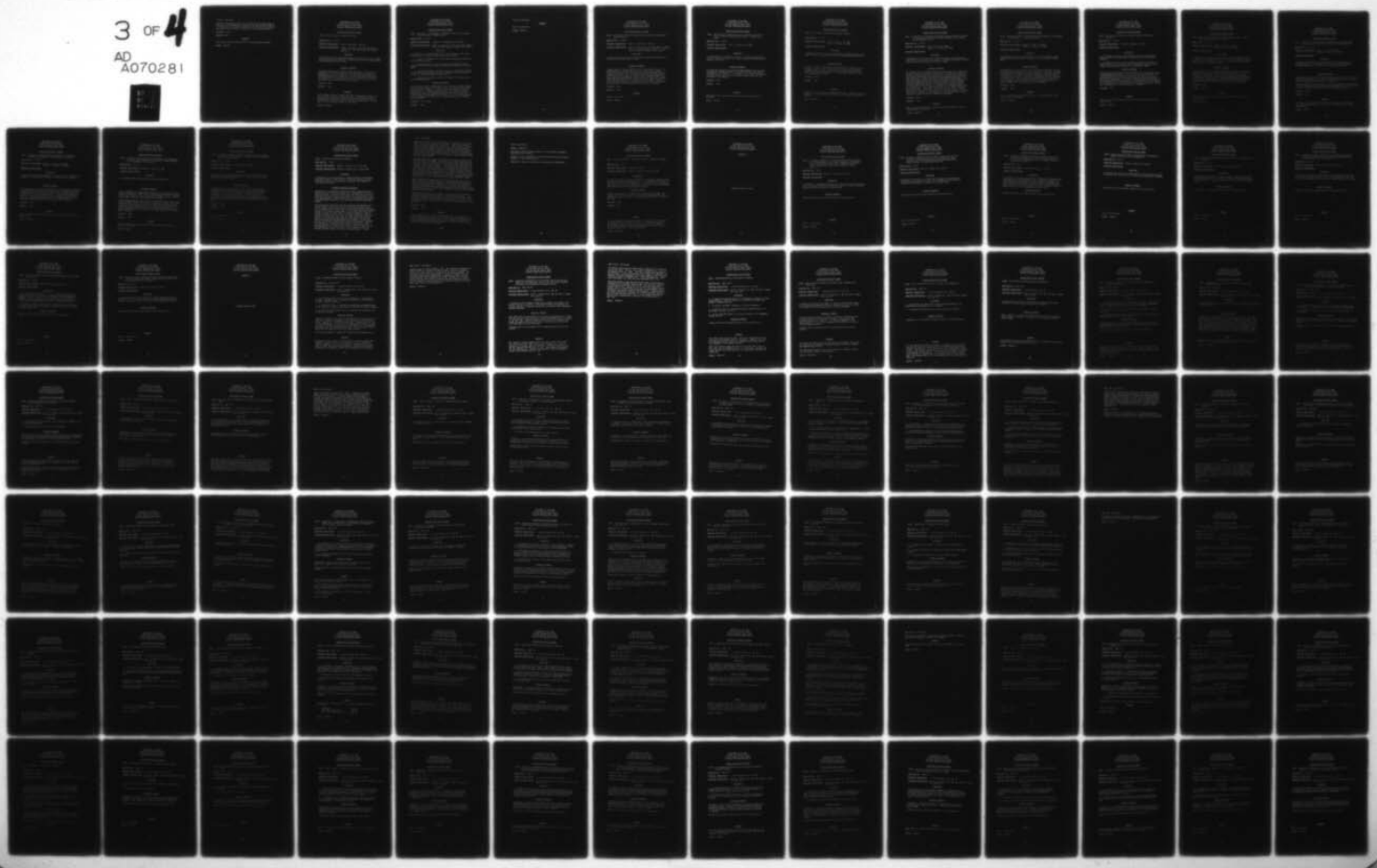

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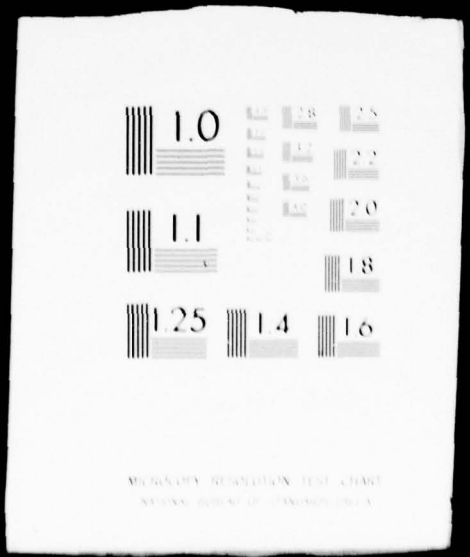

C-18-78 (Continued)

Continuous simultaneous strip chart recording will be made of PO_2 as measured by one OXYTRODE Sensor placed in the arterial and another in the venous line of the pump. Intermitten arterial and central venous PO_2 samples will be drawn and measured in the conventional manner.

Personnel: None.

Funding: None.

PROGRESS

Initial data has been collected and is currently being evaluated.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Clinical Study of Intraocular Lenses

WORK UNIT NO.: C-21-78

PRINCIPAL INVESTIGATOR: John P. Shock, M.D., COL, MC

ASSOCIATE INVESTIGATORS: John V. Van Gemert, M.D., MAJ, MC; George G. Lowell, M.D., LTC, MC; Harry W. Flynn, M.D. MAJ, MC

OBJECTIVES

To establish the safety and effectiveness of this device for use in human subjects according to guidelines recommended by the Food and Drug Administration ophthalmic advisory panel.

TECHNICAL APPROACH

Continuous monitoring of patients undergoing cataract extraction with insertion of intraocular lenses has been undertaken to satisfy the requirements of Part 812, Title 21 of the Code of Federal Regulations (Investigational Device Exemptions). Specific controls to facilitate the evaluation of the safety and efficacy of the intraocular lens are an integral part of this clinical study design.

Personnel: None.

Funding: None.

PROGRESS

From 1 February 1978 to 2 August 1978 thirteen intraocular lenses have been inserted and monitored (preoperatively, operatively, and postoperatively) according to evaluation standards established by investigational plans from McGhan and Coburn Medical Corporations. It is too early to give definitive results of this study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Intravesical Instillation of THIOTEPA at the Time of Transurethral Resection of Bladder Tumor.

WORK UNIT NO.: C-34-78

PRINCIPAL INVESTIGATOR: Stephen F. Richardson, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Mauro P. Gangai, M.D., COL, MC; Ritchie Spence, M.D., LTC, MC; Howard D. Solomon, M.D., MAJ, MC

OBJECTIVES

To study the use of THIOTEPA intravesical instillations at the time of transurethral resection of bladder tumors with regard to:

a. Amount of THIOTEPA left in the bladder following the period of instillation and washout.

b. Determination of serial blood levels of THIOTEPA following intravesical instillation at time of transurethral resection of bladder tumors.

c. Prospective study to evaluate efficacy of intraluminal THIOTEPA at the time of transurethral resection of bladder tumors in prevention or delay of recurrent/residual bladder tumors.

d. Monitoring patients carefully for evidence of toxicity, especially myelosuppression.

TECHNICAL APPROACH

At the time of surgeyr, THIOTEPA will be placed into the lbadder immediately following removal of the tumor tissue. The drug will be allowed to remain in the bladder for 2 hours and then be washed out through a rubber catheter . Bladder washings will be sent to the laboratory to determine the amount of THIOTEPA remaining in the bladder after the 2 hour period. Blood samples will be taken at 1, 3, 5, and 8 hour intervals to determine exact blood levels following absorption of THIOTEPA from the bladder.

Personnel: SP5 (1 month)

Funding: None.

C-34-78 (Continued)

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Percutaneous Epidural Stimulation for Pain Relief During First Stage of Labor.

WORK UNIT NO.: C-40-78

PRINCIPAL INVESTIGATOR: John A. Scavone, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Robert M. Young, M.D., CPT, MC; Robert L. Watson, M.D., COL, MC; Alexander G. Juden, Jr., M.D., COL, MC; Richard R. Ritter, M.D., COL, MC

OBJECTIVES

To evaluate the effectiveness of percutaneous epidural stimulation for analgesia during first stage of labor.

TECHNICAL APPROACH

A lumbar epidural catheter will be placed in the routine manner. Following placement, baseline maternal vital signs will be recorded. Fetal monitoring will be as routinely done during continuous epidural analgesia for labor. The, low frequency, weak epidural stimulation will be delivered through the catheter using a standard Shimoji type pulse generator (OBECA 1461). Vital signs of the mother will be monitored and recorded every five minutes for twenty minutes and every fifteen minutes thereafter. Fetal heart rate and utiner contractions will be monitored and recorded simultaneously and continuously.

Personnel: None.

Funding: None.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: The Reduction of Low Back Pain as a Function of the Interaction of Physical Therapist and Patient. (Health Care Study)

WORK UNIT NO.: C-43-77

PRINCIPAL INVESTIGATOR: Jane E. Gierhart, LTC, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate the treatment of low back pain and evaluate both the physical treatment of the patient and the interaction between physical therapist and patient.

TECHNICAL APPROACH

Utilizing questionnaires furnished the MEDDAC/MEDCEN by the principal investigator, information about the patient's low back pain and the treatment will be collected. For purposes of this study, low back pain is defined as any pain of acute or chronic nature from T-10 to the tuberosity of the ischium.

Personnel: None

Funding: None

PROGRESS

Raw data has been completed and is now ready to be statistically evaluated.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Pool Therapy for Medial Meinisectomy Patients.

WORK UNIT NO.: C-27-78

PRINCIPAL INVESTIGATORS: Jane M. Huffaker, 2LT, AMSC
Carol E. Petersen, 2LT AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effects of a specific therapeutic swimming program on knee range of motion and quadriceps strength following medial memisectomy.

TECHNICAL APPROACH

Patients selected for the study will be alternately assigned to one of two groups. Group 1, the control group, will receive the standard treatment twice a day for a period of three weeks, and Group 2 will receive the standard program once a day plus pool therapy once a day for the same period of time.

