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Fitzsimons Army Medical Center
Denver, Colorado 80240

Clinical Investigation Service

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30 June 1975

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Subject report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1975 and other known presentations and publications by the Fitzsimons Army Medical Center professional staff. The research protocols described were conducted under the provisions of AR 40-38, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans,

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Block 19. Key Words

publications, presentations of research data (at national, international and regional science meetings)
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protocol registration
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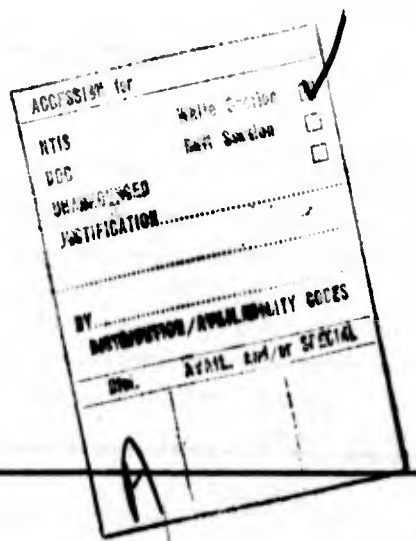
technological base (personnel and equipment)
experimental design (statistical tools, etc.)

Block 20. Abstract

AR 70-25, Use of Volunteers as Subjects of Research and FAMC Reg. 40-8, Clinical Investigation Program, FAMC, to insure the medical safety, well being, preservation of rights and dignity of human subjects who participated in these investigations.



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CLINICAL INVESTIGATION PROGRAM

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30 JUNE 1975

CLINICAL INVESTIGATIONS (U)

FITZSIMONS ARMY MEDICAL CENTER

DENVER, COLORADO 80240

FOREWORD

This report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1975 and other known presentations and publications by FAMC professional staff.

The research protocols described in this report were conducted under the provisions of AR 40-38, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans, AR 70-25, Use of Volunteers as Subjects of Research, and FAMC Reg. 40-8, Clinical Investigation Program, FAMC, to insure the medical safety, well being, preservation of rights and dignity of human subjects who participated in these investigations.

I would personally like to express my appreciation and gratitude to both the investigators and those many people who have given our Service their support and whose contributions are vital to the success of the clinical research effort.

Clinical Investigation Service is especially grateful to MAJOR GENERAL JAMES A. WIER, MC, Commanding General, Fitzsimons Army Medical Center, his professional and administrative staffs, and to the Commanding Officers and staffs of other supporting activities for the cooperation and assistance provided the Clinical Investigation Service in our efforts to accomplish our mission. Finally, I would like to recognize the outstanding work, dedication, and whole-hearted corroboration of my entire staff. I would especially like to thank my secretary, Mrs. Val McCrill and Mrs. Chris Montoya, clerk-stenographer, without whose assistance and support this report would not have been possible.

Donald G Corby

DONALD G. CORBY, M.D.
COL, MC
Chief, Clinical Investigation Service

In conducting the research described in this report, the investigator(s) adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee or the Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.

PUBLICATIONS

PUBLICATIONS

MEDICINE

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PRESENTATIONS

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Cardiology

Brundage, B. H.: Coronary Artery Surgery - What Price? High Country Cardiac Conference, Vail, CO, January 1975.

Kleiner, J. P., and Nelson, W. P.: High Altitude Pulmonary Edema - A Rare Disease? Regional Meeting of American College of Physicians, Colorado Springs, CO, January 1975.

Nelson, W. P.: Deceptions in Cardiology - Confusin-Fusin. American College of Physicians Regional Meeting, Colorado Springs, CO, January 1975.

Nelson, W. P.: EKG Impulse Conduction - Confusin-Fusin. High Country Cardiac Conference, Vail, CO, January 1975.

Dermatology

Earhart, R. N., et al: Pseudo-Kaposi Sarcoma. American Academy of Dermatology, Chicago, Illinois December 1974.

Endocrinology

Block, M. B., Nilsen, L. B., Hoftman, J. P., Hofeldt, F. D.: New Variety of Multiple Endocrine Adenomatosis Type IIb. Arizona Regional Meeting, American College of Physicians, Scottsdale, Ariz. 1-2 Nov. 1974.

Hofeldt, F. D.: Galactorrhea, What Does Its Presence Indicate? Regional Meeting of American College of Physicians, Colorado Springs, Colorado, January 1975.

Hofeldt, F. D.: New Approaches to the Study of Hypoglycemia. Regional Meeting for Affiliates of the American Diabetes Association, Denver, CO, December 1974.

Hofeldt, F. D.: Thyrotoxicosis and Hypoparathyroidism. American Association of Critical Care Nurses, Denver, CO, April 1975.

Gastroenterology

Sherr, H. P., Stifel, F. B., and Herman, R. H.: Effect of Cholera Toxin (C.T.) on Rabbit Jejunal Glycolytic (GLY) and Gluconeogenetic Enzymes (GNG). American Gastroenterological Association, San Antonio, TX, May 1975.

Pulmonary Disease

Christensen, W. I.: Genitourinary Tuberculosis. Colorado Trudeau Society, Estes Park, Colorado, August 1974.

Nephrology

Butkus, D. E.: Lipoid Nephroses. 1st University of Colorado Medical Center Symposium on Renal Disease, Aspen, Colorado, August 1974.

Pulmonary Function Laboratory

Hazlett, D. R., Ashmore, R. E. and Crumrine, J. W.: A Comparison of "End Tidal" FEV_1 and the "End Tidal FEV_1 Equivalent. 40th Annual Scientific Assembly of The American College of Chest Physicians, New Orleans, LA, 3-7, Nov. 1974.

Hazlett, D. R., Edge, R. and Dunlap, D.: Computer Assisted Measurement, Calculation and Integrated Interpetation of Spirometry and Helium Dilution Lung Compartments. Annual Meeting of the Biomedical Engineering Society, New Orleans, LA., 10-12 April 1975.

Hazlett, D. R., Edge, R. and Dunlap, D.: Real Time Measurement, Calculation and Integrated Interpetation of Spirometry and Helium Dilution Lung Compartments. 10th Annual Meeting of The Association for the Advacement of Medical Instrumentation. Boston, Mass. 14-21 March 1975.

Hazlett, D. R. and Fogg, H.: A New Respiration Monitor Using A Digital Integrator Technique. 10th Annual Meeting of the Association for the Advacement of Medical Instrumentation, Boston, Mass., 14-21 March 1975.

Hazlett, D. R., and Fogg, H.: A New Respiration Monitor Using A Digital Intergrator Technique. Annual Meeting of the Biomedical Engineering Society, New Orleans, LA., 10-12 April 1975.

Hazlett, D. R., Zajtchuk, R. and Nessan, V. J.: Measuring Heart Valve Cross Sectional Areas by an Electrical Impedance Technique. Annual Meeting of the Biomedical Engineering Society. New Orleans, LA., 10-12 April 1975.

Kindig, N. B. and Hazlett, D. R.: A Comparison of Estimation Methods for Steady State DLLO In Normal Subjects. Annual Meeting of the Biomedical Engineering Society, New Orleans, LA., 10-12 April 1975.

Kindig, N. B. and Hazlett, D. R.: Correcting Bates (End Tidal) Estimate of Pulmonary Diffusing Capacity for Breathing Patterns. 10th Annual Meeting of the Association for the Advacement of Medical Instrumentation, Boston, Mass., 14-21 March 1975.

Kindig, N. B. and Hazlett, D. R.: Time Delay Effects In The Estimation Of Pulmonary Diffusing Capacity. 12th Annual Rocky Mountain Bioengineering Symposium and 12 Annual International ISA. Biomedical Science Instrumen-

OBSTETRICS AND GYNECOLOGY

Woods, W. M.: Evaluation of the Pereyra, Marshall-Marchetti-Krantz, Kennedy & Kelly Procedure for Treatment of Urinary Stress Incontinence. American College of OB-GYN, Armed Forces District, November 1974.

Llorens, A. S.: Methods of Detection of Endometrial Cancer, American Cancer Society, Mid-winter session, Vail, Colorado, February 1975.

Llorens, A. S.: Chemotherapy of Endometrial Cancer, American Cancer Society, Mid-winter session, Vail, Colorado, February 1975.

Llorens, A. S.: Management of Ovarian Cancer, American Cancer Society, Mid-winter session, Vail, Colorado, February 1975.

Llorens, A. S.: Management of Postoperative Pelvic Abscess, American College of Obstetrics and Gynecology, Armed Forces District, Washington D.C., November 1974.

Llorens, A. S.: Method of Control of Intractable Pain, Secondary to Advanced Pelvic Cancer, American College of OB-GYN, Armed Forces District, Washington D.C., October 1975.

Powers, J. S.: Migrating Placenta, American College OB-GYN, Armed Forces District, November 1974.

PEDIATRICS

Bertolone, S.: Chemotherapy of Childhood Brain Tumors. Conference on Current Concepts and Conflicts of Childhood Cancer, Buffalo, NY, September 1974.

Larson, S., Yeatman, G., Riccardi, V.: A Report of Two Cases of 46XX, 11q-. The National Foundation-March of Dimes Annual Birth Defects Conference, Kansas City, MO, June 1975.

Mease, A., Yeatman, G., Pettett, G., Merenstein, G.: A Syndrome of Ankylosis, Facial Anomalies and Pulmonary Hypoplasia Secondary to Fetal Neuromuscular Dysfunction. The National Foundation-March of Dimes Annual Birth Defects Conference, Kansas City, MO, June 1975.

Merenstein, G. B.: People Factors, Effects on Transport. 69th Ross Conference on Pediatric Research Iatrogenic Problems in Neonatal Intensive Care, Hilton Head, SC, May 1975.

Merenstein, G.: Open Air Radiant Heat Incubators: Bacterial Contamination. 69th Ross Conference on Pediatric Research Iatrogenic Problems in Neonatal Intensive Care, Hilton Head, SC, May 1975.

Merenstein, G.: Transport of the Newborn by Ground and by Air.: Neonatology Round Table, American Academy of Pediatrics Spring Meeting, Denver, CO, April 1975.

Merenstein, G.: Umbilical Artery Catheters and Heparin. 69th Ross Conference on Pediatric Research Iatrogenic Problems in Neonatal Intensive care Hilton Head, SC, May 1975.

Pettett, G.: Air Transport of Sick Neonates. Aspen Conference on Perinatal Research, Aspen, CO, August 1974.

Pettett, G.: Importance of Perinatal Nutrition. Rocky Mountain Nutrition Associates, Denver, CO, October 1974.

Plunkett, D. C.: "Risk Factors for Childhood Neoplasia" - Neoplasia in Children Conference, Vail, Colorado, 4 April 1975.

Plunkett, D. C.: "The Spleen and the Pediatrician" - Department of Pediatrics, University of Cincinnati School of Medicine, 20 May 1975.

Plunkett, D. C.: "Thrombocytopenic States" - Department of Pediatrics, Letterman Army Medical Center, San Francisco, California, February 1975.

Sanders, J.: Approaching the Adolescent Patient. Annual Meeting of the South Carolina Pediatric Society Seminar, Hilton Head Island, SC, August 1974.

Sanders, J.: VD - A Social Epidemic. Annual Meeting of the South Carolina Pediatric Society Seminar, Hilton Head Island, SC, August 1974.

Spaulding, H.: Extrinsic Allergic Alveolitis. Annual Pulmonary Disease Symposium, FAMC, Denver, CO, September 1974.

Spaulding, H. S., Jr., Nelson, S., Branch, B. L., Pfuetze, B. M., and Wood, D.: Altered Cardiovascular and Metabolic Responses to Epinephrine Following the Administration of Ephedrine and Terbutaline to Normal Men. The 31st Annual Meeting of the American Academy of Allergy, San Diego, California, 18 Feb 1975.

Weisman, L., Woodall, J., Merenstein, G.: Constant Negative Pressure in the Treatment of Diaphragmatic Paralysis. The National Foundation-March of Dimes Annual Birth Defects Conference, Kansas City, MO, June 1975.

Woodall, J.: Early Discharge of Low Birth Weight Infant. Aspen Conference on Perinatal Research, Aspen, CO, August 1974.

Yeatman, G., Riccardi, V.: Partial Trisomy of Chromosome 14. The National Foundation-March of Dimes Annual Birth Defects Conference, Kansas City, MO, June 1975.

OCCUPATIONAL THERAPY SECTION

Becker, T. W.: The Combined Speech/Language Programs. American Occupational Therapy Association, Washington, D.C., October 1974.

Becker, T. W.: The Combined Speech/Language Programs. Colorado Occupational Therapy Association, Denver, CO, January 1975.

OTHALMOLOGY

Cottingham, A. J.: Clinical and Laboratory Studies of Benign Mucous Membrane Pemphigoid. Bascom-Palmer Eye Clinic Resident's Day, Miami, Florida, June 1975.

Cottingham, A. J.: Further Observations on the Diagnosis, Etiology, and Treatment of Endophthalmitis. American Ophthalmologic Society Meeting. Greenbriar, Virginia, May 1975.

Cottingham, A. J.: Further Observations on the Use of Vitrectomy in Endophthalmitis. Bascom-Palmer Eye Clinic Resident's Day, Miami, Florida, June 1975.

Cottingham, A. J.: Vitrectomy in Experimental Endophthalmitis. The Association for Research in Vision and Ophthalmology, Inc., Sarasota, Florida, May 1975.

Manson, R. A.: Accommodative Esotropia - A Sequel to Congenital Esotropia. American Academy of Pediatric Ophthalmology, Lake Tahoe, Nevada, February 1975.

ORTHOPEDICS

Ballard, A.: Treatment of Patellar Dislocations. S.O.M.O.S. Meeting. Colorado Springs, CO., November 1974.

Donley, J. M.: Definitive Treatment of Severely Injured Foot. Rocky Mountain Orthopedic Association. Denver, CO., December 1974.

Eversmann, W. W.: Functional Rehabilitation of the Amputee. Orthopedic Nurses Association. Denver, CO., November 1974.

Gilchrist, A. K.: Surgical Care of the Traumatized Foot. Colorado Podiatry Association, Denver, CO., May 1975.

Glancy, G. L.: Compartment Syndrome. Orthopedic Nurses Association. Denver, CO., November 1974.

Hackethorn, J. C.: Management of Open Fractures and Cast Bracing. S.O.M.O.S. Meeting. Colorado Springs, CO., November 1974. Rocky Mountain Association. Denver, CO., December 1974.

Hackethorn, J. C., Burkhalter, W. E., Donley, J. M., and Bailey, J. C.: Review of One Hundred Fifty-Six Cases of Open Femoral Fractures Treated with Traction and Brace Casting. AAOS Meeting, San Francisco, Calif. March 1975.

Landon, T. W.: The Absence of the Neural Arch of C1. Rocky Mountain Association. Denver, CO., December 1974.

Risch, E. D.: The Posterior Compartment Syndrome. Rocky Mountain Orthopedic Association. Denver, CO., December 1974.

Terry, R. L.: Tumoral Calcinosis. S.O.M.O.S. Meeting. Colorado Springs, CO., November 1974.

OTOLARYNGOLOGY

Loovis, C. F.: ABCs of Hearing Aid Evaluation. Hearing Seminar, Colorado Speech and Hearing Association, Denver, CO., Sept. 26, 1974.

Hasbrouck, J. M.: Further Comparison of Two Different Schedules for Disfluency. ASHA convention, Las Vegas, Nevada, November 6, 1974.

THORACIC SURGERY

Heydorn, W. H.: Mediastinoscopy. 29th Annual Symposium on Pulmonary Diseases, FAMC, Denver, CO., September 1974.

Schuchmann, G. F.: Surgical Management of Bullous Emphysema. 29 Annual Symposium on Pulmonary Diseases, FAMC, Denver, CO., September 1974.

Strevey, T. E.: Pulsus Paradoxus in the Postoperative Patient. American Heart Association Hi-country Cardiac Conference. January 1975.

Zajtchuk, R., Corby, D. G., Miller, J. G., O'Barr, T. P.: Treatment of Digoxin Toxicity with Activated Charcoal. 24th Annual Scientific Session American College of Cardiology, Houston, TX., February 1975.

UROLOGY SERVICE

Buntley, D. W.: Ureteritis Cystica Associated with Heparin Therapy. South Central Section Meeting of the AUA, September 1974.

Dobbs, R. M.: Renal Anomalies Associated with the Unna-Thost Syndrome. Kimbrough Transactions of the Urological Seminar, November 1974.

Fauver, H. E.: Another Episode in the Continuing Saga of Vasectomy. Kimbrough Transactions, Urological Seminar, November 1974.

Fauver, H. E.: Mutilocular Cyst of the Kidney. IBID

Fauver, H. E.: Mutilocular Cyst of the Kidney. South Central Section Meeting of the AUA, September 1974.

Haden, J. B.: Management of Vesico-Vaginal and Ureteral Vaginal Fistulae. Kimbrough Transactions of the Urological Seminar, November 1974.

Jackson, J. E.: Autotransplantation of Hemi-nephrectomized Kidney in Dogs. South Central Section Meeting of the AUA, September 1974.

Jackson, J. E.: Autotransplantation of Hemi-nephrectomized Kidney in Dogs. Kimbrough Transactions of the Urological Seminar, November 1974.

Weigel, J. W.: Management of Pheochromocytoma. Kimbrough Transactions of the Urological Seminar, November 1974.

Weigel, J. W.: Management of Pheochromocytoma. South Central Section Meeting of the AUA. September 1974.

DENTISTRY

Clifford, A. G.: Partnerships in Fixed and Removable Prosthodontics. The American Academy of Crown and Bridge Prosthodontics, Chicago, ILL., February 1975.

Clifford, A. G.: Tissue Retraction and Impressions. United States Army Institute of Dental Research, Washington, DC., September, 1974.

Grove, H. F.: Various Types of Full Immediate Denture Impressions and Trays. Rocky Mountain Mid-winter Dental Meeting, Denver, CO., January 1975.

Hoffman, W. Jr.: Posterior Tooth Form. United States Army Institute of Dental Research, Washington, DC., November, 1974.

Stringer, J. L., Snyder, A. J.: Periodontal-Restorative Interactions. Metropolitan Denver Dental Society Mid-winter Meeting, Denver, CO., January 1975.

UNIT SUMMARY SHEET

UNIT SUMMARY SHEET

Clinical Investigation Program, FAMC

Clinical Investigation efforts by FAMC personnel in FY 74 culminated in the publication of 108 articles and the presentation of 109 manuscripts at national, international, and regional scientific meetings. As of 30 June 1975, there were 82 research protocols on the CIS register. Additionally, twelve projects were completed and eleven terminated.

