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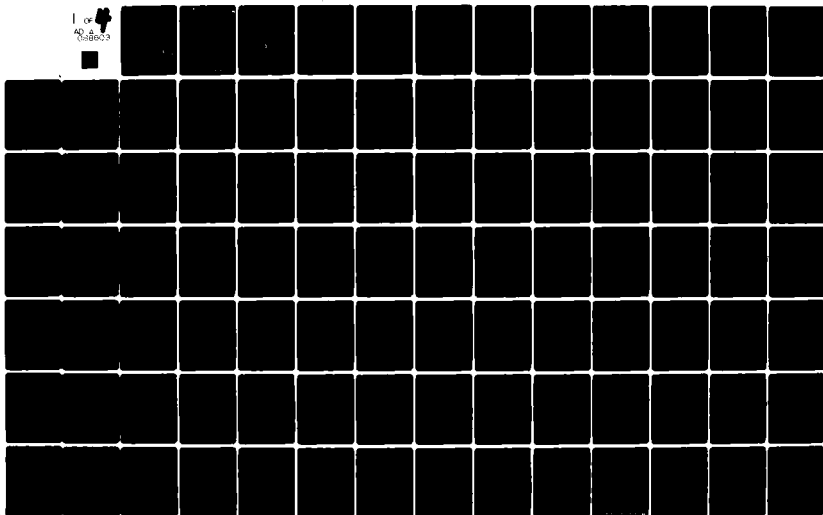
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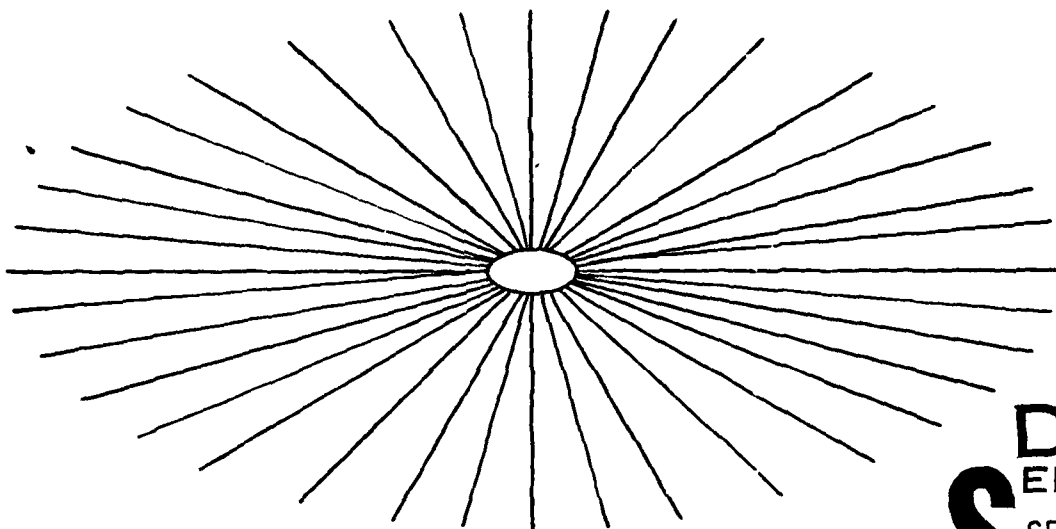
Laboratory Report No. 15

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Block 19. Key Words

publications, presentations of research data (at national, international and regional science meetings)
post graduate educational programs
protocol training and support programs
protocol registration
protocol status (ongoing, completed, terminated)
technological base (personnel and equipment)
experimental design (statistical tools, etc.)

Block 20. Abstract

Management of Clinical Investigation Protocols and Reports, Use of Volunteers as subjects of research and AR 40-38, as amended, Clinical Investigation Service, policies and procedures, to insure the medical being, preservation of rights and dignity of human subjects who participated in these investigations.

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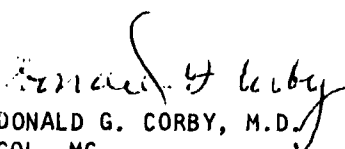
FOREWORD

This report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and Human Use Committee and registered with the Clinical Investigation Service during Fiscal Year 1979 along with 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, as amended, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans, AR 79-25, Use of Volunteers as Subjects of Research, and HSC Reg. 40-23, management of Clinical Investigation Protocols and Reports, to insure the medical safety, well being, preservation of rights and dignity of human subjects who participated in these investigations.

In conducting the research described in this report, the investigator(s) adhered to AR 70-18, Laboratory Animals, Procurement, Transportation, Use, Care, and Public Affairs and 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.

Clinical Investigation Service is especially grateful to MAJOR GENERAL Raymond H. Bishop, Jr., 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 Proto/Ed Asst, Ms. Val McCrill and Mrs. Nancy Moran, Secy, without whose assistance and support this report would not have been possible.


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

PUBLICATIONS

PUBLICATIONS

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Aeling, J.L.: Potpourri of Dermatologic Cases. Presented: Annual Med Surg Europa, Garmish, Germany, May 1979.

Davies, B.F.: Leopold Syndrome. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Duke, D.W.: Arteriovenous Malformation with Skin Lesions Simulating Kaposi Sarcoma. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Fitzpatrick, J.E.: Angiolymphoid Hyperplasia with Eosinophilia. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Gentry, R.H.: Cutaneous Leishmaniasis. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Graff, G.E.: Eosinophilic Fasciitis. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Sausker, W.F.: Cutaneous Manifestations of Chronic Myelogenous Leukemia. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Thompson, P.B.: Cutaneous Plasmacytomas. Presented: Annual Meeting of American Academy of Dermatologists, San Francisco, CA, Dec 1978.

Endocrinology Service

Dodson, E., Charles, A., Waldeck, N., O'Barr, P., Hofeldt, F., Ghaddar, V. and Telepak, R.: Comparison of Total Body Scans with Serum Thyroglobulin Levels in Patients with Treated Thyroid Cancer. Presented: The Endocrine Society, Anaheim, CA, 13-15 June 1979.

Dodson, L.E., Treece, G. and Hofeldt, F.D.: Effect of GnRH on Postmenopausal Gonadotropins and Prolactin Levels: Influence of Short Term Glucocorticoid Administration. Presented: The Endocrine Society, Anaheim, CA, 13-15 June 1979.

Endocrinology Service - continued

Hofeldt, F.D.: Laboratory and Clinical Assessment of Common Thyroid Disorders. Presented: The Third Air Force Nurse Practitioner Workshop, USAF Academy, Colorado Springs, CO, 18-22 June 1979.

Hofeldt, F.D.: The Estrogen Controversy. Presented: Regional Conference in Internal Medicine, Fitzsimons Army Medical Center, Aurora, CO, 1-2 February 1979.

Treece, G.L.: Syndrome of Medullary Carcinoma of the Thyroid. Presented: 1st Annual Regional Internal Medicine Course, Fitzsimons Army Medical Center, Aurora, CO, 1-2 February 1979.

Treece, G.L.: The Effect of Dexamethasone on Postmenopausal Gonadotropin: Influence of LHRH on Prolactin. Presented: 61st Annual Endocrine Society Meeting, Anaheim, CA, 13-15 June 1979.

Pulmonary Function Lab

Kindig, N.B.: Physiologic Deadspace; Influence of Pattern of Breathing. Presented: 32nd Annual Pulmonary Symposium, Fitzsimons Army Medical Center, Aurora, CO, Sep 1979.

Perry, M.E.: Plethysmographic Determinations of the Alveolar Pressure/Flow Patterns. Presented: 32nd Annual Pulmonary Symposium, Fitzsimons Army Medical Center, Aurora, CO, Sep 1979.

Zimmerer, R.W.: Simulated Diffusion Testing. Presented: 32nd Annual Pulmonary Symposium, Fitzsimons Army Medical Center, Aurora, CO, Sep 1979.

CLINICAL INVESTIGATION SERVICE

Brown, G.L. and Heggors, J.: Medical Mycology: Assessment of Bacteriologic and Serologic Parameters of Clinically-Important Mycoses in Normal and Immunologic Comprised Host. Presented: American Medical Technologist Educational Seminars, Denver, CO, July 1979.

Charles, A., Sharma, B., Waldeck, N., Dodson, E., Noble, S.: Use of an in vitro Cytotoxicity Assay for the Direct Evaluation of Immune Mechanisms in Diabetic Patients. Presented: 39th Annual Meeting of American Diabetes Association, Los Angeles, CA, June 1979.

Corby, D.G.: Decreased α -Adrenergic Receptors in Newborn Platelets: Cause of Abnormal Response to Epinephrine. Presented: VIIth International Congress on Thrombosis and Haemostasis, London, England, July 1979.

Damato, James J.: Rapid Methods for Differentiating Mycobacterium Species. Presented: University of N.Colorado, Greeley, CO, Oct 1979.

Clinical Investigation Service - continued

Hofmann, J.: Introduction to Micro Surgery. Presented: Surgical Seminar, Fort Collins, CO, April 1979.

Rothlauf, Mary V.: Isolation of Mycobacteria from Undecontaminated Specimens Using Selective 7H10 Medium. Presented: ASM, Denver, CO., Sep 1979.

Zolock, D.T.: Meaning of Non-parallel 1,25 (OH)₂D₃ Mediated Response Relationship in Intestine and Bone to Dose and Time. Presented: Fourth International Workshop on Vitamin D, Berlin, West Germany, Feb 1979.

DEPARTMENT OF DENTISTRY

Balserak, R.J.: Alginate Impressions. Presented: Area Dental Laboratory Workshop, Lowry AFB, Denver, CO, 5 Apr 1979.

McDonald, F.L.: Mucogingival Defects, Origin and Treatment. Presented: Vicenza Army Hospital, Vicenza, Italy, 6 Dec 1978.

McDonald, F.L.: Periodontal Surgery for the General Dentist. Presented: Vicenza Army Hospital, Vicenza, Italy, 7 Dec 1978.

DEPARTMENT OF NURSING

Adams, N.R.: Blood Gas Interpretation. Presented: Colorado Nurses' Association, CHAUTAUQUA '79, 7-9-10 Aug 79.

Adams, N.R.: Neurological Assessment. Presented: Council of Nursing Inservice Coordinators, Colorado Springs, CO, 9 Feb 79.

Crittenden, F.: Adjustment to Chronic Illness. Presented: Multiple Sclerosis Society of Colorado and Beth Israel Education Center, Aug 79.

Crittenden, F.: Pathophysiology of Diabetes. Presented: Diabetic Educator's Conference for American Diabetes Association, Colorado Affiliate, Nov 78.

Haag, G.P.: Maternal Physiology. Presented: Colorado Association of Nurse Anesthetists, April 1979.

Turner, B.S.: The Neonatal Clinical Specialist: The Role and Utilization. Presented: Mead-Johnson Conference, Vail, CO, Jun 78.

DEPARTMENT OF OB-GYN

Bobitt, J.R.: Abnormal Antepartum Fetal Heart Rate Tracings, Failure to Intervene, and Fetal Death: Review of Five Cases Reveals Potential Pitfalls of Antepartum Monitoring Programs. Presented: Infectious Disease Symposium, Boca Raton, Florida, Dec 1979.

OB-GYN - continued

Bobitt, J.R.: Abnormal Antepartum Fetal Heart Rate Tracings, Failure to Intervene, and Fetal Death: Review of Five Cases Reveals Potential Pitfalls of Antepartum Monitoring Programs. Presented: The Infectious Disease Society of Obstetrics and Gynecology, Tubingen, West Germany, April 1979.

Bobitt, J.R.: Group B Streptococcus: Microbiologic and Clinical Observation Associated with Quantitative Antepartum Culture. Presented: Annual Meeting of the Infectious Disease Society for Obstetrics and Gynecology, Tubingen, West Germany, 1979.

Bobitt, J.R.: Group B Streptococcal Neonatal Infection: Obstetric Update. Presented: Annual Meeting of the Infectious Disease Society for Obstetrics and Gynecology, Tubingen, West Germany, 1979.

Bobitt, J.R.: Specific Bacterial Infections: Group B Streptococcus and Listeria. Presented: Infectious Disease Symposium, Boca Raton, Florida, December, 1979.

Bobitt, J.R.: Specific Bacterial Infections: Group B Streptococcus and Listeria. Presented: The Infectious Disease Society of Obstetrics and Gynecology, Tubingen, West Germany, April 1979.

DEPARTMENT OF PEDIATRICS

Kilbride, H.W.: Myocardial Infarction in the Neonate with Normal Heart and Coronary Arteries. Presented: Eighth Annual Army Association of Cardiology Meeting, Tacoma, Wash., 17-19 May 1979.

Merenstein, G.B.: Colorado Perinatal Care Council: A Model for Health Care Planning. Presented: Aspen Conference on Perinatal Research, Aspen, CO, July 1979.

Merestein, G.B.: History of Neonatal Transport. Presented: Second Annual Conference on Neonatal Transport, Denver, CO, 4-6 Apr 79.

Merenstein, G.B.: Moderator, Indications for and Outcome of Maternal Air Transport, Denver, CO, Feb 1979.

Merenstein, G.B.: Newborn Transport. Presented: Department of Pediatrics, Uniformed Services, University of the Health Sciences, Wash., D.C., May 1979.

Merenstein, G.B.: Spectrum of Group B Streptococcal Infections. Presented: Department of Pediatrics, Uniformed Services, University of Health Sciences, Wash., D.C., May 1979.

Merenstein, G.B.: Workshops on Perinatal Transport. Presented: National Perinatal Association, St. Louis, Missouri, Nov 1978.

Pediatrics - continued

Merenstein, G.B.: Who Selects Patients for Maternal Transport?
Presented: Fourth Annual Conference on Neonatal-Perinatal Medicine,
Tucson, Arizona, 17-19 May 1979.

Merenstein, G.B. and Todd, W.A.: Workshop on Perinatal Infection.
Presented: Idaho State Perinatal Project, Pocatello, Idaho, Nov 1978.

Parry, W.H.: Alpha₁ Antitrypsin Deficiency. Presented: European
Pediatric Seminar, Berchtesgaden, Germany, 2 Mar 1979.

Parry, W.H.: Cystic Fibrosis--An Update. Presented: European
Pediatric Seminar, Berchtesgaden, Germany, 27 Feb 1979.

Parry, W.H.: Pulmonary Anatomy and Physiology--Clinical Considerations.
Presented: European Pediatric Seminar, Berchtesgaden, Germany,
26 Feb 1979.

Parry, W.H.: Sudden Infant Death Syndrome. Presented: European
Pediatric Seminar, Berchtesgaden, Germany, 1 Mar 1979.

Parry, W.H.: Status Asthmaticus. Presented: European Pediatric
Seminar, Berchtesgaden, Germany, 28 Feb 1979.

Parry, W.H.: Tuberculosis. Presented: European Pediatric Seminar,
Berchtesgaden, Germany, 28 Feb 1979.

Parry, W.H.: Workshop on Neonatal Bleeding and Abuse. Presented: European
Pediatric Seminar, Berchtesgaden, Germany, 1 Mar 1979.

Parry, W.H.: Workshop on Recurrent Pneumonia. Presented: European
Pediatric Seminar, Berchtesgaden, Germany, 27 Feb 1979.

Parry, W.H.: Workshop on Special Diagnostic Studies. Presented:
European Pediatric Seminar, Berchtesgaden, Germany, 28 Feb 1979.

Pierce, J.R.: Results of Agonal Blood and Spinal Fluid Cultures
from an Intensive Care Nursery. Presented: Uniformed Services
Pediatric Seminar, San Diego, CA, 11-15 Mar 1979.

Pierce, J.R.: ST Depression Suggesting Subendocardial Ischemia in
Neonates with PDA. Presented: Eighth Annual Army Association of
Cardiology Meeting, Tacoma, Wash., 17-19 May 1979.

Sanders, J.M.: Member of Faculty, AAP Continuing Education Course,
Las Vegas, Nevada, 3-5 Nov 1978.

Sanders, J.M.: Member of Faculty, AAP Continuing Education Course,
Lake Lanier, GA, 17-19 May 1979.

Pediatrics - continued

Sanders, J.M.: Member of Faculty for AAP Continuing Education Course, Mackinac Island, Michigan, 27-29 Sep 1979.

Sanders, J.M.: Member of Faculty for Annual Pediatric Postgraduate Course, Sponsored by Office of Postgraduate Medical Education, University of Colorado Medical Center, Estes Park, CO, 13-17 Aug 1979.

Sanders, J.M.: Member of Faculty, Pediatric Seminar, Sponsored by Greater Smokey Mountain Pediatric Society, Gatlinburg, Tennessee, 21-23 Jun 1979.

DEPARTMENT OF PSYCHIATRY

Golosow, N.: Homosexuality in the Service. Presented: Eisenhower Army Medical Center, Fort Gordon, GA, 23 Apr 1979.

Pierce, E.V.: Armed Forces as a Second Career. Presented: APA, Chicago, IL, 14 May 1979.

Sollod, H.H.: Workshop on Group Psychotherapy with Adolescents. Presented: American Group Psychotherapy Association Annual Meeting, New York City, N.Y., 17 Feb 1978.

PHYSICAL MEDICINE AND REHABILITATION SERVICE

Occupational Therapy Section

Daigle, W. and deLeeuw, C.: Slide Presentation: Annual Orthotic Workshop, Fitzsimons Army Medical Center, Aurora, CO, 10 May 1979.

deLeeuw, C.: Sensory Evaluation and Function of the Hand. Presented: Workshop for Orthopedic Nurses, Keystone, CO, 7-9 Dec 1978.

SOCIAL WORK SERVICE

Gemmill, R.H.: Single-Parent Family: Active Duty and Dependent. Presented: AMEDD Behavioral Science Seminar, Free University Session, Fitzsimons Army Medical Center, Aurora, CO, 19-23 Mar 1979.

DEPARTMENT OF SURGERY

Audiology Section

Bender, D.R.: Communication Problems in the Older American. Presented: National Symposium, Denver, CO, Jun 79.

Ophthalmology Service

Cottingham, A.J.: Keratoplasty. Presented: Bi-Annual Tri-Service Optometry Meeting, Fitzsimons Army Medical Center, Aurora, CO, Oct 78.

Ophthalmology Service - continued

Cottingham, A.J.: The Use of Vitrectomy Instrumentation in Anterior Segment Reconstruction. Presented: Schele Institute Trauma Symposium, Philadelphia, PA, Sep 1979.

Orthopedic Service

Ballard, A.: Common Infections. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, 1979.

Ballard, A.: Lower Extremity Torsional Problems. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, 1979.

Ballard, A.: The Milwaukee Brace, Indications and Checkout. Presented: Symposium on Spinal, Upper and Lower Extremity Orthotics, FAMC, Aurora, CO, May 1979.

Coville, F.V.: Functional Knee Braces for the Unstable or Post-Operative Knee. Presented: Symposium on Spinal, Upper and Lower Extremity Orthotics, FAMC, Aurora, CO, May 1979.

Coville, F.V.: Treatment of Residuals of Congenital Dislocated Hip in the Adult. Presented: Symposium of Children's Orthopedics, FAMC, May 1979.