Personnel: None

Funding: None

PROGRESS

One group of five patients has completed the study. Another group is in progress. Not enought data have been collected to make any statistical analyses.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Equivalent Temperature Changes Caused by Infrared and Ultrasound on the Sensory Conduction Latency of the Superficial Radial Nerve in Man.

WORK UNIT NO.: C-28-78

PRINCIPAL INVESTIGATORS: John S. Halle, 2LT, AMSC;
Charles R. Scoville, 2lt, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if the sensory nerve conduction latency of the superficial radial nerve in man is affected equally by equivalent temperature increases induced by infrared energy and ultrasonice energy.

TECHNICAL APPROACH

Ten subjects will be randomly assigned into two groups, one of which will receive an application of ultrasound initially, and the other group will receive an initial application of infrared. One week later, each group will undergo application of the modality which they had not been previously exposed to. During each session, subcutaneous temperatures of the nerve bed containing the superficial radial nerve will be continuously monitored through the use of a thermistor needle. At each .3 degree Centigrade temperature change, as caused by the appropriate modality, a nerve conduction latency over a standardized 12 centimeter length will be recorded until a total temperature change of 1.2 degrees Centigrade has been obtained. These nerve conduction latencies at the .3 degree Centigrade increments will be analyzed via a two way analysis of variance. This study is designed to determine what effect ultrasound has on nerve conduction velocity at specific temperature increases.

Personnel: None.

Funding: None.

PROGRESS

This is a new study and insufficient data has been gathered to draw any meaningful conclusions.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Patient Applied Vs. Therapist Applied Ultrasound for the Treatment of Plantar Warts: A Comparative Study.

WORK UNIT NO.: C-29-78

PRINCIPAL INVESTIGATORS: Raymond C. Ronat, 2LT, AMSC;
Richard G. Simmons, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if there is any difference in cure rates between patient applied and therapist applied ultrasound for the treatment of plantar warts.

TECHNICAL APPROACH

The therapist treated group will be treated with an ultrasonic therapy unit model ME702, built by the Mettler Electronic Corporation, following the manufacturer's suggested treatment procedures. The ultrasound will be applied using the direct contact method with the intensity adjusted to the patient's tolerace. Aquasonice transmission gel will be used as a coupling agent. The self-treated group will receive the same treatment. However, on their initial visit the self-treated group will receive instructions in the operation of the equipment.

Personnel: None.

Funding: None.

PROGRESS

This is a new study, and insufficient data has been gathered to draw any meaningful conclusions.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Effects of Perceived Vs. Subliminal Stimulus TENS on Pain Threshold.

WORK UNIT NO.: C-30-78

PRINCIPAL INVESTIGATOR: Frank B. Underwood, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if there is any difference in the pain threshold of normal subjects before and during the application of an electrical stimulus.

2. To determine if there is any difference in the pain threshold of normal subjects during the application of subliminal versus perceived stimulus transcutaneous electrical nerve stimulation (TENS).

TECHNICAL APPROACH

The pressure pain threshold of normal subjects will be determined using a Transcutaneous Pain Gauge, in the ulnar nerve area of the hand. Perceived stimulus TENS will then be applied to the ulnar nerve at the elbow and the distal phalanx of the fifth digit. The pain threshold will again be determined. Subliminal stimulus TENS will then be applied to the other arm after determining the pain threshold of the other hand. After application, the pain threshold will again be determined. The data will be analyzed with a two-way analysis of variance.

Personnel: None.

PROGRESS

This is a new study, and insufficient data has been collected to make any analysis.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Media Testing of Patient Education Video Tape 1092: "Open Heart Surgery and Physical Therapy".

WORK UNIT NO.: C-31-78

PRINCIPAL INVESTIGATORS: Stephen D. Ryan, 2LT, AMSC
Gaetano G. Scotece, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To date none of the video tapes for physical therapy patient education at BAMC have been formally evaluated. This project represents a pilot study of the effectiveness and validity of these teaching aides with regard to their prospective audiences.

TECHNICAL APPROACH

Patients admitted for open heart surgery will be asked to participate. A written pretest will be administered to each patient. Upon completion, the patient will be taken to the physical therapy clinic to view video tape 1092. After viewing is completed, the patient will be returned to the ward where he will be given the post-viewing test. The tests will be corrected upon completion and the results used to explain any objectives the patient missed or did not understand.

Personnel: None.

Funding: None.

PROGRESS

This is a new project, and insufficient data has been collected to make any analysis.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Compatative Study of Energy Consumption Between Normal Treadmill Walking Vs. Walking While Grasping Horizontal Handrails.

WORK UNIT NO.: C-32-78

PRINCIPAL INVESTIGATORS: Kerry Z. Huston, 2LT, AMSC
Kathleen R. Westfall, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To measure the difference in oxygen consumption in normal walking at three miles per hour (4.83 km per hour) on a 9% grade while grasping horizontal handrails vs. walking with the arms freely swinging.

TECHNICAL APPROACH

Subjects will be tested after three practice sessions of 10 min. duration each on the treadmill set at 3.5 mph, 9% grade. Equal practice of holding and not holding horizontal handrails is performed.

Testing includes two tests randomly scheduled in holding-not holding sequence, each of 15 minutes duration. Respired gas is collected the last 1½-2 min. of the 15 min. walk, and analyzed for oxygen consumption values.

Personnel: None.

Funding: None.

PROGRESS

Ten subjects have completed the three practice walks. Eight subjects have already completed the testing. Data collection will be analyzed upon completion.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Degree of Knee Extension as it Relates to Symptomatic Chondromalacia Following Physical Exercise.

WORK UNIT NO.: C-36-78

PRINCIPAL INVESTIGATORS: Pamela E. Prentice, 2LT, AMSC
Deborah J. Robertson, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relationship between the degree of knee extension and symptomatic chondromalacia following a prolonged exercise program.

TECHNICAL APPROACH

Participants will follow the same physical training program as outlined by the ANC/AMSC Officer Basic Training Course. Following the physical training program, each participant will be tested for the presence of chondromalacia using the compression test. This involves having the subject in a sitting position and actively bending and extending the knee while pushing down on the knee cap. Following this test, each person will again be measured for the dgree of knee extension.

Personnel: None.

Funding: None.

PROGRESS

This is a new study, and insufficient data has been collected to make any analysis.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Effects of the Application of Transcutaneous Electrical Nerve Stimulation on Peripheral Cutaneous Temperature as Measured in the Great Toe.

WORK UNIT NO.: C-37-78

PRINCIPAL INVESTIGATOR: Elizabeth J. Finan, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether TENS can alter peripheral blood flow.

TECHNICAL APPROACH

Prior to beginning the study, the volunteer will be instructed in how to adjust the TENS unit. When the unit is adjusted to the proper intensity the foot will "tingle". The volunteer will be asked to keep it adjusted at the output level that causes the mildest tingling.

After cleansing the toes with alcohol, a paper tape will be used to tape a special thermoccuple on the pad of each great toe. Then a jelly-like substance will be applied, electrodes or wires will be placed over the jelly and attached with paper tape. The investigator will watch the thermocouple temperature and start the test when temperatures stay constatn. Temperatures will be recorded at 5 minute intervals for appoximately 20 minutes.

Personnel: None.

Funding: None.

PROGRESS

This is a new project, and insufficient data has been collected for analysis at this time.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Heart Rate Response in Normal Subjects to Use of the Blow Bottle and the Spirocare Unit: Comparison with the Response to the Valsalva Maneuver.

WORK UNIT NO.: C-38-78

PRINCIPAL INVESTIGATOR: John Fromuth, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine and compare the heart rate response in normal subjects while using a blow bottle, while using a spirocare unit, and while performing a Valsalva maneuver.

TECHNICAL APPROACH

Volunteers will be asked to perform each of the three techniques. An EKG will be done to record heart rate before, during and after each exercise. The EKG recordings will be analyzed to determine the Valsalva ratio for each procedure. The Valsalva ratio is equivalent to the maximal RR interval recorded following release of strain divided by the minimal RR interval recorded during strain. Within subject and between subject comparisons will then be carried out.

Personnel: None.

Funding: None.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Child Advocacy Resources Expansion.

WORK UNIT NO.: C-8-76

PRINCIPAL INVESTIGATOR: Hubert A. Kelley, D.S.W., LTC, MSC

ASSOCIATE INVESTIGATORS; Michael F. Marley, Dir., Project CARE

OBJECTIVES

To demonstrate the effectiveness of community/Army/Air Force/Welfare Department planning in the provision to military families of broad spectrum services for the prevention, diagnosis, and treatment of child abuse and neglect.

TECHNICAL APPROACH AND RESULTS

Demonstration of systematic planning by multiple military/civilian agencies was the first project objective. Accomplishment of this objective required a study of existing needs and resources and conceptualization of basic methods and procedures for case detection, evaluation and management. Efforts were closely coordinated with installation child advocacy (ACAP) officers and child protection committees (CPCMT).

The second project objective was the integration and expansion of a community-wide referral and resources network for maximum utilization of community and military services by troubled military families. Project CARE provided a broad range of educational seminars and presentations to a variety of professional and lay audiences at BAMC, the Academy of Health Sciences, and in the general community. Topics included the subtle and overt signs of family stress and child abuse/neglect, child advocacy regulations and state laws, reporting procedures, the multidisciplinary approach and functions of the Army Child Protection and Caase Management Team (CPCMT), liaison between military and civilian agencies and treatment alternatives. BAMC and Fort Sam Houston audiences included Intensive Care Nurses, ward nursing supervisores, OB-GYN clinic nurses, chaplains, legal and law enforcement offices, ACS volunteers, school teachers, child care workers, and AHS students in various training programs. Several

C-8-76 (Continued)

parenting education classes were conducted for studnets at Cole High School on post and in the Well Baby Clinic. CARE also funded two major San Antonio child abuse conferences. CARE produced a child advocacy resource handbook for military and civilian professionals, conducted an ongoing public awareness campaign through the distribution of posters and other printed materials on local installations, and coordinated the recruitment of military families to become foster parents for the Department of Human Resources. Audio visual materials are also being produced.