Objectives: To encourage the performance of clinical investigations by AMEDD personnel, especially by personnel assigned to Army hospitals where post graduate educational programs are conducted. To aid in the planning, development, support, and execution of experimental clinical studies, both in patients and by directly related laboratory work, into clinical problems of significant concern in the necessary health care of members of the military community. To provide the physician experience in research and investigative procedures. To provide a base for continued training in such organized inquiries for those personnel who will become teaching chiefs and medical consultants in the Army Medical Department.

Technical Approach: Provides direction, management, and support as outlined under provisions of AR 40-38, Clinical Investigation Program; AR 40-7, Use of Investigational Drugs in Humans; AR 70-25, Use of Volunteers as Subjects of Research, and MCR 40-8, Clinical Investigation Service, FAMC. Provides guidance, assistance, and support to the Center staff in matters pertaining to the program. Coordinates the FAMC program with higher headquarters and other facilities.

Manpower: Current and authorized strength is outlined.

Description	Grade	MOS	Br	Auth	Actual	Name
C, Clin Rsch	06	3116	MC	1	1	Corby
C, Immuno Sec	05	3307	MS	1	1	Brown
Internist	04	3139	MC	1	1	Adler
Lab Admin	03	3314	MS	1	1	Marsteller
C, Surg - Rsch Labs	03	3200	VC	1	1	Miller
C, Micro Sec	03	3307	MS	1	1	Calcagno
Physiologist-PhD	03	3327	MS	0	1	Daniels
Biochem	03	3309	MS	0	1	Yancy
NCOIC	E7	92B4R		1	1	Johnson
C. Med Lab NCO	E7	92B4R		1	1	Underhill
SR O.R. SP	E5	91D3R		1	1	Moore
Med Lab Sp	E5	92B2R		1	1	Scholbe
Med Lab Sp	E4	92B2R		1	1	Givens
Med Lab Asst	E4	92B2R		1	1	Clifton

Description	Grade	MOS	Br	Auth	Actual	Name
O.R. Sp	E5	91D2R		1	1	Smith
O.R. Sp	E4	91D2R		1	1	Roslan
Vet Sp	E4	91T2R		1	1	Michelon
Clerk Typist	E4	71B20		1	1	Twining
Ch, Med Lab NCO	E8	92B4R		NTD	1	Davis
Microbiol-PhD	13	0403	GS	1	1	O'Barr
Microbiol	09	0403	GS	4	4	Lima
						Rothlauf
						Tull
						Preston
Med Technol	09	0644	GS	1	1	Rush
Biochem	09	1320	GS	1	1	Goad
Microbiol	07	0403	GS	6	6	Cromwell
						Gray
						Kile
						Kolb
						Calgoy
						Paine
Rsch Chem	07	1320	GS	2	2	McNamara
						Noble
Bio Lab Tech	07	0404	GS	1	1	Hakes
Animal Tech	05	0404	GS	1	1	Roslan
Secy-DMT	05	0318	GS	1	1	McCrill
Animal Caretaker	05	7706	WG	2	2	Beltran
						Hitchcock
Clerk-Steno	04	0318	GS	1	1	Montoya

	FY-75 Program	FY-76 Program
Civilian Pay	282,143	
Travel	1,012	1,400
Supplies	109,972	120,000
Equipment	75,291	85,000
Contracts	15,300	19,000
Other (Military)	314,199	

PROGRESS:

CIS under the guidance of COL Donald G. Corby, MC, has completed a total reorganization. This has resulted in the establishment of an administrative section and five functional laboratories. The new TDA has facilitated lines of command, communication, research support, and provided a viable teaching environment.

The Service has completed its move from five widely scattered facilities located throughout the medical center into the laboratories formerly occupied by the U.S. Army Medical Research and Nutrition Laboratories (now LAIR). This has resulted in a cohesive research facility offering support in immunology, microbiology, a tuberculosis reference laboratory, biochemistry, coagulation, surgical research, and veterinary animal care.

Completion of graduate level training in Statistical Analysis by the Chief, CIS, the Laboratories Administrator and other staff members, along with the updating of a 9830 Hewlett-Packard Programmable Calculator has resulted in providing both experimental design and statistical evaluation of data to FAMC investigators.

CIS is in the process of submitting to HSC a request for urgent minor construction ($300,000) for an Animal Care Facility: This project is required to provide accredited facilities for breeding, care and maintenance of research animal colonies. This construction will comply with mandatory requirements of the Department of Agriculture and the American Association for Accreditation of Laboratory Animal Care.

Office of the Chief:

The office of the Chief, CIS, assumes all administrative and clerical responsibilities of the Service and provides the following functions:

1. Exercises overall management responsibility for clinical research activities at this Center, to include planning, coordination, staff supervision, execution and review of all authorized clinical investigative projects which entail funding or other support by the Clinical Investigation Service.

2. Monitors all other clinical research efforts in medicine and surgery, and maintains a central protocol and publications file.

3. Develops a technological base of personnel and equipment by means of independent in-house research within current financial and manpower constraints.

4. Provides administrative and technical guidance and assignment of personnel (civilian and/or military) to subordinate sections.

5. Provides expertise in experimental design and a wide variety of statistical tools (t-tests, chi square, analysis of variance, and multiple regression) to help the investigator correctly set up his research and analyze his data.

Immunology Section:

The capabilities of the Immunology Section, CIS encompass two major areas: ongoing protocol support and training programs.

Protocol support is accomplished by providing the following:

1. Techniques employed in serological research.

2. Systematic approaches for isolation and characterization of serum proteins and related antigens preparative studies.

3. Lymphocyte blast transformation assays using tridiated systems: Antigen stimulation, non specific mitogens (PHA, CON-A, PWM), and mixed lymphocyte systems.

4. Methods for special studies of abnormal hemoglobins.

5. Established immunological procedures involving:

   a. Electrophoresis (cellulose acetate, polyacrylamide, starch and agar gels)
   b. Chromatography (affinity, ion exchange, sieve, thin layer).
   c. Isoelectric focusing.
   d. Ultracentrifugation.
   e. Spectrophotometry.
   f. Densitometry.
   g. Radioisotope labelling.
   h. Production, purification, quantitation of antibodies to known antigens.

Facilities of the Immunology Section, CIS have been made available for immunological training to Fitzsimons staff, Colorado State University and Colorado Medical Center. Main emphasis is immunology training for Adult and Pediatric Allergy Fellows.

Microbiology Section:

The two independent subsections of the Microbiology Section, CIS, provide the following support:

1. Medical Microbiology Subsection:

   Provides support for ongoing protocols requiring isolation and identification of pathogenic micro-organisms, development of new isolation media and culture collection systems. Current capabilities include: Isolation and identification of Group B Hemolytic Streptococcus, and potential pathogens of upper respiratory tract.

2. Mycobacteriology Subsection:

The mycobacteriological training centers around the isolation, identification and antimicrobial susceptibility of mycobacteria, including M. tuberculosis and mycobacteria other than M. tuberculosis (MOTT). Availability of clinical specimens allows evaluation of new media and isolation techniques. New methods currently established are: (1) use of a selective medium permitting direct culture of undecontaminated specimens, and (2) use of a new technique for determining growth temperature range for identification of MOTT.

Biochemistry Section:

This Section has made available a broad spectrum of laboratory support for

protocols from the Departments of Medicine and Surgery. Generally, this involves the determination of drugs, biochemicals, metabolites and hormones through the application of radioimmunoassays, labeling with radioactive compounds, and a variety of spectrophotometric or fluorometric procedures. In examples of specific studies, complete endocrine profiles are furnished for groups of study patients, histamine release from sensitized leukocytes is monitored, and possible drug-induced changes in the serum content of free fatty acids are examined.

Surgical Research Laboratories Section:

The Surgical Research Laboratories Section currently houses species of animals from mice to large dogs and with construction of a new housing facility this capability will expand to include primates and larger domestic animals. Assistance in the areas of surgery, physiology, and veterinary care are provided for the support of research by a staff which includes a veterinary surgeon, a Ph.D. physiologist, veterinary technicians, operating room technicians, and animal caretakers. Multiple diagnostic and monitoring tools, a wide range of therapeutic procedures, and necropsy capabilities are available and enable the section to support a wide range of protocols. Microvascular surgery, organ transplantation, and cardio-pulmonary bypass procedures are currently being performed and the facilities, equipment and staff are varied enough to enable adaptation to new procedures with relative ease.

Coagulation Laboratory Section:

The Coagulation Laboratory Section, CIS, provides laboratory support for the study of hemostatic conditions, techniques for investigating the various parameters of the clotting mechanisms, and research into platelet function of newborns. In addition, this section provides timely and necessary assistance to the Coagulation Laboratory of the Department of Pathology, FAMC.

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MEDICINE

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Ongoing (0), Completed (C), or Terminated (T), Published (P) or Submitted for Publication (SP).

Ongoing (0), Completed (C), or Terminated (T), Published (P) or Submitted for Publication (SP).

DETAIL SHEETS

MEDICINE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Tuberculosis Research Follow-up Program.

WORK UNIT NO: 67/100

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To facilitate proper collection of research records of tuberculosis patients and to provide a central repository for all such records. (Procedural Guide, Number 40-957, dated 27 May 1957).

TECHNICAL APPROACH

All patients admitted to the Tuberculosis Service have research files made which include representative x-rays, clinical summaries, bacteriology printouts of smear and culture data and any other records deemed appropriate for the individual case. These files are expanded when follow-up x-rays, reports and cultural data are obtained from our own clinic follow-up or from other hospitals. The information obtained is used to analyze various aspects of clinical tuberculosis, treatment results, and specific types of tuberculosis.

Manpower (in professional man years):

	FY 74:	0.25/yr
	FY 75:	0.25/yr
Funding (in thousands)	FY 74:	0
	FY 75:	0

PROGRESS

This project has to date accumulated detailed information on over 25,000 patients with tuberculosis. It is most assuredly the best file of its

PROGRESS - continued

type in the United States and will continue to contribute significantly to future data computations and papers in the field of clinical tuberculosis.

The modern concepts of therapy for tuberculosis stem from data such as we have in this file. These concepts include short-term hospitalization for treatment of active tuberculosis, early discharge from follow-up after medical therapy, frequency of pleural tuberculosis in young adults with pleural effusion and positive skin tests, and the incidence of extra pulmonary tuberculosis in the population of tuberculosis infected individuals.

Publications:

(1) Christensen, W. I.: Genitourinary Tuberculosis at Fitzsimons Army Medical Center from 1961 to Present. (To be published in Medicine, July 1974).

(2) Buchanan, B. D.: Atypical Tuberculosis Due to Type I and Type III Atypical Mycobacteria. (In preparation for publication).

Presentations:

(1) Christensen, W. I.: Genito-urinary Tuberculosis at FAMC from 1961 to Present. Presented: 25th Annual Pulmonary Disease Symposium, FAMC, September 1972.

(2) Christensen, W. I.: Genito-urinary Tuberculosis at FAMC from 1961 to Present. Presented: Regional American College of Physicians Meeting, Colorado Springs, CO, January 1973.

(3) Christensen, W. I.: Genito-urinary Tuberculosis at FAMC from 1961 to Present. Presented: Hugh Mahon Lectureship Award Competition, FAMC, May 1973 (submitted as research paper).

(4) Christensen, W. I.: Drug Resistant Tuberculosis from Vietnam. Presented: 25th Annual Pulmonary Disease Symposium, FAMC, September 1972.

(5) Nelson, R. A.: Tuberculosis of the spine (Potts' Disease). Presented J. J. Waring Chest Conference. Estes Park, CO. August 1974.

WORK UNIT 67/100

PROGRESS - continued

(6) Nelson, R. A.: Pleural and Lymph Node Tuberculosis: Presented at the Course Clinical Management and Control of Tuberculosis. Presented three times yearly by National Jewish Hospital, Denver, CO.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Primary Drug Resistance to Antituberculosis Chemotherapeutic Agents.

WORK UNIT NO.: 69/104

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
George L. Brown, LTC, MSC

OBJECTIVES

To determine the impact of overseas military commitments in areas highly endemic for resistant tuberculosis on the tuberculosis control and treatment of the United States military and civilian populations.

TECHNICAL APPROACH

The approach was to determine if active duty patients with positive tuberculin cultures had ever served in Vietnam. If the patient had served in that area an attempt was then made to establish family history, skin test results, and chest x-ray evaluation. In some cases the overseas contact history was important.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

This project is now being finalized since there is very little input of new cases of tuberculosis acquired in Vietnam. Our total experience has been analyzed and the drug resistance rate in disease acquired in Vietnam was between 7-8%. This is about two times the incidence of primary drug resistance in cases acquired in this country, but only about one-half the predicted incidence in the mid 1960's.

WORK UNIT 69/104

PROGRESS - continued

Publications: None

Presentations:

(1) Nelson, R. A.: VA-Armed Forces Research Conference, Columbus, Ohio, January 1971.

(2) Nelson, R. A.: 25th Annual Symposium on Pulmonary Disease, FAMC, September 1972.

STATUS:

Completed

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Chemotherapy of Tuberculosis: Cooperative Study 33 (Rifampin).

WORK UNIT NO.: 71/107

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: George Brown, LTC, MSC
Mary V. Rothlauf, M.S., DAC

OBJECTIVES

Pilot studies and clinical trials have shown rifampin to be very effective in treatment of advanced pulmonary tuberculosis. Its proper place in the hierarchy of antituberculosis drugs and in multiple drug regimens for treatment of tuberculosis can be defined only by more extensive clinical studies. This study will answer these questions by using four drug regimens, all administered orally in a single daily dose.

TECHNICAL APPROACH

Cases of moderately advanced and far advanced pulmonary tuberculosis who qualify according to the terms of the protocol are randomized into 4 treatment groups and treated as follows: 1) INH & RMP; 2) INH + EMB; 3) EMB + RMP; 4) INH + EMB + RMP. Fifteen hospitals among the VA-Armed Forces group are participating and the data collected is being sent to Dr. James Raleigh, Houston VA, director of this protocol.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0.6
FY 75: 1.0

PROGRESS

This is a cooperative research project with the VA and Armed Forces. To date, approximately 50 patients have been entered into the protocol

WORK UNIT 71/107

PROGRESS - continued

from Fitzsimons and a total of about 1400 patients have been entered in all. The results regarding comparative efficacy of the various drug regimens have not been divulged to the individual investigators; however, the Advisory Committee has indicated that there have been no detrimental effects resulting from the use of one regimen over another.

The data regarding input into the study drug side effects, and problems regarding the quality of the data are discussed twice each year by the Executive Committee of this research protocol. COL Roald A. Nelson, MC, FAMC, has been designated the military member of this committee and as such represents the Army and the Air Force hospitals involved in the study.

New patient input into this study has ended. The statistical analysis of the results is now being finalized. The Executive Committee for this protocol met in Montreal, Canada in May 1975 and the final draft for publication will be sent to all participants in the near future.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Clinical Demonstration of Pulsus Alternans.

WORK UNIT NO.: 72/112

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To demonstrate by a laboratory, non-invasive technique a practical way to detect pulsus alternans.

TECHNICAL APPROACH

A plan to demonstrate a simple method of detecting pulsus alternans at the bedside is underway.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 74:	0
	FY 75:	0.5

PROGRESS

Technical difficulties have continued to prevent completion of this project. The mini-transducer obtained for pulse registration has not been operational and it has not been possible, through local efforts, to have the transducer repaired. It will be returned to Holland for repairs and hopefully on its return this project can be completed. The only lacking portion is the objective registration of an event which is readily demonstrable by bedside appraisal.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Effective Respiratory Maneuvers on the Bedside Diagnosis of Cardiac Murmurs.

WORK UNIT NO: 73/115

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: James R. Wheeling, LTC, MC

OBJECTIVES

To establish the information value of various respiratory maneuvers, (phasic respiration, Mueller maneuver, and Valsalva maneuver) in the clinical diagnosis of cardiac murmurs and to correlate this behavior with diagnostic cardiac catheterization, including intracardiac phonocardiography.

TECHNICAL APPROACH

The "bedside" appraisal of cardiac murmurs remains in a very important consideration in the diagnosis of innocent and significant heart murmurs and the clarification as to their origin. A neglected aspect of such appraisal is the behavior of cardiovascular sound events with respiratory maneuvers and during phasic respiration. Previous studies haved tended to deny the significance of respiratory change in the correct diagnosis of various lesions. Such studies were not, however, correlated with exaggerated respiratory maneuvers (Mueller maneuver and Valsalva maneuver), and were not correlated with intracavity sound recordings. The present study will make such correlation. If respiratory maneuvers are found to be predictably altered right or left-sided valvular lesions, their emphasis will be an important addition to routine clinical evaluation of patients.

Patients seen for cardiovascular evaluation will be studied "at the bedside" with a decision as to the behavior of any cardiac murmurs with respiration. Such events will be recorded on phonocardiograms during quiet respiration and during exaggerated respiratory maneuvers (Mueller and Valsalva maneuver). When necessary for other reasons, cardiac diagnostic studies will be accomplished during which intercardiac phonocardiography will be recorded with repetition of the same respiratory maneuvers. The objective findings of cardiac catheterization, intercardiac phonocardiography, will then be correlated with external phonocardiograms and the "clinical" auscultatory findings.

WORK UNIT 73/115

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Phonocardiographic registration of this auscultatory phenomenon continues. It has still not been possible to achieve consistently satisfactory intracardiac, phonocardiographic recordings in the Cardiac-Diagnostic Laboratory. Efforts continue and this project is regarded as worthwhile and will be completed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: A Controlled Clinical and Laboratory Evaluation of Co-Seasonal Injection Therapy in the Treatment of Allergic Rhinitis and Asthma.

WORK UNIT NO.: 73/117

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: T. P. O'Barr, Ph.D., DAC

OBJECTIVES

To determine whether there is significant clinical improvement with the co-seasonal administration of allergy extract and to assess patient's allergy extracts.

TECHNICAL APPROACH

Patients with seasonal allergic rhinitis who are seen either while symptomatic or immediately prior to periods of anticipated seasonal symptoms are selected for study. Allergy extracts are administered on a daily basis. The immunologic changes monitored by serum RAST and blocking antibody titers and leukocyte histamine release.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 2.0
FY 75: 2.0

PROGRESS

Approximately six patients were treated to maintenance this year with daily injections of allergy extract. Blood is available prior to and following extract build-up in all individuals. Two individuals, in addition, had leukocyte histamine release which will be performed prior to and on completion of rush build-up plus following the allergy season, and the symptomatic response of the latter two individuals during the weed season will be available.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Assessment of the Indoor Allergen Load in Colorado

WORK UNIT NO.: 73/124

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To quantitatively assess the occurrence of mold spores and house dust mites in the Colorado area.