Eversmann, Jr., W.W.: Common Fractures: Wrist to Fingers. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, Aug 79.

Eversmann, Jr., W.W.: Congenital Anomalies of the Upper Extremity. Presented: Symposium of Children's Orthopedics, FAMC, Aurora, CO, 1979.

Eversmann, Jr., W.W.: Initial Evaluation of Hand. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, Aug 79.

Eversmann, Jr., W.W.: Radial Nerve Compression Syndromes. Presented: Hand Surgery Conference, Denver, CO, July 79.

Eversmann, Jr., W.W.: Unusual Cases. Presented: Hand Surgery Conference, Denver, CO, July 79.

Glancy, G.L.: Corns, Nails, Bunions. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, 1979.

Glancy, G.L.: Newer Casting Materials. Presented: Orthopedics for the Family Practice and Emergency Medicine Physician, Aspen, CO, 1979.

Orthopedic Service - continued

Goldberg, B.: Biomechanical Principles of Spinal Orthotics.
Presented: Symposium on Spinal, Upper and Lower Extremity Orthotics,
FAMC, Aurora, CO, May 1979.

Goldberg, B.: Neck and Backache. Presented: Orthopedics for the
Family Practice and Emergency Medicine Physician, Aspen, CO, 1979.

Goldberg, B.: Spondylolisthesis - Evaluation and Treatment.
Presented: Symposium of Children's Orthopedics, FAMC, Aurora, CO, Jan 79.

Plastic Surgery Service

Shesol B.: Changing Concepts of Lymphedema. Presented: Annual
Meeting of the Rocky Mountain Society of Plastic & Reconstructive
Surgeons, Keystone, CO, Feb 79.

Rich, J.D.: Reconstruction of Post-traumatic Skull Defects. Presented:
Annual Meeting of the Rocky Mountain Society of Plastic & Reconstructive
Surgeons, Keystone, CO, Feb 79.

Speech/Language Rehabilitation Section

Hasbrouck, J.M.: Auditory Perceptual Disorders. Presented: English
and Foreign Language Department, USAFA, CO, 17 May 79.

Hasbrouck, J.M.: Auditory Perception, Disorders, Evaluation, and
Treatment; How to Study Program. Presented: U. S. Air Force Academy,
CO, 1 Mar 79.

Hasbrouck, J.M.: Auditory Perceptual Disorders; How to Study Program.
Presented: U. S. Air Force Academy, CO, 18 Aug 79.

Hasbrouck, J.M.: Auditory Perceptual Disorders. Presented: Pikes
Peak BOCEES, Colorado Springs, CO, 24 Aug 79.

Hasbrouck, J.M.: Auditory Perceptual Disorders. Presented: Weld
County BOCEES, Greeley, CO, 28 Feb 79.

Hasbrouck, J.M.: Screening for Auditory Perceptual Disorders.
Presented: U.S. Air Force Academy, CO, 30 Jul 79.

McMahan, D.: Conflicting Professional Opinions. Presented: Academy
of Rehabilitation Audiology, Denver, CO, 17 Nov 79.

Urology Service

Dobbs, R.M.: Clotting Predisposition in Carcinoma of the Prostate.
Presented: AUA Meeting, New York, May 1979.

Wilson, T.M., Dunnington, G.W., Fauver, H.W., Dobbs, R.M. and Peterson,
N.E.: Synthetic Ureteral Prosthesis With Polytetrafluoroethylene
Tube. Presented: Kimbrough Urological Seminar, San Antonio, TX,
Nov 78.

UNIT SUMMARY SHEET

UNIT SUMMARY SHEET

Clinical Investigation Program, FAMC

Clinical Investigation efforts by FAMC personnel in FY 79 culminated in the publication of 100 articles and 123 presentations and lectures at national, international, and regional scientific meetings. As of 30 September 1979, there were 146 research protocols on the CIS register. Of these, 93 projects were ongoing and 53 were new registrations.

Objectives:

To encourage the performance of clinically-oriented research by personnel assigned to the Fitzsimons Army Medical Center (FAMC). To aid in the planning, development, support, and execution of experimental clinical studies, both in patients and by directly related laboratory work, into the clinical problems of significant concern in the health care of members of the military community. To provide physician experience in research and investigative procedures by furnishing a highly educated and trained staff of specialists, laboratory facilities, administrative services and funding for: supplies, equipment, consultants, publications and reprints. To achieve continuous improvement in the quality of patient care by providing an atmosphere of inquiry, maintaining high professional standing and accreditation of advanced health programs.

The Clinical Investigation Program differs from Medical Research and Development in that the emphasis is on the health care problems existing in our patient populations, i.e.; active duty, retired, and dependents and not solely on medical problems affecting combat readiness and the fighting strength. It is, by its nature, and integral part of the triad of patient care and medicine. It promotes and supports the finest ideals and traditions of Military Medicine and enhances the vitality of the teaching programs which in turn elevates the standard of medical care. The research program operates on the premise that all approved protocols will be supported to the fullest extent allowed by current funding. This concept allows for a larger number of physicians and ancillary personnel to participate in research rather than as in the grant system used elsewhere. This means that virtually every investigator is given a chance to pursue his research without having to compete for funds with "established" names in the field.

Technical Approach

This support, direction and management is carried out under the aegis of AR 40-38, as amended, Clinical Investigation Program; AR 40-7, Use of Investigational Drugs in Humans; AR 70-25, Use of Volunteers as Subjects in Research; AR 70-18, Laboratory Animals, Procurement, Transportation, Use, Care, and Public Affairs; HSC Reg 40-23, Management of

Clinical Investigation Protocols and Reports; MCR 40-8, Clinical Investigation Service (CIS), FAMC and HSC 40-23. This Service provides guidance, assistance, and coordinates the FAMC program with higher headquarters and other facilities.

Manpower: Current authorized strength is outlined.

<u>Description</u>	<u>Grade</u>	<u>MOS</u>	<u>Br</u>	<u>Auth</u>	<u>Actual</u>	<u>Name</u>
C, Clin Invest Svc	G6	60P9B	MC	1	1	Corby
C, Immuno Sec	06	68A9A	MS	1	1	Brown
Internist	05	61F9C	MC	0	1	Charles
Lab Admin	04	68F00	MS	1	1	Quigg
C, Surg Rsch Labs	04	64F9D	VC	1	1	Hofmann
C, Micro Sec	04	68A00	MS	1	1	Damato
Physiologist	C3	68J00	MS	1	1	Harbell
Biochem	03	68C00	MS	1	1	Zolock
NCOIC	E7	92B4R		1	1	Underhill
C, Med Lab NCO	E7	92B4R		1	1	Engle
Sr. O.R. SP	E6	91D3R		1	1	Smith, N.
Bio Sci Asst	E6	01H20		0	1	Glab

<u>Description</u>	<u>Grade</u>	<u>MOS</u>	<u>Br</u>	<u>Auth</u>	<u>Actual</u>	<u>Name</u>
Bio Sci Asst	E5	01H20		1	1	Kramer
Bio Sci Asst	E5	01H20		1	1	Gallegos
Bio Sci Asst	E5	01H20		1	1	Chadwick
Bio Sci Asst	E4	01H20		1	1	Harrington
Vet Sp	E6	91T3R		0	1	Rich
Chemist	13	0403 GS		1	1	O'Barr
Microbiol	09	0403 GS		3	3	Lima Rothlauf Paine
Med Technol	09	0644 GS		1	1	Rush
Biochem	09	1320 GS		1	1	Swanson
Microbiol	07	0403 GS		6	6	Rangel Kile Youmans Morse Ledoux Nelson
Rsch Chem	07	1320 GS		3	3	McNamara Noble Waldeck
Bio Lab Tec	07	0404 GS		1	1	Hakes
Animal Bio Lab Tech	07	0404 GS		1	1	Jones
Animal Tech	05	0404 GS		1	1	McCrill
Ed Asst	06	0318 GS		1	1	McCrill
Animal Caretaker	05	7706 WG		2	2	Beltran Hitchcock
Clerk-steno	04	0318 GS		1	0	

	FY 77	FY 78	FY 79
Civilian Pay	382,810	363,962	381,352
Travel	3,856	3,660	5,584
Supplies	158,153	161,431	179,883
Equipment	80,000	28,500	108,165
Contracts	20,029	16,429	16,397
Other (Military)	267,269	293,432	349,116

Progress

CIS received from Health Services Command (HSC) a microbiology training position. This program brings in a qualified aspirant at the GS05 entrance level and, upon successful completion of a rigorous training program, allows for non-competitive promotion to GS07 and finally the GS09 Microbiologist journeyman level.

Historically, Fitzsimons Army Medical Center has provided leadership in the identification and treatment of tuberculosis in the military community. The unique ongoing computer storage and analyses of mycobacteriologic data from tuberculin patients used for laboratory followup of specimens, quality control, and analyses of clinical data provides clinical support not found in any other USA MED laboratory. Additional in-depth mycobacterial studies on patients, i.e., serum drug levels, serum inhibition tests, identification of mycobacteria other than M. tuberculosis are also provided. In accordance with the Commanders' directive, CIS provides mycobacteriology (TB) support (processing clinical specimens and reference cultures) to the following centers:

MEDDAC Units: Ft. Carson, Ft. McPherson, Ft. Leavenworth, Ft. Ord, Ft. Riley, Ft. Sill

Army Medical Centers: Letterman, Tripler, Madigan

USAF Facilities: Scott AFB, Baker's Field, Minot AFB

Additionally, TB reference laboratory support is furnished to the Communicable Disease Center, Atlanta, GA., PHS, Pine Ridge Reservation, S.D.

The Surgical Research Laboratory (SRC) Section supports research and training protocols and provides the laboratory animal care for CIS. The Research Animal Support now includes a daily small animal population of approximately 700 animals, 20 large animals, and a small colony of

of primates. The scope of support includes clinical laboratory techniques, cardio-pulmonary bypass, electron microscopy, surgical research and pre- and post-operative care of research subjects. The SRL has expanded its service capabilities during the past year to include histopathology and tissue culture techniques which are utilized in several protocols as well as in a system for monitoring the health of the laboratory animal colony. CIS has re-submitted an urgent minor construction request for an Animal Care Facility. This vivarium was approved and has been scheduled for funding and construction in FY81. A complete listing of the training provided by SRL is located on CIS detail sheet "Training Support, SRL, CIS" immediately following the Annual Progress Reports.

The Mycobacteriology Laboratory sub-section, Microbiology Section, CIS, has maintained College of American Pathologists (CAP) accreditation as an Extent Two Laboratory.

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DETAIL SHEETS

MEDICINE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Tuberculosis Research Follow-up Program.

WORK UNIT NO: 67/100

PRINCIPAL INVESTIGATOR: Roald 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): 0.1/yr

Funding (in thousands) FY 78: 4.0
FY 79:

PROGRESS

No progress report has been received on this study to date. Clinical Investigation Service has been advised that this study is to be terminated.

WORK UNIT 67/100

Publications:

- (1) Christensen, W. I.: Genitourinary Tuberculosis: Review of 102 Cases. Medicine 53:377, 1974.
- (2) Buchanan, B. D.: Atypical Tuberculosis Due to Type I and Type III Atypical Mycobacteria. (Submitted for Publication).
- (3) Gerace, J., Nelson, R. A.: Incidence of Drug Resistant Tuberculosis in Oriental Females Treated at Fitzsimons Army Medical Center and Scott Air Force Base Medical Center. (In preparation.)

Presentations:

- (1) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: 25th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1972.
- (2) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: Regional American College of Physicians Meeting. Colorado Springs, Colorado, January 1973.
- (3) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: Hugh Mahon Lectureship Award Competition, Fitzsimons Army Medical Center, Denver, Colorado, May 1973 (submitted as research paper).
- (4) Christensen, W. I.: Drug Resistant Tuberculosis from Vietnam. Presented: 25th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1972.
- (5) Nelson, R. A.: Tuberculosis of the Spine (Potts' Disease). Presented J. J. Waring Chest Conference. Estes Park, Colorado, August 1974.
- (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, Colorado.
- (7) Buchanan, B.: Atypical Tuberculosis. Presented: 28th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1975.
- (8) Nelson, R. A.: Extra Pulmonary Tuberculosis. Presented: Fitzsimons Army Medical Center, Denver, Colorado, September 1975.
- (9) Christensen, W. I.: Genitourinary Tuberculosis. Presented: At the course, Clinical Management and Control of Tuberculosis. Sponsored by National Jewish Hospital, Denver, Colorado, three times yearly.

WORK UNIT 67/100

Presentations - continued

- (10) Gerace, J., Nelson, R.A., Byrd, R.: Drug Resistant Tuberculosis in Oriental Females. Presented: Annual Meeting of American Thoracic Society, San Francisco, California, May 1977.
- (11) Nelson, R.A.: Extrapulmonary Tuberculosis. Presented: Walter Reed Army Medical Center Grand Rounds - 20 January 1978.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Active Antigens in House Dust.

WORK UNIT NO.: 73/135

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, 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, mite products and cotton degeneration products.

TECHNICAL APPROACH

Skin test data from over 200 patients will be analyzed for correlation between positive skin tests to house-dust, cat dander, dog dander, house dust mite and cotton antigen along with the commercial Hollister-Stier and Greer dust. The ability of cat, dog and cotton to inhibit grass specific IgE antibody as determined by RAST testing will be determined. Cross immunoelectrophoresis for antigen identification and cross immunoelectrophoresis with inhibition will be performed. The antisera for this will be raised in rabbits. Likewise, cross radioimmuno-electrophoresis will be performed in order to identify those antigens that are important in human disease.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 78: 0.5
FY 79: 0.5

PROGRESS

During this period RAST inhibition and RAST adsorption studies were performed using pooled allergic serum and RAST disks for aged cotton lintens, cat dander, dog dander, house dust mite, human epidermal antigen and various commercial house dust preparations.

Publications:

- (1) Mansfield, L.E. and Nelson, H.S.: Allergens of Commercial House Dust Extracts. (Abst) J of Allergy and Clinical Immunology, March 1979.

WORK UNIT NO.: 73/135

Presentations:

- (1) Mansfield, L.E. and Nelson H.S.: Allergens of Commercial House Dust Extracts. Presented: Annual Meeting of the American Academy of Allergy, New Orleans, La., 25 March 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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 78: 0.0
FY 79: 0.0

PROGRESS

Two patients were treated with L-Asparaginase, both of them by the Pediatric Hematology-Oncology Service for acute lymphocytic leukemia. Both patients tolerated L-Asparaginase well but both are dead of progressive leukemia.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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): 0.2/yr

Funding (in thousands) FY 78:	0
FY 79:	0

PROGRESS

Fourteen patients were treated with Daunomycin as part of induction therapy for their acute leukemia. Two patients experienced local reactions due to inadvertent infiltration and necrosis; both have healed satisfactorily with little residual discomfort. One patient (MC) died of an acute cardiomyopathy of unknown etiology. Although this might have been due to the Daunomycin, postmortem myocardial examination was not consistent with drug-induced cardiotoxicity. There were no unexpected reactions in the other patients.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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, Ph.D., COL, MSC

OBJECTIVES

To determine whether there are any alterations of serum protein profiles in myeloproliferative and plasmaproliferative diseases.

To determine whether there are any alterations of serum protein profiles and lymphocyte transformation in myeloproliferative and plasmaproliferative diseases.

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.4/yr

Funding (in thousands)	FY 78:	2.0
	FY 79:	1.0

PROGRESS

Two patients with myeloproliferative and twenty-nine with plasmaproliferative disorders were studied immunologically. I. Myeloproliferative Disorders: Results recorded were as follows: No monoclonal gammopathies, serum immunoglobulin levels were recorded within normal limits, Lymphocyte blast transformation to PHA was suppressed. II. Plasmaproliferative Disorders: Results recorded were as follows: Thirteen subjects studied had IgG monoclonal gammopathies with evidence of free light chains in the serum. Seven patients were found to have elevated serum IgM levels

WORK UNIT 74/101

PROGRESS - continued

with monoclonal gammopathies, differentiated as IgM type. One patient each with IgA and IgD monoclonal gammopathy was studied. One case denoting immunoglobulin light chain disorder was recorded.

Publications:

- (1) Brown, G.L., DiBella, N.J., and Corby, D.G.: IgE-IgM Kappa Gammopathy Associated with Lymphocytic Lymphoma. Federation Proceedings 35:438, 1976.
- (2) DiBella, N.J., and Brown, G.L.: Immunologic Dysfunction in the Myeloproliferative Disorders. Cancer 42:149, 1978.

Presentations:

- (1) DiBella, N.J. and Brown, G.L.: Cellular and Humoral Immunity in the Myeloproliferative Disorders. Presented: Annual Joint Meeting of the American College of Physicians and American Society of Internal Medicine, Colorado Regional Meeting, Colorado Springs, CO, January 15, 1976.
- (2) Brown, G.L., DiBella, N.J., and Corby, D.G.: IgE-IgM Kappa Gammopathy Associated with Lymphocytic Lymphoma. Presented: Anaheim, California, April 12, 1976.
- (3) DiBella, N.J., and Brown, G.L.: In-depth Immunologic Evaluation of Myeloproliferative and Plasmaproliferative Disorders. Clinical Investigation Service Seminar, April 1978.

STATUS:

Ongoing

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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, COL, MC

ASSOCIATE INVESTIGATORS: Gary L. Treece, LTC, MC
T.P. O'Barr, Ph.D., DAC
A. Shackelford, MT, DAC
Leonard R. Sanders, CPT, MC
Leonard E. Dodson, MAJ, MC

OBJECTIVES

The objectives of the hypoglycemic study is to continue to investigate in our large clinic population the glucose-insulin-glucagon and prolactin interrelationships and the response of counter-regulatory hormones to hypoglycemic stress. This project is a continuation of a previous project initiated in 1969 at the University of California Medical Center, Moffatt Hospital, San Francisco, California.

TECHNICAL APPROACH

The clinical research portocol involves evaluation of control subjects and hypoglycemic patients to assess the interrelationships of beta cell and alpha cell responsiveness to oral and intravenous glucose administration. Based upon findings in controls and patients with disease states, a classification system has been proposed. The data have allowed for an understanding of the basic pathophysiology of reactive hypoglycemia disorders. The clinical studies are being conducted in the Department of Medicine, Endocrine Clinic, with the assistance of an assigned GS-9 to perform blood sampling and assist during the testing. During the glucose tolerance test, the patient has an indwelling catheter for frequent sampling of blood glucose, is continually monitored by 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, prolactins and cortisols are sampled and values are determined by a sensitive radioimmunoassay. The procedure is designed to provide a minimum of patient inconvenience in the performance

WORK UNIT NO.: 74/110

TECHNICAL APPROACH - continued

of these well standardized procedures. Many normal individuals experience a low blood sugar state sometime after glucose administration, 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 to defend the stress of a low blood glucose state. This approach allows strict definition of bona fide reactive hypoglycemia and clearly distinguishes it from the benign low blood glucose states.