The third CARE objective was the expansion of existing treatment and prevention services at BAMC. Systematic social work intake and evaluation processes were utilized and included home visits with military families. Family and adolescent crisis intervention, counseling, and treatment services were expanded. A uniform reporting system for all suspected child abuse and neglect cases involving Army personnel and their families was developed and piloted at BAMC. Uniform procedures for case presentation and follow-up to the CPCMT were utilized. Assessment and intervention guidelines were compiled into a social work procedures manual. Crisis child care services were contracted at the Fort Sam Houston child care center and the San Antonio Children's Center.

CARE facilitated numerous conferences between military and civilian service provides to identify, discuss, and resolve legal and jurisdictional issues and increase awareness of professional and organization roles and responsibilities. CARE's role as a liaison and advocate resulted in the conceptualization and dissemination of a procedures manual, delineating policies on the interface between civilian and military child advocacy service deliveres.

Care's final objective was to conduct a policy study on the military community's response to the problems of child abuse and neglect. The study was developed with the support and input of military and civilian social work administrators, including representatives of the Office of The Surgone General, Health Services Command, and the Department of Human Resources.

Personnel: None.

Funding: None.

PROGRESS

Final priorities of the project are identification of alternatives to assure continuation of services and activities initiated by the project; writing and disseminating the project's final report; distribution of project audio-visual and written documents; and finalization of fiscal, personnel and logistical requirements.

C-8-76 (Continued)

Status: Completed.

Presented at Third National Conference on Child Abuse and Neglect, April 1978, New York City.

Findings are to be published in a book entitled "Children of Miliary Families: A Part and Yet Apart."

Submitted to Journal of Social Service Research for publication.

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

INVESTIGATION PROJECT RESUME

TITLE: Patient Attitudes. A Preliminary Study. (Health Care Study)

WORK UNIT NO.: C-47-77

PRINCIPAL INVESTIGATOR: Barbara M. Nardi

ASSOCIATE INVESTIGATOR: Hubert A. Kelley, D.S.W., LTC, MSC

OBJECTIVES

To begin to isolate those factors bearing on a patient's ability to cope with the conditions of hospitalization. It is hoped that the results of this initial study will (1) demonstrate the effectiveness of the survey instrument and (2) show the emergence of a pattern of factors influencing "successful" and unsuccessful" patient behavior.

TECHNICAL APPROACH

Patient interviews will be carried out at Beach Pavilion, BAMC. The sample will consist of one group of adults ages 20 through 50, and a second group age 51 and above. One hundred patients will be included in the study.

Personnel: None

Funding: None

PROGRESS

It was found that the open-ward setting is conducive to the formation of community between patients and staff. A relationship exists between higher levels of patient adjustment and a sense of community. An additional finding is that older patients seem to adjut better in the open setting than do younger individuals.

Status: Completed.

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

APPENDIX A

GYNECOLOGY ONCOLOGY GROUP

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

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan Alone Versus Adriamycin and Cyclophosphamide Versus Hexamethylmelamine and Melphalan in Patients with Ovarian Carcinoma: Suboptimal Stage III, Stage IV and Recurrent Equivalent to Stages III and IV (Phase III).

WORK UNIT NO.: GOG 22

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if combination chemotherapy is more effective than Melphalan alone in achieving remission and improving survival in Stage IV and sub-optimal patients with Stage III ovarian cancer.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Women with Cervical Cancer Stage IIB, IIIB, IVA, Confined to the Pelvis and/or Para-aortic Nodes with Radiotherapy Alone versus Radiotherapy plus Immunotherapy (Intravenous C-Parvum - a killed germ) Phase III)

WORK UNIT NO.: GOG 24

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of the study is to assess the therapeutic effectiveness of immunotherapy (intravenous C-parvum) used concommitantly with radiation in patients with advanced carcinoma of the uterine cervix.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan Therapy Alone versus Melphalan plus Immunotherapy (Corynebacterium Parvum) in the Treatment of Women with Stage III (Optimal) Epithelial Carcinoma of the Ovary.

WORK UNIT NO.: GOG 25

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the relative effectiveness of Melphalan or Melphalan plus immunotherapy (Corynebacterium parvum) as adjunctive therapy to at least laparotomy and debulking of as much tumor as is prudent, and, total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy when technically feasible in Stage III optimal epithelial tumors of the ovary in a randomized prospective study.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies.

WORK UNIT NO.: GOG 26

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of chemotherapeutic agents in patients whose malignancies have been resistant to high priority methods of treatment.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Clinical-Pathologic Study of Stage I and II Carcinoma of the Endometrium.

WORK UNIT NO.: COG 33

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the incidence of pelvic and aortic lymph node metastases associated with Stage I and II adenocarcinoma of the endometrium and the relationship of these node metastases to other important prognostic factors.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Study of Adriamycin as an Adjuvant After Surgery and Radiation Therapy in Patients with High Risk Endometrial Carcinoma, Stage I and occult Stage II.

WORK UNIT NO.: GOG 34

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatment in the high risk Stage I and, optionally, high risk Stage II occult endometrial carcinoma.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Surgical Pathologic Study of Women with Squamous Cell Carcinoma of the Vulva.

WORK UNIT NO.: GOG 36

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine by observations of 5-year survival and disease-free interval the validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histologic grade, and site and number of positive lymph nodes in Stage I-IV carcinoma of the vulva.

2. To rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols for subsets of disease identified.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Randomized Study of Radiation Therapy versus Pelvic Node Resection for Patients with Invasive Squamous Cell Carcinoma of the Vulva Having Positive Groin Nodes.

WORK UNIT NO.: GOG 37

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the benefit and morbidity of adding adjunctive radiation therapy to pelvis and groin for patients found to have positive groin nodes at the time of radical vulvectomy and bilateral groin dissection.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new project.

Status: Ongoing.

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

APPENDIX B

SOUTHWEST ONCOLOGY GROUP

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

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy of Acute Leukemia in Adults.

WORK UNIT NO.: SWOG 7416/17

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine whether with the use of sequential or simultaneous adriamycin and ARA-C there is significant difference in their ability to induce complete remission.

2. To study the effects of combination chemotherapy and immunotherapy on the duration of remission and survival in patients with acute leukemia.

3. To identify those patients with ALL vs AML who are vincristine and prednisone responsive.

TECHNICAL APPROACH

Patients fulfilling the criteria for treatment will be divided into two different categories, depending on their peripheral circulating blast count. Category 1 is for those patients with a circulating blast count of less than 30,000. Category 2 is for those patients with a circulating blast count equal to or greater than 30,000/cu. ml. Approximately 96 patients will be entered into each group. Therapy will be in accordance with the schema outlined in the study protocol.

The study was amended to exclude the vincristine and prednisone arm.

PROGRESS

Prognosis for CIAL patients is still superior to that for 10-day OAP patients in survival time, but no longer in length of remission or complete remission rate at all institutions. Comparing the response rate for those starting with VP treatment to patients starting with simultaneous or sequential Ad-OAP, with < 30,000 blasts, the complete

response rates are similar (60% vs. 56%). For patients receiving simultaneous Ad-OPA vs. sequential Ad-OAP as primary induction treatment, there was no real evidence of a superiority for either treatment. For patients achieving CR on simultaneous or sequential Ad-OPA, there was no evidence that patients maintained on remission with OAP + BCG had longer remission than patients on OAP alone. Patients at M. D. Anderson received only OAP + BCG but detailed analysis revealed no differences in length of remission between these patients and those receiving OAP or OAP + BCG at other institutions.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy Utilizing BCNU, Hydroxyurea and DTIC (BHD) with and without BCG, and DTIC with BCG in the Treatment of Patients with Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7424/25

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To compare the effectiveness of BHD (3-drug regimen) alone, BHD in combination with BCG, and DTIC in combination with BCG for remission, induction, duration of remission and survival in patients with disseminated malignant melanoma.

TECHNICAL APPROACH

Since BCNU, DTIC and Hydroxyurea are principally myelosuppressive, dosage and time intervals were calculated to avoid the maximum toxicity occurring at the same time. Separate randomizations are set up for patients with normal and impaired bone marrow reserve, as well as for patients with brain metastases and liver metastases.

Treatment will be in accordance with the schema outlined in the study protocol.

PROGRESS

The complete + partial response rates were 30% for BHD, 29% for BHC + BCG, and 19% for DTIC + BCG. There is some evidence ($p = .107$) of difference in response rates by treatment. Combining the patients on BHD and comparing them with those on DTIC, the response rates are 30% and 19%, respectively. Patients receiving DTIC + BCG had a significantly poorer response rate ($p = .05$).

SWOG 7424/25 (Continued)

The patient characteristics significantly related to CR + PR rate at the 5% level were: age ($p = .01$), stage at diagnosis ($p = .01$), and performance status ($p = .001$). Favorable patients were those who were 30 years or older (28% response rate), stage 0 at diagnosis (53% response rate) and asymptomatic active (38% response rate). Factors moderately related to response were: brain involvement ($p = .09$), liver involvement ($p = .09$), and lung involvement ($p = .10$).

Combining patients on BHD and those on BHD + BCG, the advantage in response rate for patients receiving BHD + BCG over DTIC + BCG was in patients age 30-59 years (36% vs 13%), patients with stage 1 disease (38% vs 18%), patients at all levels of performance status, patients with or without brain metastases, patients without liver metastases, and patients without lung metastases. Though there was no overall difference in response rate between patients receiving BHD and those receiving BHD + BCG, it is of interest that the response rate in patients 60 or older was 12% on BHD and 32% on BHD + BCG.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy in Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7426/27

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC: Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness of two chemotherapy regimens or chemo-immunotherapy for remission induction in previously untreated non-Hodgkin's lymphoma patients.

2. To evaluate systematic restaging of clinical remissions..

3. To test the value of continued maintenance immunotherapy vs. no maintenance treatment for CR's.

4. To test the effectiveness of continued treatment with chemoimmuno-therapy for PR's.

TECHNICAL APPROACH

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The overall response rate is 59%. There are no significant differences in CR rate between induction treatments. Similarly there are no differences between induction treatments within either the diffuse lymphomas or the nodular lymphomas.