TECHNICAL APPROACH

Mold studies are to be conducted in selected Denver area homes, utilizing the volumetric Anderson mold sampler and culture plates. House dust samples are to be collected from a variety of Denver homes and examined for the presence of house dust mites thought to be a principal component of house dust antigen.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

No further studies have been done on this protocol during the present year. The next requirement is to obtain a pure cotton degredation antigen for skin testing and adsorption studies and repeated attempts through several channels to find old bales of cotton have been unsuccessful.

Publications: None

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Deceptions in Cardiology: Cancellation of Abnormal Electrocardiographic Patterns by an Additional Abnormal Event.

WORK UNIT NO.: 73/126

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

This prospective study will seek examples of the normalization of pre-existing abnormal ECG changes by additional myocardial alterations (such as myocardial infarction, myocardial hypertrophy, etc.). It is anticipated that sufficient examples will demonstrate and prove the "cancellation effect" of one abnormality by another.

TECHNICAL APPROACH

Comparison of electrocardiograms before and after "a new cardiac event" for examples of, and clarification of the cancellation effects of one abnormality by the appearance of another.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 74	0.5
	FY 75	0

PROGRESS

Additional examples have been obtained during the past year. We have now encountered examples which we did not previously think of as indicative of this phenomenon. A draft of the total project remains in rough draft form awaiting one or two additional, or better examples. It is anticipated that publication of this material and completion of the research project will be shortly forthcoming.

WORK UNIT 73/126

PROGRESS - continued

Publications: None

Presentations:

(1) Nelson, W. P.: Deceptions in Cardiology; Electrocardiographic Confusion Resulting from Fusion of Electrical Impulses. Presented: Regional Meeting, American College of Physicians, Colorado Springs, CO, January 1975.

(2) Nelson, W.P.: Dilemmas in Cardiac Diagnosis and Therapy: "Confusin-Fusion". Presented: Colorado Heart Assn. Program, Vail, CO, January 1975.

(3) Nelson, W.P.: Cancellation of Myocardial Infarction Patterns, Mercy Hospital Symposium on Acute Coronary Care, Denver, CO, May 1975.

(4) Nelson, W.P.: Confusing Cancellations, Nefarious Normalization and Confusin-Fusion. Presented: Post-Graduate Course in Internal Medicine, Colorado University Medical School Program, Estes Park, Colorado, July 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Effect of Ephedrine on the Physiologic Responses to Exercise and Epinephrine Infusion.

WORK UNIT NO.: 73/132

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: NONE

OBJECTIVES

To further investigate the effect of ephedrine on the metabolic and cardiovascular responses of normal individuals to catecholamine stimulation.

TECHNICAL APPROACH

Metabolic and cardiovascular responses to epinephrine and treadmill exercise were evaluated before and after the administration of ephedrine sulphate in normal pharmacologic doses. In addition, similar responses were studied before and after the administration of Terbutaline, a newly approved, more selective Beta-2 sympathomimetic bronchodilator.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 74:	1.0
	FY 75:	0

PROGRESS

Studies have continued under this protocol, particularly measuring the response to short, vigorous and long-term, less vigorous treadmill exercise.

Publications:

(1) Subsensitivity to Epinephrine Following the Administration of Epinephrine and Ephedrine to Normal Individuals. Harold S. Nelson, M.D., Harry Spaulding, M.D., Richard Summers, M.D., Dale Wood, M.D., Journal of Allergy and Clin. Immunol. 55:299;1975.

WORK UNIT 73/132

Publications - continued

(2) Altered Cardiovascular and Metabolic Responses to Epinephrine Following the Administration of Ephedrine and Terbutaline to Normal Men. Harry S. Spaulding, Jr., M.D., Harold S. Nelson, M.D., L. Bernard Branch, M.D., Bruce M. Pfuetze, M.D., Dale Wood, M.D. Presented at the 31st Annual Meeting of the American Academy of Allergy, San Diego, Calif, 18 February 1975. Published in abstract form in the Journal of Allergy and Clinical Immunology, February 1975.

Presentations:

Nelson, H. S.: Altered Cardiovascular and Metabolic Responses to Epinephrine Following the Administration of Ephedrine and Terbutaline to Normal Men. Presented at the 31st Annual Meeting of the American Academy of Allergy, San Diego, Calif., 18 February 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Response of Nonsensitized Atopic Individual to Long-Term Injections of Allergy Extract.

WORK UNIT NO. 73/133

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: George L. Brown, LTC, MSC
Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

To determine whether clinically-significant sensitization of atopic individuals can occur if they receive antigen in their injection therapy to which they were not originally sensitive.

TECHNICAL APPROACH

Individuals requiring hyposensitization who are initially not sensitive to black walnut or sycamore extract, received one of these two extracts in their Allergy Injection Therapy and are periodically skin tested to both. Blood samples are drawn monthly for one year for alternate analysis of IgE and blocking antibody levels.

Manpower (in professional man years): 0.01/yr

Funding (in thousands) FY 74: 1.0
FY 75: 0.5

PROGRESS

Nine individuals have been entered into the study and have either completed the anticipated course of injections or discontinued shots on their own volition. The laboratory studies have not been performed since RAST antigens for sycamore are not yet available.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Active Antigens in House Dust.

WORK UNIT NO.: 73/135

PRINCIPAL INVESTIGATOR: Leslie B. Branch, LTC, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To determine to what degree the reactivity of house dust extract is related to its contents of cat dander, dog dander, and mites.

TECHNICAL APPROACH

Different lots of house dust from different manufacturers will be put through Sephadex columns charged with specific antibody to: (1) cat dander, (2) dog dander, (3) mite. These extracts which have had one or more of the above specific antigens removed will be used to skin test individuals in the allergy clinic. Their reactivity will be compared to the original extract.

PROGRESS

At present, this protocol has not been started. It is expected the protocol should be accomplished within the next year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Nature and Extent of Hourly Variations in Diffusing Capacity

WORK UNIT NO.: 73/138

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine if the reported diurnal variations in DLCO actually exists.

TECHNICAL APPROACH

Single breath diffusing capacities will be obtained in 10 volunteers, every hour between 0800 hours of one day and 0800 hours of the following day fasting and after a standard meal.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Fifteen subjects have been studied. DLCO appears to vary inversely with serum triglyceride levels after a single high fat meal. Detailed analysis of the data in preparation for publication is now underway.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Treatment of Asthma by Behavior Therapy.

WORK UNIT NO.: 73/139

PRINCIPAL INVESTIGATOR: Thomas L. Creer, Ph.D.

ASSOCIATE INVESTIGATOR: Anthony Hoffman, Ph.D.

OBJECTIVES

To evaluate the effectiveness of systemic desensitization by reciprocal inhibition in the treatment of bronchial asthma.

TECHNICAL APPROACH

Children with bronchial asthma, particularly those in whom there is some evidence of psychological precipitation of attacks will be instructed in the technique of systemic desensitization by reciprocal inhibition and the results of therapy monitored over a six-month period of time.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 74: 0

PROGRESS

Several patients at Fitzsimons were studied under this protocol. The data was incorporated into reports on patients treated by similar means at CARIH.

Publications and Presentations: None specifically on data from this protocol.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: A Controlled Study of Provocative Food Testing, Sponsored by the Food Committee of the American Academy of Allergy

WORK UNIT NO.: 73/140

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To evaluate injection provocative food testing as a method for diagnosing food allergy.

TECHNICAL APPROACH

This study is part of a cooperative effort by The Food Allergy Committee of The American Academy of Allergy. Unknown extracts are supplied to the investigators who in a double-blind fashion administer these food extracts by injection and record any resulting symptoms. Each food is administered twice in random fashion and the response to the two injections will be compared.

Manpower (in professional man years): .1/yr

Funding (in thousands)		
	FY 74:	0.3
	FY 75:	0

PROGRESS

No further patients were studied under this protocol this year.

Publications and Presentations: None.

STATUS:

This protocol was terminated by the Food Allergy Committee 1 July 1975.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Intensive Chemotherapy of Recurrent and Disseminated Bronchogenic Carcinoma

WORK UNIT NO.: 73/143

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: Roald A. Nelson, COL, MC

OBJECTIVES

To improve the survival in patients with inoperable bronchogenic carcinoma.

TECHNICAL APPROACH

Patients with bronchogenic carcinoma which is disseminated (extrathoracic metastases) or recurs after radiotherapy, and otherwise meet the eligibility requirements for the study, are treated with combination chemotherapy. The combination includes two non-FDA approved drugs, CCNU and hexamethylmelamine, plus methotrexate.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0.0

PROGRESS

Nineteen patients were treated with the three-drug combination as described in the protocol. Eighteen had bronchogenic and one had squamous carcinoma of the trachea. All patients completed at least one 21 day course of therapy and are evaluable. Objective remissions were observed in only 3/18 (17%): complete 1; partial (>50%) 1; incomplete (<50%) 1. The patient with CR was the only drug death on day 21. Remission duration was 3 months in the patient with PR and 8 months + in the patient with the incomplete response. One patient with oat cell Ca. had no progression for 5 months but 2 other patients with oat cell and all

WORK UNIT 73/143

PROGRESS - continued

other patients experienced progressive disease.

Significant GI toxicity was observed in 6 of 19; severe thrombopenia (50,000/mm^3) in 12 of 19; severe neutropenia (2,000 mm^3) in 6 of 19; nadir of marrow was d. 21-28. One patient died of drug-related sepsis and two experienced life-threatening hemorrhage. We conclude that this combination demonstrates no increased effectiveness compared with single-agents and is excessively toxic.

Presentations: None

Publications: "Combined CCNU, Hexamethylmelamine and Methotrexate for Bronchogenic Carcinoma." DiBella. N.J., Nelson, R.A. and Norgard, M.J. Proceedings American Association for Cancer Research and American Society of Clinical Oncology 16:264 (1173), 1975.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Anti-Neoplastic Therapy with L-Asparaginase (NSC-109229)

WORK UNIT NO.: 73/144

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with acute lymphoblastic leukemia (ALL), refractory to standard chemotherapy, with L-asparaginase.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with L-Asparaginase as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0.0

PROGRESS

Two patients have been treated:

(1) B. A. - acute lymphocytic leukemia; complete response, relapsing 3 weeks later.

(2) H. L. - blast crisis of chronic granulocytic leukemia, progression of disease.

No toxicities were observed in these patients.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Anti-Neoplastic Therapy with CCNU (NSC-79037) /1-2-chloroethyl)-3-cyclohexyl-1-Nitrosoureal/.

WORK UNIT NO.: 73/145

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with advanced Hodgkin's disease, bronchogenic carcinoma or brain tumors (primary or metastatic) with CCNU.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with CCNU as per protocol.

Manpower (in professional man years): 0.06/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Eleven patients have been treated:

(1) C. M. - CNS fibrosarcoma; progression.
(2) C. C. - Astrocytoma; no change.
(3) H. G. - Glioblastoma multiforme; 50% response.
(4) R. L. - Oat cell carcinoma of lung; stable for 6 weeks, then progression.
(5) J. F. - Squamous cell ca of lung; no change.
(6) C. L. - Glioma; less than 50% remission.

WORK UNIT NO.: 73/145

PROGRESS - continued

(7) M. N. - Glioblastoma multiforme; no change.
(8) M. S. - Glioblastoma multiforme; 50% remission
(9) L. S. - Adenocarcinoma; subjective response then progression.
(10) J. H. - Bronchogenic carcinoma; (with hexamethylmelamine) progression.
(11) P. M. - Squamous cell ca of lung; no change for 5 months, then progression.

Moderate thrombocytopenia at 3-5 weeks has been observed, without significant bleeding or other toxicity.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Anti-Neoplastic Therapy with DTIC (NSC 45388)

WORK UNIT NO.: 73/146

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with advanced Hodgkin's disease, recurrent or disseminated melanomas and sarcomas with DTIC (NSC 45388) / 5(3,3-Dimethyl-1-triazeno) imidazole-4-carboxamidel /.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with DTIC as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Three patients have been treated:

(1) M L. - Melanoma, no change.
(2) U. E. - Partial response (oral lesions receded, no change in pulmonary lesions).
(3) S. W. - Melanoma, progressive.

Malaise and vomiting experienced by one patient but not the others.

Publications and Presentations: None

STATUS

Completed: drug now available from FDA.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Treatment of Psoriasis with Pyrimethamine.

WORK UNIT NO.: 73/147

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine whether pyrimethamine has any therapeutic effectiveness in psoriasis.

TECHNICAL APPROACH

Patients whose psoriasis is long-standing (over 12 months) and refractory to more conservative measures, are placed on pyrimethamine. This drug is given once weekly at twelve-hour intervals for three doses. Every four weeks the dose is increased by 0.25 mg/kg, beginning at 0.75 mg/kg every twelve hours.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Seven patients were begun on this study. Patient #1 (WØ) had a 20% improvement after dose escalation to 1.0 mg/kg, but voluntarily discontinued the protocol for personal reasons. Patient #2 (SØ) had to be discontinued from this study due to an elevation of his liver function tests (SGOT 30 to 400, alkaline phosphatase 55 to 110) after the first dose of pyrimethamine. However, he admitted to ingestion of alcohol during this time. Due to unreliability, therapy was not restarted following return of chemistries to normal. Patient #3 (DØ) obtained a complete response at 1.5 mg/kg dosage level by day 116, and was successfully maintained on 1.0 mg/kg (every 12 hours for 3 doses once weekly). His liver function tests were normal but because of the possible hepatotoxicity observed in the second patient, he

PROGRESS - continued

underwent a percutaneous liver biopsy. This showed severe fatty metamorphosis with minimal early fibrosis. He denied excessive use of alcohol. His BSP was 25% and has slowly decreased over the five months since the drug was discontinued to 14%. Patient #4 obtained a 50% improvement at the 1.5 mg/kg level also by day 116. Due to bad taste and moderately severe nausea, however, therapy had to be discontinued. A liver biopsy on this patient was unremarkable. Patient #5 (PØ) obtained 95% response at the 1.25 mg/kg level by day 117. His therapy was discontinued and he has remained in remission since February 1974 with conservative therapy. Patient #6 (KØ) with extensive psoriasis and psoriatic arthritis has had the best response. Due to the severity of his disease, he was begun on a higher dose (1.0 mg/kg) which resulted in thrombopenia (75,000 per cu mm) and neutropenia (2,800 per cu mm) from which he recovered promptly with folate and discontinuation of the drug. Subsequently he was restarted at the 0.5 mg/kg level obtaining a 100% response of his psoriasis and an 80% response in his arthritis by day 50. He has since been maintained on 0.5 mg/kg weekly with normal liver functions and hematologic tolerance. Attempts at reducing the dosage or frequency of administration have resulted in flareups of his disease. A liver biopsy after 7 months of therapy revealed no evidence of hepatotoxicity. Patient #7 (BØ) also had extensive psoriasis but failed to respond at the 1.75 mg/kg level or two pulses at the 2.0 mg/kg level. At this dose level, he experienced moderately severe nausea and vomiting usually beginning 12-16 hours after the first dose of each weekly pulse, with malaise and anorexia. His liver function tests remained normal. He has subsequently responded to oral methotrexate given once weekly. This is an important observation since methotrexate and pyrimethamine are thought to inhibit folate metabolism by the same mechanism, e.g., blocking of dihydrofolate reductase. Hence, one would expect a cross-resistance between the two drugs.

Publications:

Manuscript in preparation for submission.

Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Anti-Neoplastic Therapy with Adriamycin (NSC 123127)

WORK UNIT NO.: 73/148

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with advanced Hodgkin's disease, lymphosarcomas, acute leukemia, bladder tumors, neoblastomas, breast carcinoma, and sarcomas with Adriamycin.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with Adriamycin as per protocol.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Eleven patients have been treated:

(1) B. H. - Adeno ca, primary unknown; subjective without objective improvement.

(2) C. S. - Osteogenic sarcoma, given with radiation; no evidence of metastases to date.

(3) G. A. - Osteogenic sarcoma, metastatic; no response.

(4) J. R. - Retroperitoneal rhabdomyosarcoma; no response.

(5) R. L. - Oat cell ca of lung; stable for 6 weeks, then progression.

WORK UNIT 73/148

PROGRESS - continued

(6) T. T. - Squamous cell ca of larynx; 50% response of lesions.

(7) W. J. - Squamous cell ca of lung; no response.

(8) W. R. - Osteogenic sarcoma; over 50% remission.

(9) W. M. - Squamous cell ca of sinus; no response.

(10) R. G. - Diffuse, histiocytic lymphoma; less than 50% remission (with cytoxan, vincristine & prednisone).

(11) E. R. - Epidermoid ca of esophagus; stable for 3 months, then progression.

Project will be terminated when Adriamycin becomes FDA-approved.

Publications and Presentations: None

STATUS:

Completed; drug now available from FDA.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Use of Daunomycin (NSC-82151) in Acute Leukemia

WORK UNIT NO.: 73/149

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To permit use of a drug of proven efficacy in acute leukemia, but which is not yet FDA-approved.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with Daunomycin as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Seven patients have been treated:

(1) B. D. - CML blast crisis; no response.

(2) B A. - Acute lymphocytic leukemia; partial response (combined with cytosine arabinoside).

(3) L. C. - CML blast crisis; no response.

(4) S. S. - Acute myelocytic leukemia (with cytosine arabinoside); partial response.

WORK UNIT 73/149

PROGRESS - continued

(5) W. E. - Acute myelocytic leukemia (with cytosine arabinoside); partial response.

(6) D. C. - CML blast crisis; no response.

(7) F. H. - Acute myelomonocytic leukemia (with ARA-C); complete remission.

Severe bone marrow hypoplasia was observed in 4 of 7 patients.

Publications and Presentations: None

STATUS:

Ongoing

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Anti-Neoplastic Therapy with BCNU (NSC 409962) / 1,3-BIS (2-chloroethyl)-1-Nitrosoureal /

WORK UNIT NO.: 73/150

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with inoperable or recurrent melanoma, gastrointestinal tumors or brain tumors (primary or metastatic) and refractory multiple myeloma with BCNU.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with BCNU as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0.0
FY 75: 0

PROGRESS

Eight patients were treated:

(1) F. B. - Melanoma - Over 50% remission of 8-9 months' duration.

(2) M. Z. - Hodgkin's disease; no response.