Manpower (in professional man years): 2.0/yr

Funding (in thousands)	FY 78:	8.0
	FY 79:	10.0

PROGRESS

The study continues to recruit patients with the clinical disorder of reactive hypoglycemia and continues to expand the present knowledge and data on these subjects. At the present time the data has been placed on the MISO computers and will shortly be available for retrieval. The biostatistical analysis of data may be somewhat difficult inasmuch as statistical programs are not available at Fitzsimons and it may require the use of computers with these programs located at Ft. Sam Houston. The project is to be continued as an ongoing, active Endocrine project with the assignment to the Associate Investigator list of newly arrived personnel and research fellows. The accumulative data on these patients within the next year will be undergoing data analysis for interpretation of the alterations seen in metabolic parameters in these patients.

Publications:

- (1) Hofeldt, F.D.: Transitional Low Blood Glucose States. Rocky Mountain Medical Journal, 76:30-34, 1979.
- (2) McCowen, K.D., Adler, R.A., O'Barr, T.P., and Hofeldt, F.D.: Clinical Implications of Flat Oral Glucose Tolerance Test. Military Medicine, 144:177-179, 1979.

Presentations:

- (1) Sanders, L.R.: Reactive Hypoglycemia. Presented: Grand Rounds, University of Colorado Medical Center, Denver, CO, 13 Mar 1979.
- (2) Sanders, L.R.: Reactive Hypoglycemia. Presented: Medical Grand Rounds, Denver General Hospital, Denver, CO, 15 Mar 1979.
- (3) Sanders, L.R.: Reactive Hypoglycemia. Presented: Endocrine Grand Rounds, University of Colorado Medical Center, Denver, CO, 11 Apr 1979.

WORK UNIT NO 74/110

Presentations - continued

- (4) Sanders, L.R.: Reactive Hypoglycemia. Presented: Medical Grand Rounds, St. Joseph's Hospital, Denver, CO, 4 May 1979.
- (5) Hofeldt, F.D.: Reactive Hypoglycemia. Presented: Noon Medicine Conference, Presbyterian Aurora Hospital, Aurora, CO, 14 Sep 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 75/102

PRINCIPAL INVESTIGATOR: John M. Haas, COL, MC

ASSOCIATE INVESTIGATOR: Troy H. Williams, COL, 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 the approved formulary drugs. In order for patients to be entered into this protocol evidence had to be provided that the patients were indeed refractory to or experienced unacceptable side effects with standard drugs available and initial report forms were to be completed and submitted to the sponsor before the drug was made available. The clinical investigators had to be experienced in the use of antihypertensive therapy and familiar with the requirements and precautions associated with the new drug testing. The cases treated had to be documented in regard to side effects, safety, and the antihypertensive efficacy of the drug and frequent reports of patient progress as well as laboratory data submitted to the supplier of the drug and in turn to the FDA.

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 78:	0.0
FY 79:	0.0

PROGRESS

This protocol was continued exclusively by Dr. John M. Haas, during Fiscal Year 1979 and only five patients were followed on Minoxidil therapy and no

WORK UNIT NO.: 75/102

PROGRESS - continued

new patients had been added to the study. From September 1979 to December 1979, Colonel Troy H. Williams was listed as the principal investigator due to the retirement of Dr. John M. Haas and the protocol was continued primarily in an effort to establish continuity for these five patients who were controlled on Minoxidil therapy. In December 1979, the Minoxidil was approved by the FDA for general use and Upjohn Company reflected that they were not particularly interested in continuing this protocol. Since there were only five patients entered into the protocol it is the opinion of the Cardiology Service that it is not worthwhile to continue these patients on an investigative basis but they can be followed in the Cardiology Clinic for control of their hypertension on a routine basis now that Minoxidil is an approved drug. As such, the protocol has been terminated and records returned to the sponsoring pharmaceutical company.

Publications:

- (1) Kleiner, J., Ball, J.H., and Nelson, W.A.: The Out Patient Treatment of Refractory Hypertension with Minoxidil. (Abst.) Colorado Regional ACP Meeting Rocky Mountain Medical Journal, p 534, December 1975.
- (2) Earhart, R.N., Ball, J.H., Nuss, D.D., and Aeling, J.L.: Minoxidil-Induced Hypertrichosis: Treatment with Calcium Thioglycolate Depilatory. Southern Medical Journal, Vol 70, No 4, April 1977.

Presentations:

- (1) Kleiner, J., Ball, J.H., and Nelson, W.A.: The Out Patient Treatment of Refractory Hypertension with Minoxidil. Regional ACP Meeting, Colorado Springs, Colorado, 15-17 January 1976.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

ASSISTANT INVESTIGATOR: None

OBJECTIVES

To compare the efficacy and side effects of two different 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

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Most observation and sample collection from the patients has now been completed. Grass studies have been completed; however, blocking antibody to grass pollen still remains.

REFERENCES

1. Nelson, H.S.: A Three-Year Comparison of Immunotherapy with Aluminum Precipitated and Glycine Saline Grass Extracts. (Abst.) Ann

WORK UNIT 75/107

Publications: - continued

of Allergy, 42:123, 1979.

Presentations:

- (1) Nelson, H.S.: A Three Year Comparison of Immunotherapy with Alum Precipitated and Glycero-Saline Grass Extracts. Presented: American College of Allergists, San Francisco, CA, 29 Jan 79.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Antineoplastic Therapy with CIS-Platinum (II) Diamminechloride
(NSC 119875).

WORK UNIT NO.: 75/110

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: John C. Michalak, LTC, MC

OBJECTIVES

To treat patients with advanced solid tumors, primarily testicular tumors.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with CIS-Platinum as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Three patients were treated with CIS-Platinum prior to it becoming commercially available. One has died of progressive disease, a second one is alive but with progressive disease and the third one is alive without evidence of disease. Moderately severe nausea and vomiting were experienced in all three instances, but no significant renal toxicities were observed.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Fractionation of *Kochia*(*Kochia scoparia*) Pollen with Isolation
of *Kochia* Pollen Extract Antigens.

WORK UNIT NO.: 75/116

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: Mark R. Stein, LTC, MC
Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

This study is designed to extract raw kochia polen and purify it through chemical fractionation. It will attempt to isolate antigenic molecules of significance in human allergy (to this plant).

TECHNICAL APPROACH

Raw kochia defatted pollen has been extracted in distilled water and aliquots separated. This material has been used to immunize rabbits emulsified in Freund's complete adjuvant, and rabbit antisera have been obtained. Allergic human sera are currently available at -70°C. *Kochia* discs will be used in the direct RAST to determine which human sera will be pooled and in the indirect RAST to determine antigenic activity of isolated kochia fractions. Macaque monkeys will also be used by pca to test the extract potency.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 78: 1.0
FY 79: 1.0

PROGRESS

No progress occurred during this year because of the departure of Dr. Stein. It is hoped that this protocol can be reactivated at a later date.

Publications and Presentations: none.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A study of the Stability of Allergy Extracts Under Varying Conditions.

WORK UNIT NO.: 75/118

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To systematically explore the effects of several stabilizers on the loss of potency of allergy extracts at different concentrations, volumes and time intervals.

TECHNICAL APPROACH

Varying dilutions of Russian thistle allergy extract will be prepared from identical freeze-dried lots. These will be stabilized with varying concentrations of human-serum albumin or tween or glycerine or no stabilizaing agent. They will be placed in both siliconized and plain vials. New dilutions will be set up periodically during the course of a year and at the end of one year's time, the continuing potency of the extracts will be compared using skin testing in human volunteers and RAST inhibition curves.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	1.0
	FY 79:	1.0

PROGRESS

The first two phases of this study have been completed. Additional questions have arisen as a result of these first two studies and data presented by other investigators. Accordingly, further comparisons are planned between RAST inhibition and titrated skin tests as measures of residual extract potency.

Publications:

- (1) Nelson, H.S.: Effect of Diluent and Conditions of Storage on Allergy Extract Potency. (Abst.) J of Allergy Clin Immunol, March 1979.
- (2) Nelson, H.S.: The Effect of Preservatives and Dilution on the

Deterioration of Russian Thistle (Salsola pestifer), A Pollen Extract.
J Allergy Clin Immunol, 63:417, 1979.

Presentations:

- (1) Nelson, H.S.: Effect of Diluent and Conditions of Storage on Allergy Extract Potency. Presented: American Academy of Allergy, New Orleans, LA., 24 March 1979.
- (2) Nelson, H.S.: The Effect of Preservatives and Dilution on the Deterioration of a Pollen Extract-Russian Thistle (Salsola pestifer). Presented: Annual Meeting of the American Academy of Allergy, Phoenix, Arizona, March, 1978.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A New Measure of Anatomic Dead Space During Steady State
Studies: Theory - Component Design.

WORK UNIT NO.: 76/100

PRINCIPAL INVESTIGATOR: Michael E. Perry, LTC, MC

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

OBJECTIVES

To develop a method to measure anatomic dead space during steady state diffusing capacity studies. To develop a valve to be used in the measure of anatomic dead space during steady state diffusing capacity studies.

TECHNICAL APPROACH

Using the theory of the experiment already developed by the use of digital computer analysis and simulation and using the six port rotary valve designed specifically for this protocol, an anatomic dead space will be measured on a group of normal volunteers. This data will be compared with anatomic dead space as measured by the Fowler technique. If correlation occurs, then further modification of the rotary valve will be made to allow for automatic operation during diffusion studies.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: 5.0
FY 79: 0

PROGRESS

The original principal investigator has departed this station. A subsequently-approved protocol replaced this study.

Publications:

- (1) Kindig, N.B., Hazlett, D.R.: A Precision measure of anatomic dead space: Theory. Ann Biomed Engineer 6:33-47, 1978.
- (2) Kindig, N.B., Hazlett, D.R.: Alveolar Air Equations Modified for breathing Pattern. Federation Proceedings 37:867, 1978.

WORK UNIT NO.: 76/100

Publications-continued

- (3) Kindig, N.B., Hazlett, D.R.: An Integral Form Solution of a CO Gas Transport Equation. Biomedical Sciences Instrumentation 14:151-155, 1978.
- (4) Kindig, N.B., Zimmerer, R.W., Hazlett, D.R.: Computer Simulation. Clinical Engineering (submitted for publication).
- (5) Kindig, N.B., Hazlett, D.R., Filley, G.F.: Timing and Volume Averaging in Single Breath DLCO Measurements. The Physiologist, (submitted for publication).

Presentations: none

STATUS

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Anti-neoplastic Therapy with Methyl CCNU (NSC95441)/1-(2-Chloroethyl)-3-(4-Methyl Cyclohexyl)-1-Nitrosourea.

WORK UNIT NO.: 76/102

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with inoperable, recurrent or disseminated colorectal carcinoma with MeCCNU.

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

Three patients were treated with MeCCNU for metastatic adenocarcinoma of the colon and rectum. All three patients have tolerated the drug without serious toxicity. Two patients are stable and one has had progression of the adenocarcinoma.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Objective Measure of CNS Development in Children.

WORK UNIT NO.: 76/103

PRINCIPAL INVESTIGATORS: R. John Morgan, Ph.D. (CSU, CO)
John H. Buscemi, LTC, MC

ASSOCIATE INVESTIGATORS: John W. Steadman, Ph.D. (CSU, CO)
C. Norman Rhodine, Ph.D. (CSU, CO)
Paul W. Daugherty, B.S. (CSU, CO)
James W. Howell, B.S. (CSU, CO)

OBJECTIVES

A long-term goal of the proposed research is to develop a clinical method of assessing central nervous system (CNS) development in children too young to be tested using behavioral methods. Early diagnosis of abnormal CNS development is of paramount importance in early institution of therapy which influences the prognosis. Such early diagnosis is not possible using testing methods which require verbal or written communication skills.

TECHNICAL APPROACH

The proposed research will develop a quantitative method of assessing CNS development and the data base for normal subjects. Abnormal development of the CNS, such as mental retardation, will be the subject of a later research. This study is designed to find parameters of the Electroencephalogram (EEG) which will be reliable quantitative measures of CNS development and establish the normal range of these parameters. The variation of these parameters with age in normal children will be established and statistically tested for significance.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Progress on this project has slowed considerably secondary to lack of funding at Colorado State University. Only fifteen patients were

WORK UNIT NO.: 76/103

PROGRESS - continued

evaluated in the previous fiscal year. Total objective is two hundred and fifty patients prior to the evaluation of the data.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of Testicular Function in Patients Receiving
Cytotoxic Therapy.

WORK UNIT NO.: 76/105

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATOR: Nicholas J. DiBella, COL, MC

OBJECTIVES

To determine if there are abnormalities in testicular function resulting from cytotoxic therapy. To determine whether correction of such hormone deficiencies is beneficial to the patients, particularly by improving their bone marrow function or other testosterone related parameters such as muscle strength, weight gain, etc.

TECHNICAL APPROACH

The patient population under study is that of male patients over the age of 18 years with proven malignancy who are undergoing chemotherapy. To be included in the study the patients must have an expected survival of at least three months, sign a Volunteer Agreement form and be receiving any single cytotoxic agent or combination of such agents. Patients who have received pelvic irradiation or who have undergone bilateral orchidectomy or who have had known diseases of the testes prior to the institution of therapy will be excluded from the study.

Prior to therapy each patient will have a LH, FSH, testosterone and estradiol drawn and a semen analysis obtained. Sexual history will also be monitored in the form of a questionnaire. Patients with decreased testosterone or increased LH will be treated with 200 mg of testosterone enanthate IM every two weeks. All patients will continue to have endocrine studies drawn and questionnaires filled out during their chemotherapy.

Manpower (in professional man years) 0

Funding (in thousands) FY 78: 0
FY 79: 0

WORK UNIT NO.: 76/105

PROGRESS

No progress on this protocol was made during the past year. It is hoped that some progress can be seen during the next year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Evaluation of Nasal Secretory IgE.

WORK UNIT NO.: 76/109

PRINCIPAL INVESTIGATOR: Bruce Martin, MAJ, MC, USAF

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC
John McDonnell, MAJ, MC

OBJECTIVES

To determine whether a localized secretory IgE response can occur to selected aero allergens in the absence of cutaneous mast cell sensitization and to determine whether this is associated with nasal mast cell sensitivity to these antigens.

TECHNICAL APPROACH

Patients who present to the allergy clinic with a seasonal history of allergic rhinitis but with negative tests to the suggested aero allergens will be the principal subjects for investigation, in addition there will be positive and negative control groups. All groups will be studied by skin testing, serum RAST for the suspected aero allergens, nasal RAST for the suspected aero allergens and nasal antigen challenge.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	1.0
	FY 79:	0.5

PROGRESS

Patients study was completed by September 1978 and laboratory evaluation of the results was completed during this year.

Publications:

- (1) McDonnell, J., Martin B. and Nelson H.S.: Evaluation of Specific IgE in Nasal Secretions of Patients with Seasonal Rhinitis and Negative Skin Tests. (Abst.) J. of Allergy Clin Immunol, March 1979.

Presentations:

- (1) McDonnell, J., Martin, B. and Nelson, H.S.: Evaluation of Specific IgE in Nasal Secretions of Patients with Seasonal Rhinitis and Negative Skin Tests. Presented: American Academy of Allergy, New Orleans, LA, 25 March 1979.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Study of the Effect of Ibuprofen (Motrin) on Platelets in Normal Subjects.

WORK UNIT NO.: 76/111

PRINCIPAL INVESTIGATOR: John C. Michalak, LTC, MC

ASSOCIATE INVESTIGATORS: Robert Claypool, LTC, MC
Judy Barber, GS-9, DAC
Pat Rush, GS-9, DAC

OBJECTIVES

To determine the effect of Ibuprofen on the platelets of a control group of patients who do not have inflammatory joint disease and who are on no other medications.

TECHNICAL APPROACH

Baseline coagulation studies including bleeding time, protime, partial thromboplastin time, platelet count, platelet adhesivity, platelet aggregation with epinephrine, thrombin, collagen, ADP and ristocetin were obtained on 20 normal individuals following informed consent. Repeat studies were done at 24 hrs, 7 days and 8 days to determine if and how long Ibuprofen affected platelet function.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: 0.0
FY 79: 0.0

PROGRESS

No further work has been done on the Motrin protocol. The initial study was felt to be inadequate due to difficulties with the aggregometer and patient compliance. When thromboxane levels are available, this study might be more meaningful and could be restarted.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Study of the Effect of Tetracycline and Pleural Drainage
on Pleural Effusion in Cancer Patients.

WORK UNIT NO.: 76/112

PRINCIPAL INVESTIGATOR: John C. Michalak, LTC, MC

ASSOCIATE INVESTIGATORS: Michael Barry, LTC, MC
Michael Langin, CPT, MSC
Antti G. Maran, MAJ, MC

OBJECTIVES

To determine in a prospective, randomized, double-blind fashion if pleural drainage and tetracycline are better than pleural drainage alone in the treatment of pleural effusion in cancer patients.

TECHNICAL APPROACH

Patients with biopsy-proven malignancy with malignant infusion are being randomized to closed chest tube drainage alone or closed chest tube drainage with tetracycline. This is being done in a double-blind manner by the Pharmacy Service so ward physicians do not know if the patient is given tetracycline or the vitamin solution which looks the same as tetracycline.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 78: 0.0
FY 79: 0.0

PROGRESS

Presently twenty-one patients have been placed on the study. The code has not yet been broken so it is yet uncertain which patients have been treated with closed chest tube drainage alone or closed chest tube drainage with tetracycline.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Chemolmmunotherapy of Malignant Melanoma.

WORK UNIT NO.: 76/115

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To test the efficacy of BCG and BCG plus DTIC in malignant melanoma.

TECHNICAL APPROACH

Stage I - BCG by scarification weekly for 3 months, then every other week for 21 months.

Stages II & III - DTIC every 21 days with BCG on days 7, 12 and 17 of a 21 day cycle.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Six patients have been treated with adjuvant BCG. Other than local reactions to BCG, there were no unusual toxicities observed in these patients. Four of the patients were alive and free of disease when last seen. The other two patients have had recurrence and dissemination of the malignant melanoma.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 78

TITLE: The Effect of Dexamethasone on Gonadotropins in Post-Menopausal Women.

WORK UNIT NO.: 76/116

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATOR: Leonard Dodson, MAJ, MC

OBJECTIVES

To clarify the mechanism whereby glucocorticoids may interfere with gonadotropin secretion or release in post menopausal women. This is of interest because of the high frequency of gonadal dysfunction in patients, male and female with endogenous as well as exogenous Cushing's syndrome.

TECHNICAL APPROACH

The patient population to be studied are healthy post menopausal women on no medications. A post menopausal woman will be defined as any woman with elevated plasma gonadotropin levels as a result of physiologic ovarian failure or with prior surgical extirpation of the ovaries. A baseline 0800 plasma FSH, LH, cortisol and prolactin levels will be drawn on two consecutive days prior to the subjects taking 2mg qid po of Dexamethasone on three consecutive days. A.M. FSH, LH, cortisol and prolactin levels will be obtained daily during the Dexamethasone treatment. In order to define the site of the anticipated Dexamethasone suppression of the gonadotropins an LH-RH infusion test will be performed by giving a single IV bolus of 100ug of LH-RH on the day prior to and on the third Dexamethasone treatment day. Blood for FSH and LH, cortisol and prolactin will be drawn at -15, 0, 15, 30, 45, 60, 90 and 120 minutes after LH-RH injection.