CHOP + BCG produced longer CR duration than either CHOP + Bleo or COP + Bleo, but all differences were not significant. Patients had longer survival than other patients, but again differences were not significant.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: VBAP in Multiple Myeloma (Vincristine, BCNU, Adriamycin and Prednisone).

WORK UNIT NO.: SWOG 7432

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To evaluate the frequency and degree of response with VCR, BCNU, adriamycin, prednisone combination (VBAP) in patients who failed to respond or relapsed on alkylating agents with or without prednisone.

TECHNICAL APPROACH

Patients with the diagnosis of multiple myeloma are eligible who have received Melphalan or Cytoxan with or without prednisone and have recovered from previous toxicity. The study was amended to allow VBAP treatment for all patients relapsing on any SWOG protocol and to include lymphoma patients.

Treatment was in accordance with the schema outlined in the study protocol.

PROGRESS

An overall 25% response rate has been observed using VBAP Of patients who had previously responded to alkylating agents and later relapsed, the response rate was 33%.

The VBAP program appears to be a useful addition to therapy for myeloma patients in relapse from melphalan.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: 5-FU + Mitomycin-C vs. 5-FU + MeCCNU in GI Malignancies.

WORK UNIT NO.: SWOG 7434

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.C., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine and compare the toxicity and effectiveness of two combination chemotherapies in GI carcinomas.

2. To compare the results with the results observed in SWOG 730.

TECHNICAL APPROACH

Treatment will conform with the schema outlined in the study protocol.

PROGRESS

The data demonstrates that 5-FU combined with Mitomycin-C has a higher response rate than 5-FU and Methyl-CCNU for treatment of advanced carcinoma of the pancreas. Unfortunately this is not translated in longer survival. The decision was made to keep the 5-FU + Mitomycin-C arm open for esophageal cancer patients. The objective is to obtain a more accurate estimate of response rate of esophageal cancers to this treatment. The response rate is very encouraging and the study has now been completed.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum for GU-GYN Malignancies, Phase II.

WORK UNIT NO.: SWOG 7438

PRINCIPAL INVESTIGATOR: J. Dean McCracken, LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To evaluate the activity of cis-platinum in patients with malignant diseases of the genitourinary and gynecologic organs.

TECHNICAL APPROACH

CACA, 75 mg/M^2, as a single intravenous injection will be administered every 3 weeks. A minimum of 15 patients in each histologic subtype will be studied.

PROGRESS

The response rates have been somewhat inferior to published observations, being 33.4% for testes and 14.7% for ovary.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Skin Test Protocol for Evaluation of Cellular Immunity in Patients with Neoplasia.

WORK UNIT NO.: SWOG 7475

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine if response to chemotherapy, duration of remission or survival of patients with cancer correlate with cellular immune competence as judged by skin test evaluation prior to therapy.

2. To determine which skin tests are ideal for this type of immunocompetence.

3. To delineate more clearly by means of three types of skin tests the immunologic defect in the cancer patient.

TECHNICAL APPROACH

Patients who have not received chemotherapy in the prior three month period and who are to be registered on a SWOG therapy protocol are eligible for entry into this protocol.

Skin tests are administered as outlined in the study protocol.

PROGRESS

Analysis of skin tests are being done within specific disease protocols where clinically relevant data are more readily available. Data from this study will provide normal control data and baseline data in broad disease categories.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Piperazinedione: In Patients with Metastatic Malignant Melanoma, Phase II.

WORK UNIT NO.: SWOG 7506

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To investigate the efficacy of Piperazinedione in patients with metastatic malignant melanom.

TECHNICAL APPROACH

A minimum of 25 patients will be entered into the study. The initial dose of Piperazinedione will be 12 mg/M^2 administered by intravenous infusions q 3 weeks for patients with adequate marrow reserved. Inadequate marrow reserve will receive initial dose of 9 mg/M^2 IV infusion q 3 weeks. Courses will be administered at 3-week intervals as tolerated. Subsequent courses should not be repeated until the nadir of blood counts has been reached, and the counts are recovering. Subsequent doses of Piperazinedione will be adjusted in relation to nadir blood counts according to the schedule outlined in the study protocol.

PROGRESS

Twenty-five patients have been entered on this study with 17 evaluable patients. It is a negative study and is closed.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: 5-FU, MeCCNU + Radiotherapy with or without Testolactone for Localized Adenocarcinoma of the Exocrine Pancreas.

WORK UNIT NO.: SWOG 7509

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effect on survival of intensive radiotherapy and chemotherapy (5-FU and MeCCNU) of localized pancreatic adenocarcinoma.

2. To evaluate any beneficial effect of testolactone when added to this regimen.

TECHNICAL APPROACH

Patients with histological confirmation of adenocarcinoma of the exocrine pancreas with localized disease are eligible for enrollment in this study protocol.

Treatment regimen is as outlined in the schema accompanying the study protocol.

PROGRESS

Initially, severe toxicity was noted which necessitated deleting the second dose of Methyl-CCNU. Preliminary analysis suggests that 5% to 10% of the patients will approach a two-year survival. The addition of Testolactone had no benefit to the program.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Chemotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel.

WORK UNIT NO.: SWOG 7510

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness of the combination of MeCCNU + 5-FU as adjuvant chemotherapy.

2. To judge whether oral BCG adds to effectiveness.

TECHNICAL APPROACH

Patients with histologically proven Duke-C adenocarcinoma of large bowel with no proven residua or metastatic disease and nor prior chemotherapy or radiotherapy are eligible for entry into this protocol.

Treatment regimen will confomr with the schema outlined in the study protocol.

PROGRESS

It does not appear that there will be a difference in skin test reactivity between patients with locally advanced colon cancer (Duke B_2 and C) and normal subjects.

At this point, there is no statistical difference in the disease-free interval between those patients on the 5-FU + MeCCNU arm or 5-FU + Methyl-CCNU + BCG limb.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: VP-16 in Adults with Metastatic Adenocarcinoma of the Breast.

WORK UNIT NO. SWOG 7514

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of VP-16 in adult patients with metastatic adenocarcinoma of the breast.

TECHNICAL APPROACH

Eligibility: Patients with a histologically confirmed diagnosis of adenocarcinoma of the breast with metastasis who are not eligible for studies of higher priority.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Some activity in breast cancer with VP-16 has been seen, especially at the 75 mg/M^2 dose level (1 PR and 2 improved of 28 evaluable patients). The myelotoxicity, mainly leukopenia, seen at this dose level suggests this to be the correct starting dose. It was felt that the results warrant further trials with VP-16 possibly in combination with Adriamycin.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Phase III Study of Squamous Cell Carcinoma of the Head and Neck Region.

WORK UNIT NO.: SWOG 7519

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTICATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To determine whether a three drug combination treatment program will give a superior response rate and/or a longer remission duration than methotrexate alone in patients with squamous cell carcinoma of the head and neck region.

TECHNICAL APPROACH

Approximately 60 patients will be entered into the study. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

Thie study compares MTX in a 3-day intramuscular schedule every 21 days with MTX in the same schedule given every 6 weeks plus methyl-CCNU given once every 6 weeks and bleomycin administered during the 5th and 6th week. Response rates between the two arms are not different (31% for the 1-drug versus 21% for the 3-drug) but CR's were 10% versus 1% ($p < .05$) favoring the single drug. There was a high percentage of early deaths in the 3-drug arm (19% versus 4%, $p < .01$). Performance status did not

SWOG 7519 (Continued)

differ significantly between the two arms. A significantly higher number of patients in the 1-drug arm received inadequate trials on the basis of no toxicity, i.e. 60% 0-1 grade arm. The degree of toxicity was higher in responders receiving three drugs compared to one drug ($p<.05$), 64% versus 31% grade 2 or more toxicity, suggesting that higher response rates might be achieved particularly in the single drug arm. The survival for all eligible patients was statistically longer in the single drug arm compared to the 3-drug arm, 215 days versus 105 days, $p<.01$. There was a difference in median survival of responders of 337 days for the 1-drug arm compared to 158 days in the 3-drug arm, but it is too early to assess significance since there is a large percentage of censored observations.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Phase II Study of Galactitol in Advanced Cancer Patients.

WORK UNIT NO.: SWOG 7520

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D, MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy and toxicity of Galactitol in the treatment of advanced carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with measurable metastatic disease not eligible for studies of higher priority or other potentially more effective drugs.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Partial responses have been observed in three patients; three have had no response; 1 increasing disease. Two patients had decreased creatinine clearances and six had mild to moderate myelosuppression.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy with or without Immunotherapy in High Risk Melanoma Patients: An Adjuvant Study.

WORK UNIT NO.: SWOG 7521

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine efficacy of BHD in preventing recurrence of disease and prolonging survival of patients who have received definitive surgical treatment for their primary lesions.

2. To determine the efficacy of BHD+BCG in preventing metastases and prolonging the disease-free interval.

3. To determine the immunocompetence of these patients.

TECHNICAL APPROACH

Eligibility: All patients with histologically confirmed diagnosis of malignant melanoma previously untreated with chemotherapy or radiotherapy who are within 4 weeks of surgical excition of active disease.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

Sixty-four class I patients have been registered. No deaths have been reported. There are 118 class II patients either fully or partially evaluable. So far there is no statistical difference in the two arms. There has been 30% severe life-threatening toxicity in the class II arm of the study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy, Splenectomy with or without Immunotherapy in the Treatment of Chronic Myelogenous Leukemia.

WORK UNIT NO.: SWOG 7522

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To study the effects of chemotherapy, splenectomy and/or immunotherapy on leukemic cytogenetics, immune status, appearance of blastic transformation, and any influence in overall survival.

TECHNICAL APPROACH

Eligibility: All patients with confirmed diagnosis of benign phase CML not previously treated with any of the agents used in this study.

Treatment will conform to the schema outlined in the study protocol.