(3) M. E. - Melanoma; progression after 4 months of stable disease.

(4) M. L. - Melanoma; 50% remission.

(5) U. E. - Partial response (with DTIC and hydroxyurea).

WORK UNIT 73/150

PROGRESS - continued

(6) O. J. - Melanoma; progession (with DTIC).

(7) J. G. - Adenocarcinoma; progression (with 5FU).

(8) W. F. - Adenocarcinoma of stomach; progression (with 5FU).

Publications and Presentations None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Clinical and EEG Evaluation of Vasodilator Therapy as a Means of Preventing Migraine Disorders

WORK UNIT NO.: 73/154

PRINCIPAL INVESTIGATOR: Jon H. Buscemi, MAJ, MC

ASSOCIATE INVESTIGATOR: Dale Schultz, MAJ, MC

OBJECTIVES

To determine if the frequency and/or severity of migraine attacks in susceptible individuals can be altered by daily prophylactic treatment with oral vasodilators; and to determine if the EEG has predictive value regarding response to such therapy.

TECHNICAL APPROACH

(Experimental Design - Clinical Study): Patients, after being counseled and having given written informed consent, will enter into the study, and will receive 3 month trials on each of 3 treatment regimens: (1) Control - no prophylaxis; (2) Isoxsuprine HCl (Vasodilan) - 10 mg TID; (3) Placebo - 1 tablet TID. The severity and incident (number of attacks bi-weekly) will be recorded on each patient during the period of study. The data will be analyzed by means of a 2 way ANOVA with repeated measures.

(Laboratory determination of predictive value of Electroencephalogram): An EEG with hyperventilation will be performed. If a definite change in brain rhythms occurs during this activation process, Vasodilan will be given and the patient will be asked to go through hyperventilation again. A decrease in the hyperventilation response might correlate with a good therapeutic result with prophylactic treatment, for the slowing (build-up) which frequently occurs in the EEG during hyperventilation is felt to be a consequence of vasospasm.

WORK UNIT 73/154

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Investigation of the response from the initial seven patients included in this study reveals that the data provided by these patients is extremely confusing and almost uninterpretable. The data presented by the patients on their recording cards were variable to a high degree, and seemed to have no relationship to the administration of the medications involved. Questioning of the patients with regard to the clinical response to the medications seemed to indicate, however, that there is no significant difference noted by them during either of the three months trial periods of their individual studies. In view of the apparent lack of response to treatment with Vasodilan and the virtually uninterpretable data derived from the individual patients concerned, it is the opinion of the undersigned that this particular project is not leading to any supportable conclusions, and we have elected to terminate this investigation.

Publications and Presentations: None

STATUS: Terminated

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: FAMC's Clinical Experience with Cromolyn Sodium in the Management of Problem Cases of Asthma

WORK UNIT NO.: 73/158

PRINCIPAL INVESTIGATOR: Wendell E. Petty, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To gather information on the effectiveness and establish guidelines for use of Cromolyn Sodium in the treatment of bronchial asthma and to assess the long-term results of therapy with bronchial asthma.

TECHNICAL APPROACH

Patients who were considered suitable candidates for the trial of Sodium Cromolyn in the treatment of bronchial asthma were asked to maintain a symptom index score card for two weeks prior to and four weeks following the introduction of the drug. Wherever possible, patients were contacted one year later, were administered a questionnaire, and again asked to maintain two weeks symptom-medication diary.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Original input in the study was terminated in March 1974 with a total of 80 patients being placed on Cromolyn Sodium, according to the protocol. Results of the initial response were analyzed during the current year. Follow-up data was obtained on 46 patients of the total of 80, and this data is currently being analyzed.

Publications: None

Presentations:

Black, J. W.: Fitzsimons Army Medical Center (FAMC) Clinical Experience with Chromolyn Sodium (Disodium Cromoglycate). Presented: Hugh Mahon Lectureship Award Competition, Fitzsimons Army Medical Center, Denver, CO, 13 June 1974.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Immuno-chemical Evaluation of Myeloproliferative and Plasmaproliferative Diseases

WORK UNIT NO.: 74/101

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC

OBJECTIVES

To determine whether there are any disturbances of immunoglobulin production or of delayed hypersensitivity in the myeloproliferative diseases. To apply new immunochemical techniques for the characterization of monoclonal gammopathies and other dysproteinemias.

TECHNICAL APPROACH

This is an in-depth immunologic evaluation of patients with myeloproliferative and plasmaproliferative disorders.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 74: 1.5
FY 75: 1.5

PROGRESS

(1) Myeloproliferative disorders: Thirty-five patients have been studied on one or two occasions. The average stimulation index (S.I.) of these patients' peripheral lymphocytes was considerably lower than that of control patients. Specifically the average S.I.'s using PHA were as follows:

Normals controls	80-140
Agnogenic myeloid metaplasia (AMM)	4.6
Chronic myelogenous leukemia (CML)	2.9
Smoldering acute myelogenous leukemia	14.5
Paroxysmal nocturnal hemoglobinuria (CPNH)	28.8
Idiopathic thrombocythemia (IT)	5.1

PROGRESS - continued

Polycythemia Vera (PV)	58.0
Refractory anemia	0.7

Of particular interest is the observation that the baseline control values (prior to stimulation with PHA) were considerably higher in patients with some myeloproliferative disorders including AMM, CML and IT.

Hence these figures may reflect only relative impairment in delayed hypersensitivity (DHS), since the S.I. is the ratios of thymidine uptake of stimulated vs. control lymphocytes. Indeed skin testing of these patients with common antigens revealed intact DHS in 32 of 35 patients.

Quantitative immunoglobulin determinations yielded averages that fall within the range of normal, but with considerable scatter above and below this normal range. This was the case for Ig G, A and M. Total complement activity has been normal. C3 and C4 levels are currently being determined.

(2) Plasma proliferative disorders: Eleven new patients were studied. Five were found to have no protein abnormalities. Five patients had IgG myeloma, K-chain in nature. Two of these also had free light chains in the urine. A patient with lymphoma was found to have IgM- K complexed with IgE, a finding not previously reported.

Publications: Manuscript in preparation reporting patient with lymphoma and IgM-K IgE complex.

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Ill Winds that Blow No One Any Good I: Enhanced Gas Transport by Inhalation of Negative Air Ions

WORK UNIT NO.: 74/102

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine if gas transport can be improved by negative air ion inhalation.

TECHNICAL APPROACH

Ten volunteers will undergo pulmonary function testing before, during, and every hour after inhaling negative air ions for approximately 8 hours.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 0.5
FY 75: 0

PROGRESS

The electromagnetic storage device and its controller is ADP equipment and cannot be purchased without specific approval. The project cannot be completed without this equipment.

The air ion collector, Keithley direct current electrometer and medion negative air ion generator will be used in a pulmonary study of the effects of air ions on lymphocyte activation.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Diurnal Variations in Lung Volumes in Fasting and Postprandial Subjects

WORK UNIT NO.: 74/103

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine if there is significant primary diurnal variation in lung volumes or if fluctuations in lung volume are secondary to eating.

TECHNICAL APPROACH

Ten volunteers will have lung volumes measured by a helium dilution technique every hour from 0800 hours of one day to 0800 hours of the next day, on two consecutive days. On one day, the subject will continue a fast that began at 1800 hours the day before. On the other day a standard meal will interrupt the fast after the 0800 hour lung volume measurement. The subject will be alternated so that half will have the standard meal the day before the fast day.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Fifteen subjects have been studied. Lung volumes appear to vary inversely with serum triglyceride levels. Detailed data analysis in preparation for publication of results is now underway.

Publications and Presentations: None

STATUS:

Completed.

WORK UNIT 74/106

PROGRESS - continued

In phase III of this study we have found that oophorectomy and adrenalectomy arrested the rate of tumor progression compared with controls, by a factor of approximately 2:1. Yet lymphocyte transformation by PHA, measured by the stimulation index at 50 days after oophorectomy-adrenalectomy was considerably lower than in the tumor bearing animals who had not undergone the procedure.

We also measured the animals' ability to produce humoral antibody response to sheep RBC's. A significant impairment in both the IgG and IgM response was noted in the DMBA treated rats versus the controls.

We also attempted to induce a delayed hypersensitivity skin test response to an extract derived from this tumor. However, both control and DMBA-treated animals failed to respond to this extract.

In the next phase of this study we plan to:

(1) Assess lymphocyte transformation between day 10 and 50 following the oophorectomy-adrenalectomy.

(2) Assess the humoral response to sheep RBC's following this procedure.

(3) Assess the effect of sham surgery on lymphocyte transformation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Serum IgA Levels in Atopic Individuals and Their Relation to Immediate Skin Test Reactivity and Serum IgE Levels

WORK UNIT NO.: 74/107

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: L. Bernard Branch, LTC, MC

OBJECTIVES

To determine if individuals with significant allergies have increased incidence of abnormal IgA levels.

TECHNICAL APPROACH

Blood is drawn on each patient who undergoes complete skin testing in the Allergy Clinic. Immunoglobulin levels will be determined on these patients and the IgA levels will be correlated with the IgE levels and the degree of positive skin tests.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 74:	0.3
	FY 75:	0.5

PROGRESS

Blood was collected on 690 individuals undergoing skin testing in the Allergy Clinic. Immunoglobulin levels were determined on these blood specimens. Correlations were made between the presence of immediate skin tests and the levels of IgE and IgA and also between the immunoglobulin levels in the presence or absence of hypersensitivity in those individuals who had delayed hypersensitivity skin tests performed in the Allergy Clinic.

Publications and Presentations:

Serum IgA and Delayed Hypersensitivity Skin Tests in Allergic Patients, by L. Bernard Branch, M.D., Harold S. Nelson, M.D., and Richard Lipcak, M.D.

WORK UNIT NO.: 74/107

Publications and Presentations - continued

Presented by Dr. Branch at the 31st Annual Meeting of the American Academy of Allergy, San Diego, California, February 19, 1975, published in abstract form in the Journal of Allergy and Clinical Immunology, February 1975. Serum IgA and Delayed Hypersensitivity Skin Tests in Allergy Patients by L. Bernard Branch, M.D., LTC, MC, presented at the 27th Annual Symposium on Pulmonary Diseases, Fitzsimons Army Medical Center, 12 September 1974 and published in proceedings at the 3rd Annual Meeting Association of Military Allergists, page 50.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Controlled Study of Dander Immunotherapy

WORK UNIT NO.: 74/108

PRINCIPAL INVESTIGATOR: Melvin Hoffman, MAJ, MC

ASSOCIATE INVESTIGATORS: Sheldon Spector, M.D., National Jewish Hospital, Denver, Colorado

OBJECTIVES

Determine the efficacy of immunotherapy with cat and dog dander as determined by symptomatic improvement and improvement in pulmonary function measurements; and determine changes, if any, in bronchial sensitivity, skin tests, RAST, total IgE and neutralizing antibody after specific, high dose, long-term immunotherapy with cat and/or dog dander extract and ascertain if these parameters have predictive value.

TECHNICAL APPROACH

Patients have been selected who have asthma and demonstrate allergy to cat or dog, but who refuse to remove the animal from their home environment. They are to have skin testing, bronchial challenges, and serum samples drawn at the end of the fall pollen season and at the beginning of the spring pollen season each year of the study. The study will be terminated when the participants have received a minimum of 150,000 PNU's of cat or dog extract. Their serums will be evaluated for IgE, specific IgE utilizing the Rast procedure, and for blocking Ab. In addition, the patient's clinical status will be followed through the use of two different symptom evaluation forms and through serial measurement of pulmonary function utilizing the Wright Peak Flow Spirometer.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 1.5
FY 75: .5

PROGRESS

The same 10 patients have continued under observation and treatment during the fiscal year. No new patients were added.

WORK UNIT 74/108

PROGRESS - continued

Publications and Presentations: None.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Safety and Efficacy of Albuterol Tablets when Administered Chronically in the Treatment of Reversible Obstructive Airway Disease.

WORK UNIT NO.: 74/109

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Dudley Raine, MAJ, MC

OBJECTIVES

To compare the efficacy of two doses of oral Albuterol to the standard Ephedrine Sulfate, 25 mg. four times daily.

TECHNICAL APPROACH

The response to these drugs will be compared over a three and one-half month period by use of daily symptom cards, twice daily peak flows and every two weeks, measure response to the drug under observation in the Allergy Clinic.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

A total of 16 patients have completed this study. No further patients are being entered. The results are presently being analyzed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Reactive Hypoglycemia: An Analysis of Glucose-Insulin-Glucagon Interrelationships and Counter Hormonal Regulatory Factors

WORK UNIT NO.: 74/110

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, LTC, MC

ASSOCIATE INVESTIGATORS: Robert A. Adler, MAJ, MC
Steven Plymate, LTC, MC
T. Philip O'Barr, Ph.D., DAC

OBJECTIVES

The objective of the hypoglycemic study is to continue to investigate in our large clinic population the glucose-insulin-glucagon interrelationship and the response of counter-regulatory hormones to hypoglycemic stress.

TECHNICAL APPROACH

The clinical research project involves evaluation of control patients and patients with clinical abnormalities in low blood glucose states to assess the interrelationships of beta cell and alpha cell responsiveness to oral and intravenous glucose administration. Based upon the findings in control patients and patients with disease states, a classification system has been proposed and experience in determining the base pathophysiology of reactive hypoglycemic disorders has been assessed. The clinical studies are being conducted in the Department of Medicine, Endocrine Clinic, with the assistance of an assigned GS-5 to perform blood sampling and assistance during the conducted tests. During the glucose tolerance test, the patient has an indwelling catheter for frequent sampling of blood glucose and is continually monitored with a cardiac monitor system and blood glucoses are assessed immediately after sampling by the Ames Reflectance Meter. After glucose administration, blood insulins, glucagons, growth hormones and cortisols are sampled and the values are determined by sensitive radioimmunoassay systems. The procedure is designed to provide a minimum of patient inconvenience in the performance of these well standardized procedures. All normal individuals experience a low blood sugar state sometime after glucose administrations and the clinical significance of a low blood glucose state is observed by recording appropriate adrenergic symptoms at the nadir of the glucose and determining if there is a counter hormonal responsiveness in defending the low blood glucose state

WORK UNIT 74/110

TECHNICAL APPROACH - continued

as a manifest by timely rises in cortisol and growth hormone indicating hypothalamic-pituitary-end-organ stress.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 74: 7.0
FY 75: 4.0

PROGRESS

Ninety-three oral glucose tolerance tests have been performed and 30 intravenous glucose tolerance tests in conjunction with this research protocol. Data from these studies has provided important clinical information for patient management but has also allowed a major understanding into describing the hypoglycemic disorders and to developing a logical approach to therapy. Such information has allowed us to write a major review article which will appear in the August 1975 issue of Metabolism.

Publications:

(1) Hofeldt, F.D., review article "Reactive Hypoglycemia" in Metabolism.

(2) Hofeldt, F.D., Adler, R.A., Herman, R.H., "Postprandial Hypoglycemia: Fact or Fiction?" Editorial for JAMA.

(3) Hofeldt, F.D., Lufkin, E.G., Hall, S., Dippe, S., Davis, J.W., Levin, S., Forsham, P.H., "Alimentary Reactive Hypoglycemia: Effects of DBI and Dilantin on Insulin Secretion", Military Medicine.

(Published Abstracts):

(1) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Those With Reactive Have Delayed or Excessive Insulin Response. Internal Medicine News 8:4:35, 1975.

(2) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Response to Oral Glucose in Reactive Hypoglycemia Often Delayed or Excessive. Family Practice News 5:2:64, 1975.

(Completed Papers Pending Publication):

(1) McCowen, K.D., Adler, R.A., O'Barr, P.P. and Hofeldt, F.D., "Clinical Implications of the Flat Oral Glucose Tolerance Test", submitted to the Archives of Internal Medicine.

WORK UNIT 74/110

Presentations:

(1) New Approaches to the Study of Hypoglycemia. Regional Meeting for Affiliates of the American Diabetes Association, 7 December 1974.

(2) Endocrine Grand Rounds, University of Colorado, Denver, Colorado, 3 April 1975, Topic: Endocrine Update 1975, Reactive Hypoglycemia.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Correcting Bates (End Tidal) Estimates of Diffusing Capacity for Breathing Patterns. I: Theoretical Analysis.

WORK UNIT NO.: 74/111

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: Neal B. Kindig, Ph.D.

OBJECTIVES

To find a mathematical and/or a graphical relationship between the End Tidal technique and a diffusing capacity calculated by the single breath technique and/or physiologic dead space techniques of Filley and/or Asmussen and Neilsen.

TECHNICAL APPROACH

The Bates correction factor and estimates related to transient response will be developed using digital simulation based on the equations and procedures of Kindig and Hazlett, Quarterly Journal of Experimental Physiology 59: 311-329, 1974. For a given set of parameters, to include pulmonary diffusing capacity, volumes and breathing patterns, the externally measured quantities such as impediment, uptake and end tidal concentration will be computed. Then, the standard Bates formula will be used to compute an estimate of pulmonary diffusing capacity. The ratio of the assumed "true" to the estimated pulmonary diffusing capacity is the correction factor. The correction factor will be displayed on a graph on which only the most significant parameters will be considered the alternate approach is to estimate the "true" diffusing capacity directly from the external measureable parameters, such as tidal volume, frequency, and expiratory flow rate.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 4.0

PROGRESS

Discrepancies are known to exist between the estimates of pulmonary diffusing capacity for carbon monoxide when measured by the three

WORK UNIT NO.: 74/111

PROGRESS - Continued

most common methods. These are the Bohr (average steady state) Bates (end tidal) and the single breath methods. Our previous work has shown that one contribution to the discrepancy results from the usual lack of knowledge of the breathing patterns. We have investigated this extensively for comparing the Bohr and end tidal estimates with some experimental confirmation. A preliminary investigation of the end tidal method indicates that the graphical procedure which was developed for the Bohr method is also applicable to the end tidal method except that the effective sample delay time must be obtained by a different analysis of the breathing pattern. A preliminary method of doing this has been developed. Since the end tidal sample delay is larger than the Bohr (average) sample delay, a set of universal curves and a sample delay estimation technique needs to be developed for specific application to the end tidal method. Now that funding has improved effective 17 Oct 75 progress on this protocol will be rapid.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Small Airway Disease (SAD) II: A Simplified Method for Detecting Small Airway Disease

WORK UNIT NO.: 75/101

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: Robert W. Zimmerer, Ph.D.