Manpower (in professional man years): 0.5/yr

Funding (in thousands)	FY 78:	2.0
	FY 79:	2.0

WORK UNIT NO.: 76/116

PROGRESS

Seven postmenopausal women have completed all or part of the protocol. Mean pre-dexamethasone basal LH, FSH, prolactin and cortisol levels were respectively 64.6 (mIU/ml), 140.0 (mIU/ml), 7.3 (ng/ml) and 11.5 (ug/dl) (n=7). Mean peak pre-dexamethasone, post GnRH LH, FSH, prolactin and cortisol levels were respectively 253.0 (390%), 201.1 (144%), 20.8 (286%) (p 0.05) and 12.50 (108%) (n=7) as compared to basal levels. Post-dexamethasone mean basal (0800) LH, FSH, prolactin and cortisol levels were respectively 93.4, 169.8, 8.5 and 1.3 (n=5). Only cortisol levels were significantly different from pre-dexamethasone levels (p.0.10) and 1.8 (138%) (n=5) as compared to basal levels post-desamethasone. There was no significant difference between the LH, FSH, prolactin levels response to GnRH pre- and post-dexamethasone, although peak prolactin levels post GnRH occurred at 45 minutes pre-dexamethasone and 90 minutes post-dexamethasone (p 0.01). In three subjects a saline placebo injection prior to giving GnRH did not influence the levels of prolactin, cortisol, LH or FSH.

It is therefore concluded that short term treatment with dexamethasone did not affect the hypophyseal response to GnRH. Suppression of tonically elevated LH and FSH also was not observed. However, it was observed, for the first time, that GnRH stimulated prolactin in postmenopausal subjects with the response being delayed by dexamethasone. The mechanism and significance of this latter observation remains speculative but deserves further study.

In this regard, it planned to seek approval for the use of GnRH in premenopausal women, males, additional postmenopausal women and hyperprolactinemic subjects, delving further into this observation.

Publications: none

Presentations:

(1) Treece, G., Dodson, L.E. and Hofeldt, F.D.: Effect of GnRH on Postmenopausal Gonadotropins and Prolactin Levels: Influence of Short Term Glucocorticoid Administration. Presented: 61st Annual Endocrine Society Meeting, Anaheim, CA, June 13-15 Jun 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
Fitzsimons Army Medical Center
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: A Non-Invasive Plethysmographic Measure of Transthoracic Pressure During Maximal Expiratory Maneuvers.

WORK UNIT NO.: 76/117

PRINCIPAL INVESTIGATOR: Michael E. Perry, LTC, MC

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

OBJECTIVES

To develop a Non-Invasive Plethysmographic method to measure Transthoracic Pressure during maximal expiratory maneuvers.

TECHNICAL APPROACH

Ten adult volunteers drawn from military and civilian staff assigned to the Pulmonary Function Laboratory will be the test population. Each individual will be subjected to Spirometry, Frequency Dependence of Functional Residual Capacity, Flow Volume Loops, Compartment Studies, Frequency Dependence of Compliance, and to Forced Vital Capacity maneuvers in the Body Plethysmograph.

Manpower (in professional man years): 0.4/yrs

Funding (in thousands)	FY 78:	5.0
	FY 79:	0

PROGRESS

The original principal investigator has departed this station. A subsequently-approved protocol replaces this study.

Publications: none

Presentations:

- (1) Zimmerer, R.W., Hazlett, D.R.: Whole Body Plethysmographic Monitoring of Airway Dynamics During Maximal Exhalation.

WORK UNIT NO.: 76/117

Presentations - continued

Presented: American Association for Medical Instrumentation,
San Francisco, CA, March 1977.

- (2) Zimmerer R.W., Perry, M.E., Hazlett, D.R.: Airway Resistance and Alveolar Pressure Measurement. Presented: 31st Annual Conference of Engineering in Medicine and Biology, Atlanta, GA, October 1978.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Comparison of the Clinical and Immunological Response of Pre-Seasonal and Co-Seasonal vs. Post-Seasonal Initiation of Allergy Immunotherapy.

WORK UNIT NO.: 77/103

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, LTC, MC

ASSOCIATE INVESTIGATORS: William R. Tipton, LTC, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To investigate in patients who present to the allergy clinic just prior to or during their symptomatic pollen season, whether it is advantageous to begin immunotherapy at that time or postpone the initiation of specific treatment until a specified period following the end of the pollen season.

TECHNICAL APPROACH

Fifteen pairs of relatively well matched new patients presenting to the allergy clinic at FAMC will undergo the usual allergy evaluation. One group of patients will have allergy immunotherapy delayed until after the season of the specific pollen has passed, with the initiation of therapy beginning one month at the end of the season, the other group will begin their allergy immunotherapy at the time the person is evaluated and within two months of the specific pollen season. A blood sample and nasal provocation testing and nasal RAST testing will be performed upon initial evaluation. These procedures will be repeated just prior to the next season and immediately after the first and second pollen seasons. Patients will keep a symptom score diary during both pollen seasons.

Manpower (in professional man years): 0.0/yr

Funding (in thousands): FY 78: 0
FY 79: 0

WORK UNIT NO: 77/103

PROGRESS

No work was undertaken under this protocol this year.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of Immunoglobulins and Immunoglobulin Bearing Lymphocytes
in Asthma.

WORK UNIT NO.: 77/104

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, LTC, MC

ASSOCIATE INVESTIGATORS: Craig Jacobson, CPT, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To determine whether patients with bronchial asthma have mean immunoglobulin levels which are lower than normal for their age or have abnormalities of lymphocytes as determined by surface markers.

TECHNICAL APPROACH

All asthmatic patients seen in our Clinic as much as possible were evaluated by means of a data sheet and had sera drawn for immunoglobulin studies. A portion of this group will be recalled and have appropriate studies and have blood drawn for lymphocyte markers.

Manpower (in professional years): 0/02/yr

Funding (in thousands) FY 78: 2.5
FY 79: 0

PROGRESS

No further patients were studied during this period. Analysis of the data continues.

Publications and Presentations: none

STATUS:

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Evaluation of Cross Allergenicity Among Pollen Extracts of
Members of Chenopodiaceae and Amaranthaceae.

WORK UNIT NO.: 77/105

PRINCIPAL INVESTIGATOR: Richard W. Weber, LTC, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To evaluate the cross allergenicity between pollens of the weed families Chenopodiaceae and Amaranthaceae, and to ascertain whether sensitivity to select members of these families can be distinguished or whether cross-reactivity with strong allergens abrogates such a discrimination.

TECHNICAL APPROACH

Twelve members of Chenopod-Amaranth families will be studied. Rabbit antisera will be raised to each weed extract and studied with Ouchterlony immunodiffusion and inhibition of passive hemagglutination. Sera collected from patients with positive skin tests will be used for RAST inhibition studies.

Manpower (in professional man years): 0.5/yr

Funding (in thousands)	FY 78:	1.0
	FY 79:	1.0

PROGRESS

No further work was performed under this protocol due to the transfer of the principal investigator to Europe.

Publications:

- (1) Weber, Richard W., Nelson, H. S.: The material was submitted to the 1978 Hugh Mahon Lectureship Award Competition where it was awarded second prize.

Presentations: none

STATUS:

Ongoing.

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CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Durham, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Effect of Chronic Non-Immunologically Mediated Bronchial
Constriction of Bronchial Smooth Muscle.

WORK UNIT No.: 77106

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, M.D.

ASSOCIATE INVESTIGATORS: William H. Glab, SP6
John Hofmann, CPT, VC

OBJECTIVES

To determine if the hyperactivity or constriction of the bronchial smooth muscle in asthmatic patients is the cause of the bronchial smooth muscle hypertrophy found in the asthmatic lung; and secondly, to determine if bronchodilators as presently used have any protective effect against this hypertrophy.

TECHNICAL APPROACH

Guinea pigs will be subjected to non antigen mediated bronchoconstriction from the age of weaning to sexual maturity. Pulmonary functions and histological data will be obtained in depth as the guinea pigs are sacrificed.

Impact on (in professional man years): 0.0/yr

Funding (in thousands): FY 78: 1.2
FY 79: 0.0

PROGRESS

Work was performed under this protocol due to separation of the principal investigator from the service.

Publication and other results: none

Comments:

References:

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: L-Dopa Stimulation of Glucagon in Obesity.

WORK UNIT NO.: 77/107

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATOR: William Georgitis, CPT, MC

OBJECTIVES

It has been suggested that obese subjects have a deficiency of glucagon reserve. L-Dopa is known to cause a rise in glucagon levels in normal weight subjects. This study was designed to observe the effect of L-Dopa on serum glucagon levels in obese subjects compared to normal weighted controls.

TECHNICAL APPROACH

The patient populations to be studied include 10 normal weight, non-diabetic subjects; 10 obese, non-diabetic subjects and 10 obese, diabetic subjects. In the latter group, subjects taking insulin and/or oral hypoglycemic agents will be excluded from the study. Diabetic subjects will be defined on the basis of a standard 3-hr glucose tolerance test. Subjects with a history of cardiovascular disease, glaucoma, melanoma, peptic ulcer disease, psychosis, and patients taking MAO inhibitors will be excluded from the study. All subjects will be on a weight maintaining 150 gram carbohydrate diet three days prior to the study. If not previously documented in the subject's medical records a 3-hour glucose tolerance test will be performed on a day prior to L-Dopa administration. Subsequently, after an overnight fast all will be given a 7.5 mg/kg dose of L-Dopa by mouth at 8:00 a.m. In the supine position venous blood samples will be obtained from an indwelling scalp vein catheter at -15, 0, 15, 30, 45, 60, 90, 120 and 180 minutes for determinations of plasma glucose, growth hormone, insulin, glucagon and prolactin.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 78: 0.0
FY 79: 0.0

WORK UNIT NO.: 77/107

PROGRESS

With the addition of CPT Georgitis as coinvestigator, it is anticipated that the protocol will be completed during the next fiscal year. No data is yet available. Several control and obese subjects have been studied or are scheduled for the protocol.

Of concern in the design of the protocol is whether L-dopa should be administered in a dose per weight (mg/kg) or a single dose for each subject (i.e., 500 mg). To resolve this concern, several control subjects will receive different doses of L-dopa to determine whether or not there is a maximal effective dose. Review of available information on the pharmacology of L-dopa will also be required.

Publications and Presentations: none

STATUS:

Ongoing.

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CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: A Comparison of the Clinical and Immunologic Response to
Grass Pollen Extract With or Without the Addition of Glycerin.

WORK UNIT NO.: 77/108

PRINCIPAL INVESTIGATOR: William R. Tipton, COL, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To determine whether there is a difference in the immunologic response to allergy injection therapy if the vehicle for the pollen extract contains glycerin as opposed to saline.

TECHNICAL APPROACH

Alternate patients beginning immunotherapy with grass pollen extract were placed on one of the two types of grass extract. They received immunotherapy with this extract through two pollen seasons and blood was collected for IgE and blocking antibody levels before and following each pollen season.

Manpower (in professional man years): 0.1/yr

Funding (in thousands):	FY 78	0
	FY 79	0

PROGRESS

Patients' study is completed and the final serum samples have been collected. Studies of IgE and IgG antibodies are currently being performed.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARM/ MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Further Investigation of the Esophago-bronchial Reflex Mechanism,
and on the Association Between Gastroesophageal Reflux and Asthma.

WORK UNIT NO.: 77/109

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, M.D.

Associate Investigators: Peter Hameister, LTC, MC
Harry S. Spaulding, Jr., COL, MC
W. Nicholas Glab, Sp6
Nigel Smith, Sp6

OBJECTIVES

To demonstrate that reflexes exist between the lower esophagus and the lungs and that they are vagally mediated and can cause bronchoconstriction.

TECHNICAL APPROACH

A group of 20 Mongrel dogs were artificially given esophagitis by frequent hydrochloric acid infusions. These dogs were then intubated under anesthesia and had an intra-esophageal instillation of hydrochloric acid. Pulmonary functions were measured pre and post. In addition the esophagus was distended and pulmonary functions were repeated in a similar manner. As the third part of the experiment the vagus nerves were cut and studies of pulmonary function before and after hydrochloric acid profusion.

Manpower (in professional man years): 0

Funding (in thousands) FY 78: 0
FY 79: 5.0

PROGRESS

Hydrochloric acid provocation caused a significant fall in total respiratory resistance. Distention of the esophagus also caused a significant decrease in total respiratory resistance suggesting bronchoconstriction. A second group of five dogs whose vagal nerves were interrupted had ablated responses to acid and distention. These results indicate a possible reflex vagal arc can modulate smooth muscle tone. They may also suggest that a similar mechanism by which gastroesophageal reflux could induce bronchoconstriction in patients with asthma.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effect of Chronic Oral Propranolol on Glucose Tolerance.

WORK UNIT NO.: 77/110

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATORS: none

OBJECTIVES

To determine what effect propranolol given orally for the treatment of hypertension and angina pectoris has on intravenous and oral glucose tolerance tests in light of recent case reports of hyperglycemia non-ketotic coma attributed to propranolol therapy (Podolsky, 1973).

TECHNICAL APPROACH

Patients with hypertension being started on propranolol therapy will be the subjects for this study. A baseline IVGTT and 5-hr OGTT will be obtained prior to therapy. The initial dose of propranolol will be 40 mg qid po. A repeat IVGTT and 5-hr OGTT will be obtained at 2 and 6 weeks of therapy. In some subjects, hydrochlorthiazide will be added to the propranolol therapy and a repeat IVGTT and 5-hr OGTT obtained after 1 month of combined therapy. The effect of propranolol on glucose disappearance rate (K value) and glucose tolerance will be examined. The effect of propranolol on insulin and glucagon levels will also be examined.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Work on this protocol began at MAMC when the principle investigator was in fellowship. The results obtained on six subjects was reported in the MAMC CIS 1977 report. Approval was given on 7 Jun 77 to transfer the protocol to FAMC CIS with the protocol to remain ongoing at MAMC

WORK UNIT NO.: 77/110

PROGRESS - continued

with both groups to combine efforts. However, it has been decided to terminate the MAMC CIS involvement and to have the FAMC investigators complete the protocol. Although no progress has been seen recently it is anticipated that the protocol will near completion during the next year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Investigation of the Effects of Antihistamines and Aspirin
on the Late Skin Test Reaction.

WORK UNIT NO.: 77/111

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, M.D.

ASSOCIATE INVESTIGATOR: Joseph A. Smith, LTC, USAF, MC

OBJECTIVES

To discover if prostaglandins may play a role in the late reaction
to allergy skin testing.

TECHNICAL APPROACH

Ten to twelve patients who demonstrate late cutaneous reactions to
various allergens, ragweed or Timothy grass, will be utilized in
this study. They will be given a combination of different histamine
antagonists prior to being skin tested and likewise, will receive a
therapeutic dose of Aspirin prior to being skin tested in order to
evaluate the possible mode of development of the late cutaneous
reaction. Skin tests will be evaluated as to their size and will
be analyzed by planometry and the effects of the various drug
regimens of the skin tests compared.

Manpower (in professional man years) 0.1/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Study of patients under this protocol has been completed. Evaluation
of the data is completed and is currently in press.

Publications:

- (1) Smith, J.A., Mansfield, L.E. and Nelson, H.S.: The Effect of
Cimetidine on the Immediate Cutaneous Response to Allergens,
Ann Allergy, 42:353, 1979.

WORK UNIT NO.: 77/111

Publications - continued

- (2) Smith, J.A., Mansfield, L.E., deShazo, R. and Nelson, H.S.: An Evaluation into the Pharmacologic Inhibition of the Immediate and Late Cutaneous Reaction to Allergen, J of Allergy & Clin Immunol in press.

Presentations:

- (1) Smith, J.A., Mansfield, L.E., deShazo, R., and Nelson, H.S. "An Evaluation into the Pharmacologic Inhibition of the Immediate and Late Cutaneous Response to Allergens". Presented: American Academy of Allergy, New Orleans, Louisiana, 25 Mar 79.

STATUS:

complete.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Study of the Diagnostic Role of Serum and Bone Marrow
Lactate Dehydrogenase Isoenzymes (LDH).

WORK UNIT NO.: 77/112

PRINCIPAL INVESTIGATOR: John C. Michalak, LTC, MC

ASSOCIATE INVESTIGATORS: Thomas Alford, CPT, MC

OBJECTIVES

To determine if serum or bone marrow LDH isoenzymes are an aid to diagnosis or a parameter to follow in a variety of hematological and oncological disease states.

TECHNICAL APPROACH

Adult patients who are having a bone marrow performed for diagnostic reasons will have 2-3cc of additional blood aspirated from the bone marrow and 10cc of peripheral blood evaluated for total LDH and LDH isoenzymes. Informed consent emphasizes the additional phlebotomy and prolongation of the bone marrow biopsy procedure. No follow-up studies are needed.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

No further patients have been added to the protocol during 1979. From the initial 76 patients studied, further evaluation should be done in those patients with acute leukemia and malignant lymphomas.

Publications:

- (1) Michalak, J.C., Alford, T.J., and Herbst, K.D.: Bone Marrow Lactate Dehydrogenase (LDH) in Lymphoma and Acute Leukemia. Blood, Volume 50, Supplement 376, 1977.

Presentations: none

STATUS:

Completed.

075

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A Study of Terbutaline Aerosol in the Treatment of Patients
with Bronchial Asthma.

WORK UNIT NO.: 77/113

PRINCIPAL INVESTIGATORS: Joseph A. Smith, LTC, USAF, MC
Harold S. Nelson, COL, MC
Richard W. Weber, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the effectiveness of freon propelled metered dose aerosol terbutaline as a bronchodilator administered on a regular four times a day basis. Two specific considerations were (1) whether the bronchodilator response was sustained with chronic administration and (2) to compare the relative effectiveness of terbutaline as a sole medication to that of theophylline in optimum doses as a sole medication.

TECHNICAL APPROACH

This study consisted of two parts: In the first part, 15 patients were taken off all beta adrenergic bronchodilators for a period of two weeks. The response to aerosolized terbutaline was then measured following which they were placed on a metered dose inhalation of aerosolized terbutaline, four times a day for twelve weeks. During this period, their response to terbutaline was measured in the Allergy Clinic every two weeks. At the beginning and at the end of the twelve week period, double-blind comparisons were made in the Allergy Clinic between the bronchodilator response over a four hour period of time to placebo or to terbutaline. In the second portion of the study, patients were placed on optimal theophylline; they then received optimal theophylline and aerosolized terbutaline for a week during which time they measured their pulmonary function at home four times daily, on a Wright peak flow meter. Following one week, they were placed on a cross over double-blind in which they received one active drug and one placebo for two weeks. At the end of this time, another open week of observation ensued in which they received both active drugs, following which they went into a second double-blind period in which the active drug of the previous two week double-blind was replaced by a placebo - while they received the second drug in its active form.