PROGRESS

Sixty-three patients have been entered into this study. Twenty-two have had spelenctomy. Thirty-three had no toxicity during induction, toxicity was unknown in 15 cases, and 7 FUO's were documented associated with drops in white cell count.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Advanced Large Cell Undifferentiated and Adenocarcinoma of the Lung Using the Combination of Methotrexate and Methyl-CCNU.

WORK UNIT NO.: SWOG 7523

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC: Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To determine the effectiveness, response rates, and duration of response of Methotrexate and Methyl-CCNU in large cell undifferentiated and adenocarcinoma of the lung.

TECHNICAL APPROACH

Eligibility: Patients with diagnosis of large cell undifferentiated or adenocarcinoma of the lung with extensive disease and no prior treatment with nitrosourea or methotrexate.

Treatment will conform with the schema outlined in the study protocol.

PROGRESS

Response rates by cell types are: 13% for adenocarcinoma and 15% for undifferentiated large cell patients. The survival of all adenocarcinoma patients is not at all significantly different from that achieved by large cell patients.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy in Stages III and IV Ovarian and Endometrial Cancer.

WORK UNIT NO.: SWOG 7524

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness of chemotherapy alone vs. chemoimmunotherapy for remission induction in Stages III and IV ovarian and endometrial carcinoma.

2. Test the effectiveness of chemotherapy plus immunotherapy vs. chemotherapy in maintaining complete remissions.

3. To test effectiveness of continued chemotherapy plus immunotherapy vs. chemotherapy in inducing a complete remission or maintain in partial remission in patients with occult disease at restaging or in patients achieving only partial remission during 12 month induction therapy.

TECHNICAL APPROACH

Eligibility: Patients with histologically conformed ovarian carcinoma or endometrial carcinoma Stage III or IV with no prior chemotherapy or concurrent progestational agent therapy are eligible. Adenocarcinoma of cervix and germ cell of the ovary are eligibile.

Therapy will be according to the schema outlined in the study protocol.

PROGRESS

In the ovarian arm, 43 patients have been registered on the adriamycin-cytoxan + BCG and 44 patients have been registered on adriamycin-cytoxan alone. IN the endometrial arm, 17 patients have been registered on AC + BCG and 21 patients on AC alone. Toxicity has been well tolerated in both arms. BCG reactivity of 3+ and 4+ are reasonably good.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Patients for Early Testicular Cancer with Irradiation and Chemotherapy with Vinblastine and Bleomycin.

WORK UNIT NO.: SWOG 7525

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if a combination of irradiation and chemotherapy can improve the 2 year disease free interval and 5 year survival in certain morphologic subtypes of Ib and II nonseminomatous testicular tumors.

2. To determine which sequence of irradiation and chemotherapy more favorably influences remission maintenance, survival and possibly cure.

TECHNICAL APPROACH

Eligibility: Previously untreated patients with histologically proven Stage IB and II pure embryonal and pure teratocarcinomas, mixed cell types with seminomatous elements.

Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

Forty-four patients have been registered on this study since its activation. Three patients have failed.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Immune Evaluation of Lymphoma in Unmaintained Remission.

WORK UNIT NO.: SWOG 7580

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the immune status of patients with lymphoma who have been successfully treated and are in remission without therapy.

2. To correlate the presence of immune deficits with histologic type of lymphoma, pathologic stage, types of therapy and interval since therapy.

3. To correlate the immunologic profile with long term follow-up of patients in terms of disease relapse, second malignancy and duration of survival.

TECHNICAL APPROACH

Eligibility: Any patient with histologically proven Hodgkin's or non-Hodgkin's lymphoma, who has completed therapy and has had at least 3 months of unmaintained remission.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

This study evaluated skin test reactivity as an indicator of immune competence in a large population of lymphoma patients who were in unmaintained remission for 3-186 months following intensive chemotherapy (CT), radiation therapy (RT) or both CTRT). Ninety-eight patients with Hodgkin's disease (HD) or non-Hodgkin's lymphoma (NHL) were skin tested with 5 recall antigens (NA) and phytohemagglutinin (PHA), immunized with the neoantigens (NA) keyhole limpet hemocyanin

(KLH) and dinitrochlorobenzene (DNCB) and challenged with these NA 3 weeks later. PHA skin test was normal in all groups. Stages of disease, histology and time since treatment did not significantly affect the incidence of anergy. In fact, of 30 patients in remission for greater than 3 years, 67% were anergic to KLH and 45% to DNCB. Thus, treated lymphoma patients have a long-lasting deficit in response to neoantigens although most have a normal response to recall antigents. This deficit may result in impaired defense mechanisms.

Status: Ongoing.

King, G.W., Grozea P. and LoBuglio, A.F.: Neoantigen Response in Successfully Treated Lymphoma Patients. Abstract submitted to American Socity of Clinical Oncologists for consideration for presentation.

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

INVESTIGATION PROJECT RESUME

TITLE: Effect of Schedule of Activity of 5-Azacytidine in Acute Leukemia.

WORK UNIT NO.: SWOG 7603

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the activity and toxicity of single dose vs. continuous 5-day infusions of 5-Azacytidine in patients with acute leukemia.

TECHNICAL APPROACH

Eligibility: Patients with bone marrow diagnosis of acute leukemia who are ineligible for or who have relapsed on a leukemia protocol of higher priority.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

Among 68 patients, there were 6 CR's and 1 PR. No responses were seen with the 750 mg/M^2 dose. There were 2 CR's and 1 PR among 22 evaluable patients treated with 300 mg/M^2 x 5 days and 2 CR's amont 15 evaluable patients treated with 200 mg/M^2/d x 7 days. Toxicity appears to be significantly less with the continuous infusion. The 12 patients with CNS toxicity were sent to the Unusual Complications Committee for evaluation. The report stated that 10/12 were probably not drug related toxicity, however, the drug may have caused drowsiness in the other 2.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Disseminated Testicular Cancer with Vinblastine, Bleomycin, Cis-Platinum, Chlorambucil and Actinomycin-D.

WORK UNIT NO.: SWOG 7610

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness of Vlb, Bleo and Cis-platinum in remission induction.

TECHNICAL APPROACH

Eligibility: Patients of an age with Stage III metastatic testicular carcinoma who have not been previously treated with any of the selected agents.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

One hundred and twenty-five patients have been registered. The complete response rate is 50% with an 8+ month median duration of remission. Renal dysfunction has not been a major problem.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum for Refractory Sarcomas.

WORK UNIT NO.: SWOG 7611

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of cis-platinum in the treatment of patients with advanced sarcomas refractory to adriamycin combinations.

TECHNICAL APPROACH

Eligibility: Patients with a biopsy confirmed diagnsis of soft tissue or bony sarcoma and not eligible for a higher priority protocol. Patients must have measurable disease.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

Sixty-six patients have been registered, 61 of these are fully evaluable. Three of 41 patients with soft tissue sarcoma have responded. With only 3 remissions out of 41 evaluable patients, DDP appears to have a low degree of antitumor activity. Since there are only 8 patients with boney sarcomas entered on the study, it is too early to comment on the activity of DDP, although it appears to be inactive.

Status: Onging.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Preoperative Adjuvant Therapy in Rectal Carcinoma.

WORK UNIT NO.: SWOG 7618

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if adjuvant preoperative radiotherapy and chemotherapy will yield a higher incidence than expected of Duke A lesions in a high risk group.

2. To determine the survival of patients with an without regional node metastases.

TECHNICAL APPROACH

Eligibility: Patients with CA of the rectum judged by the surgeon to have clinically resectable disease by abdominoperineal resection.

Therapy will conform to the schema outlined in the study protocol.

PROGRESS

Approximately 140 patients are necessary for this randomized study. Patient accrual continues to be extremely slow averaging approximately one patient per month.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Ftorafur in the Treatment of Metastatic Adenocarcinoma of the Colon and Rectum.

WORK UNIT NO.: SWOG 7619

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of Ftorafur in disseminated adenocarcinoma of the colon and rectum.

TECHNICAL APPROACH

Eligibility: Patients must have biopsy proven adenocarcinoma arising from the colon or rectum and have clinically measurable recurrent or disseminated disease.

Therapy will be administered as outlined in the schema of the study protocol.

PROGRESS

This non-myelosuppressive agent produced remissions in 13% of the evaluable patients. Survival of responders was significantly longer than non-responders. A signifficant amount of CNS and gastrointestinal toxicity was encountered.

Status: Completed.

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

TITLE: Chemotherapy or Chemotherapy + Immunotherapy Following Initial Surgery and/or Radiotherapy for Treatment of Early Squamous Cell Carcinoma of the Head and Neck.

WORK UNIT NO.: SWOG 7620

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LT, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ. MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant chemotherapy or chemoimmunotherapy after initial surgery, radiotherapy or combination approach have resulted in no clinically evident disease.

2. To accumulate immunologic data in treated and untreated patients withthis malignancy.

TECHNICAL APPROACH

Eligibility: Patients with no evidence of clinical disease three months after completion of surgery or irradiation.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

Entry into this study has been extremely slow. As a consequence the study has been amended as follows:

1) The study will be restricted to Stages I and II of the following sites: tonsil, oropharynx, posterior tongue, pyriform sinus, hypopharynx and subglottic region.

2) Patients will be registered at initial staging prior to evaluation of primary therapy.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin vs. Adriamycin plus Cis-platinum in Transitional Cell Bladder Carcinoma.

WORK UNIT NO.: SWOG 7624

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the efficacy of Adriamycin vs. Adriamycin + Cis-platinum in recurrent or disseminated transitional cell bladder carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven T_4 transitional cell bladder carcinoma, T_3 if there is a general contraindication to radical surgery; recurrent or residual cases after surgery, radiotherapy or both; and M_1 cases of liver, osseous, pulmonary or other metastasis.

Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

Very few patients have been registered. The hematologic toxicity has been very tolerable. The GI toxicity has been more severe on the combined treatment arm. Renal toxicity has been minimal. There is no apparent difference in response rates thus far.

Status: Onging.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Chemotherapy for Advanced Sarcoma of the Bone and Mesothelioma Utilizing Rubidazone and DTIC.