OBJECTIVES

To expand the capabilities of the Collins spirometer to include the detection of small airway disease by employing an additional respiratory maneuver. And, in addition, to support this concept by employing additional pulmonary function tests not available in a basic pulmonary function laboratory.

TECHNICAL APPROACH

a. Ten adult volunteers who have never smoked, who have no allergies or asthma, no history of pulmonary infection and who have not had an upper respiratory infection in the past six months will be defined as the normal population.

b. Ten adult smokers who have normal routine pulmonary function tests will be defined as the test population.

c. Pulmonary function test will include spirometry, frequency dependence of functional residual capacity, flow volume loops, compartment studies by helium dilution, compartment studies by body plethysmography, arterial blood gases, frequency dependence of nitrogen washout and frequency dependence of compliance.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 4.0

PROGRESS

Ten smokers and five nonsmokers have been studied so far. Frequency dependence of compliance is abnormal in all of the smokers averaging

WORK UNIT NO.: 75/101

PROGRESS - Continued

53.2% and normal in the nonsmokers averaging 98.2%. The frequency dependence of nitrogen washout had to be abandoned early in the project due to equipment failure but if this is to be reinstituted, approximately $3,000 will be needed. Sixty percent of the smokers had a notch in the first portion of the spirogram and 70% of the smokers had roughening in the mid-portion of the curve whereas none of these findings were present in the normal nonsmoker. Eighty percent of the smokers had an abnormal increase in fuctional residual capacity during the maximum voluntary ventilation maneuver whereas none of the normal nonsmokers had an increase in the functional residual capacity more than 200 cc. By definition both groups had a normal vital capacity, forced expiratory volume in one second and a FEV_1 percent. The maximum mid-expiratory flow rate was abnormal in only one smoker and normal in all the nonsmokers. The critical flow of the flow volume loop was less than 80% of predicted in 60% of the smokers and was all within normal limits in the nonsmokers.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Minoxidil as an Antihypertensive in Patients Refractory to Available Medications.

WORK UNIT NO.: 75/102

PRINCIPAL INVESTIGATOR: John H. Bail, LTC, MC

ASSOCIATE INVESTIGATOR: John P. Kleiner, MAJ, MC

OBJECTIVES

The objective of this protocol is to provide an alternative treatment for patients whose blood pressure is refractory to available drugs or who have experienced unacceptable side effects from them. In fulfilling this purpose, the sponsor has been given three important responsibilities by the Food and Drug Administration: (1) Evidence must be provided that the patient(s) in question indeed is refractory to or experiences unacceptable side effects with standard drugs. The Initial Report Form should be completed and submitted to the sponsor before drug is shipped; (2) The clinical investigators should be (a) experienced in antihypertensive therapy, (b) familiar with the requirements and precautions associated with new drug testing, and (c) fully informed about the drug on the basis of the protocol supplements and by consultation with the research physician and other minoxidil investigators; and (3) The cases treated must be documented in regard to side effects, safety and the antihypertensive efficacy of the drug in such fashion that the sponsor and, in turn, the FDA are completely and currently informed.

TECHNICAL APPROACH

Stable investigation of the etiology of the hypertension will have been carried out prior to consideration of minoxidil. Assessment of end-organ damage will be part of the record. Behavior of the blood pressure will be documented.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.0

PROGRESS

Since inception of this project, 11 patients have been treated with Minoxidil. Sufficient clinical data has been accumulated for presentation

WORK UNIT 75/102

PROGRESS - continued

to clinical meetings. Along these lines, an abstract has been submitted to the Regional American College of Physicians Meeting in Colorado Springs for January 1976. No publications have resulted from this project yet, but it is anticipated that several will be submitted in the next 6 months. Currently the project is ongoing and will continue for some time.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Incidence of IgG Skin Sensitizing Antibodies in an Allergic Population

WORK UNIT NO.: 75/103

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: L. Bernard Branch, LTC, MC

OBJECTIVE

To determine the incidence of IgG skin sensitizing antibodies among a large group of patients previously skin tested in the Fitzsimons Allergy Clinic.

TECHNICAL APPROACH

Passive sensitizing of monkeys using previously collected serum from patients with positive skin tests. The serum will be, in some instances, treated with immunoadsorbents to remove the IgE or IgG immunoglobulins to determine which fraction contains the skin sensitizing antibodies in that particular individual.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 75: 0.0

PROGRESS

Work on this protocol has not been initiated.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Feasibility and Clinical Application of Precordial ST Segment Mapping

WORK UNIT NO.: 75/104

PRINCIPAL INVESTIGATOR: John P. Kleiner, MAJ, MC

ASSOCIATE INVESTIGATOR: Bruce H. Brundage, LTC, MC

OBJECTIVES

Initial phase of this study will be directed in determining the feasibility and clinical application of precordial ST segment mapping. In addition to examining the hypothesis that the millimeter sum of ST segment deviation is related to infarct size, we will also attempt to confirm or deny reports of a high rate of infarct extension as measured by precordial ST segment mapping during the post-infarction convalescent.

TECHNICAL APPROACH

Patients admitted to the Coronary Care Unit with definite anterior or lateral myocardial infarctions, will have a precordial ST segment mapping performed within 24 hours of admission. They will subsequently have daily precordial ST segment maps performed for eight days and then on alternate days, until the fourteenth day. Cardiac enzymes (SGOT, LDH and CPK) will be measured, and symptoms and medications recorded on days in which the ST segment precordial maps are performed.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0.0

PROGRESS

At the present time, a relatively limited number of patients have been available for study. One apparent conclusion is that such a study on a large scale basis can be performed only with the aid of a computerized electrocardiographic system. At the present time, this study will be continued as initially described, until the feasability of a more far reaching study is determined.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Incidence of Bronchoconstriction Induced by Aspirin, F.D. & C. Dyes, and Food Preservatives in a Group of Severe Perennial Asthmatics.

WORK UNIT NO: 75/105

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Melvin Hoffman, MAJ, MC

OBJECTIVE

To determine the incidence of untoward reactions to aspirin, dyes and preservatives in patients with severe and moderately severe bronchial asthma.

TECHNICAL APPROACH

Patients with severe and moderately severe bronchial asthma will be challenged, first openly with aspirin, various food dyes and preservatives in increasing dosages. If these appear to cause attacks of asthma or significant decrease in pulmonary function, challenges will be repeated in double-blind manner.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0

PROGRESS

Twenty patients have been completely studied and the material is undergoing analyses.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Effect of Corticosteroids on Immunoglobulin Levels in Asthmatic Patients.

WORK UNIT NO.: 75/106

PRINCIPAL INVESTIGATOR: William C. Posey, LTC, MC (USAF)

ASSOCIATE INVESTIGATOR: None

OBJECTIVE

To determine whether short courses of high-dose corticosteroids administered to asthmatic patients affect their immunoglobulin levels.

TECHNICAL APPROACH

Blood will be collected on patients who receive brief high-dose courses of corticosteroid treatment with follow-up immunoglobulin levels over a period of several weeks after completion of the treatment.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0

PROGRESS

A number of patients have been studied, but the laboratory studies have not been performed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: A Comparison of the Results of Hyposensitization With Aqueous Grass Extract and Aluminum Precipitated Aqueous Extracted Grass Extract in the Treatment of Patients with Allergic Symptoms Due to Grass Allergy.

WORK UNIT NO.: 75/107

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVE

To compare the efficacy and side effects of two types of FDA approved grass extracts.

TECHNICAL APPROACH

Alternate consenting patients requiring grass hyposensitization will receive the aqueous or the alum-precipitated extract. Their charts will be carefully monitored for incidence of local and systemic reactions, number of injections required to reach maintenance therapy. Symptoms during grass pollen exposure, and antibody changes as a result of hyposensitization will be measured.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0

PROGRESS

Approximately 70 patients are currently in the study, which is in progress.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: A Comparison of Varying Dosage Schedules of Aerosolized Terbutaline in the Treatment of Bronchial Asthma.

WORK UNIT NO.: 75/108

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Wendell E. Petty, MAJ, MC

OBJECTIVE

To evaluate two aspects of aerosol terbutaline response.

TECHNICAL APPROACH

In one study, patients will receive a fixed dose of terbutaline aerosol administered in either one, two or four doses over a period of four minutes. In the second part, subjects will receive one of two doses of aerosol terbutaline or aerosol isoproterenol at 20-minute intervals until they develop side effects, or receive a total of seven doses.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0

PROGRESS

The anticipated 12 patients have completed each part of the study and data is currently being analyzed.

Publications and Presentations: None

STATUS:

Ongoing.

SURGERY

blank

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Evaluation of Peripheral Nerve Injuries at Fitzsimons General Hospital.

WORK UNIT NO.: 72/202

PRINCIPAL INVESTIGATOR: Anthony Ballard, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

The purpose of this study is to evaluate the functional recovery, sensory and motor, of these upper extremity peripheral nerve injuries. This will be carried out by visits to the individual patients by the responsible investigator and his assistant to determine the status of motor recovery and sensory recovery following treatment. Not since WW II has any number of peripheral nerve injuries been examined as long as 2 years following the injury and in no situation has it ever been possible to examine this many peripheral nerves utilizing only 2 investigators.

TECHNICAL APPROACH

To determine functional recovery, both motor and sensory, following neurolysis and/or neurorrhaphy at Fitzsimons Army Medical Center in a group of patients who have been treated here from 1966 through 1970.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Since 1966 to June 1970, the Orthopedic Service has treated approximately 500 peripheral nerve injuries in the upper extremity. In 1966, the Chief of Orthopedics, Fitzsimons Army Medical Center, instituted a system by which the Tumor Registry would maintain records

WORK UNIT 72/202

PROGRESS - continued

and obtain periodic reports from these patients on the status of their peripheral nerve return. Consequently, available to us are the names and addresses of approximately 500 patients involved in upper extremity peripheral nerve injury cases. The majority of these patients, at the time of this writing, are in the Midwest; i.e. from Chicago toward Denver and probably none of them are south of Kansas City.

The initial investigator was Dr. William E. Burkhalter who has since departed this station. This is a continuing project and repeated annual reports have been received through the Tumor Registry at Fitzsimons Army Medical Center from the various patients who have sustained peripheral nerve injuries. The reports are being correlated with the anticipation of presentation of this material in 1977. Information is insufficient at this time to make a more definitive statement regarding the status of these peripheral nerve injuries.

Publications and Presentations: None

STATUS:

Ongoing.

WORK UNIT 72/209

PROGRESS - continued

At the present time there are twenty-five patients involved in the study. All have been placed in prostheses with the stump in adduction. Movies taken before and after therapy show that improvement is demonstrated in gait when the stump is placed in adduction.

The results gathered thus far are being prepared for publication and presentation at the American Academy of Orthopedic Surgeons for their meeting in January 1977. In addition, in cooperation with the Department of Physical Therapy, an exhibit is being prepared for their forthcoming national meeting.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Treatment of Urinary Tract Trauma in the Laboratory Animal.

WORK UNIT NO.: 73/219

PRINCIPAL INVESTIGATOR: Myron E. Page, MAJ, MC

ASSOCIATE INVESTIGATORS: John W. Weigel, COL, MC
Howard E. Fauver, LTC, MC

OBJECTIVES

It has been the objective of this continuing study to develop techniques for auto-transplantation of the canine kidney with a high degree of technical skill. Following this, auto-transplantation was done following partial nephrectomy. Pertinent observations were made and currently we are determining the feasibility of auto-transplantation of the right kidney into the left iliac fossa following occlusion of the vena cava above the point of renal venous drainage. Appropriate flow and pressure studies are being done. The aim of this project is to determine its possible application in the human in conditions such as tumor or trauma destroying the venous drainage on the right and the adjacent areas of vena cava.

TECHNICAL APPROACH

This surgery is done via a midline abdominal incision. The left kidney is left in place as we have no facility for dialysis and acute tubular necrosis is common in the transplanted kidney. Renal transplantation is done utilizing the right kidney into the left renal fossa with anastomosis to the iliac vessels. Pressure measurements are obtained as noted above. The dogs are studied two-weeks postop.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 74: 6.0
FY 75: 6.0

PROGRESS

We currently have 12 viable animals two-weeks post-transplantation which have been adequately studied. Following analysis and presentation and

PROGRESS - continued

publication of this data, we will determine the feasibility of various venous shunts in this condition.

Publications:

(1) Levisay, G.L.: Renal Autotransplantation in the Dog. Proc. of the Kimbrough Urological Seminar, Jan. 74.

(2) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Proc. of the South Central Section, AUA, Denver, CO, 15-19 Sept 74 (published).

(3) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion to be published in Proc. of the Kimbrough Urological Seminar, Seattle, Wash. 5 Oct 75.

Presentations:

(1) Levisay, G.L.: Renal Autotransplantation in the Dog. Presented: Kimbrough Urological Seminar, Washington, D.C., Jan 74.

(2) Levisay, G.L.: Renal Autotransplantation in the Dog: Presented: South Central Section Meeting of the AUA, Denver, CO 15-19 Sep 74.

(3) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Presented: South Central Section of the AUA, Denver, CO, 15-19 Sep 74.

(4) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Presented: Kimbrough Urological Seminar, San Antonio, TX, 14-19 November 1974.

(5) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion to be presented at the Kimbrough Urological Seminar, Seattle, Wash. Oct 5, 75.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Acalculous Biliary Tract Disease

WORK UNIT NO.: 73/221

PRINCIPAL INVESTIGATOR: Robert W. Steyskal, MAJ, MC

ASSOCIATE INVESTIGATORS: Joseph H. Baugh, COL, MC
Thomas P. O'Barr, Ph.D., DAC
Lewis A. Mologne, COL, MC

OBJECTIVES

To evaluate diagnostic methods in patients exhibiting biliary tract symptoms but having normal oral cholecystograms. (a) Evaluation of cholecystokinin in conjunction with oral cholecystography in acalculous biliary tract disease; (b) Evaluation of duodenal bile drainage for evidence of cholesterol crystals and lithogenic bile, i.e. bile with excess cholesterol, in acalulous biliary tract disease; (c) Evaluation of radiomanometry with pressures in the gallbladder and common duct in acalulous biliary tract disease.

TECHNICAL APPROACH

All patients who exhibit biliary tract symptoms and have a normal oral cholecystogram will be entered into the study. All patients will undergo the following diagnostic workup to exclude other systemic diseases: CBC with sed rate, serum and urinary amylase determinations, upper G.I. series, Barium enema, intravenous pyelography, gastroduodenoscopy. All patients will receive cholecystokinin oral cholecystography. All patients will receive cholecystokinin duodenal drainage and the bile collected will be examined for cholesterol crystals and analyzed for bile salts, cholesterol and lecithin.

If meeting the requirements for surgery, the patients will undergo: radiomanometry; collection of bile from gallbladder and common duct for analysis of bile salts, cholesterol and lecithin; cholecystectomy; common duct exploration if indicated; sphincterotomy if indicated.

WORK UNIT 73/221

TECHNICAL APPROACH - continued

Postoperative followup: Patients will be followed at three-month intervals for two years and then yearly for evidence of similar symptoms that existed prior to surgery. At the six month followup, patients will undergo cholecystokinin duodenal collection for analysis of bile.

The number of patients entered into the study will be determined by the analysis of the data obtained from the first twenty patients.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 74: 0
FY 75: 1.0

PROGRESS

There has been no significant progress in this project during the past year. As mentioned in last year's report there was considerable delay in receiving approval from AIDRB, and when this approval was finally received, the principal investigator was totally occupied perforiming the duties of a senior surgical resident. Although Dr. Steyskal had intended to work on this project during the past year, and hence was continued as the principal investigator, his clinical duties and demands throughout the year precluded his devoting any significant time or effort to this project. This project still has merit and should be completed. However, when this project will be completed is indeterminate at the present time.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Gortex Grafts for Replacement of Superior Vena Cava

WORK UNIT NO.: 74/200

PRINCIPAL INVESTIGATOR: William H. Heydorn, COL, MC

ASSOCIATE INVESTIGATOR: Russ Zajtchuk, LTC, MC
George Schuchmann, LTC, MC

OBJECTIVE

To evaluate the performance of Gortex grafts as a replacement for the superior vena cava in dogs.

TECHNICAL APPROACH

Mongrel dogs weighing over thirty kilograms will be anesthetized. A right thoracotomy will be performed and the superior vena cava will be removed and replaced with a Gortex graft. Twenty to 25 dogs will be utilized. If there are early failures in the initial ten dogs a proximal arterio-venous shunt will then be utilized.

Following surgery, tetracycline (1 gram per 24 hours) will be administered prophylactically for five days.

Animals will be sacrified at approximately 40 days to determine the gross and microscopic (if available) status of the graft.

A high patency rate would encourage us to consider the use of this material in two patients in whom superior vena caval replacement may be identified. However, the use of Gortex in a clinical situation is not a part of this protocol.

Manpower (in professional man years): 0.45/yr

Funding (in thousands) FY 74: 0
FY 75: 6.5

PROGRESS

Thirty-three dogs have been followed long term.

WORK UNIT NO.: 74/200

PROGRESS - continued

Only one dog is yet to be studied. Four animals are being followed for long term results. The results of this project were submitted for presentation at the American College of Surgeons in October and rejected. A paper reporting the results is being prepared for publication.

Publications and Presentations: None

STATUS:

Completed.

TLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Preparation and Use of Stroma-Free Hemoglobin Solution in Hemorrhagic Shock and Cardiopulmonary Bypass Surgery

WORK UNIT NO.: 74/201

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: George Brown, LTC, MSC
Joseph H. Baugh, COL, MC
Ben Eiseman, M.D. (Consultant)

OBJECTIVES

To develop blood substitute that will remain within the vascular space and be able to oxygenate tissues. To make the solution free of pyrogenicity and antigenicity, free from interference with typing and cross-matching, free of toxicity to visceral function, and possess a reasonable biologic half-life.

TECHNICAL APPROACH

Method of preparation of the stroma-free hemoglobin. Solution will be based on affinity chromatography. Solution will be evaluated for purity in vitro and in vivo.

Manpower (in professional man years): 3.0/yr

Funding (in thousands) FY 74: 1.8
FY 75: 2.0

PROGRESS

Work up to date demonstrates that it is possible to remove stroma from hemoglobin solution by affinity chromatography. Preparation is being made to present the preliminary results at a national meeting.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Treatment of Digoxin Toxicity with Activated Charcoal

WORK UNIT NO.: 74/202

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
John G. Miller, CPT, VC
Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

Evaluate activated charcoal in the treatment of digoxin toxicity

TECHNICAL APPROACH

Dogs were made digoxin intoxicated and subsequently treated with activated charcoal. Digoxin levels in serum, urine and bile were determined in treated and control groups.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 75: 1.2

PROGRESS

Results were presented at the American College of Cardiology Meeting last February 1975, in Houston, Texas. The first phase of the project has been terminated and the second phase is being carried out under the direction of COL Corby.