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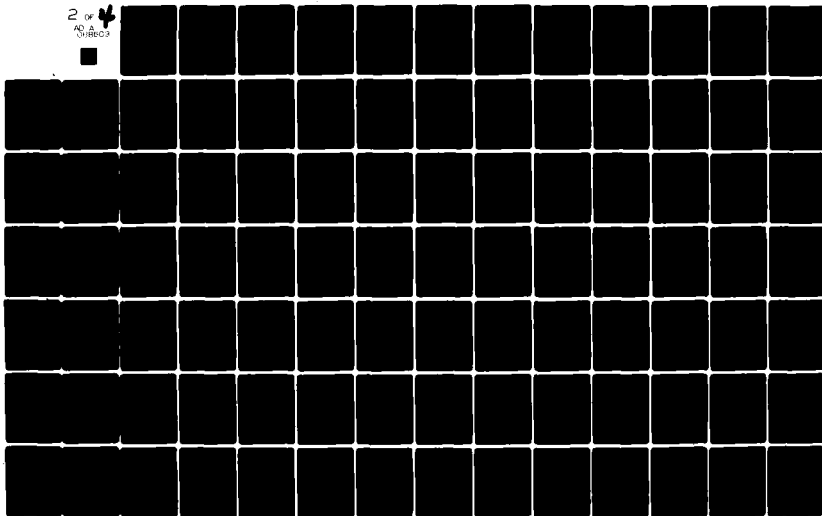
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WORK UNIT NO.: 77/113

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 78: 0.0
 FY 79: 0.0

PROGRESS

Data concerning patients studied under this protocol has been completed.

Publications:

- (1) Smith, J.A., Weber, R.W. and Nelson, H.S.: Comparison of Aerosolized Terbutaline and Optimal Dose Theophylline in the Management of Bronchial Asthma. (Abst.) Ann Allergy, 42:121, 1979.
- (2) Smith, J.A., Weber, R.W. and Nelson, H.S.: Long-term Use of Aerosolized Terbutaline in the Treatment of Bronchial Asthma-The Development of Subsensitivity. (Abst.) American Review of Respiratory Disease, 119:170S, 1979.

Presentations:

- (1) Smith, J.A., Weber, R.W., and Nelson, H.S.: Comparison of Aerosolized Terbutaline and Optimal Dose Theophylline in the Management of Bronchial Asthma. Presented: American College of Allergists Annual Meeting, San Francisco, CA, 29 Jan 79.
- (2) Smith, J.A., Weber, R.W. and Nelson, H.S.: Long-term Use of Aerosolized Terbutaline in the Treatment of Bronchial Asthma-The Development of Subsensitivity. Presented: American Thoracic Society, Las Vegas, Nevada, 14 May 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effect of Propranolol in Patients with Reactive Hypoglycemia.

WORK UNIT NO.: 77/114

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATORS: Fred D. Hofeldt, COL, MC
Anellie Shackelford, MT, DAC

OBJECTIVES

To investigate the therapeutic efficacy of chronic oral propranolol (Inderal) administration on the symptoms and metabolic defects of patients with postabsorptive (reactive) hypoglycemia.

TECHNICAL APPROACH

The subjects will be those with persistent symptomatology despite prior drug or dietary therapy for any of the forms of reactive hypoglycemia. A baseline 5-hr oral glucose tolerance test (GTT) using 100 grams of glucose and a 3-day 150 gram carbohydrate preparatory diet will be obtained. A dietary, drug and symptom history will also be recorded in the form of a questionnaire. Propranolol (160 mg qd po) or placebo will then be administered double blindly for one month. A repeat 5-hr GTT will be performed and a second questionnaire obtained at the end of the month. For a second month the alternate drug is administered and another 5-hr GTT and questionnaire obtained. The effect of glucose, insulin, glucagon, growth hormone, cortisol and prolactin levels during the 5-hr GTT will be compared.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	1.0

PROGRESS

Preliminary results on four subjects administered propranolol only for one month suggest an improved symptom complex on the drug.

WORK UNIT NO.: 77/114

PROGRESS - continued

However, placebo effect cannot be ruled out. The glucose nadir during the GTT on propranolol tended to be higher without any change in basal or postprandial insulin, glucagon, cortisol or prolactin levels. Basal growth hormone levels were not effected but postprandial growth hormone levels were Higher.

Although no progress has been made recently on this portocol, the SGO has obtained an FDA IND number and both placebo and drug have been received by the investigators from Ayerst. It is anticipated that much progress on this protocol will ensue over the next year.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Development of Specific and Cross Subsensitivity in the Tracheal Tissues of Guinea Pigs Treated with Isoproterenol and Aminophylline.

WORK UNIT NO: 78/102

PRINCIPAL INVESTIGATORS: W. Ronald Tipton, M.D.

ASSOCIATE INVESTIGATORS: Joseph Souhrada, M.D., Ph.D., National Jewish Hosp.
Helen Morris, M.D., National Jewish Hospital
Harold S. Nelson, COL, MC

OBJECTIVES

This study is designed to measure the development of the subsensitivity to two drugs, Isoproterenol and Theophylline by examining both their dilating response on histamine contracted tracheal rings and their ability to increase levels of cyclic-AMP in tracheal tissue and parenchymal lung tissue. Cyclic-AMP is considered to be "second messenger" in inducing smooth muscle relaxation and initiated by these two drugs. In each system, evidence will be sought of subsensitivity not only to the drug administered to the animal, but also to the other drug in the study and to combine stimulation to both drugs. Data will also be sought concerning the effect of H₁ and H₂ antagonists on the actions of these drugs.

TECHNICAL APPROACH

Guinea pig tracheal and peripheral lung strips will be analyzed for cyclic nucleotide levels as well as physiological response to various mediators as previously described. Modifications to existing equipment will enable the investigators to do the tension studies at Fitzsimons, Army Medical Center.

Manpower (in professional man years) 2.5/yr

Funding (in thousands) FY 78: 3.6
 FY 79: 3.0

PROGRESS

In addition to the presentation at the Annual Pulmonary Symposium, September 1979, the work was accepted and presented at the American

WORK UNIT NO.: 78/102

PROGRESS - continued

Thoracic Society, May 1979. It was co-winner of the Hugh Mahon Award at Fitzsimons Army Medical Center for 1979. The paper is to be submitted shortly for publication. The equipment is now available for further studies at Fitzsimons Army Medical Center as outlined in the objectives.

Publications: none

Presentations:

- (1) Tipton, W.R., Jacobson, K., Nelson, H.S., Morris, H., Souhrada, J.: Dynamics and Mechanism of Guinea Pig Trachea Subsensitvity to Isoproterenol. Presented: 31st Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Aurora, Colorado, Sept 1978.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Trial of Lithium Carbonate to Prevent or Reduce Neutropenia
in Dogs Receiving Radiation.

WORK UNIT NO.: 78/103

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
W. Nicholas Glab, SP6, B.S.
Donald B. Mercill, DAC, B.S.

OBJECTIVES

To determine the efficacy of lithium carbonate in preventing or
reducing the neutropenia due to myelotoxic irradiation.

TECHNICAL APPROACH

Dogs will be maintained at myeloproliferative lithium levels for 21
days, after which half will receive 175 rads of whole body radiation.
Bone marrow biopsy, complete blood count with differential, and serum
colony stimulating factor will be monitored during the course of the
study and compared with control animals.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 78: 2.5
 FY 79: 0.2

PROGRESS

Dogs did not experience increases in granulopoiesis in response to lithium
levels of 1.5-2.0 mEq/h. Therefore, a dog will not serve as a
model animal for this study. Additionally, the concept of lithium
usage to prevent the neutropenia common in cancer radiation and
chemotherapeutics has been validated in human studies.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Study of Coagulation Parameters in Patients with Suspected
Deep Vein Thrombophlebitis Before and After Venography.

WORK UNIT NO.: 78/104

PRINCIPAL INVESTIGATOR: Joseph R. Haskett, Jr., CPT, MC

ASSOCIATE INVESTIGATORS: John C. Michalak, LTC, MC
Judy Barber, GS-09, DAC
Patricia Rush, GS-09, DAC

OBJECTIVES

To determine if coagulation parameters which have been associated
with hypercoagulable states are altered by lower extremity venography.

TECHNICAL APPROACH

Following informed consent all adult patients who are referred to the
Department of Radiology for venography are screened with a variety of
clotting studies to include: fibrinogen and fibrin degradation products,
protamine sulfate paracoagulation test, thrombin generation index,
and serum anti-thrombin 3 before venography and 24 hours after to
determine if there is a change in the patients coagulation parameters
from the procedure and dye.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

As mentioned last year, patient accrual has been slow. To improve
patient accrual, an amendment to the protocol will be needed to study
patients before and after studies such as intravenous pyelograms. Dr.
Stephen Oswald will work on the amendment and hope the protocol will
restart by March 1980.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Ifosfamide plus Fluorouracil in the Treatment of Pulmonary Carcinoma.

WORK UNIT NO.: 78/105

PRINCIPAL INVESTIGATOR: Eduardo R. Pajon, Jr., MAJ, MC

ASSOCIATE INVESTIGATOR: Nicholas J. DiBella, LTC, MC

OBJECTIVES

To obtain results of treating pulmonary carcinoma with a combination of ifosfamide and fluorouracil and to determine the maximum effective dose of the above combination.

TECHNICAL APPROACH

Since March 1978 after Surgeon General approval of the protocol, all patients with unresectable known oat cell carcinoma of the lung have been eligible for study. A total of seven patients at Fitzsimons have been entered on this study. Additional patients have been entered on the study from the other corporate institutions and will not be reported here. All patients have been treated with the combination drugs, 5-day infusion of ifosfamide and weekly doses of 5-FU repeated monthly with followup of clinical and laboratory parameters.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

Since inception of the study a total of thirty-nine patients with advanced lung cancer were treated with the combination of IF 1200mg/M² iv push d1-5 and 5FU 450mg/M² iv d8,15,22. Cycles were repeated monthly. Of 31 evaluable patients there were 5 PR (16%) lasting 1 1/2, 3, 4, 13, and 14+ months and 16 Stable disease (52%) lasting 2-8 months with a median of 3 months. Only patients without prior CT responded. Moderate hematuria occurred in 12 of 129 courses of IF. Significant proteinuria occurred in 20 courses of IF. No patient

WORK UNIT NO.: 78/105

Progress - continued

experienced irreversible renal toxicity. Hematological and gastrointestinal toxicities were generally mild. These results suggest that the addition of 5FU to IF may actually result in lower response rates than when IF is used alone.

Publications: none

Presentations:

- (1) Pajon, E. Mahmood, T., Jennings, W., diBella, N.: Ifosfamide and 5Flourouracil in the Treatment of Advanced Lung Cancer.
Presented: Colorado Clinical Oncology Group, Denver, CO,
17 Nov 79.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effects of the Evaluation of the Frequency of Pollen Allergen
Injections During the Pollen Season.

WORK UNIT NO.: 78/106

PRINCIPAL INVESTIGATOR: Brian S. Dantzler, MAJ, MC
Bryant R. Fortner, MAJ, MC

ASSOCIATE INVESTIGATORS: William R. Tipton, COL, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To establish if the more frequent use of hyposensitization injections during the specific pollen season for which patients are receiving immunotherapy, is immunologically or clinically better than a less frequent schedule.

TECHNICAL APPROACH

Two groups of 10-12 patients relatively well matched in regard to severity of symptoms, serum IgE levels and nasal provocation sensitivity to the specific pollens involved will be compared. One group will receive their allergy immunotherapy on a once weekly basis. One group will receive it on a three weekly basis. These two groups will be compared on the basis of nasal provocation before and after the season. Specific serum IgE antibodies before and after the season. Specific IgG - before and after the season. Finally, they will all complete a twice daily symptoms score. All of this data will be compared in an attempt to evaluate which mode of therapy is more beneficial to the patient. The aim of the study is to determine if a once weekly schedule offers a significant therapeutic benefit in relationship to patient and government cost as opposed to the three weekly schedule.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

No progress was made on this protocol for the past year. It has been

WORK UNIT NO.: 78/106

PROGRESS - continued

revised slightly and patients have been identified with an anticipated starting date of mid December 1979. The revised protocol has been submitted for consideration.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Evaluation of the Efficacy of Animal Dander Allergy
Immunotherapy in Perennial Rhinitis.

WORK UNIT NO.: 78/107

PRINCIPAL INVESTIGATORS: Alvin J. Aubry, MAJ, MC
Gary P. Carpenter, MAJ, MC
Bryant R. Fortner, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL. MC

OBJECTIVES

To evaluate the reponse to immunotherapy with commercial cat and dog extracts in patients with marked skin test reactivity to these antigens and perennial symptoms.

TECHNICAL APPROACH

Patients markedly sensitive to cat or dog dander extract and having perennial respiratory symptoms are randomly placed on either cat and dog dander or placebo extracts for a period of at least one year. During this period of time the tissue threshold is measured by periodic titrated skin tests and titrated nasal and conjunctival challenges and the immunologic response is measured by specific RAST and blocking antibody titers.

Maypower (in professional man years): 0

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

At the present time twenty-three patients have been enrolled in the study. They are reporting to the Allergy Clinic at periodic intervals for measurement of tissue threshold to cat and dog dander allergens. At the same time blood is obtained which will be stored until the completion of this study at which time the antibody levels will be determined.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Investigation into the Generation of Antigen Specific
Suppressor Cells During Allergy Immunotherapy.

WORK UNIT NO.: 78/108

PRINCIPAL INVESTIGATORS: Lyndon E. Mansfield, LTC, MC
George L. Brown, Ph.D., COL, MSC
Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

The object of this study is to evaluate the development of antigen specific regulatory cells during allergy immunotherapy, and to ascertain whether these cells suppress formation of IgE. In this investigation a new technique known as co-culture will be used.

TECHNICAL APPROACH

Ten patients beginning allergy immunotherapy will be evaluated. They will have blood drawn for lymphocyte studies including antigen stimulated blastogenesis. The total amount of IgE generated from these cultures with different concentrations of antigen; total amount of specific IgE generated from these cultures, upon stimulation by different concentrations of antigen, will be evaluated. These cells will also be co-cultured with normal person's lymphocytes and the same procedure performed. After a period of time when these patients are able to reach allergy maintenance immunotherapy, the procedure will be repeated. One alteration will be that these patient's cells will be co-cultured with a new non-treated allergic patient's cells, which will also undergo antigen stimulation. The object of this technique will be to show that during the course of immunotherapy, the changes in specific IgE generated under stimulation by antigen is decreased by the development of a T suppressor cell mechanism.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 78:	5.0
	FY 79:	0.0

WORK UNIT NO.: 78/108

PROGRESS

No work was performed under this protocol this year due to separation of the principal investigator from the Service.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 78/109

PRINCIPAL INVESTIGATORS: Hugh P. McElwee, MAJ, MC
James J. Damato, MAJ, MSC

OBJECTIVES

To determine if patients with cirrhosis have a higher incidence of
bacteremia following endoscopy than normal patients.

TECHNICAL APPROACH

Control patients and patients with cirrhosis have baseline and serial
post procedural blood cultures drawn. Blood cultures are collected
for both aerobic and anaerobic organisms. Positive results are recorded
and if necessary patients are notified and treated.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 78: 0.5
FY 79: 0.5

PROGRESS

To date we have only performed studies on eleven patients. One cirrhotic
patient had transient bacteremia but no others have been positive.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Study of the Chlorpromazine Induced Inhibitor of Blood Coagulation.

WORK UNIT NO.: 78/110

PRINCIPAL INVESTIGATOR: Norman J. Martin, MAJ, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To determine the frequency of the previously described nonspecific inhibitor of blood coagulation which may be associated with long-term chlorpromazine therapy.

TECHNICAL APPROACH

Adult patients who were selected were all those who presented to Ward 7, South Psychiatry, Denver, VA Hospital, and Psychiatry Service, Fitzsimons Army Medical Center. These patients were those who were receiving either chlorpromazine, other phenothiazine derivatives, or chlorpromazine in combination with other phenothiazines or neuroleptics. The control group consisted of psychiatric patients who were not receiving chlorpromazine. Only those patients judged mentally competent by a primary physician not connected with this study were selected. Informed written consent was received from all patients which explained the study and required phlebotomy. Additional studies were performed on plasma from those patients with prolonged prothrombin and partial thromboplastin times. Toxic patients will be subjected only to phlebotomy. Approximately 30cc of blood will be required from each patient per baseline study.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

WORK UNIT NO 78/110

PROGRESS

No progress is reported since the principal investigator never initiated the study. Dr. Martin has since been transferred to Letterman Army Medical Center.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Further Investigation of Gastroesophageal Reflux and Reflex
Bronchoconstriction.

WORK UNIT NO: 78/111

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

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To more clearly prove that the association between gastroesophageal
reflux and asthma is reflex mediated.

TECHNICAL APPROACH

In order to ascertain the importance of any relationship between
gastroesophageal reflux and asthma, the following subjects under-
went investigation as documented in the protocol: Six normal sub-
jects with hiatal hernia and reflux, three subjects with asthma
hiatal hernia and reflux and eight subjects with asthma and reflux.
Baseline pulmonary functions were obtained before and after and
intra-esophageal double-blind challenge with 0.1N HCl. No unusual
problems were encountered. The data was analyzed and recorded.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78:	0.5
FY 79:	0.5

PROGRESS

From July 78 through January 79 the above patients were studied. The
protocol was completed. The three control groups, the normals, the
patients with reflux and no history of asthma and those patients with
asthma who did not have reflux showed no significant change in pul-
monary function measurements on hydrochloric acid provocation. In
thirteen patients who had a clinical history of reflux and asthma and

WORK UNIT 78/111

PROGRESS - continued

a positive Bernstein test, there was a significant increase in total respiratory resistance upon acid stimulation. When these patients received antacids with relief of symptoms, there was a return to baseline. This work supported a previous study that suggested a reflex mechanism could be involved in the clinical association between asthma and gastroesophageal reflux.

Publications: none

Presentations:

- (1) Spaulding, H.S., et al: Further Investigation of Gastroesophageal Reflux and Reflex Bronchoconstriction. Presented: American Academy of Allergy, New Orleans, LA, April 1978.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Investigation of Laser Nephelometry for Measurement of
"Blocking Antibody"

WORK UNIT NO: 78/112

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVE

To evaluate the feasibility of measuring blocking antibody titers to allergy extracts by use of laser nephelometry.