WORK UNIT NO.: SWOG 7625

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy in terms of rate of response of combination chemotherapy with the 2-drug regimen RubiDIC (Rubidazone + DIC) in patients with metastatic sarcomas of bone and mesothelioma.

2. To determine the duration of remission and survival pattern of patients on this study and compare them with that of patients with metastatic bone sarcomas and mesothelioma on previous SWOG or M.D. Anderson Hospital protocols using adriamycin containing regimens.

3. To determine the toxicity of the regimen especially with regard to cardiac toxicity.

TECHNICAL APPROACH

Eligibility: Patients with a biopsy-confirmed diagnosis of bony sarcoma or mesothelioma with measurable metastases who have already received appropriate surgical therapy and who have not received prior adriamycin, daunorubicin, rubidazone, DIC or BIC are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study is closed to chondrosarcomas and mesotheliomas. Thus far, this is a negative study but some patients are still needed in the osteogenic category.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: ROAP Induction of Chemotherapy for Acute Leukemia Patients Over the Age of 50.

WORK UNIT NO.: SWOG 7626

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of the 4-drug combination chemotherapy regimen ROAP (rubidazone, vincristine, arabinosyl cytosine and prednisone) in remission induction chemotherapy in patients with acute leukemia over the age of 50.

2. To determine the toxicity of the regimen.

TECHNICAL APPROACH

Eligibility: All patients age 50 or greater with a diagnosis of acute leukemia who have received no extensive prior therapy (defined as one course or less of any other chemotherapeutic agent or combination of agents) will be eligible for this study. The diagnosis of acute leukemia will be made on bone marrow smear clot section and/or biopsy. An absolute infiltrate of 50% leukemic cells or greater is required. Absolute infiltrate is defined as the total blase cell percentage (%) multipled by the bone marrow cellularity percentage divided by 100.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Of the 172 entered in this study, 52 are evaluable. There are 50% CR's (84% CR if early deaths are excluded). There is evidence of positive response but it is too early to evaluate.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Chemotherapy/Radiotherapy/Immunotherapy for Oat Cell Cancer of the Lung.

WORK UNIT NO.: SWOG 7628

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To use combination chemotherapy, local radiotherapy, and maintenance chemotherapy or chemoimmunotherapy in the treatment of oat cell carcinoma of the lung in order to improve the quality and duration of survival.

TECHNICAL APPROACH

Eligibility: Histologically proven diagnosis of oat cell carcinoma or small cell undifferentiated carcinoma of the lung.

Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

Patients with limited disease now receive the full split-course. An analysis is being prepared of those treated in this fashion, vs. those who received only 3000 rads, especially with respect to the incidence of local recurrence.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Refractory Epidermoid Carcinoma of the Head and Neck.

WORK UNIT NO.: SWOG 7629

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy and toxicity of cis-platinum and mannitol in the treatment of refractory epidermoid head and neck carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with epidermoid carcinoma of the head and neck region with measurable disease, who are not eligible for protocols of higher priority.

Therapy is administered according to the schema outlinedin the study protocol.

PROGRESS

30% of evaluable patients had excellent PR's. These were all previously heavily treated patients. The median duration of survival in responders is in excess of 119 day. Renal toxicity was minimal, as was immunological toxicity. It appears that this is an active regimen in head and neck cancer that lends itself to outpatient therapy and is well tolerated.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Advanced Prostatic Cancer.

WORK UNIT NO.: SWOG 7630

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare rate of response of hydroxyurea versus adriamycin + cytoxan.

2. To compare the duration of survival in patients with nonmeasurable disease.

3. To estimate the response rate to each crossover regimen.

TECHNICAL APPROACH

Eligibility: All patients with advanced Stage D prostatic cancer who have not received Hydroxyurea, Adriamycin, or Cyclophosphamide.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

Sixty-one patients have been entered on study since its activation. It is too early for any significant evaluation.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality for Recurrent Breast Cancer.

WORK UNIT NO.: SWOG 7632

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. Establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal-chemotherapeutic approach.

2. Determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.

3. Correlate hormonal manipulations with estrogen and progesterone receptors where possible.

TECHNICAL APPROACH

Only patients who have been surgically and/or radiotherapeutically treated with the intent to cure their primary disease are eligible. In addition, patients with castration are eligible.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

There have been 109 patients registered. Responses to Tamoxifen have been seen in 10/47 (21%) patients, 2/15 in the premenopausal group and 8/32 in the postmenopausal group. Eight patients have movedinto the second phase of the study, Tamoxifen + oophorectomy. One partial response occurred in a premenopausal patient who failed to respond to Tamoxifen alone. Responses to Tamoxifen have lasted 40+ to 202+ days.

SWOG 7632 (Continued)

Ten patients have been treated with chemotherapy in the final phase of the study and 4/10 have responded. Toxicity has been negligible.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Rubidazone in Adults with Previously Treated Acute Leukemia and Patients with CML Blast Transformation.

WORK UNIT NO.: SWOG 7633

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficay of rubidazone in adult patients with previously treated acute leukemia and in patients with CML blast transformation.

2, To determine the toxicity of the drug in the above patients with special reference to patients having prior therapy with adriamycin.

TECHNICAL APPROACH

Eligibility: Adult patients with acute leukemia having had prior chemotherapy and patients with CMLBT will be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Data is being analyzed and a manuscript is being prepared.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of MeCCNU plus BTGdR and Mitomycin-C plus BTGdR in the Treatment of Refractory Disseminated Colorectal Carcinoma.

WORK UNIT NO.: SWOG 7634

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To evaluate the effectivenes of MeCCNU plus BTGdR vs. Mitomycin-C plus BTGdR for remission induction or for relapsing patients from prior chemotherapy.

TECHNICAL APPROACH

Eligibility: All patients with disseminated colorectal carcinoma who are not eligible for studies of higher priority.

Therapy will be in accordace with the schema outlined in the study protocol.

PROGRESS

Neither combination is effective in previously treated patients, and the study is now closed to all previously treated patients. Both arms remain open for patients with no prior therapy.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality Treatment for Limited Squamous Carcinoma of the Lung.

WORK UNIT NO.: SWOG 7635

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether chemotherapy with adriamycin and/or immunotherapy with levamisole, improve median survival of split-course radiotherapy used alone in the treatment of patients with limited extent, squamous bronchogenic carcinoma.

2. To determine the qualitative and quantitative toxicity of each treatment regimen.

TECHNICAL APPROACH

Eligibility: All patients with a histologically confirmed diagnosis of limited squamous carcinoma of the lung are eligible provided they have received no previous chemotherapy or radiation therapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

In 8 months 41 patients have been registered. This is short of the projected accrual. No outward complications have been reported to date. It is too early to say whether the study is positive, but patients have now been followed for as long as two years without evidence of unexpected or synergistic toxicity.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Hexamethylmelamine in Advanced Breast Cancer.

WORK UNIT NO.: SWOG 7636

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Peter S. Kennedy, M.D., MAJ, MC; Dan W. Luedke, M.D., MAJ, MC

OBJECTIVES

1. To determine the responsiveness of patients to hexamethlmelamine.

2. To determine whether pyridoxine given prophylactically will prevent the neuropathy associated with long-term hexamethylmelamine administration.

TECHNICAL APPROACH

Eligibility: Patients with advanced breast cancer not eligible for a higher priority study.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

No CR's or Pr's reported in this group of previously treated patients. In view of this, the study is closed.

Status: Completed.

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

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin, Mitomycin-C, and 5-FU in Gastric Carcinoma.

WORK UNIT NO.: SWOG 7639

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine and to document both response rates and the toxicities of two different combinations of Adriamycin, Mitomycin-C and 5-FU in the management of surgically incurable adenocarcinoma of the stomach.

2. To compare the effectiveness of these two regimens.

TECHNICAL APPROACH

Eligibility: Patients must have unresectable gastric adenocarcinoma and an objectively measurable lesion. No prior exposure is permitted to Adriamycin, Daunomycin, Mitomycin-C or Porfiromycin. If previous chemotherapy has been given, full recovery from its effects must have been achieved before this regimen is started.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

It is still too early to make any statements comparing the toxicity or effectiveness of these two regiments.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: CIA vs. Ifosfamide Alone in Extensive Squamous Lung Cancer.

WORK UNIT NO.: SWOG 7701

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if Ifosfamide, Adriamycin, CCNU is a more effective combination than Ifosfamide alone or in combination with Adriamycin in the treatment of patients with extensive non-oat cell carcinoma of the lung who are not eligible for curative radiotherapy.

2. To measure the relative efficacy of this regimen on survival.

3. To determine the qualitative and quantitative toxicity of the regimen.

TECHNICAL APPROACH

Eligibility: All patients with a histologically confirmed diagnosis of extensive non-oat cell carcinoma of the lung are eligible, provided they have received no previous chemotherapy.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

Based on fully evaluabe patients, a preliminary response analysis is as follows:

Ifosfamide	4/18 PR
Ifosfamide + Adriamycin	5/22 PR
CCNU + Ifosfamide + Adriamycin	6/12 PR
	15/52

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Radiation Therapy in Combination with BCNU, DTIC or Procarbazine in Patients with Malignant Gliomas of the Brain.

WORK UNIT NO.: SWOG 7703

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus Procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed primary central nervous tumors of the following histologic types are eligible: Astrocytoma, grade 3 and 4 (glioblastoma multiforme).

Therapy will follow the schema outlined in the study protocol.

PROGRESS

On the RT + BCNU arm, there are 21 patients registered, with 9 evaluable and 1 partially evaluable. These include 3 CR's, 1 PR, 3 no change, and 3 with increasing disease. On the RT + DTIC limb, 19 patients have been registered of which 13 are evaluable. There have been 1 CR, 3 PR, 4 with stable disease, 4 with increasing disease, and 1 patient showed subjective improvement but refused further therapy.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy/Immunotherapy for Multiple Myeloma.

WORK UNIT NO.: SWOG 7704

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness of three intermittent pulse chemotherapy combinations VMCP + VCAP vs. VMCP + VBAP vs. MP for induction of remissions in previously untreated patients with multiple myeloma.