Publications: Treatment of Digoxin Toxicity with Activated Charcoal, published in the American Journal of Cardiology, Volume 35, February 1975.

Presentations: Presented at the American College of Cardiology Meeting last February 1975 in Houston, Texas.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Heart Valve Model Cross-Sectional Area Measurement by Electrical Impedance Technique

WORK UNIT NO.: 74/203

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATOR: David R. Hazlett, COL, MC
Joseph H. Baugh, COL, MC

OBJECTIVES:

To improve heart valve cross-sectional area measurement.

TECHNICAL APPROACH

Impedance measurements were made at various openings and increasing hematocrit in the model. Subsequently this was done in dogs across aortic and pulmonic valves. Comparisons made between measured areas by impedance and anatomic measurements.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.35

PROGRESS

Preliminary studies indicate that this method may be used in determining heart valve areas. This method appears to be more reliable than the current ways of calculating the areas i.e., Gorlin's formula.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 82040

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Role of Hypercoagulability in Patients Undergoing Myocardial Revascularization

WORK UNIT NO.: 75/200

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: James J. Bergin, COL, MC
William R. Hamaker, COL, MC
Judy A. Barber, DAC
Patricia A. Rush, DAC

OBJECTIVES

To identify hypercoagulable patients undergoing saphenous vein aorto-coronary bypass operations. To institute rational treatment of such patients.

TECHNICAL APPROACH

Patients undergoing coronary artery bypass surgery will be evaluated preoperatively and on 3rd, 6th, 8th, 10th, 14th and 21st postoperative days. Parameters which will be evaluated include platelet count, platelet adhesivity, activated partial thromboplastin time, factor VIII assay, thrombin generation index, CBC, SMA-18, two-hour post-prandial glucose, serum cholesterol, triglycerides, anti-thrombin III levels and lipo-protein electrophoresis. Those patients found to be hypercoagulable will be treated appropriately.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 3.0

PROGRESS

We found that many of the patients undergoing surgery became hyper-coagulable postoperatively and occlude their grafts early. Hopefully, with appropriate treatment we can salvage some of these patients.

Publications: None

Presentations: Preliminary data will be presented at the American College of Chest Physicians in October 1975, at Anaheim, California.

STATUS:

Ongoing.

CLINICAL INVESTIGATIONS

blank

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Measurement of Adenine Nucleotide Release in Platelets of Newborns

WORK UNIT NO.: 71/301

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To further define in biochemical terms the nature of the qualitative defect of newborn infants.

TECHNICAL APPROACH

The release of adenine nucleotides (AN) from platelets following aggregation and the AN content of platelets will be measured in normal term infants and from infants whose mothers received drugs (ASA or parenteral analgesic agents) prior to delivery.

Manpower (in professional man years): .25/yr

Funding (in thousands)	FY 74:	0.5
	FY 75:	0.5

PROGRESS

This study is completed. A sensitive assay for the measurement of AN using firefly luminescence has been developed, and AN content and the release of these compounds following aggregation with collagen and epinephrine has been studied in normal full term newborn platelets. These findings, when compared with those found in normal adults, confirm earlier work (Corby, D. G. and Schulman, I., J. Peds, 79:307-313, 1971) and indicate that the functional platelet defect is impaired capability to release endogenous adenosine diphosphate.

WORK UNIT 71/301

PROGRESS - continued

Platelet release defects have more recently been classified as (1) "storage pool" defects where subnormal levels of nucleotides are available for release from the dense granules of the platelets and (2) abnormalities in the platelet release mechanism per se. Although our earlier studies demonstrated decreased adenine nucleotide content in newborn platelets, the data did not determine whether this deficit was in the storage pool. Studies of nucleotide labelling and specific activity with 8-C-14 adenine were normal, suggesting that the nucleotide deficits of both metabolic and nonmetabolic pools are similar. Manuscript has been submitted for publication to Thrombosis and Hemostasis Hemorrhagica.

Publications:

(1) Corby, D.G.: Mechanism of Platelet Dysfunction in Newborn Infants. Ped. Res., Vol. 8, No. 4, April 1974. (Abstract)

Presentations:

(1) Corby, D.G., Shigeta, F.H., and Zuck, T.F.: Speculations on the Implications of Newborn Platelet Defects. Presented: III Congress, International Society on Thrombosis & Hemostasis, APS-SPR, Washington, D.C., May 1974.

(2) Corby, D.G., (intr. by Wm. E. Hathaway): Mechanism of Platelet Dysfunction in Newborn Infants, Society for Pediatric Research, APS-SPR, Washington. D.C., May 1974.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Comparison of Metabolic and Functional Changes in Defects of Platelet Function.

WORK UNIT NO.: 73/302

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATORS: None

OBJECTIVES

To correlate biochemical and functional parameters to gain a better understanding of the pathophysiology of functional or qualitative platelet disorders.

TECHNICAL APPROACH

Platelet function studies (aggregation, adhesion, platelet factor-3 availability, bleeding times, and adenine nucleotide (AN) content and the release of these compounds following aggregation with collagen and epinephrine will be measured in patients with various congenital and acquired disorders of platelet function. These results will be correlated with appropriate metabolic studies including levels of adenyl cyclase and glycolytic enzymes in platelets and other body tissues. In some instances, patients will be studied prior to and after initiation of therapeutic measures designed to correct the altered metabolic state.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 74: 0.5
FY 75: 0.5

WORK UNIT 73/302

PROGRESS

This past fiscal year, study on this project has concentrated mainly in two areas: (1) The evaluation of the platelet functional defects in patients with various forms of glycogen storage disease. The progress on this study is summarized in the following abstract: Platelet function was evaluated in 13 patients with Cori type I, III, VI and IX glycogen storage disease. Only patients with glucose-6-phosphatase deficiency demonstrated evidence of platelet dysfunction. The most prominent findings were prolonged bleeding time, reduced platelet adhesion, and defective collagen and epinephrine-induced aggregation. Nucleotide content of platlets was normal, but release of adenosine diphosphate was markedly impaired. These data suggest an intrinsic defect in the platelet release reaction. The reversibility of abnormal platelet function on the 10th to 12th day of total parenteral nutrition suggests that the defect is secondary to the metabolic changes associated with glucose-6-phosphatase deficiency and occurs as the platelet is developing in the megakaryocyte rather than while circulating in the plasma. (2) Soon after initiation of this work, it became obvious that techniques must be developed in our laboratory to separate platelets from their plasma mileux. Concentration of human platelets by Sepharose 2B gel filtration has been advocated as an attractive method for study of functional platelet abnormalities. (Levy-Toledano, S., et al., Rev. Europ. Etudes Clin. et Biol., 1972, 27:313). However, platelets concentrated in this manner have failed to aggregate normally in our laboratory, a finding also noted by other workers. To determine whether nucleotide release occurred during filtration, ADP content of native platelet-rich plasma (PRP) was compared with the content of the platelet effluent. During filtration, platelets from five normal persons lost a mean of 40% (range, 44% -70%) of their initial ADP. The PRP from two persons had been previously incubated with 14-C adenine, and radioactive nucleotides were demonstrated chromatographically in the plasma effluents of these samples, suggesting that at least a portion of the released nucleotides originated from the metabolic pool. These studies suggest that technical refinements of gel filtration are necessary before this method can be considered appropriate for concentrating platelets to be used in functional studies. Future studies are planned involving better technique for platelet isolation.

Publications:

(1) Corby, D. G., Shigeta, F. H., Greene, H. L., and Stifel, F. B.: Platelet Dysfunction in Glycogen Storage Disease Type I (GSDI): Reversal with Total Parenteral Alimentation (TPA). (Abst.) Clin. Res. 21:304, 1973.

WORK UNIT 73/302

Publications - continued

(2) Corby, D. G., Preston, K. A., Shigeta, F. H., O'Barr, T. P., and Zuck, T. F.: Adverse Effect of Gel Filtration on the Adenine Nucleotides of Human Platelets. (Abst., p. 107), III Congress, International Society on Thrombosis Hemostasis (Vienna, Austria), June 1973.

(3) Corby, D. G., (Intr. by Wm. E. Hathaway): Mechanism of Platelet Dysfunction in Newborn Infants. J. Ped. Res., Vol. 8, No. 4, April 1974.

(4) Corby, D.G., Preston, Karen A., O'Barr, Thomas P.: Adverse Effect of Gel Filtration on the Function of Human Platelets. Proceedings of The Society For Experimental Biology and Medicine 146, 96-98 (1974).

(5) Corby, D.G., Putnam, Charles W., Greene, Harry L.: Impaired Platelet Function In Glucose-6-Phosphatase Deficiency. The Journal of Pediatrics. Vol. 85, No. 1, pp. 71-76, July, 1974.

Presentations:

(1) Corby, D.G., Shigeta, F.H., Greene, H.L., and Stifel, F.B.: Platelet Dysfunction in Glycogen Storage Disease Type I (GSDI): Reversal with Total Parenteral Alimentation (TPA). Presented: Western Society for Pediatric Research, Carmel, CA, February 1973.

(2) Corby, D.G., Preston, K.A., Shigeta, F.H., O'Barr, T.P., and Zuck, T.F.: Adverse Effect of Gel Filtration on the Adenine Nucleotides of Human Platelets. Presented: III Congress, International Society on Thrombosis Hemostasis, Vienna, Austria, June 1973.

(3) Corby, D.G.: Mechanism of Platelet Dysfunction in Newborn Infants, Society for Pediatric Research, APS-SPR, Washington, D.C., May 1974.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Computer Storage and Analyses of Mycobacteriologic Laboratory Data from Tuberculous Patients

WORK UNIT NO.: 73/305

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
Joseph Martinez, DAC

OBJECTIVES

To establish and maintain an in-depth data base of mycobacteriological data on FAMC Tuberculosis Service patients.

TECHNICAL APPROACH

Since 1968 all mycobacteriologic results on FAMC tuberculosis patients have been stored in a computer file. Presently 2000 patient records encompassing 45,000 bits of information have been accumulated in the computer file. Patient data include: smear and culture results, drug susceptibilities of mycobacterial isolates, initial drug therapy data, serum tests, data on special study patients, and experimental data on methodology studies.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 74: .5
FY 75: .5

PROGRESS

In December 1973 all computer capability provided by USAMRNL was terminated since September 1974, with the assistance of personnel from MISO, update of the mycobacteriology computer file has been in progress. Old files have been transferred to MISO storage. In addition 250 new patient files encompassing 5000 messages have been added.

PROGRESS - continued

Many old programs have been rewritten for use with MISO hardware. As demand occurs, additional old programs are rewritten and new ones are designed. It is anticipated that the capability for data queries will be greatly increased from the former capability.

Publications:

Blair, E.B., and Tull, A.H.: Computer Storage and Analyses of Laboratory Data From Tuberculosis Patients. II Analyses of Systems Data on Sputum Specimens. Accepted for publication American Review of Respiratory Diseases.

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Immunologic Responses against Spermatozoa in Vasectomized Men

WORK UNIT NO.: 73/308

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Gerald L. Levisay, MAJ, MC
Joseph Lima, DAC
Michael Gray, DAC

OBJECTIVES

To evaluate humoral and cellular immunologic responses in man at intervals post-vasectomy. This study will further clarify possible sequelae for auto-immune disease which may follow this operation.

TECHNICAL APPROACH

Clotted and heparinized blood samples are collected from each subject prior to surgery and at monthly intervals post-vasectomy. Sperm specimens are obtained prior to surgery; seminal plasma and free sperm antigens are prepared. Serum samples are evaluated for humoral anti-sperm globulins against homologous and pooled sperm antigens, functional type(s) of anti-sperm immunoglobulins are determined. Cellular immunity to sperm component(s) are evaluated by lymphocyte transformation studies.

Manpower (in professional man years): 0.8/yr

Funding (in thousands) FY 74: 4.0
FY 75: 1.5

WORK UNIT 73/308

PROGRESS

Pabbits were immunized with human sperm; the developed anti-sera were used for a comparative study of various serological methods for the detection of spermatozoal antibody. A modified sperm agglutination test using viable and spermatozoa was found to be a reproducible and a sensitive test for anti-sperm globulin detection. Cellular immune responses on 23 subjects to sperm antigens showed no evidence for immune mechanism impairment as demonstrated by phytohemaglutinin, poke-weed mitogen, and sperm antigen lymphocytic stimulation. All subjects tested showed development of humoral antibody for sperm occurring on the thirtieth day after surgery. Maximum titers were recorded on the sixth month with residual humoral antibody activity remaining on the twelfth month. IgG and IgM remained unchanged during a twelfth month observation. A two-fold increase in circulating IgG was noted on the second month; normally IgG levels were recorded by the fourth month.

Publications and Presentations:

Brown, G.L. et al.: Humoral and Cellular Immunologic Responses in Man at Intervals Post Vasectomy. Manuscript in preparation.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Microbiological Research in Tuberculosis

WORK UNIT NO.: 74/300

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
James D. Hakes, DAC
J. Graham Kolb, M.S., DAC

OBJECTIVES

To evaluate and/or design new methods for improving diagnostic laboratory procedures in mycobacteriology and to maintain an in-depth data base of laboratory results on tuberculous patients.

TECHNICAL APPROACH

Continuing projects are designed to use clinical materials from FAMC tuberculosis service patients. Specific studies under this project: (I) Comparison of Middlebrook 7H11 OA Agar with Modifications thereof, with Lowenstein-Jensen in an effort to improve isolation of mycobacteria from clinical specimens; (II) Tests for identification of mycobacterial species; (III) Evaluation of a holding medium for transport of specimens for isolation of mycobacteria.

Manpower (in professional man years) 0.5/yr

Funding (in thousands) FY 74: 1.2
FY 75: 1.6

PROGRESS

Evaluation of the media comparison data reaffirms that the Mitchison's selective OA agar is a medium of choice for isolation of mycobacteria from raw clinical specimens. This is evident where small numbers of organisms are involved and also in the isolation of mycobacteria other

WORK UNIT 74/300

PROGRESS - continued

than M. tuberculosis (Mott), particularly Runyon Groups I and III. Data from the media comparison study are being prepared for publication.

Some M. tuberculosis strains require CO_2 on primary isolation. We would like to know if incorporation of bicarbonate into 7H11OA would be stimulatory for mycobacteria. A limited trial comparing 7H11OA with 7H11OA + bicarbonate in a range of concentrations (0.1, 0.05, 0.01, 0.005 M) is currently in progress.

Use of "Dri-Blocks" for determination of temperature growth range of Mott has been incorporated as a routine procedure for identification of these organisms. A description of the method is being prepared for publication.

Methods of determining enzymatic activity are evaluated in an attempt to develop rapid, reproducible and routine tests for this Mott identification.

Evaluation of a modified Cary and Blair transport medium for use as a holding/transport medium for the isolation of mycobacteria is in process. Preliminary results indicate that this modified holding medium can maintain viable mycobacterial organisms.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Mycoplasma and Infertility: Therapeutic Results of Doxycycline Therapy

WORK UNIT NO.: 74/301

PRINCIPAL INVESTIGATOR: James S. Powers, MAJ, MC

ASSOCIATE INVESTIGATORS: Larry B. Norfleet, MAJ, MC

OBJECTIVES

To see if mycoplasma hominis or ureoplasma predominate in our infertility patients. If so, a double-blind control study will be done in which one-half of the patients will be treated with doxycycline or placebo to observe effects on pregnancy rate.

TECHNICAL APPROACH

Patients in the infertility clinic at FAMC, GYN Service, with no demonstrated organic cause of infertility will be grouped into placebo or antibiotic group and followed for one year.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 74: 1.0
FY 75: 0.5

PROGRESS

Since the inception of this project, some sixteen patients have been studied in detail and grouped according to the protocol specifications. To date there have been no pregnancies in patients who were treated but not included in the protocol, however, at this point no determination can be made as to the effects of treatment of the patients suffering from primary infertility with antibiotics. All patients treated with Vibramycin, having positive cultures for ureoplasm or mycoplasma hominis, showed eradication of the organisms after therapy.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Stimulation of Labor by a Single Dose of Intra-Amniotic Steroid

WORK UNIT NO.: 74/302

PRINCIPAL INVESTIGATOR: James S. Powers, MAJ, MC

ASSOCIATE INVESTIGATORS: Jay M. Hill, COL, MC
Gerald B. Merenstein, LTC, MC

OBJECTIVES

To stimulate a normal labor pattern in otherwise normal patients who have passed their due date vs. a control group of similar patients who receive saline placebo.

TECHNICAL APPROACH

Women judged by clinical evaluation and due dates to be at 41 week's gestation will, after amniocentesis and ultra sonography, be randomized to receive injections of short-acting steroids or placebo intra-amniotically. Onset of labor, clinical course and complications will be recorded and analyzed.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

This project has resulted in adverse effect in at least one patient and premature rupture of membranes without labor in another patient. After consultation with the staff, Department of OB-GYN, FAMC, it has been decided that this project, at least in its current phase, should be terminated due to the adverse effects on the patient population. Therefore, recommendation is made that this project be terminated and this was done by DF to COL Corby in February 1975.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Depletion of Liver Glycogen During Endotoxemia

WORK UNIT NO.: 74/303

PRINCIPAL INVESTIGATOR: Thomas P. O'Barr, Ph.D., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To examine the possibility that endotoxin acts on adrenergic receptors to cause a cyclic AMP mediated stimulation of liver phosphorylase.

TECHNICAL APPROACH

Two hundred gram Holtzman rats, which were injected eighteen hours prior to use with saline (controls) or 100 ug of Salmonella typhimurium endotoxin, will be anesthetized with pentobarbital. After opening the peritoneal cavity a catheter will be placed in the hepatic portal vein. One hundred milligrams of D-glucose will be injected into the renal vein and blood samples collected into heparinized tubes from the portal vein at 5 min intervals for 60 min. Plasma will then be recovered and held at -20 C until analyzed for glucose and insulin.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0.5
FY 75: 0.75

PROGRESS

Blood glucose values rose to a maximum at 5 min and began to fall off from that time until at 60 min they were back to fasting levels in the case of the controls. With the endotoxemic animals, the blood glucose levels at 60 min had dropped well below that of the fasting value into the area of hypoglycemia. Insulin values showed a concomitant rise with glucose, although the peak response occurred at 30 min. With the endotoxemic animals, 1 1/2 to 2 fold more insulin was produced and maintained at a high level for a longer time. Additional experiments are being designed to examine the possibility that the hypoglycemic state of the poisoned animals is related to the over production of insulin in response to blood glucose.