TECHNICAL APPROACH

Currently available rabbit antisera for specific antigens from registered protocols will be used as well as currently available sera from patients in an approved study. Approximately 100 human serum samples will be tested for the presence of blocking antibody to a minimum of two allergen's each. It has been shown that in some assay systems the Laser Nephelometer Curve can measure as little as 10 ng/ml serum protein. A standard curve will be constructed with allergen and varying dilutions of rabbit antisera for this allergen. This curve will be obtained and plotted graphically three times to show reproducibility. The same rabbit antisera will be evaluated with passive hemagglutination for titer which will be used as reference. Each human serum sample will be mixed with a standard amount of allergen and the change in turbidity will be compared to the dilutions of the standard rabbit serum. Blocking at

antibody values can be expressed in nephelometry units or can be related back to the passive hemagglutination titer. In most cases, there will be no requirement for dilutions of the human serum as such. Many specimens can be tested with minimal technician time and the equipment input. The technique of applying laser nephelometry for blocking antibody evaluation when perfected can be adapted to measure other antibodies of the IgG class, or IgM class resulting post immunization levels for numerous types of particulate and non-particulate types of vaccines.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	1.0
	FY 79:	1.5

WORK UNIT NO 78/112

PROGRESS

It was demonstrated employing rabbit antisera and appropriate antigens, a curve could be generated by the laser nephelometer which reflected serial dilutions of the antisera. Similar changes could be shown in serum taken from allergy patients prior to and during the course of allergy immunotherapy when these serum specimens in dilutions were mixed with allergen extracts. It did not however prove to be a very sensitive means of measuring blocking antibody.

Publications: none

Presentations:

- (1) Mansfield, L.E.: Laser nephelometry in the measurement of blocking antibodies. Presented: Annual Meeting of the American College of Allergists, Miami Beach, Florida, 22 January 1980.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effects of Salicylic Acid on Fatty Acid Oxidation in Rat
Skeletal Muscle Mitochondria.

WORK UNIT NO.: 78/113

PRINCIPAL INVESTIGATOR: Robert E. Jones, CPT, MC

ASSOCIATE INVESTIGATOR: Gerald S. Kidd, MAJ, MC

OBJECTIVES

The principal objective of this protocol is to elucidate the mechanism of salicylate-induced enhancement of fatty acid oxidation. The major investigative effort has been placed upon studying the kinetics of fatty acid:CoASH ligase (AMP) (E.C. 6.2.1.3).

TECHNICAL APPROACH

Rat skeletal muscle mitochondria are isolated from the quadriceps femoris muscle group. Ligase activity is determined with a radio-chemical-millipore filter procedure. Salicylic acid, in varying concentrations, is co-incubated in the reaction mixture which contains ATP, Mg(2+), (3H)CoASH and palmitic acid. Statistical analysis is performed with the Student's paired t test.

Manpower (in professional man years): 0.17

Funding (in thousands) FY 79: 0.8

PROGRESS

Salicylic acid enhances the enzymatic rate of fatty acid:CoASH ligase (AMP). It appears this action is mediated by increasing the enzyme affinity for substrate (palmitic acid). In kinetic terms, salicylic acid lowers the Michaelis constant (K_m) from 0.0035 mM in controls to 0.0022 mM ($p < 0.007$) without altering the maximal velocity (V_m). Similar parameters have been determined for CoASH, Mg(2+) and ATP. Dose response curves are pending.

WORK UNIT 78/113

Publications:

- (1) Jones, R.E. and Askew, A.W.: Effects of Salicylic Acid on Fatty acid Oxidation in Muscle Mitochondria. (Manuscript in preparation).

Presentations:

- (1) Jones, R.E.: Pharmacological Augmentation of Fatty Acid Oxidation: Potential Benefits in Untrained Individuals. Presented: Army Science Conference, 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Treatment of Systemic Scleroderma with Minoxidil (U-1858).

WORK UNIT NO.: 78/114

PRINCIPAL INVESTIGATOR: Paul B. Thompson, MAJ, MC

ASSOCIATE INVESTIGATORS: John L. Aeling, COL, MC
Robert G. Claypool, COL, MC
Steven R. Bailey, CPT, MC

OBJECTIVES

To determine if Minoxidil is a useful, vasoactive drug for the control of systemic scleroderma and the associated Raynaud's phenomena.

TECHINAL APPROACH

Patients with systemic scleroderma are entered into this double-blind cross-over study, using Minoxidil in low doses and followed at bi-weekly and monthly intervals. Hospital admissions as indicated for dosage increase and the performance of laboratory studies.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: 0.0
FY 79: 6.0

PROGRESS

In June of 1979, the first patient was admitted to the protocol, having received the drug and suitable placebo from Upjohn and Company in Kalamazoo, Michigan. Since June, approximately six patients have been entered into the Minoxidil protocol, each suffering from progressive systemic scleroderma. No patient, to this date, has suffered any adverse reactions secondary to the medication or placebo, and final report on the significance of the study awaits the one year mark, when the code can be broken and the appropriate figures compared for statistical significance.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Effect of Immunotherapy on the Tissue Threshold to Allergen:
Correlation with Alterations in Serum IgE and Blocking Antibody.

WORK UNIT NO.: 78/115

PRINCIPAL INVESTIGATORS: B. S. Dantzler, MAJ, MC
W. R. Tipton, COL, MC

ASSOCIATE INVESTIGATORS: T. P. O'Barr, Ph.D., DAC
H. S. Nelson, COL, MC

OBJECTIVES

To attempt to confirm early reports of a decreased sensitivity to the skin and conjunctiva to allergens occurring within a few weeks of immunotherapy, and to attempt to correlate these changes, if found, with changes in serum levels of specific IgE and specific blocking antibody.

TECHNICAL APPROACH

1. Patients: Patients studied will have seasonal allergic rhinitis due to weed pollen, they will have been selected for pollen extract immunotherapy on the basis of the usual clinical criteria, will never have received immunotherapy in the past, and will give informed consent to participate in the study.
2. Treatment: Treatment will be with aqueous pollen extract which will be reconstituted from lyophilized extract (Greer). Fresh vials will be reconstituted every two weeks and fresh dilutions for measurement of tissue reactivity will be made the day they are utilized.
3. Challenges: Prior to initiation of immunotherapy, every two weeks during immunotherapy, and at the completion of three months, the following measurements will be made:
 - a. Nasal challenge threshold.
 - b. Prick test threshold employing aqueous extract (10-fold solutions performed in duplicate).

WORK UNIT 78/115

TECHNICAL APPROACH - continued

c. Conjunctival threshold employing aqueous extract (10-fold dilutions). For the first and last measurement, threshold will also be determined to an unrelated pollen allergen not included in the patient's immunotherapy.

d. Immunologic studies: At the same time as the challenges, blood will be obtained for immunologic studies. These will include RAST for the treated and untreated allergen, blocking antibody by passive hemagglutination, RAST inhibition, or other methods which will be worked on during the course of the study. If possible, leukocyte histamine release will be performed at the beginning and end of the study period.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 78:	2.0
	FY 79:	2.0

PROGRESS

This study has been completed.

Publications:

- (1) Dantzler, B.S., Tipton, W.R., O'Barr, T.P., Nelson, H.S.: The Effect of Immunotherapy on the Tissue Threshold to Allergen: Correlation with Alterations in Serum IgE and Blocking Antibody. (abst.) American Academy of Allergy, Atlanta, GA, Feb 1980.
- (2) Abstract for von Pirquet Award, American College of Allergy.

Presentations:

- (1) Dantzler, B.S., Tipton, W.R., O'Barr, T.P., Nelson, H.S.: The Effect of Immunotherapy on the Tissue Threshold to Allergen: Correlation with Alterations in Serum IgE and Blocking Antibody. Presented: Annual Pulmonary Symposium, Fitzsimons Army Medical Center, Aurora, CO, September 1970.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Effect of Positive and Negative Air Ions on Pulmonary Functions
in Patients with Bronchial Asthma.

WORK UNIT NO: 78/116

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To evaluate the short-term response of patients hospitalized with
bronchial asthma to an increase in the ambient concentration of negative
ions.

TECHNICAL APPROACH

Patients with bronchial asthma whose clinical condition is stable and
medication is constant will be exposed on two consecutive days for
two consecutive periods of six hours to either an increased concentration
of positive or negative small air ions. Response will be monitored
by Pulmonary Function Studies.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	5.0

PROGRESS

Funding has been obtained and the equipment ordered but the study
itself has not begun.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Effect of Parasitic Infestation on Immediate Skin Test Reactions.

WORK UNIT NO: 78/117

PRINCIPAL INVESTIGATORS: Praphan Phanuphak, M.D., Ph.D.
Harold S. Nelson, COL, MC
Lyndon E. Mansfield, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To determine whether antiparasite antibodies of the IgE class present in high concentrations in patients with infestations are able to saturate receptors in the mast cell and in so doing block mast cell sensitization by IgE antibody directed toward inhaled allergen.

TECHNICAL APPROACH

Evidence for mast cell IgE receptor saturation will be sought by comparing the direct immediate wheal and flare skin test to circulating levels of IgE specific for that same allergen. The clinical portion of the study will be performed in Thailand by Dr. Phanuphak. The laboratory support will be performed at Fitzsimons.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 78: 0.0
FY 79: 0.0

PROGRESS

This study has not yet been instituted.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A precision measurement of anatomic deadspace using multiple inert gas analysis, comparison with Fowler's technique and application to steady-state diffusion estimates.

WORK UNIT NO: 78/118

PRINCIPAL INVESTIGATOR: Michael E. Perry, LTC, MC

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

OBJECTIVES

To experimentally confirm a proposed new procedure for anatomic deadspace measurement which has important advantages over conventional techniques.

TECHNICAL APPROACH

Ten normal adult volunteers and ten abnormal adult volunteers will serve as the test population. Deadspace measurements are first performed on each subject using the technique of Fowler. Deadspace measurement will then be performed on each subject using the multiple inert gas technique.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 78: 5.0
FY 79: 5.0

PROGRESS

Extensive modification was made concerning the recording technique during both the Fowler and Kindig maneuvers. Inspiratory volume is accounted for during Fowler technique as well as expiratory flow rate and both are corrected for gas viscosity. Six normal patients have been extensively studied to date and very precise measurements could be made by both techniques, the range of values being approximately 15cc. There are consistent differences in some individuals, however, between the two techniques which we feel at this time is most likely due to a time dependent variation in mixing deadspace volume particularly evident in the Fowler technique.

WORK UNIT 78/118

Publications:

- (1) Kindig, N.B., Martin, B., Morgan, E., Filley, G.F.: "Ventilation Variations at Constant Load Exercise". Federation Proceedings 38, 1050, 1979.
- (2) Kingig, N.B., Zimmerer, R.W., Hazlett, D.R.: Automation and Profile; Computer Simulation:. Clinical Engineering, Six, 68-69, 1978.
- (3) Hazlett, D.R., Zimmerer, R.W., Kindig, N.B.: "Ultrasound in Tissue Characterization:. Medical Instrumentation, 11:24, 1979.
- (4) Kindig, N.B., Editor: "Proceedings of the 16th Annual Rocky Mountain Bioengineering Symposium and 16th International ISA Biomedical Sciences Instrumentation Symposium". Biomedical Sciences Instrumentation, 15, Instrument Society of America, Pittsburg, 1979.

Presentations:

- (1) Kindig, N.B.: Physiologic Deadspace; Influence of Pattern of Breathing. Presented: 32 Annual Pulmonary Symposium, FAMC, Aurora, CO, September 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: The Effect of Aspirin on Platelet Aggregation in Aspirin Sensitive Asthmatics.

WORK UNIT NO: 78/119

PRINCIPAL INVESTIGATORS: Robert A. Gillham, LTC, MC, USAF
Richard E. Danziger, CDR, MC, USN

ASSOCIATE INVESTIGATORS: Harold S. Nelson, COL, MC
T.P. O'Barr, Ph.D., DAC

OBJECTIVES

To determine whether the intolerance to aspirin and other related substances manifested by some patients with bronchial asthma could be diagnosed by an in vitro test. Since these drugs have in common the inhibition of cyclo-oxygenase and that inhibition of prostaglandin synthesis is felt probably to be related to the idiosyncratic reactions to the drugs, the in vitro model chosen was the inhibition of platelet aggregation and generation of thromboxane.

TECHNICAL APPROACH

The plan is to utilize the platelet aggregation assay which is already being performed in the clinical investigation laboratory. The first stage will involve studying 5 or 6 normal individuals. These individuals will have their platelet aggregation measured following the in vitro addition of incremental amounts of aspirin to their platelet rich plasma. Following the preliminary work to establish a dose response curve for the effect, both in vivo and in vitro of aspirin exposure on the platelet aggregation of normal individuals, similar studies will be performed in patients with known aspirin sensitivity. The in vitro doses of aspirin employed in an aspirin sensitive patient's platelet system will be similar to those employed in the normal individuals, which should encompass the range from no response to completed response. Pulmonary function studies will be performed on the asthmatic patients employing a Jones Pulmonar both prior to the ingestion of aspirin. In addition to the usual visual measurement of platelet aggregation, quantitation of platelet aggregation will be attempted by assay of Thromboxane B₂ by a method currently being developed in the clinical investigation laboratory.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 78: 1.0
FY 79: 1.0

WORK UNIT NO 78/119

PROGRESS

A number of variables have been examined in order to develop a reproducible and sensitive assay for the prostaglandin inhibiting actions of aspirin. After the development of these assays, patients with and without aspirin sensitivity have been investigated. Thus far it has not been possible to distinguish between the normal and aspirin intolerant patient by any assay method which has been employed.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Diabetic Treatment Study: Assessment of Metabolic Control and Change in Quality of Life Following Short Term Treatment of Diabetic Patients with Tolazamide.

WORK UNIT NO.: 78/120

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, COL, MC

ASSOCIATE INVESTIGATORS: Gary L. Treece, LTC, MC
Francis G. Henderson, MD, Upjohn Monitor
J.T. Keene, Upjohn Medical Associate
Annie Shackelford, MT, DAC
Leonard R. Sanders, CPT, MC

OBJECTIVES

The objective of this double blind pilot study is to determine if the methodology employed will adequately determine whether maturity-onset, non-ketotic diabetic patients feel and function differently when their blood sugars are controlled.

TECHNICAL APPROACH

Patients with moderate diabetes mellitus are introduced into a double blind study where they will be treated with placebo or with Tolazamide tablets. The dose of the placebo and the Tolinase is regulated according to blood sugar determinations on frequent follow-up of patients. In addition to controlling the metabolic parameters of the disease as measured by hemoglobin A1C, fasting blood glucose determinations and symptomatic state of the patient, the patient will complete a questionnaire which will assess his quality of life.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)	FY 78:	0.2
	FY 79:	0.0

PROGRESS

To date, 7 patients have entered the study and are now in the long term follow-up phase of the study. It has been determined by the Upjohn Company that on preliminary analysis of data from three centers by the

WORK UNIT 78/120

PROGRESS - continued

Monitor of the study that this study is not determining quality of life differences in patients on placebo versus Tolazamide. For this reason, the study has been requested to enter no new patients and to continue the long term follow-up for the duration of the study on those patients currently in the study.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Determination of Possible Cross Activity Between Western
Grass Pollens and the More Common Northern Grass Pollens

WORK UNIT NO: 78/121

PRINCIPAL INVESTIGATOR: Bruce G. Martin, MAJ, MC, USAF

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVE

To study the cross allergenicity of extracts of common western prairie
grasses and to compare them to the already well-studied northern
pasture grasses and Bermuda grass.

TECHNICAL APPROACH

The principal approach has been to employ the RAST inhibition technique
to determine cross allergenicity.

Manpower (in professional man years): 0.2/yr

Funding (in thousands): FY 78: 1.0
FY 79: 1.0

PROGRESS

RAST allergen disks have been prepared for eight of the grasses of
interest. A serum pool has been prepared from blood of patients with
4+ prick tests to various grass extracts. RAST inhibition is currently
being performed employing disks to pooled serum and thirteen different
grass extracts as inhibitors. In addition, correlations of skin test
results and isoelectric focusing have been employed to compare cross
reactivity and similarity of protein profiles.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effects of Dietary Fructose in Diabetes Mellitus.

WORK UNIT NO.: 78/122

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, COL, MC

ASSOCIATE INVESTIGATORS: Phyllis A. Crapo, UCHSC, Denver, CO
Jerrold M. Olefsky, M.D., UCHSC, Denver, CO
Orville G. Kottlerman, UCHSC, Denver, CO
Jon Insel, M.D., UCHSC, Denver, CO

OBJECTIVES

To see if different kinds of simple carbohydrates (fructose, glucose, sucrose) elicit different postprandial plasma glucose, insulin and glucagon response when administered to diabetic patients (as simple agents or in test meals). It is hypothesized that there is a striking and therapeutically significant difference in postprandial responses in normals versus diabetic patients.

To assess longer term (three weeks) effects of feeding diets enriched with fructose, rice and bread on the postprandial response to test meals and twenty-four hour plasma glucose and insulin levels, glucose tolerance, VLDL-TG production rates, plasma triglycerides and HDL levels. It is hypothesized that such a diet will lead to a significant reduction in the day assessed profile of plasma insulin, glucose and lipid levels and that there will be improved glucose tolerance in diabetics treated.

To assess the postprandial response to natural cooked foods (cake and ice cream) which have been prepared with either fructose or sucrose. This aim takes advantage of the fact that fructose is a natural nutrient sweetener of greater potency than glucose or sucrose which can be readily incorporated into the Western diet and may well be very pertinent in regards to the present controversy regarding the cyclamates and saccharin as artificial food sweeteners. If fructose plays an unimportant role in carbohydrate metabolism, its use as a food sweetener might have therapeutic values in management of large diabetic populations.

TECHNICAL APPROACH

Three groups of subjects will be studied to include 1) chemical diabetics, 2) adult onset, non-ketotic diabetics with significant fasting hyperglycemia (plasma glucose levels greater than 140 mg% on three different occasions) and 3) age and weight matched diabetic control patients. These patients will undergo acute studies where their hormonal responses will be determined to glucose, sucrose and fructose and chronic studies where the patient will be fed diets containing mixed test meals of various starches containing calories of fructose or sucrose and glucose. Postprandial hormonal responsiveness again will be measured. Each of the diets will be fed for a period of 3 weeks. At the end of this time the postprandial plasma glucose, insulin and glucagon responses will be determined following the ingestion of 50 grams of glucose, sucrose and fructose. (As described above.) Likewise, each patient's tolerance will be tested with a standard glucose to tolerance test before and after the 3 weeks of the chronic dietary period. The influence of diet on triglyceride metabolism will be determined by the measurement of VLDL-TG production rate and fasting triglyceride levels, before and after the dietary period.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 78: 0.1
FY 79:

PROGRESS

This study has not yet been initiated.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A comparison of the Zimmerer and Dubois techniques of airway resistance measurements by body plethysmography.

WORK UNIT NO: 78/123

PRINCIPAL INVESTIGATOR: Michael E. Perry, LTC, MC

ASSOCIATE INVESTIGATORS: Robert W. Zimmerer, Ph.D., Consultant
Robert J. Browning, B.S., DAC

OBJECTIVES

To compare a clinically untried measurement of airway resistance with a standard technique.