2. For patients proven to have at least a 75% tumor regression after induction, to compare the value of 12 months of chemoimmunotherapy maintenance VMCP + Levamisole in comparison to VMCP alone.

3. To establish baseline and serial data on immunologic status in these patient groups.

TECHNICAL APPROACH

Eligibility: All previously untreated patients with multiple myeloma (all stages) are eligible; without prior cytotoxic chemotherapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

There is no way to discern between the results in the three arms due to the marked imbalance of registrations. However, a preliminary review of experience at M.D. Anderson Hospital for VMCP + VCAP and VMCP + VBAP is most encouraging.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy for Stages III and IV Ovarian Carcinoma Resistant to Adriamycin-Cyclophosphamide or Single Alkylating Agent.

WORK UNIT NO.: SWOG 7706

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To use a combination of 5-FU, hexamethylmelamine and platinum in an attempt to induce complete and partial clinical remissions in patients with stages III and IV ovarian carcinoma who have failed to respond to or have relapsed following remission from Adriamycin-cyclophosphamide therapy.

2. To use a combination of 5-FU, hexmethylmelamine, platinum and Adriamycin to induce complete and/or partial remissions in patients with stages III and IV ovarian carcinoma who have failed on or relapsed from previous alkylating agent therapy.

TECHNICAL APPROACH

Eligibility: Patients must have a diagnosis of ovarian carcinoma established by biopsy. Epithelial type neoplasms (e.g. serous cystadenocarcinoma, undifferentiated adenocarcinoma, endometrioid adenocarcinoma, mucinous cystadenocarcinoma, mesonephroid adenocarcinoma) are to be included.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

It is too early for significant evaluation. Three patients on the 4-drug arm had severe leukopenia. Other toxicity has been very tolerable.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Previously Treated Patients Using VBAP, Phase II.

WORK UNIT NO.: SWOG 7707

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To evaluate the frequency and completeness of response with vincristine, BCNU, Adriamycin and prednisone combination (VBAP) chemotherapy in patients with malignant lymphoma (non-Hodgkin's disease and Hodgkin's disease) who have received prior therapy and are not eligible for higher priority studies.

TECHNICAL APPROACH

Eligibility: Patients of any age with Hodgkin's disease or non-Hodgkin's lymphoma who have become refractory to prior treatment and who are not eligible for studies of higher priority.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Of the 41 evaluable patients, 12 are Hodgkin's disease and 29 are non-Hodgkin's lymphoma. There are 3/12 responses in the Hodgkin's disease group (1 CR and 2PR) and 12/29 responses in the non-Hodgkin's group (2 CR and 10 PR). These would be the minimum response rates of the 41 patients and may increase as more data becomes available.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy in Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7713/14

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness, in terms of rate of response to two chemoimmunotherapy regimens (CHOP+Levamisole vs. CHOP + Levamisole_BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma.

2. For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with Levamisole vs. no maintenance therapy.

3. For patients with impaired cardiac function (not eligible for treatment with Adriamycin), with mycosis fungoides, or with only a partial response to II courses of treatment with CHOP-Levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + Levamisole.

4. To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.

5. To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.

6. To establish baseline and serial data on immunologic status in both chemoimmunotherapy groups.

TECHNICAL APPROACH

The patient must have the diagnosis of non-Hodgkin's lymphoma established by biopsy. All histologic types of non-Hodgkin's lymphoma,

according to the Rappaport classification will be eligible. Patients with chronic lymphocytic leukemia are ineligible.

PROGRESS

Seventy-five patients are entered. There is no analysis as it is too early.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Tamoxifen in Renal Cell Carcinoma.

WORK UNIT NO.: SWOG 7716

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the response rate and survival in patients with disseminated renal cell carcinoma treated with Tamoxifen.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven disseminated renal cell carcinoma who have not received anti-estrogen agents before are elibible. Expected survival should be a minimum of 8 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Management of Patients with a Metastatic Adenocarcinoma of Unknown Primary.

WORK UNIT NO.: SWOG 7717

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the yield of various diagnostic procedures in finding the site of tumor origin in patients who present with metastatic adenocarcinoma with no obvious primary source.

2. To compare the efficacy of combination chemotherapy using 5-FU, Adriamycin and Cytoxan vs. 5-FU alone in the palliative management of patients with metastatic adenocarcinoma of unknown origin.

3. To assess the hematologic toxicity of the chemotherapy regimen on treated patients.

TECHNICAL APPROACH

Eligibility: Patients with metastatic adenocarcinoma with no obvious primary source are eligible for diagnostic evaluation. In addition they should meet the following criteria:

1. Should have histopathologic confirmation of their disease.

2. Patients must have measurable disease and an expected survival of 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality for Removable Lung Cancer.

WORK UNIT NO.: SWOG 7718

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if immunotherapy in the form of Levamisole and postoperative intrapleural BCG prolonges the median disease-free interval and survival of resected (T_1 or T_2, N_0, M_0) non-small cell carcinoma of the lung.

2. To determine whether immunotherapy in the form of Levamisole and intrapleural BCG prolong the median disease-free interval and survival of non-small cell carcinoma of the lung (T_3, N_{any}, M_0) or (T_{any}, N_1, or N_2 M_0) treated with resection and subsequent postoperative radiotherapy.

TECHNICAL APPROACH

Eligibility: Patient must have potentially resectable squamous, adeno or large cell carcinoma of the lung.

Therapy will follow the schema outlined in the study protoco.

PROGRESS

The study was amended in 3 respects: 1) patients now will be reigstered and randomized only once, postoperatively; 2) the radiation therapy approach has been modified to include supraclavicular fields, when appropriate; 3) patinets with grossly complete resections (Stage II) will be eligible.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Addition of CCP and Bleomycin to VBAP in Relapsing and Resistant Myeloma Patients, Phase II.

WORK UNIT NO.: SWOG 7719

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the frequency, degree and duration of response with cis-platinum (DDP) and bleomycin (Bleo) added to vincristine-BCNU-Adriamycin-prednisone combination (VBAP) to combinations of melphalan and/or cyclophosphamide with prednisone (M/C+P).

2. To compare results with previous SWOG trials of VBAP in such patients.

TECHNICAL APPROACH

Eligibility: Patients with the diagnosis of multiple myeloma who are no longer responding to or have not responded to melphalan/cyclophosphamide with prednisone.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Accrual rate has been slow. In those entered into the study, toxicity does not appear to be excessive.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Management of Oligoblastic Leukemia.

WORK UNIT NO.: SWOG 7720

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC, Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To collect data on the clinical course of patients with acute oligoblastic (smoldering) leukemia, a subgroup of acute leukemia patients who do not meet hg requirements of the current Southwest Oncology Group chemotherapy protocol which requires greater than a 50% absolute leukemic infiltrate.

2. To compare the randomly assigned immuno-stimulant effect of levamisole on half this group of patients, as opposed to those receiving no specific treatment.

3. To maintain data on those patients in this group who subsequently attain a marrow status, which qualified them to transfer to active chemotherapy protocols.

TECHNICAL APPROACH

Eligibility: Any previously untreated patient with a diagnosis of acute non-lymphocytic leukemia (excluding blast crisis of CGL), whose absolute marrow blast cellularity is less than 50%, should be registered in this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Diglycoaldehyde in Adult Acute Leukemia, Phase II Study.

WORK UNIT NO.: SWOG 7723

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the response of adult acute leukemia to diglycoaldehyde.

2. To study the toxicity of the drug.

TECHNICAL APPROACH

Eligibility: Patients will all cell types of acute leukemia will be eligible for the study. They will be in relapse after an initial response to other therapies or they may have failed to responde.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Diglycoaldehyde in Metastatic Malignant Melanoma, Phase II Study.

WORK UNIT NO.: SWOG 7724

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the response of metastatic malignant melanoma to diglycoaldehyde.

2. To study the toxicity of the drug.

TECHNICAL APPRAOCH

Eligibility: Patients with disseminated disease who have relapsed or are resistant to regimens in a higher priority will be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

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

INVESTIGATION PROJECT RESUME

TITLE: CMPF vs. CMPF + Levamisole for ER$^-$ Patients with Breast Cancer.

WORK UNIT NO.: SWOG 7725

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the respective effects of Levamisole on the duration of response and survival of patients with advanced breast cancer concurrently treated with maintenance chemotherapy after a successful remission induction trial of continuous Cooper regimen.

2. To accumulate data on immunologic variables under the conditions of chemotherapy alone and combined chemotherapy and immunotherapy with Levamisole of advanced breast cancer.

TECHNICAL APPROACH

Eligibility: Only patients prove to be ER negative are eligible. Patients with measurable lesions and no previous experience of chemotherapy other than adjuvant chemotherapy. Life expectancy of 2 months is assumed.

Therapy will follow the schema outlined in the study protocol

PROGRESS

Only 13 patients are registered and are all too early for analysis.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Advanced Carcinoma of the Breast with Rubidazone.

WORK UNIT NO.: SWOG 7726

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy and toxicity of Rubidazone as determined by response rate and median duration of response in patients with disseminated carcinoma of the breast who have not received prior therapy with Adriamycin or other anthracycline antibiotics alone or in combination.

TECHNICAL APPROACH

Eligibility: All paitnes not eligible for higher priority Southwest Oncology Group studies with histologically proven advanced metastatic carcinoma of the breast who have not previously received Adriamycin or other anthracycline antibiotics. Patients must have a life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemoimmunotherapy Utilizing BCNU, Hydroxyurea and DTIC with Levamisole vs. DTIC plus Actinomycin-D in the Treatment of Patients with Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7727

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine remission induction rates, remission duration, survival and toxicity in patients with disseminated malignant melanoma treated with BCNU, hydroxyurea and DTIC (BHD), BHD plus Levamisole, and intermittent single high dose DTIC plus Actinomycin D in a prospective, randomized clinical study.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven disseminated malignant melanoma who have not been previously treated with any of the protocol agents shall be eligible. Patients must have measurable disease and estimated survival of at least 2 months.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Fourteen patients have been registered on this study. It is too early for any significant evaluation.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemoimmunotherapy Utilizing BCNU, Hydroxyurea and DTIC with Levamisole vs. DTIC plus Actinomycin-D in the Treatment of Patients with Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7727

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine remission induction rates, remission duration, survival and toxicity in patients with disseminated malignant melanoma treated with BCNU, hydroxyurea and DTIC (BHD), BHD plus Levamisole, and intermittent single high dose DTIC plus Actinomycin D in a prospective, randomized clinical study.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven dissminated malignant melanoma who have not been previously treated with any of the protocol agents shall be eligible. Patients must have measurable disease and estimated survival of at least 2 months.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Fourteen patients have been registered on this study. It is too early for any significant evaluation.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-diamminedichloroplatinum in Refractory Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7730

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of high intermittent doses of cis-diamminedichloroplatinum in patients with advanced malignant melanoma refractory to higher priority protocol(s).