WORK UNIT 74/303

PROGRESS - continued

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Clinical Application of TSH Radioimmuno Assay

WORK UNIT NO.: 74/305

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: T.P. O'Barr, Ph.D., DAC
Nassar Ghaed, LTC, MC

OBJECTIVES

To establish a specific homologous radioimmuno assay for thyrotropin, TSH.

TECHNICAL APPROACH

The radioimmuno assay developed uses anti-human TSH material from the NIH. TSH standard used is from the Medical Research Council in England. 125-I is attached to standard TSH via a Sephadex Column method and forming chloramine T.

Manpower (in professional man years): .25/yr

Funding (in thousands) FY 74: .2
FY 75: 2.0

PROGRESS

This radioimmuno assay has been developed and has turned out to be a sensitive and specific assay. The serum from many patients has been studied and has had important clinical implications. However, thyrotropin releasing hormone (TRH) has not been released by the FDA yet and, therefore, many of the studies planned with this assay have not been started. As soon as the TRH is released, further protocols will be submitted for several clinical studies.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Effect of Oral Water Loading on Plasma Prolactin

WORK UNIT NO.: 75/300

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATOR: T. P. O'Barr, Ph.D., DAC

OBJECTIVES

To further clarify the effect of oral water loading on plasma prolactin secretion in various clinical states.

TECHNICAL APPROACH

Normal patients, pituitary tumor patients, people with idiopathic cyclicedema, and patients with drug-induced hyperprolactinemia will be tested for prolactin response to an oral water load.

Prolactin is measured by radioimmunoassay. Radio recepto assay of prolactin is also planned.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.70

PROGRESS

This test has been performed in several patients, but some testing was suspended until the prolactin radioimmunoassay was refined. The assay now is working well, and the radio receptor assay is being developed.

Publications:

(1) Adler, R.A., Noel, G.L., Wartofsky, L., Frantz, A.G.: Failure of Ali Water Loading and Intravenous Hypotonicsaline to Suppress Plasma Prolactin in Man (In Press, Journal of Clinical Endocrinology and Metabolism, August 1975).

(2) Hofeldt, F.D., Adler, R.A., Boland, M.J., Block, M.B.: Galactorrhea: What Does It Mean? Rocky Mountain Medical Journal 73:252, 1975.

WORK UNIT 75/300

Presentations:

Galactorrhea and Prolactin. Endocrine Grand Rounds, University of Colorado Medical Center, 23 January 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FTIZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Circulatory and Homoral Changes In Dogs During Acute Pancreatitis

WORK UNIT NO.: 75/301

PRINCIPAL INVESTIGATOR: William L. Daniels, CPT, MSC

ASSOCIATE INVESTIGATORS: John C. Miller, CPT, VC
Thomas P. O'Barr, Ph.D., DAC
James A. Seab, Jr., MAJ, MC

OBJECTIVES

To determine changes that occur in heart rate blood pressure, serum glucagon and serum insulin during acutes pancreatitis.

TECHNICAL APPROACH

a. Ten animals will be studied to determine the effects of acute pancreatitis.

b. Blood pressures and electrocardiograms will be recorded.

c. Blood samples will be drawn hourly to measure plasma glucagon, plasma insulin and serum amylase.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0.2

PROGRESS

Six animals were studied in an attempt to determine to optimum method of inducing pancreatitis. It has been determined that acute pancreatitis can be induced within eight hours by injecting autologous bile into the pancreatic duct. Three animals have been studied using this procedure.

Publications and Presentations: None

STATUS:

Ongoing.

OBSTETRICS AND GYNECOLOGY

blank

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Evaluation of "Pereyra-Harer" Procedure in Treating Urinary Stress Incontinence.

WORK UNIT NO.: 67/351

PRINCIPAL INVESTIGATOR: Willard M. Woods, MAJ, MC
James E. Brown, CPT, MC

ASSOCIATE INVESTIGATOR: Keith F. Deubler, COL, MC

OBJECTIVES

To evaluate the Pereyra method of urethro-vesical suspension as a means of treatment for patients with true urinary stress incontinence. To evaluate the long term effect of all forms of surgically corrected urinary stress incontinence.

TECHNICAL APPROACH

This project is an attempt to define the long term effect of one type of surgical repair for urinary stress incontinence in the female. Patients with urinary stress incontinence receive a complete urological work-up. The Bonney-Marchetti-Read "Stress test" is used to select surgical candidates. The chain cystogram is utilized as described by Green to define cases as Type I or Kennedy urethro-vesical plications as the primary surgical procedure used for control of Krantz procedure or a Pereyra-Harer procedure, depending on whether an abdominal or vaginal approach is indicated by the patient's other symptoms and findings. The long term follow-up is done through the modality of patient questionnaire on a six monthly basis. This will ultimately give sufficient data to define the relative merits of different surgical approaches in our treatment of this clinical problem.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 0
FY 75: 0

WORK UNIT 67/351

PROGRESS

The original objective and paper work were completed in November 1974 according to the original protocol. Since completion of the paper, a slightly modified objective has been assigned as follows: The Tumor Registry will continue to report the successes and failures of each type of surgically corrected urinary stress incontinence; however, our surgical approach will be somewhat modified in that we will do initial vaginal repairs by the Kennedy-Kelly without Pereyra procedure on both Type I and Type II chain, depending on their clinical situation. The primary objective will now be to simply evaluate all forms of surgically correctable urinary stress incontinence on all types of defects, using the same technical approach in the previous protocol.

Publications: None

Presentations:

1. Buffone, David A.: Evaluation of the "Pereyra-Harer" Procedure in Treating Urinary Stress Incontinence. Presented: The Armed Forces District Meeting of the American College of OB-GYN, Las Vegas, NV, October 1970.

2. Woods, W.M.: Evaluation of the "Pereyra-Harer" Procedure in the Treating of Urinary Stress Incontinence. Presented: Armed Forces District Meeting of the American College of OB-GYN, Washington, D.C., November 1974.

3. Woods, Willard M.: Operative Treatment of Urinary Stress Incontinence Evaluation of the Pereyra, Kennedy-Kelly, and Marshall-Marchetti-Krantz Procedures. Hugh Mahon Lectureship Award Competition, Fitzsimons Army Medical Center, Denver, CO, June 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Gynecologic Follow-up after Tubal Surgery for Sterilization.

WORK UNIT NO.: 73/353

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

1. To determine the incidence of GYN problems following tubal surgery for sterilization in a five-year postoperative follow-up.

2. To determine the failure rate of various types of tubal surgery for sterilization.

3. To determine complications (operative) of various types of tubal surgery for sterilization.

4. To determine morbidity (postoperative) from various types of tubal surgery for sterilization.

5. To determine patient's estimates of the value of the procedure.

TECHNICAL APPROACH

The long-term results of sterilization by tubal surgery as opposed to other means of sterilization will be evaluated by registering all these patients in the tumor registry and following their progress for several years by a questionnaire on a biannual basis.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 74:	0
	FY 75:	0

WORK UNIT 73/353

PROGRESS

The three-year collection of cases to be followed for five years is to completed as of the end of July 1975; with follow-up being maintained on these patients by questionnaire for a total of five years.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Prophylactic Use of Cephaloridine in Elective Total Vaginal Hysterectomies.

WORK UNIT NO.: 73/354

PRINCIPAL INVESTIGATOR: Alfred S. Llorens, COL, MC

ASSOCIATE INVESTIGATORS: George L. Brown, LTC, MSC
Thomas J. Hickman, MAJ, MC
Ann H. Tull, DAC
Dennis L. Ludwig, CPT, MSC

OBJECTIVES

The purpose of this research project is to evaluate Cephaloridine as a "prophylactic" antibiotic in elective total vaginal hysterectomies. This study will correlate postoperative morbidity as expressed by the specific pathogenic bacterial type isolated from vaginal cultures and the incidence of postoperative morbidity following the use of prophylactic antibiotic both pre and postoperatively. A total of 200 patients randomized into 100 patients each group (prophylactic antibiotic and non-prophylactic antibiotic group) will be evaluated.

TECHNICAL APPROACH

The patients undergoing vaginal hysterectomy for sterilization are entered into the study. In a double-blind manner these patients either received placebo or Loridine pre and postoperatively. After an appropriate number of patients are studied, the code is broken to determine whether prophylactic antibiotics have an effect on morbidity in vaginal hysterectomy for sterilization.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 74: 5.0
FY 75: 1.0

WORK UNIT 73/354

PROGRESS

Since inception of this study only 66 patients have been entered; of these, approximately one-half fall into placebo and one-half into the Loridine group. Because of the difficulty obtaining cultures, it has been decided to terminate the study. Preliminary study of the data show that those patients who received prophylactic antibiotics (Loridine) only 3% showed febrile morbidity. In contrast, those that did not receive prophylactic antibiotics, 19% showed febrile morbidity. This is considered to be a significant difference.

Publications: None

Presentations:

Abstract submitted to the Armed Forces District Meeting of the American College of OB-GYN, San Antonio, Texas, October 1975.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Migrating Placenta Previa

WORK UNIT NO.: 74/351

PRINCIPAL INVESTIGATOR: James S. Powers, MAJ, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To illustrate through an obstetrical case history, the phenomenon of placental migration from one region of the uterus to another.

TECHNICAL APPROACH

Studying a case history from the obstetrical clinic which documented anterior placenta previa marginalis which through serial ultrasound documentation was observed to actually move away from the cervical os to the anterior fundal area.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 75: 0

PROGRESS

The project is complete and actual documentation has been shown in the paper.

Publications:

Has been submitted to the Southern Medical Journal for publication and is currently awaiting acceptance.

Presentations:

23rd Annual Armed Forces District Seminar, Washington, D.C., Nov 1974, presented to the meeting.

STATUS:

Completed.

PEDIATRICS

blank

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Daunomycin in the Treatment of Acute Leukemia in Childhood (ALL).

WORK UNIT NO.: 73/407

PRINCIPAL INVESTIGATOR: Daniel C. Plunket, COL, MC

ASSOCIATE INVESTIGATOR: S.J. Bertolone, MAJ, MC

OBJECTIVES

To investigate (1) effect of Daunomycin in inducing remission in acute leukemia refractory to other chemotherapeutic agents and (2) the effect of Daunomycin added to Prednisone and Vincristine Induction remission regimen in patients with ALL not responding to Prednisone and Vincristine alone.

TECHNICAL APPROACH

Daunomycin to be utilized in an attempt to induce remission in acute leukemia refractory to other chemotherapeutic agents and also utilized with Prednisone and Vincristine induction in patients with acute lymphatic leukemia not responding to Prednisone and Vincristine.

Manpower (in professional man years): .02/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

This drug was used in two patients. Neither patient achieved a complete response. There was one partial response.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Use of L-asparaginase in Acute Leukemia in Childhood (ALL)

WORK UNIT NO.: 73/408

PRINCIPAL INVESTIGATOR: Daniel C. Plunket, COL, MC

ASSOCIATE INVESTIGATOR: S. J. Bertolone, MAJ, MC

OBJECTIVES

L-asparaginase is to be used in an attempt to induce remission in patients with ALL refractory to other medication.

TECHNICAL APPROACH

To utilize this drug in an effort to induce remission in patients with acute lymphatic leukemia resistant to other chemotherapeutic agents. A weekly dosage of 10,000 units/M2 is utilized.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 74; 0
FY 75: 0

PROGRESS

FY 74-75 - two patients with ALL were entered. Both patients had previous ALL relapse. Both patients achieved complete remission, although for only very short duration.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Treatment of Acute Myelocytic, Myelomonocytic and Erythroleukemia of Childhood (Non-ALL, Non-AUL).

WORK UNIT NO.: 73/409

PRINCIPAL INVESTIGATOR: Daniel C. Plunket, COL, MC

ASSOCIATE INVESTIGATOR: S. J. Bertolone, MAJ, MC

OBJECTIVES

To investigate chemotherapeutic drug combination in improving survival of these forms of childhood leukemia.

TECHNICAL APPROACH

Patients in these diagnostic categories are given a regimen of cytosine-arabinoside and cyclophosphamide.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

No patients were entered on study.

Publications and Presentations: None.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Effect of Positive Transpulmonary Pressure on Effective Pulmonary Blood Flow, Cardiac Output, Functional Residual Capacity, and Dynamic Pulmonary Compliance in Idiopathic Respiratory Distress Syndrome in Neonates

WORK UNIT NO.: 73/413

PRINCIPAL INVESTIGATOR: William H. Parry, LTC, MC

ASSOCIATE INVESTIGATOR: Gerald B. Merenstein, LTC, MC

OBJECTIVES

Although positive transpulmonary pressure has been shown to be effective in the treatment of the idiopathic respiratory distress syndrome, few physiologic studies have been performed to delineate the reasons for its effectiveness. It is the purpose of this study to obtain data on various cardiopulmonary parameters in order to increase understanding of the physiologic effects of positive transpulmonary pressure in the neonate ill with the idopathic respiratory distress syndrome.

TECHNICAL APPROACH

A non-invasive method utilizing the body plethysmograph will be utilized to gain information on various cardiopulmonary physiologic parameters both prior to institution of positive transpulmonary pressure and after institution of the technique.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 6.0
FY 75: 0

PROGRESS

All equipment has been purchased and has arrived. Presently the equipment is being assembled and being put in working order. It is

WORK UNIT 73/413

PROGRESS - continued

that the initial subjects will be studied in about one month's time.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Clinical Evaluation of Effective Thyroxine Ratio in Newborns

WORK UNIT NO.: 74/400

PRINCIPAL INVESTIGATORS: Gary Pettett, MAJ, MC
Gerald B. Merenstein, LTC, MC

ASSOCIATE INVESTIGATORS: None

OBJECTIVES

To show that the effective thyroxine ratio (ETR) is an accurate, single test for determining thyroid status of newborns, obviating technical and interpretive errors of the Resin T_3 uptake, T_4 by column and free thyroxine index.

TECHNICAL APPROACH

Samples of whole blood were obtained from 30 consecutive healthy newborns from the FAMC Newborn Nursery. Mallinkrodt Laboratories supplied test kits for direct measurement of ETR and Red-o-Mat T_3 and T_4 measurements. A free thyroxine index was calculated from these values. The purpose of the study was to determine thyroid function in the neonatal period and test the applicacy of the ETR measurement as a standard of thyroid function.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 0.5
FY 75: 0.5

PROGRESS

The project has now been completed. Data has been analyzed, and the project is being written up in anticipation of submission for publication within the next few months.

Publications and Presentations: None.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

Title: Treatment of Meconium Aspiration

WORK UNIT NO.: 74/405

PRINCIPAL INVESTIGATOR: Gentry W. Yeatman, CPT, MC

ASSOCIATE INVESTIGATOR: John B. Woodall, MAJ, MC

OBJECTIVES

To evaluate the effectiveness of suction and/or pulmonary lavage in meconium aspiration.

TECHNICAL APPROACH

It was planned to induce meconium aspiration in newborn animals and determine a LD_{50}. Subsequently, various groups of tracheal lavaged and untreated animals were to be compared to "normal animals" from the same litter.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 74:	0.2
	FY 75:	0.2

PROGRESS

Initially, we attempted to induce meconium aspiration in the New Zealand white rabbits and then performed tracheal lavage. This was found to be technically impossible to do in a controlled manner. Subsequent attempts to obtain large pregnant dogs or induce pregnancy with any acceptable frequency or predictability has also been unsuccessful.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Posterior Polar Cataracts and Steroid Therapy in Children

WORK UNIT NO.: 74/406

PRINCIPAL INVESTIGATOR: Harry S. Spaulding, Jr., COL, MC

ASSOCIATE INVESTIGATOR: Hyman L. Chai, M.D.

OBJECTIVES

To determine the incidence of posterior subcapsular cataracts in a group of children with severe bronchial asthma treated with corticosteroids. This is to be compared to a population of approximately 100 normal nonatopic children age 6-16 who will be studied at Fitzsimons Army Medical Center. The main objective is to determine if the incidence of cataracts in a normal population is of a similar incidence to that of a population of the same age who have been treated with steroids.

TECHNICAL APPROACH

a. Approximately one hundred subjects with no documented history of allergy will be subjected to routine allergy testing with only ten antigens and utilizing prick testing only.

b. Subjects will be divided into ones without any overt allergy, those with history of allergy and eczema, and those with a history of allergy but who have not been on steroids.

c. In addition to the skin tests, 10 cc's of blood will be obtained at the time of testing for the purpose of doing IgE levels as well as total eosinophil counts.

d. The only other procedure to be followed in this protocol will be a slit lamp examination by an ophthalmologist.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 75: 0

WORK UNIT 74/406

PROGRESS

Chai has shown at the National Asthma Center that slit lamp studies in ninety-two children, all except one of who had been on steroids prior to admission for many years, revealed that ten (10.8%) had clear evidence of cataracts. Twenty-one or (22.8%) additional children had uncertain findings but not clearly positive for cataracts. Four (4%) of the positive had eczema. Six (6%) did not. Ten (47.7%) of the suspicious cases had eczema. Eleven (52.3%) did not. Ninety-one children had been on steroids for years. Sixty-one (66.3%) of children with essentially the same steroid history had no evidence of cataracts or even suspicion thereof. Dr. Spaulding has examined thirty-seven children with and without atopy who have not been on steroids at Fitzsimons Army Medical Center and to-date slit lamp examination has shown no changes. This study suggests that cataracts may be more prevalent then what was first thought if the suspicious cases are taken into account. Furthermore, no evidence is available whereby "at risk" children can be identified, hence repeated examination is necessary.

Publications:

(1) Paul Dunand, M.D.: H. Chai, M.D.; D. Walter, M.D.; H. Spaulding, M.D. and G. Meltzer, M.D.: Posterior Polar Cataracts and Steroid Therapy in Children, Journal of Allergy and Clinical Immunology, Vol. 55, #2, Pg 123-1975.

Presentations:

(1) Paul Dunand, M.D.; H. Chai, M.D.; D. Walter, M.D.; H. Spaulding, M.D. and G. Meltzer, M.D.: Posterior Polar Cataracts and Steroid Therapy in Children. Presented: Annual Meeting of the American Academy of Allergy, San Diego, California, February 1975.