TECHNICAL APPROACH

Ten normal adult volunteers and ten adult volunteers with pulmonary disease will undergo forced vital capacity maneuvers in the body plethysmograph. Data will be analyzed by the method of Dubois and simultaneously by a new method developed in this laboratory. Test results will be tabulated and the correlation between the two studies sought.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 78: 5.0
FY 79: 5.0

PROGRESS

A heated screen pneumotach (Hans Rudolph) was extensively tested and found to be much superior to the heated pneumotach used previously which provided uneven heat flux. This pneumotach heat exchange during expiration was found to be minimal. A different valving arrangement has been instituted on the plethysmograph to allow venting just prior to the forced maneuver which reduces leak artifact to a minimum. The computer program has been modified to allow for box drift during the course of the measurement, to account for pneumotach back pressure and to account for the known linear pneumotach response to flow. The computer program was also radically altered since it was discovered that numerical integration of collected data was inducing significant

WORK UNIT 78/123

PROGRESS -- continued

cumulative air. The computer program now calculates a alveolar pressure from a constant baseline corrected only for box drift. Six normal volunteers have been extensively studied to date and consistent differences were found between Dubois and our technique. We have conclusively shown that airway collapse occurs when flows temporarily exceed the flow volume envelope. Airway resistance is found not to be constant but to increase as a result of turbulence during moderate to strongly forced expiratory maneuvers.

Publications: none

Presentations:

- (1) Perry, M.E.: Plethysmographic Determinations of the Alveolar Pressure/Flow Patterns. Presented: 32nd Annual Pulmonary Symposium, FAMC, Aurora, CO, September 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A self consistent method of single breath DLCO measurement.

WORK UNIT NO: 78/124

PRINCIPAL INVESTIGATOR: Michael E. Perry, LTC, MC

ASSOCIATE INVESTIGATORS: Neal B. Kindig, Ph.D., Consultant
Robert J. Browning, B.S., DAC

OBJECTIVES

To experimentally confirm a proposed new method of DLCO measurement.

TECHNICAL APPROACH

Ten normal adult volunteers will perform standard single breath DLCO maneuvers, but will hold their breath for various predetermined times. Data will be analysed off line by computer which will correct for volume averaging and effective breath-holding time and the calculation of diffusion capacity. If the theoretical approach is self consistent the calculated diffusion capacity should remain constant regardless of breathing pattern or gas collection timing.

Manpower (in professional man years): 0.4/yr

Funding (in thousands)	FY 78:	5.0
	FY 79:	5.0

PROGRESS

A specially designed solenoid activated multivalve assembly has been purchased from Hewlett-Packard for this protocol. Fogg Systems Incorporated has completed their design of the instrumentation required for this protocol and is presently assembling the special apparatus. Our computer specialist, Mr. Robert Browning, is presently writing the computer program for the LSI 11/03 minicomputer. We expect to have this system operational by January 1980, at which time the actual data collection can begin.

WORK UNIT 78/124

Publications:

- (1) Kindig, N.B., Hazlett, D.R., Filley, G.F.: "Timing and Volume Averaging in Single Breath DLCO Measurement". The Physiologist, 21:64, 1978.

Presentations:

- (1) Zimmerer, R.W.: Simulated Diffusion Testing. Presented: 32nd Annual Pulmonary Symposium, FAMC, Aurora, Colorado, September 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Adjuvant Therapy of Premenopausal Patients with EBP (+) Breast Cancer with CMF alone versus CMF plus Tamoxifen and EBP (-) Breast Cancer with CMF alone versus Adriamycin and Vincristine followed by CMF.

WORK UNIT NO.: 78/125

PRINCIPAL INVESTIGATOR: John C. Michalak, LTC, MC

ASSOCIATE INVESTIGATORS: Nicholas J. DiBella, LTC, MC
Kyle M. Fink, M.D., Hematology/Oncology Assoc.

OBJECTIVES

1. To determine whether therapy with the antiestrogen tamoxifen has an additive effect to adjuvant chemotherapy in premenopausal patients with EBP (+) breast cancer who are at high risk for recurrence.
2. To determine whether the results of adjuvant chemotherapy with CMF can be improved by first giving 3 months of intensive chemotherapy with adriamycin and vincristine in premenopausal patients with EBP (-) breast cancer.

TECHNICAL APPROACH

This is a randomized clinical study of the Colorado Oncology Group.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 79: 0

PROGRESS

Six patients have been entered into this study during FY 79. Moderate myelosuppression has been observed in three patients requiring dose reductions. One patient (TG) experienced an allergic reaction and had to be taken off the study. Allergy evaluation preliminarily suggests the reaction was due to Methotrexate. Five of six patients continue on study without evidence of disease. The sixth patient relapsed (FW) after being off CMF for one month, with bony metastasis.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: The Systematic Evaluation of Urticaria. I. Response to Therapy.
II. Evaluation with Skin Biopsy.

WORK UNIT NO.: 78/126

PRINCIPAL INVESTIGATOR: Gary B. Carpenter, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

The objectives are: to study the histology of skin biopsies of patients with urticaria to determine the incidence of histologic evidence of vasculitis underlying this condition; to systematically evaluate the use of the current management program employed by the Allergy Clinic at Fitzsimons including routine sinus x-rays and the utilization of three sequential diet manipulations; and to evaluate in double-blind fashion the efficacy of adding Cimetidine and H₂ blocker to an H₁ blocking agent in symptomatic control of chronic urticaria.

TECHNICAL APPROACH

Specifically, standard treatment of urticaria with a histamine-type-one (H₁) blocker, hydroxyzine (Atarax), will be compared with a combination of H₁ and histamine-type-two (H₂) blocker, Cimetidine (Tagamet^R). Information will be gathered in a double-blind controlled fashion to compare the different clinical responses in the two groups.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Due to a long delay in obtaining the Cimetidine and placebos, this protocol is just getting underway.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Does Neoplastic Disease Produce a Positive Secretin Test?

WORK UNIT NO.: 78/127

PRINCIPAL INVESTIGATORS: Hugh P. McElwee, MAJ, MC
Nicholas J. DiBella, LTC, MC
Steven Bailey, CPT, MC

ASSOCIATE INVESTIGATOR: David Jarvis, SP5

OBJECTIVES

To determine if the secretin test is positive in neoplastic disease.

TECHNICAL APPROACH

The secretin test is felt to be specific for diagnosis of the Zollinger Ellison syndrome. We have an index case of one patient with oat cell carcinoma who had a positive secretin test and no evidence of Z-E at autopsy. We are therefore testing certain patients with hormonally active cancers to see if they produce positive secretin tests.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 78: 0.5
FY 79: 0.5

PROGRESS

We have tested 11 patients to date. There are no positive secretin tests in patients or controls. There is however a marked difference in the response curve of gastrin to secretin in normal vs. control patients. These differences are being further evaluated as we continue our testing.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Assessment of Postprandial Plasma Glucose, Insulin and Glucagon Response to Different Orally Administered Complex Carbohydrates in Diabetic Subjects (UCMC, Endocrine, Cooperative Study).

WORK UNIT NO.: 78/128

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, COL, MC

ASSOCIATE INVESTIGATORS: Phyllis A. Crapo, R.D., UCHSC, Denver, CO
Jerrold M. Olefsky, M.D. UCHSC, Denver, CO
Orville, G. Kolterman, M.D., UCHSC, Denver, CO

OBJECTIVES

To establish if feeding different simple and complex carbohydrates substantially affect plasma glucose and insulin values. This project will use mild diabetics, moderately severe diabetics and age and weight-matched, non-diabetic controls in a paired analysis of their response in plasma glucose, plasma insulin and plasma glucagon to 50 grams of carbohydrate presented as various meals.

TECHNICAL APPROACH

Selected diabetic patients suitable for the study were studied at the University of Colorado Medical Center, General Clinical Research Unit, where their plasma glucose, insulin and glucagon responses were determined following the ingestion of glucose, potato, rice, corn and wheat (breach starch). The test meals were given in a random order to these diabetic subjects. Statistical analysis on data will be carried out by the use of the paired t test for dependent means.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: 0.1
FY 79:

PROGRESS

The study is completed. Approximately 5 of the group of patients studied were from Fitzsimons Army Medical Center. The major findings

WORK UNIT 78/128

PROGRESS - continued

of the study were that the postprandial glucose response to different starches is quantitatively different. In order of less carbohydrate intolerance to more carbohydrate intolerance, the following ranking of starches was noted: Rice, wheat bread, corn, potatoes. Noteworthy, potatoes and glucose were equally diabetogenic in this group of patients.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Respiration During Sleep in Myxedema and Hypothyroidism

WORK UNIT NO.: 78/129

PRINCIPAL INVESTIGATOR: Leonard R. Sanders, CPT, MC

ASSOCIATE INVESTIGATORS: Fred D. Hofeldt, COL, MC
Clifford Zwillich, MD, Consultant

OBJECTIVES

The objective of this study is to determine whether patients with myxedema have abnormalities in respiration which occur during sleep which in turn might explain the daytime symptoms of fatigue and hypersomnolence.

TECHNICAL APPROACH

At least six uncomplicated, adult myxedema patients will be studied after their myxedema is confirmed by clinical examination and laboratory determinations. After myxedema is determined, the patient will have his ventilatory drives to hypoxia and hypercapnia as well as normal ventilation studies determined. He will then go to the Cardiopulmonary Research Unit at the University of Colorado where a sleep study will be performed. The study will consist of two consecutive nights of sleep where the patient will have his EEG monitored, heart monitored with an electrocardiogram, respiratory pattern monitored with a strain gauge attached to the patient's chest wall and oxygen saturation determined by the means of an ear oximeter. The patient will then be replaced with thyroid hormone and after there is documentation that the patient is euthyroid both by clinical examination and laboratory values, the above sleep study will be repeated.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 78: 0
FY 79: 0.9

PROGRESS

Since the protocol was only recently approved by the Surgeon General's

WORK UNIT 78/129

PROGRESS - continued

Office, progress in this study has been minimal and therefore will have to be reported after the patients are studied.

Publications and Presentations: none

STATUS

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Investigation of the Tumor Reduction Effect of Combined Sodium-L-Ascorbate and 5FU Chemotherapy in Transplanted B16 Melanoma of Mice.

WORK UNIT NO.: 79/100

PRINCIPAL INVESTIGATORS: N.J. Martin, MAJ, MC
George L. Brown, Ph.D., COL, MSC
Joseph Lima, DAC

ASSOCIATE INVESTIGATORS: Frederick Rangel, DAC
Wilson C. Bourg, III, MAJ, MC

OBJECTIVES

To evaluate the possible synergism of 5-fluorouracil and sodium-L-ascorbate against tumor cells in vivo.

TECHNICAL APPROACH

The B16 melanoma was transplanted into the BFD, Jackson Laboratory male mouse hosts. An optimal tumor cell number was established to provide an 18-22 day range of mouse death. This was 75,000 cells/cu.mm. In addition to this, the maximum safe dose range for 5FU was established in the BFD, hybrid Jackson mouse and this maximum safe dose of 5FU was found to be 20mg/kg.

The mice were divided into five groups; groups 1 through 4 received the B16 melanoma. Group 5 was a controlled group which received only sodium chloride injections. Group 1 received only oral vitamin C as therapy in a concentration of 0.1%. Group 2 received no ascorbate but only 5FU given on Days 2 through 10 via intraperitoneal injection. Group 3 received oral vitamin C in the previously mentioned concentration and intraperitoneal 5FU in the previously mentioned dose and concentration. Group 4 received B16 melanoma only. Group 5 received no B16 melanoma but received vitamin C at 0.1% daily until death and 5 FU at the previously mentioned concentration.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 79: 2.5

PROGRESS

Between March 1979 and October 1979, two groups of mice were evaluated. As mentioned previously, the maximum safe dose for 5FU was determined to be 20mg/kg per day by intraperitoneal injection for Days 2 through 10 by establishing lethality data with doses of 10mg/kg, 20mg/kg, 25mg/kg, 30mg/kg, and 40mg/kg. The optimal survival time to assess maximal effect of chemotherapy was established by trial and error and was found to be approximately 75,000 cells/cu.mm. inoculated intraperitoneally.

The first experiment revealed no evidence of any facilitation of the effect of 5FU either in toxicity or in beneficial effect against the tumor cells, however, it was an inadequate trial. This was an inadequate trial because for 5 days of the chemotherapy, the mice received sodium-L-ascorbate of a different pH which was not as well accepted and was, therefore, delivered to the animals in suboptimal amounts. This first one involved 60 animals.

The second experiment run was begun in the fall of 1979. It involved 75 mice. The second trial was also an inadequate study since all groups receiving 5FU had very high death rates within the first 15 days of the study. It is suspected that the 5FU concentration was too high in these groups, however, the final reason for the inordinate sensitivity to 5FU has not been determined at this time. This study was unable to conclusively show any difference between vitamin C and 5FU-treated mice with melanoma, however, it is also inadequate.

Plans are underway at this time to begin a third experiment in November 1979.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Relationship of Granuloma Annulare (GA) to Diabetes Mellitis (DM).

WORK UNIT NO.: 79/101

PRINCIPAL INVESTIGATOR: Gene E. Graff, D.O., CPT, MC

ASSOCIATE INVESTIGATORS: Bernard F. Davies, MAJ, MC
John L. Aeling, COL, MC
Fred D. Hofeldt, COL, MC
D. M. Strong, M.D., WRAMC
George L. Brown, Ph.D., COL, MSC

OBJECTIVES

To determine if an association exists between GA and DM by special laboratory test, including HLA typing.

TECHNICAL APPROACH

Patients with biopsy proven GA are studied for concurrent DM historically, clinically, and following oral and intravenous glucose challenge. HLA typing is also done. Baseline studies include: Complete physical examination, US, CBC, sedimentation rate, SMA-18, triglycerides, cholesterol, HDL, two-hour pc blood glucose, TSH, T3, T4, resin uptake T3, EKG if indicated. Parameters monitored following glucose challenge include serum insulin, glucose, glucagon, growth hormone, cortisol.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 78:	1.7
FY 79:	1.7

PROGRESS

Between September 1978 and September 1979, eleven patients have been identified for this study. Eight patients have been completely or incompletely studied. Three-hour OGT studies are pending in five patients. Preliminary results show two patients to be diabetic and one patient with idiopathic reactive hypoglycemia. HLA typing will be done terminally.

WORK UNIT 79/101

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Mechanism(s) of Insulin Resistance in Obesity (Cooperative Study Between Fitzsimons and Endocrine Division, University of Colorado Medical Center).

WORK UNIT NO.: 79/102

PRINCIPAL INVESTIGATOR: Gary L. Treece, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVE

Insulin resistance is a characteristic feature of obesity and has been causally implicated in many of the clinical complications of the obese state. However, the mechanisms responsible for insulin resistance in obesity are not known. The plan is to develop in vivo insulin dose response curves in obese human subjects in order to delineate the mechanisms of insulin resistance in obese humans and to assess the relationship between in vitro insulin binding and in vivo insulin action.

TECHNICAL APPROACH

The overall plan will be to utilize the glucose clamp technique to elucidate the in vivo insulin-glucose uptake dose response curves in insulin resistant obese patients. Additionally, hepatic glucose production will be simultaneously determined in all studies to quantitate the contribution of this variable to total glucose turnover, and to assess the ability of different steady state plasma insulin levels to suppress the liver's capacity to secrete glucose. Finally, in vitro measurements of adipocyte insulin receptors will be performed so that the relationships between overall in vivo insulin sensitivity and insulin receptors can be assessed.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: 0

PROGRESS

Seven lean subjects and 17 obese subjects have completed the protocol.

WORK UNIT NO 79,102

PROGRESS - continued

To date, the data suggests that insulin resistance in obesity is a heterogenous disorder with some patients having a pure receptor defect consisting of a decrease in the number of insulin receptors (manifest by a rightward shift of the insulin dose response curves without a change in the maximal insulin stimulated glucose disposal), whereas the majority of adult obese subjects have a combined defect consisting of both a decrease in receptor number and a significant post-receptor defect.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Evaluation of Combined H₁ and H₂ Receptor Blocking Agents in the Treatment of Seasonal Allergic Rhinitis.

WORK UNIT NO: 79/103

PRINCIPAL INVESTIGATORS: Gary B. Carpenter, MAJ, MC
Antonio Bunker-Soler, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To determine whether the addition of a blocker of the H₂ receptor would provide greater symptomatic relief in patients with allergic rhinitis than was provided by H₁ blocking agents alone.

TECHNICAL APPROACH

Patients included in this study will be those consenting adults who give an unequivocal history of symptoms of seasonal allergic rhinitis, with or without asthma, occurring in August and September. All patients will receive during their symptomatic period, Chlorpheniramine, 8mg, tid. In addition, the patients will receive either Cimetidine, 300mg tid or 1 Os-Cal tablet, tid. Os-Cal in this case will serve as the placebo control since it is of approximately the same size and similar color to Cimetidine. Medication will be dispensed in two week increments which will always include Chlorpheniramine but for each patient will alternately include either the Cimetidine or the Os-Cal. Evaluation of symptoms response will be made by having patients complete, twice daily, symptom and medication score card. If in the judgement of the physician control of the patient's symptoms is not adequate, two alternative forms of medication will be available. Ordinarily the physician will prescribe Decadron Turbinaire, two activations into each nostril tid. If in the physician's judgement it is needed because of marked swelling or rhinorrhea, the Decadron Turbinaire will be preceded by a vasoconstrictive spray. If, in the physician's opinion, the patient's symptoms warrant its use, Prednisone may be given orally, 20mg bid for three days. Volumetric pollen sampling employing an intermittent roto-slide sampler will be performed six days per week commencing 15 July and continuing until 1 Oct.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 79: 0

WORK UNIT NO 79/103

PROGRESS

Patients with a clear history of weed season allergic rhinitis and a strongly positive skin test to at least one of the weeds prevalent in Colorado, were enrolled in the study. Throughout the weed season of August and September 1979, the patients kept a twice daily symptom score card and ingested regularly an H₁ blocking agent Chlorpheniramine. In alternate two-week courses they received, in addition to the Chlorpheniramine, either an H₂ blocking agent Cimetidine, or a placebo. The data has now been collected and is being analyzed.

Publications and Presentations: none

STATUS:

Ongoing.

SURGERY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

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

WORK UNIT NO.: 71/202

PRINCIPAL INVESTIGATOR: William W. Eversmann, Jr., COL, MC

ASSOCIATE INVESTIGATOR: Bertram Goldberg, LTC, MC

OBJECTIVES

To establish a pattern of peripheral nerve repair and recovery following injuries to peripheral nerves and in most cases neurotomy of the peripheral nerve.

TECHNICAL APPROACH

These patients are followed through questionnaire and outpatient physical examination in some cases attendant to a temporary duty retired list medical board for evidences of nerve recovery and disability.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

During FY 1979 patients have continued to return for follow up evaluation and an ongoing body of knowledge and clinical data continues to be collected for this study.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 73/219

PRINCIPAL INVESTIGATOR: John A. Vaccaro, MAJ, MC

ASSOCIATE INVESTIGATOR: Howard E. Fauver, COL, MC

OBJECTIVES

Investigation of and comparison of various modes of treatment of urological trauma with emphasis on newer surgical techniques to include renal vascular repair, Bench surgery and autotransplantation.