2. To determine the nature and extent of toxicity of this agent with the use of IV hydration only or IV hydration and mannitol diuresis.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed diagnosis of malignant melanoma. Patients must have metastatic disease and measurable lesion(s) refractory to higher priority protocol(s) for malignant melanoma. Expected survival should be a minimum of 10 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Only four patients have been entered on this study, and it is too early for significant evaluation. One patient has shown 50% liver reduction after therapy.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Anguidine in Advanced Soft Tissue and Bony Sarcoma.

WORK UNIT NO.: SWOG 7731

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the level of efficacy of the drug anguidine as a single agent in the treatment of advanced soft tissue and bony sarcomas in patients who have failed to respond or have relapsed on higher priority therapeutic regimens.

2. To determine the toxicity of anguidine in a Phase II trial.

TECHNICAL APPROACH

Eligibility: The patient must have a diagnosis of soft tissue or bony sarcoma confirmed by pathologic examination of tissue and must demonstrate either primary or recurrent disease which is not amenable to control with surgery, radiotherapy, or higher priority chemotherapy. Patient must have a project life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study, and it is too early for significant evaluation.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: CMF with or without Tamoxifen in Patients with Estrogen Receptor Positive Breast Cancer, Phase III Study.

WORK UNIT NO.: SWOG 7732

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine if the antiestrogen, Tamoxifen in combination with Cytoxan, Methotrexate and 5-FU will alter the response rate, duration of response and median survival seen with Cytoxan, Methotrexate and 5-FU alone in advanced human breast cancer, in patients who are estrogen receptor positive.

TECHNICAL APPROACH

Eligibility: Histological proof of recurrent breast cancer which is progressing. Measurable disease. Estimated survival greater than 10 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study was recently activated and is too early to present any data.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Rubidazone in Relapsing Lymphoma Patients Previously Untreated with Anthracycline Derivatives.

WORK UNIT NO.: SWOG 7734

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC: Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy, in terms of response rate, duration of response and survival, of the anthracycline antibiotic rubidazone in previously treated patients with Hodgkin's or non-Hodgkin's lymphoma.

2. To determine the maximum tolerated single dose in lymphoma patients.

3. To determine the critical cumulative cardiotoxic dose of rubidazone.

TECHNICAL APPRoACH

Eligibility: Patients with histological diagnosis of Hodgkin's disease or non-Hodgkin's lymphoma who are not eligible for higher priority SWOG studies and who have had no prior anthracycline derivatives. Patients must have expected survival of 6 weeks or more.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Anguidine in Advanced Gastrointestinal Malignancies.

WORK UNIT NO.: SWOG 7735

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC, Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of anguidine and survival in terms of response rate and median duration of response, in the treatment of advanced gastrointestinal malignancies.

2. To observe any factors predisposing to excessive myelosuppression and for other toxicities not observed during Phase I studies of this drug.

TECHNICAL APPROACH

Eligilibility: All patients with histologically proven gastrointestinal malignancies coming off studies with higher priority. Patients must have surgically incurable disease and objectively measurable parameters.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This second line therapy in advanced GI cancer is just beginning to accrue patients. Data is too preliminary for analysis.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Anguidine in the Treatment of Urological Malignancies.

WORK UNIT NO.: SWOG 7736

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of anguidine in treating the major urological malignancies in terms of response rate, duration of responses, and survival.

2. To more fully study the adverse effectts of anguidine and factors important in producing such effects.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven advanced urological malignancies (bladder, prostate, testis, renal pelvis, renal cell carcinoma). Life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy of Pancreatic Adenocarcinoma with Mitomycin-C, 5-Fluorouracil and Streptozotocin.

WORK UNIT NO.: SWOG 7738

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine and document the response rates and toxicities of mitomycin-C, streptozotocin, and 5-FU compared to mitomycin-C and 5-FU in the management of disseminated pancreatic adenocarcinoma.

TECHNICAL APPROACH

Eligibility: Patients with measurable and nonmeasurable disease will be eligible for this study. Patients with distant metastases (liver, peritoneum, etc.) and/or those in whom extension of the disease is outside of a port size greater than 15 x 15 cm.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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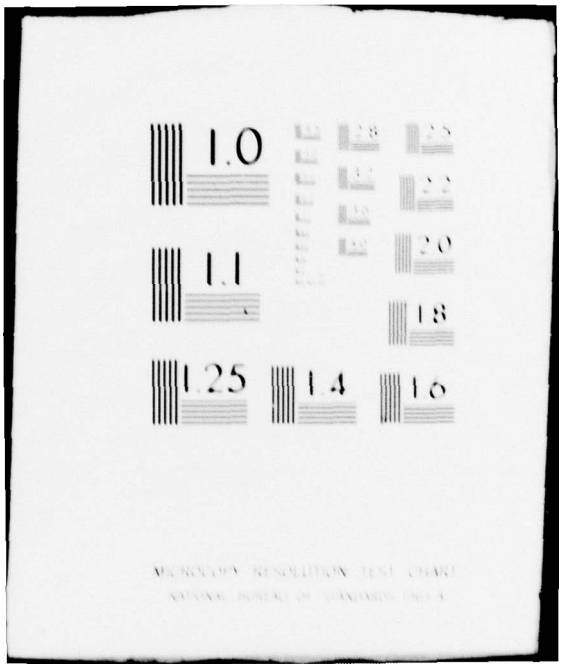
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DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Pancreatic Carcinoma with Streptozotocin + 5-FU + Mitomycin-C, Phase I-II Pilot

WORK UNIT NO.: SWOG 7771

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness as determined by response rate and survival of intra-arterial streptozotocin and systemic 5-FU and mitomycin-C in the treatment of adenocarcinoma of the pancreas with or without liver metastases localized to distribution of the celiac artery.

2. To determine the toxic effects resulting from such a combination.

TECHNICAL APPROACH

Eligibility: All patients must have a biopsy proven adenocarcinoma of the pancreas with the tumor confined to the distribution of the celiac artery (involvement of pancreas and liver only).

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Phase II Pilot Study, Combined Chemotherapy for Advanced Gastrointestinal Malignancies.

WORK UNIT NO.: *SWOG 7801*

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the anitumor effect of anguidine as measured by response rate and survival, in combination with 5-FU in patients with advanced gastrointestinal malignancies.

TECHNICAL APPROACH

Eligibility: Only patients with histologically proven adenocarcinoma arising in the liver, gallbladder, biliary tree, exocrine pancreas, stomach, small intestines, colon and rectum are eligible. Patients must not have had prior exposure to fluoronated pyrimidines or anguidine.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) vs. Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma.

WORK UNIT NO.: SWOG 7804

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of adjuvant chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potnetially curative surgery alone.

TECHNICAL APPROACH

Eligibility: Localized lesions at least extending into the submucosa and involving any of the deeper layers with the maximum allowable penetration into but not through the serosa; localized lesions extending through serosa, with or without direct extension to continuous structures; a lesion diffusely involving the wall of the stomach with or without metastases to immediately adjacent perigastric nodes, or a localized lesion of any depth with metastases to perigastric nodes in the immediate vicinity; a localized or diffuse lesion with metastases to perigastric nodes distant from primary.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Refractory Epidermoid Carcinomas of the Esophagus.

WORK UNIT NO.: SWOG 7806

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

The purpose of this study is to determine the response rate and survival, with some degree of precision, utilizing cis-diamminodichloroplatinum II (CACP) in the treatment of patients with squamous cell carcinoma of the esophagus which is growing despite more standard therapy.

TECHNICAL APPROACH

Eligibility: Patients must have a biopsy-confirmed diagnosis of epidermoid carcinoma of the esophagus.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Refractory Epidermoid Carcinoma of the Lung.

WORK UNIT NO.: SWOG 7807

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the response rate and survival in patients with epidermoid carcinomas of the lung who have demonstrated refractoriness to previous therapy utilizing Cis-Diammindichloroplatinum.

TECHNICAL APPROACH

Eligiblity: Patients must have epidermoid carcinoma of the lung confirmed, preferably by biopsy, although positive cytology is acceptable. Measurable disease is a requirement of this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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

INVESTIGATION PROJECT RESUME

TITLE: Combined Therapy with Celiac Artery Infusion 5-FU Plus Radiation Therapy Followed by Mitomycin-C and 5-FU Maintenance Chemotherapy for Treatment of Localized Adenocarcinoma of the Exocrine Pancreas.

WORK UNIT NO.: SWOG 7861

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effect on survival in localized pancreatic cancer by utilizing direct celiac artery infusion of 5-FU combined with radiation therapy and Mitomycin, 5-FU maintenance therapy.

2. To establish the toxicities of this multimodality in a pilot study and test feasibility for widespread cooperative group use.

TECHNICAL APPROACH

Eligibility: Histological confirmation of adenocarcinoma of the exocrine pancreas. Tumor margin as outlined by radiopaque clips to create a port size not greater than 225 cm^2 (approximately 15x15 cm). Alternately, patients are eligible if a similar port can be constructed based on artiographic findings or with ultrasonography. Patients with local extension of disease into stomach, vertebral body, liver or lymph node are eligible for this study as long as the field size meets the stated criteria.

Threapy will follow the schema outlined in the study protoco.

PROGRESS

This is a new study.

Status: Ongoing.

AUTHOR INDEX

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