(2) Harry S. Spaulding, M.D.: Occurrence of Cataracts in Asthmatic Children Treated with Corticosteroids. Presented: 28th Annual Fitzsimons Pulmonary Disease Symposium and 4th Annual Fitzsimons Allergy Immunology Symposium, 8-11 September 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Computer Assisted Diagnosis in a Military Hospital

WORK UNIT NO.: 74/407

PRINCIPAL INVESTIGATOR: Warren A. Todd, LTC, MC

ASSOCIATE INVESTIGATOR: Gary Pettet, MAJ, MC

OBJECTIVE

To determine if the use of a computer system will speed up the time from admission to confirmed diagnosis in those patients who have not had a confirmed diagnosis within 48 hours of hospitalization. It was also hoped that we could learn if there would be a reduction in the length and cost of hospital stay, the number and cost of laboratory studies, the number and cost of relevant laboratory studies, and the number and cost of consultations obtained.

TECHNICAL APPROACH

All admissions to the General Pediatric Service would be considered as candidates for the study. The first one hundred patients who do not have a confirmed diagnosis 48 hours after admission would be assigned randomly to either the computer group or to a control group according to an attached patient assignment table. The patient assignment table would not be revealed to the physicians caring for the patients during the first 48 hours of admission and at the same time with a 48 hour differential.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0

PROGRESS

At the present time we have approximately thirty-three patients involved in the study with a need to study a further 60+ children. The second portion of the objectives of the study, that is a reduction in length and cost of hospital stay, etc., has not been computed at present and will probably not be computed until completion of the study. At the present time we estimated at least another 18 months involved in the computer study. The project is approximately 1/3 complete. No funding is needed for completion of the study as all of the monetary supplementation has been provided through MEDITEL.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Echocardiographic Assessment of Ventricular Size and Function in Infants of Diabetic Mothers

WORK UNIT NO.: 75/400

PRINCIPAL INVESTIGATOR: G. B. Merenstein, LTC, MC

ASSOCIATE INVESTIGATORS: Gerald L. Way, MAJ, MC
William P. Nelson, COL, MC

OBJECTIVES

To determine serial dimensions of hearts of infants of diabetic mothers and to determine serial indices of myocardial contractility of hearts of infants of diabetic mothers.

TECHNICAL APPROACH

a. All LGA infants will be assessed, and those infants whose mothers satisfy White's Classification of Diabetes and Pregnancy will be evaluated.

b. Height, weight, and head circumference will be recorded.

c. Gestational aging will be done according to Dubowitz exam within seventy-two hours, and a hematocrit will be obtained.

d. Left ventricular wall thickness and left ventricular internal dimensions will be measured from the echocardiograms and compared to normal newborns at this altitude. Left ventricular function will be determined by measuring velocity of circumferential fiber shortening.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 1.0

PROGRESS

Fifteen infants with a mean gestational age of 38.5 weeks and all satisfying White's Classification were evaluated echocardiographically.

PROGRESS - continued

Two infants were eliminated from the study because of congenital heart disease. Velocity of circumferential fiber shortening, posterior wall thickness, and septal wall thickness were measured and compared to normal infants. Infants of diabetic mothers had significant decrease in circumferential fiber shortenings. Only one patient had abnormal posterior wall thickness or septal wall thickness.

There was no correlation between the patient's clinical state and circumferential fiber shortening, stroke volume, or birth weight. There was good correlation between injection fraction and circumferential fiber shortening ($r = 0.886$). Our data suggests that the cardiorespiratory symptoms seen in infants of diabetic mothers are related to decreased ventricular function.

Publications:

Way, G.L., Wolfe, R.R., Pettett, P.G., Merenstein, G.B., Simmons, M.A., Spangler, R.D., Nora, J.J.: Echocardiographic Assessment of Ventricular Dimensions in Myocardial Function in Infants of Diabetic Mothers, Pediatric Research 9:273, 1975 (Abst).

Presentations:

Way, G.: The Spectrum of Myocardopathy in Infants of Diabetic Mothers (Abst). To be Presented: Annual Meeting American Academy of Pediatrics, Cardiology Section, Washington D.C., Oct 1975. (Abstract submitted and accepted for presentation)

STATUS:

Ongoing.

PATHOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Relationship of Estrogenic Hormones to the Coagulation Balance

WORK UNIT NO.: 71/450

PRINCIPAL INVESTIGATOR: Paul W. Holley, MAJ, MC

ASSOCIATE INVESTIGATORS: James J. Bergin, COL, MC
Donald G. Corby, COL, MC
Thomas F. Zuck, LTC, MC
James S. Powers, MAJ, MC

OBJECTIVES

The objective is to continue to investigate the changes in the natural inhibitor mechanisms of coagulation brought about by female sex hormones; i.e., estrogens and combined progesterone-estrogen oral contraceptives. The main purpose for such investigation is to determine whether prospective application of the thrombin generation and anti-thrombin-III tests, either alone or with other clotting parameters, can define those patients taking exogenous hormones who would be at increased risk of developing thrombovascular disease.

TECHNICAL APPROACH

The approach is twofold: (1) To study the relationship of the two parameters to each other by various assay techniques with several different plasma and serum fractions in order to insure that they are indeed independent parameters and not mutually dependent upon each other, and (2) to study large numbers of women in various categories while they are symptomatic and asymtomatic to confirm that the tests have prognostic value, or to disprove their usefulness for this purpose.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 74: 5.0
FY 75: 5.0

WORK UNIT 71/450

PROGRESS

The thrombin generation test and the functional serum antithrombin-III determination have been discussed in previous Research Project Resumes. Studies indicate that in all patients taking estrogens, either alone or in an oral contraceptive preparation, there is a significant depression of serum functional antithrombin-III and an acceleration of thrombin generation to a somewhat lesser degree. Plasma antithrombin III is mildly depressed, also, indicating probable in vivo catabolism.

Studies in women taking exogenous estrogens (Premarin) show a lack of relationship between the dose of estrogen and the level of antithrombin III activity and thrombin generation.

Recent studies in 50 female patients, half taking the "minipill" and half taking the "micropill," have shown a similar degree of depression of serum functional antithrombin-III activity in each group. Thus it appears that the degree of decrease in serum functional antithrombin III level is unrelated to the dose of estrogen. This data is currently being prepared for publication.

The plans for study of antithrombin III activity in males with prostatic carcinoma treated with estrogens have been unsuccessful because of a paucity of patients. Therefore, this group of patients will not be studied.

Currently, studies are being undertaken in three general areas:

1. A group of teenage females with severe acne vulgaris are being treated with oral contraceptives containing four different doses of estrogen. The relationship between the clinical improvement in the acne and the blood clotting kinetics involving thrombin generation and antithrombin III depression at different dose levels will be studied.

2. Ten females of reproductive age having regular "normal" menstrual periods and not taking oral contraceptives or other medications will be studied daily during their menstrual cycle to assess change in thrombin clotting kinetics and antithrombin III depression.

3. In a group of females prior to castration, after castration but prior to estrogen replacement, and then after several months of estrogen replacement, determination of estrogen levels, thrombin generation index (TGI) and antithrombin III activity will be undertaken.

For the above studies, certain other tests, such as the APTT, PT, platelet function tests and factor assays, may be done in conjunction with the thrombin generation and antithrombin III determinations.

WORK UNIT 71/450

Publications:

(1) Zuck, T. F., Bergin, J. J., and Raymond, J. M.: Implications of Depressed Antithrombin III Association with Oral Contraceptives. Surg. Gynec. & Obstet. 133:209, 1971.

(2) Zuck, T. F., and Bergin, J. J.: Thrombotic Predisposition Associated with Oral Contraceptives. Obstet. & Gynec. 41:427, 1973.

(3) Zuck, T. F., Bergin, J. J. and Raymond, et al.: Platelet Adhesiveness in Symptomatic Women Taking Oral Contraceptives. Thromb. Diath. Hemorr. 26:426, 1971.

(4) Zuck, T. F., Bergin, J. J., and Perkins, R. P.: Antithrombin III Activity and Oestrogen Content of Oral Contraceptives. Lancet 1:831, 1973.

Presentations:

(1) Zuck, T. F.: Rates of Generation and Progressive Neutralization of Thrombin in Symptomatic Women Taking Oral Contraceptives. Presented: II Congress, International Society on Thrombosis and Haemostasis, Oslo, Norway, 1971 (Abs., P. 106).

(2) Zuck, T. F.: Shifts in Thrombin Kinetics Induced by Conjugated Equine Estrogens. Presented: III Congress, International Society on Thrombosis and Haemostasis, Washington, D.C., 1973, (Abs., P. 160).

(3) Zuck, T. F.: On the Mechanism of Antithrombin III Depression in Women Using Oral Contraceptives. Presented: IV Congress, International Society on Thrombosis and Haemostasis, Vienna, Austria, 1973, (Abs., P. 223).

(4) Zuck, T. F.: Thrombin Generation Index and Antithrombin III as Guides to Anticoagulation in the Surgical Patient. Presented: Regional Meeting of American College of Physicians, Steamboat Springs, CO, 1974.

(5) Zuck, T. F.: The Pill and Thromboembolic Disease. Presented: Colorado Heart Association, Snowmass-at-Aspen, CO, 1974.

STATUS:

Ongoing.

RADIOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Scintographic Evaluation of Thyroid Disorders - Clinical Evaluation of Oral ^{123}I Sodium Iodide.

WORK UNIT NO: 73/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of ^{123}I Sodium Iodide for oral administration supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

One to four capsules (100 to 400 uCi) of ^{123}I-Sodium Iodide Capsules will be administered orally to patients suspected of having thyroid disease. Measurement of ^{123}I accumulation in thyroid and thyroid scintography will be performed at varying time intervals. The number of subjects with known or suspected thyroid disease will be unlimited and there will be no limitation on sex or age of patients. Data obtained will be recorded on either the special patient report forms provided or in the routine fashion used to record radioiodine studies of the thyroid in the laboratory of the investigator. The quality of the scintographic images of the thyroid and the radioiodine accumulation in the gland will be evaluated and compared with that obtained using other agents previously employed by the investigator for this purpose. Adverse reactions will be reported immediately to Medi-Physics, Inc. Reports of clinical studies will be made periodically to Medi-Physics, Inc. and to appropriate state licensing agencies where applicable. Clinical evaluation of these agents as described above is considered adequate since the use of radioiodine for evaluating thyroid function and morphology is well established and the detailed studies of changes in in vivo distribution of these materials with time in human subjects is well documented in the medical literature.

WORK UNIT 73/600

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

We have not used I-123 (Sodium Iodide) due to technical problems. The procedure will be resumed in the near future.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Bone Marrow Scintigraphy and Scintigraphic Localization of Soft Tissue Tumors by Use of Indium-111 Chloride

WORK UNIT NO.: 74/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Indium-111 Chloride supplied by Medi-Physics, Inc. The evaluation of the agent is significant in that it represents a method of studying sites of erythropoiesis in bone marrow and allows scintigraphic localization of soft tissue tumors by non-invasive techniques. In selected patients, this affords clinical information which could not be obtained by other methods.

TECHNICAL APPROACH

Up to 2mc of Indium-111 Chloride or proportionally less depending on body weight supplied by Medi-Physics, Inc. will be administered intravenously to patients referred to Nuclear Medicine Laboratory for either scintigraphic evaluation of sites of erythropoiesis in bone marrow or the presence of soft tissue tumors. After administration routine scintigraphic procedures with conventional equipment for periods up to 96 hours depending on the patient's clinical situation will be peformed. The number of subjects with known or suspected hematologic disease will be unlimited and there will be no limitation on sex or the age of patients. Radionuclide will not be administered to pregnant patients or patients under the age of 18 unless the clinical situation is severely dependent upon this study. Data obtained will be recorded in the routine fashion used to record radionuclide studies. This consists of a consultation sheet from the referring physician which will be appropriately answered. Selective scans will be copied on polaroid film included with the record and returned to the patient's chart. The quality of the scintigraphic images of the bone marrow and tumor site will be evaluated so the best image is obtained. Adverse reactions will be reported immediately to Medi-Physics, Inc. and to appropriate state license and agencies where

WORK UNIT 74/600

TECHNICAL APPROACH- continued

applicable. Clinical evaluation of these agents as described above is considered adequate since the use of Indium-111 Chloride is a substitute for iron and is well established in the literature.

Manpower (in professional man years): 0/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

There has been no use of Indium 111 Chloride to date. When patients become available, the protocols will be applied.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Use of Gallium 67 Citrate in Evaluation of Patients with Known or Suspected Tumors and Pyogenic Abscesses

WORK UNIT NO.: 74/601

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Gallium 67 Citrate supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

The evaluation of this agent is significant in that it represents a method of diagnosing tumors that cannot be visualized by other conventional means, resulting in significantly more information on each patient with initial diagnosis, initial therapy and follow-up care. It will be used to localize pyogenic abscesses primarily subdiaphragmatic abscesses which cannot be localized by conventional methods. Use of this agent will enhance the diagnosis of this serious medical condition and ultimate treatment of the patient.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Thirty-nine studies using Gallium 67 Citrate for evaluation of patients with known or suspected tumors or pyogenic abscesses have been completed. The radiopharmaceutical proved adequate for the intended diagnostic purpose and again no detectable side effects were observed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Use of Indium 111 DTPA for the Study of Cerebrospinal Fluid Pathways

WORK UNIT NO.: 74/602

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Indium 111 DTPA in aqueous ionic solution (pH 7 to 8) for study of cerebrospinal fluid pathways as supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

Evaluation of this agent represents a method of studying cerebrospinal fluid pathways in selected patients with a compound that will result in significantly less absorbed radiation doses to patients than the methods currently used. The incidence of side reactions, such as fever, headaches and mild meningitis, will probably be decreased in comparison to the compound presently used.

Manpower (in professional man hours): .05/yr

Funding (in thousands) FY 74: 0
FY 75: 0

PROGRESS

Seven studies using Indium 111 DTPA for evaluation of patients with cerebral spinal fluid pathways pathology have been completed. The radiopharmaceutical proved adequate for the intended diagnostic purpose, and again no detectable side effects were observed.

Publications and Presentations: None

STATUS:

Ongoing.

HOSPITAL CLINICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: The Ontogenesis of Embryonic Hemoglobin in the American Opossum (Didelphia Virginia)

WORK UNIT NO.: 74/650

PRINCIPAL INVESTIGATOR: Nicholas C. Bethlenfalvay, COL, MC

ASSOCIATE INVESTIGATORS: George L. Brown, LTC, MSC
Jeneen K. Nelson, DAC
John G. Miller, CPT, VC
Michael R. Gray, DAC

OBJECTIVES

This is a continuation of a previously completed study, Phase I. The overall objectives are to evaluate the transient emergence of the embryonic and adult globin polypeptide chains and to define their phenotypic participation as functional hemoglobin molecule(s).

TECHNICAL APPROACH

This study is a coordinated investigation between the Immunology Section, Clinical Investigation Service, and the Outpatient Clinic, FAMC. Animal experimentation will be conducted in accordance with the principles set forth in "Guide for Laboratory Animal Facilities and Care" prepared by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences and National Research Council.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 74: 2.0
FY 75: 1.2

PROGRESS

Blood smears, hemolysates and globin (of neonates and adult animals) were prepared by standard methods. Hemoglobin phenotypes were determined by zone electrophoresis, isolectric focusing and by ion exchange column chromatography. Polypeptide chains from urea dissociated globin were separated by zone electrophoresis and column chromatography. Differences of the UV spectra of the hemoglobins were ascertained by spectrophotometric scanning.

WORK UNIT 74/650

PROGRESS - continued

Five litters of pouch young ranging from approximately five to fifty days old and their mothers were available for study. Embryonic hemoglobins were identified in the 5 and 11 day old pouch young, confirming the findings of the Phase I Study conducted at FAMC. In two litters (approximately 15 and 25 day old) a hemoglobin distinct from the embryonic and adult phenotype was shown based on electrophoretic migration, spectral absorption, and by its ability of in vitro polymerization or hybirdization as shown on re-electrophoresis. One adult animal and its litter (50 day old) was heterozygous for the common (single Hb band) and what is suspected to be an alpha chain variant (second slow Hb band). Globin of the common Hb phenotype showed 2 peaks on chromatography (one alpha - one beta) but three of the variant Hb (two alpha and one beta). Severe limitation of sample volume of blood of the younger neonates precluded preparation of globin sufficient for study. "Embryonic" hemoglobins were only seen while yolk sac megaloblast were still present on circulation.

Publications:

(1) Bethlenfalvay, N.C., Brown, G.L., and Block, M: Hemoglobins of the Opossum (Didelphys Virginia Kerr). I Developmental changes from yolk sac to definitive erythropoiesis. (In preparation).

(2) Bethlenfalvay, N.C., and Brown, G.L: Hemoglobins of the Opossum (Didelphys Virginia Kerr) II Polymorphysm. Electrophoretic and chromatographic observations. (In preparation).

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 75

TITLE: Establishment of and Training in Methods for Special Studies of Abnormal Hemoglobins

WORK UNIT NO.: 74/651

PRINCIPAL INVESTIGATOR: Nicholas C. Bethlenfalvay, COL, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC

OBJECTIVES

To establish and conduct training in methods for special studies of abnormal hemoglobins.

TECHNICAL APPROACH

Plans are to familiarize existing personnel in the performance of procedures involving biochemical study of hemoproteins using existing equipment.

Clinical studies of mutant human and animal hemoglobins have defined the effects of molecular aberrations on physiologic processes. Amino acid substitutions or deletions in the alpha, beta, gamma and delta chains dictate a variety of structural alterations which may modify hemoglobin affinity for oxygen, or affect the stability of the hemoglobin molecule. A laboratory to aid the clinician or researcher in his investigation of a mutant hemoglobin is not available in the Denver Metropolitan area. A thorough preliminary special investigation of hemoglobins almost always kindles the interest and support of established investigators in CONUS or abroad, where amino acid analyses in the end ultimately reveal the molecular lesion.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 74: 5.0
FY 75: 1.5

WORK UNIT 74/651

PROGRESS

The following procedures can now be performed: Preparation and preservation and storage of hemoglobin and globin. Zone electrophoresis of hemoglobin in various media and electrophoresis in polyacrylamide gel with isoelectric focusing. Quantitiation of Hb F. Quantitation of Hb A_2 by microcromatography. Hb stability testing by the isopropanol technique. Electrophoresis of urea dissociated globin, and qualitative and quantitative recovery of hemoglobin and its sub units using colum chromatography. Additional laboratory space is expected to enable the performance of additional procedures ultimately to include peptide mapping.

Publications and Presentations: None

STATUS:

Ongoing.

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