TECHNICAL APPROACH

Various techniques of vascular reanastomosis and autotransplantation will be performed. This will be followed by IVPs 2-4 weeks post-operatively to ascertain success or failure.

Manpower (in professional man years): 0.02/yr

Funding (in thousands)	FY 78:	1.5
	FY 79:	0.5

PROGRESS

This protocol continues as an important tool in instructing new residents in the intricacies of renal and renovascular surgery.

Publications:

- (1) Levisay, G.L.: Renal Autotransplantation in the Dog. Proc. of the Kimbrough Urological Seminar, January 1974.
- (2) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Proc. of the South Central Section, AUA, Denver, CO, 15-19 September 1974. (Published)
- (3) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion, Proc. of the Kimbrough Urological Seminar, Seattle, Washington, 5 October 1975.

WORK UNIT NO.: 73/219

Presentations:

- (1) Levisay, G.L.: Renal Autotransplantation in the Dog. Presented: Kimbrough Urological Seminar, Washington, D.C., January 1974.
- (2) Levisay, G.L.: Renal Autotransplantation in the Dog. Presented: South Central Section Meeting of the AUA, Denver, Colorado, September 1974.
- (3) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Presented: South Central Section of the AUA, Denver, Colorado, 15-19 September 1974.
- (4) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy. in the Dog. Presented: Kimbrough Urological Seminar, San Antonio, Texas, 14-19 November 1974.
- (5) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion, Washington, October 1975.
- (6) Page, M.E., and Weigel, J.W.: Exhibit-Renal Transplantation with Proximal Vena Caval. Presented: South Central Section Meeting in Urology, September 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Acalculous Biliary Tract Disease

WORK UNIT NO.: 73/221

PRINCIPAL INVESTIGATOR: None

ASSOCIATE INVESTIGATORS: None

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 acalculous biliary tract disease; (c) Evaluation of radiomanometry with pressures in the gallbladder and common duct in acalculous 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 cholecystokin 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 78:	0.0
FY 79:	0.0

PROGRESS

No new Principal Investigator was ever appointed to this study.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Screening Program for Military Children at High Risk for
Hearing Loss.

WORK UNIT NO.: 76/203

PRINCIPAL INVESTIGATOR: Susan T. Slibeck, M.S., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To screen infants and children for information indicating high risk for hearing loss so that early identification and treatment can be enhanced.

TECHNICAL APPROACH

Red Cross volunteers will screen the medical and family histories of all newborns, pediatric ward patients (0-6 years of age), and one-year old Well Baby Clinic patients through parent interviews and chart reviews. The investigator will review the gathered data for indications of high risk for hearing loss and designate children as AT RISK or NOT AT RISK. AT RISK children will be tested by an audiologist periodically for one year or until hearing loss is ruled out.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

This report concerns the active period of the High Risk Registry screening program (17 October 1976 to 31 November 1979). During that time, 1124 children were screened by 3 Red Cross volunteers; 426 of these children were considered AT RISK for hearing loss; and 86 children are currently being followed on the Registry as indicated.

WORK UNIT NO.: 76/203

PROGRESS - continued

Twenty Six children with depressed auditory acuity were identified. Audiometric testing and otologic consultation indicated significant hearing loss due to middle ear fluid, middle ear infection, or excessive cerumen. At the time of the screening, these hearing/medical problems had not been previously identified. Two of the 26 children also had a significant sensorineural loss requiring amplification with a hearing aid and special rehabilitation intervention. The ages of the four children ranged from 6 months to 3 1/2 years; thus achieving the objective of early identification and treatment.

The value of High Risk Registers is well documented: "Infants at risk for hearing impairment should be identified by means of history and physical examination" (National Joint Committee on Newborn Hearing Screening, 1973). The committee found that a High Risk Registry can increase identification of hearing impairment as much as ten fold. Reports of similar registers indicate that 1 out of 57 AT RISK children will be hearing impaired. The registry procedures used in this program have yielded a more economical result: 1 out of 186 AT RISK children were hearing impaired.

A problem which plagues and reduces the effectiveness of this program is the paucity of Red Cross volunteers offered despite repeated requests for additional help. At this time the project receives an average of 24 red Cross volunteer hours per month. Forty-five volunteer hours would provide minimal acceptable coverage.

Publications: None

Presentations

- (1) Slibeck, Susan T.: High Risk Factors for Hearing Loss. Presented: Pediatric Department, Fort Carson, Colorado December 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Use of Cyclic AMP in the Evaluation of Calcium Urolithiasis.

WORK UNIT NO.: 76/205

PRINCIPAL INVESTIGATOR: John A. Vaccaro, CPT, MC

ASSOCIATE INVESTIGATORS: Howard E. Fauver, COL, MC
Daniel W. Horne, MAJ, MC
Glenn W. Dunnington, LTC, MC

OBJECTIVES

To measure nephrogenous CAMP levels to differentiate renal causes of hypercalciuria from other causes.

TECHNICAL APPROACH

The use of various blood studies and urine collections to define the metabolic basis of stone disease in recurrent stone formers. The hallmark of these studies will be serum and urine cyclic AMP. Using these values, appropriate treatment will be prescribed to patients.

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

Funding (in thousands)	FY 78:	.3
	FY 79:	0

PROGRESS

Due to lack of manpower and increased workload on the Urology Service, we have been unable to continue with the research project and request that it be terminated.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Use of Nephrogenous Cyclic AMP In the Evaluation of Calcium Urolithiasis.

WORK UNIT NO.: 77/202

PRINCIPAL INVESTIGATOR: John A. Vaccaro, CPT, MC

ASSOCIATE INVESTIGATORS: Howard E. Fauver, COL, MC
Daniel W. Horne, MAJ, MC
Glenn W. Dunnington, LTC, MC

OBJECTIVES

The main objective of this protocol is to measure nephrogenous CAMP levels and, thus, differentiate renal causes of hypercalciurias from other causes. This can be calculated in the following manner.

$$C_{AMP} \text{ filtered} = C_{AMP} \text{ plasma} \times C_{CV} \times \text{time of collection}$$

$$CAMP \text{ nephrogenous} = CAMP_{Urine} - CAMP \text{ filtered}$$

TECHNICAL APPROACH

Serum samples for determining CAMP activity will be drawn with other appropriate lab tests on each visit per outline protocol 76/205.

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

Funding (in thousands) FY 78: .3
FY 79: 0

PROGRESS

Due to lack of manpower and increased workload on the Urology Service, we have been unable to continue with the research project and request that it be terminated.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Use of Urinary Prostaglandins in the Evaluation of Recurrent
Calculus Disease - Addendum to 76/205.

WORK UNIT NO.: 77/203

PRINCIPAL INVESTIGATOR: John A. Vaccaro, CPT, MC

ASSOCIATE INVESTIGATORS: Howard E. Fauver, COL, MC
Daniel W. Horne, MAJ, MC
Glenn W. Dunnington, LTC, MC

OBJECTIVES

Measure urinary prostaglandins as a possible cause of hypercalciuria
in recurrent stone formers.

TECHNICAL APPROACH

1. Working with protocol 76/205 the urine would be screened using a high performance liquid chromatographic separation of urinary prostaglandins F_2 , F_2a , E_1 , E_2 , and A via a phase column.
2. If a pattern of prostaglandin excretion could be determined, then a radioimmune assay could be developed for increased sensitivity of excretion.

Manpower (in professional man years): 0

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Due to lack of manpower and increased workload on the Urology Service, we have been unable to continue with this research project and request that it be terminated.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Anatomical and Physiological Development of the Flexor Tendon Sheaths in the Human Fetus.

WORK UNIT NO.: 77/204

PRINCIPAL INVESTIGATOR: William W. Eversmann, Jr., COL, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

The objectives of this study are to anatomically follow the embryological development of the flexor tendon sheaths in the human fetus to 20 weeks of age and biochemically analyze in coordination with the development of the flexor tendon sheath, the development of the contractility of the flexor muscle mass.

TECHNICAL APPROACH

Collection of human fetal specimens up to twenty weeks of age, gestational age, following voluntary interruption of pregnancy and study of **the development** of digits and the flexor tendon sheath by histological techniques and correlating this development with biochemical techniques of the flexor muscle mass contractability in order to establish a correlation between the development of the flexor muscles and the development of the flexor tendon sheath continues to be the mainstay of this project.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

During FY 1979 the Congress of the United States deleted funding for interruption of pregnancy on military personnel and their dependents in military treatment facilities. Obtaining specimens for this study then has been extremely difficult or impossible during the past fiscal year.

WORK UNIT NO.: 77/204

PROGRESS - continued

It is the hope of the investigator that changes in policy by the Congress of the United States, which may be pending in Congress at this time, will allow us to reinstate the gathering of material for this study and complete the study.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Anastomosis of the Dog Vas Deferens Using Microsurgical Technique.

WORK UNIT NO.: 78/200

PRINCIPAL INVESTIGATOR: Glenn W. Dunnington, LTC, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC
Howard E. Fauver, COL, MC
Torrence M. Wilson, MAJ, MC
John A. Vaccaro, CPT, MC

OBJECTIVES

To master the microsurgical anastomosis of the vas deferens.

TECHNICAL APPROACH

Standard bilateral vasectomy performed on mongrel male dogs. Three weeks later a two layer microsurgical anastomosis using 10-0 nylon is completed. Three weeks later the dog is sacrificed and bilateral vasograms completed.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 78: 1.3
 FY 79: 4.5

PROGRESS

Sixteen dogs have been completed and Dr. Dunnington and Dr. Wilson have mastered the use of the microscope. Dr. Vaccaro is in the process of learning the microsurgical technique.

Continued experimentation with various sutures and suture techniques has been performed. This is an indispensable tool for learning microsurgical technique. The expertise gained through this protocol has permitted the Urology Service, Fitzsimons Army Medical Center, routinely employing microsurgical vasovasostomy as a routine clinical procedure.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Clinical Study for Intraocular Lenses.

WORK UNIT NO.: 78/201

PRINCIPAL INVESTIGATORS: Andrew J. Cottingham, COL, MC

ASSOCIATE INVESTIGATORS: Richard A. Manson, COL, MC
Lance P. Steahly, LTC, MC
Floyd M. Cornell, MAJ, MC
Kevin J. Chismire, MAJ, MC
Craig A. Peterson, CPT, MC

OBJECTIVES

- 1). To determine postoperative visual acuity of patients receiving an intraocular lens, and to compare those results with those of a control group of patients who undergo cataract surgery but do not receive an intraocular lens.
- 2). To describe the occurrence and time course of postoperative ocular complications and adverse reactions both for intraocular lens implant subjects and for control subjects.
- 3). To compare the occurrence of adverse reactions and ocular complications in the implant group and in the control group, in order to delineate any significant differences.
- 4). To describe the occurrence of postoperative lens complications for the implant group, and their relationship to ocular complication.
- 5). To identify subgroups within the implant study population that are at "high risk" of particular complications as compared to the control group.

TECHNICAL APPROACH

After didactic courses, observations, laboratory practice and assistance with an experienced implant surgeon, a surgeon who can perform an accomplished cataract extraction, is then allowed to perform intraocular lens surgery under proper tutorage. Postoperative examinations include:

WORK UNIT NO.: 78/201

TECHNICAL APPROACH - continued

pachymetry, keratometry, and specular microscopy. Contraindications to surgery include: patients with good visual potential in only one eye, proliferative diabetic retinopathy, rubeosis irides, high axial myopia, and inadequately controlled glaucoma, Fuch's endothelial dystrophy, and a history of previous retinal detachments or uveitis.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Between September 1976 and February 1978, we implanted 25 intraocular lenses. Patients included 15 males and 10 females ranging in age from 53 to 83 years (mean age 68.6 years). Since March 1978, we have implanted an additional 33 intraocular lenses. Patients include 11 females and 22 males ranging from 23 to 89 years (mean age 65.7 years).

As a result of the past three years experience, we have evolved better guidelines for patient selection, better surgical techniques and improved guidance for postoperative care.

Our study includes tabulations of operative complications, postoperative complications, visual results, endothelial cell loss, corneal thickness changes, changes in corneal astigmatism, and residual refractive error.

The results of every ophthalmologist implanting intraocular lenses in the United States additionally compiled by computer in Washington, D.C. by the FDA, our results are a small part of this overall study. Final data from this massive study is to be released soon.

Publications:

- (1) Cottingham, A.J.: The Initial Fifty Intraocular Lens Implantations in an Ophthalmology Residency Training Program. Submitted for publication to the American Journal of Ophthalmology.

Presentations:

- (1) Cottingham, Jr., A.J.: "Keracoplasty". Presented: Optometry Meeting, FAMC, October 1978.
- (2) Cottingham, Jr., A.J.: Endophthalmitis - Cause and Treatment. Presented: University of Colorado Health Sciences Center, January 1979.

WORK UNIT NO 78/201

Presentations - continued

- (3) Cottingham, A.J.: Corneal Keratomycoses. Presented: University of Colorado Health Sciences Center, January 1979.
- (4) Cottingham, A.J.: Bacterial Corneal Ulcers. Presented: University of Colorado Health Sciences Center, January 1979.
- (5) Cottingham, A.J.: The Use of Vitrectomy Instrumentation in Anterior Segment Reconstruction. Presented: Scheie Institute Trauma Symposia Philadelphia, Penn, September 1979.
- (6) Cottingham, A.J.: An Analysis of the Initial Twenty-Five Intraocular Lens Implantations in an Ophthalmology Residency Training Program. Presented: 7th Biennial, Walter Reed Ophthalmology Post Graduate Course and Alumni Meeting, April 1978.
- (7) Cottingham, A.J.: An Analysis of the Initial Twenty-Five Intraocular Lens Implantations in an Ophthalmology Training Program. Presented: Bascom Palmer Eye Institute Annual Resident Alumni Meeting, June 1978.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of the Nitroblue Tetrazolium Test (NBT) in Pyogenic Arthritis Using Synovial Fluid.

WORK UNIT NO: 78/202

PRINCIPAL INVESTIGATOR: Robert M. Campbell, Jr., CPT, MC

ASSOCIATE INVESTIGATOR: Thomas G. Fry, III, CPT, MC

OBJECTIVES

To correlate the NBT test performed on synovial fluid with culture proven pyogenic arthritis in the knee joint.

TECHNICAL APPROACH

This is a coordinated study between the Orthopedic Service and Clinical Investigation Service, FAMC. Presently many patients are admitted to this facility with septic arthritis diagnosis. These subjects are subjected to joint fluid aspiration for routine studies. Many other patients with joint effusions secondary to conditions other than septic arthritis also have joint fluid aspirations for diagnostic purposes. In the present laboratory study it is planned that the remaining and not used joint fluid aspirate be evaluated for NBT reaction pattern and for serum protein studies. All patients whose joint fluid aspirates will be subjected to this protocol evaluation will be so informed and will be asked to sign a consent form. It is anticipated that approximately twenty (20) test and control subjects each will be evaluated. Control subjects are those individuals with joint effusions not due to septic arthritis conditions.

Two orthopedic housestaff will be responsible for submitting fluid to the Clinical Investigation Service for analysis. During the normal weekday laboratory hours the fluids will be processed by a CIS technician utilizing both the original technique of the NBT test as described by Park and by the cytocentrifuge technique as described by Gordon. At any other time than normal laboratory hours the NBT test will be conducted by either one of the orthopedic housestaff designated as investigators in this project. All NBT tests will be run within two hours of aspiration of the joint. When orthopedic housestaff do

WORK UNIT NO 78/202

TECHNICAL APPROACH - continued

process such slides, the actual counting of NBT positive cells on the slides will be done by laboratory personnel during normal laboratory hours to eliminate observer bias. The results of the NBT test and serum protein patterns of the joint fluid of patients with culture proved pyogenic arthritis will be compared to a controlled group of patients with joint effusions due to causes other than pyogenic arthritis.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.5

PROGRESS

As outlined in the original protocol the patients available for testing of the synovial fluid are few in number. To this date five patients have been accumulated and presently there seems to be only minimal correlation between the NBT test and the pyogenic culture proven arthritis of the knee joint.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Effects of Heterotopic Lymph Node Transplantation on Surgically Induced Lymphedema.

WORK UNIT NO: 78/203

PRINCIPAL INVESTIGATORS: Barry F. Shesol, MAJ, MC
Viktor Gottlieb, MAJ, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

The object of this project is to demonstrate that surgically induced lymphedema may be prevented by transplanting lymph node tissue into an area of prior lymphadenectomy. The degree of reduction of lymphedema is dependent upon the time that passes between the removal of lymph nodes and their replacement. Once lymphedema has occurred, lymph node transplants have little benefit, while if done initially can prevent lymphedema. The transplantation of lymph nodes may be accomplished as a microsurgical transplant, or as an island pedicle flap containing the lymphatic tissue.

TECHNICAL APPROACH

Male albino Fisher rats, weighing 300-450 grams, will be divided into five experimental groups. Each group will contain 10 animals and will be studied as outlined below:

Group I - Will serve as the control group. Each animal will undergo ipsilateral popliteal and inguinal lymphadenectomies in the left leg. At the same time a right inguinal lymphadenectomy will be done. The effect will be to create lymphedema in the left leg. Photos and measurements with a caliper at the ankle and 0.5 cm below the knee will be taken preoperatively and at days 1, 3, 7, and 10 postoperatively.

Group II- Procedure as in Group I, however, at the time of the lymphadenectomies one of the nodal groups to be discarded will be microsurgically transplanted into the vacant left popliteal fossa. Data will be collected in accord with the above schedule.

WORK UNIT NO 78/203

Group III-Procedure as in Group I, however, the left inguinal lymph node group will be rotated into the left popliteal fossa as an island pedicle instead of being discarded. Data will be collected as in Groups I and II.

Group IV- Procedure as in Group II, however, the microsurgical transplant will take place at day 3 postoperatively. (The lymph node group will come from another animal there is the 3 day time delay.)

Group V - Procedure as in Group IV, however, the microsurgical transplant will take place at day 7 postoperatively. A total of 75 animals would cover accidental deaths and other attrition.

Manpower (in professional man years): 0.0/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Since the approval of this project, no significant progress has been made. This has been due to the limited time available to the investigator because of studying for the Plastic Surgery Boards. Now that the boards are over and there is a resident in Plastic Surgery to help in the manpower for this project, plans are underway for initiating the project by mid March 1980. Time required to complete this project should be no more than three or four months.

Publications:

- (1) Shesol, B.F., Viktor, Gottlieb: Preliminary Data and Technique for The Effects of Heterotopic Lymph Node Transplantation on Surgically Induced Lymphedema. Journal of Plastic and Reconstructive Surgery, Vol 63, No 6, Jun 79.

Presentations:

- (1) Shesol, B.F.: Heterotopic Lymph Node Transplantation. Presented: Ivy Society Resident's Competition(3rd prize), Hershey, Penna., 1978.
- (2) Shesol, B.F.: Heterotopic Lymph Node Transplantation. Presented: Chief Resident's Meeting(1st prize basic science), Hershey, Penna., 1978.

STATUS

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Alterations of Hematostatic Mechanisms in Patients Undergoing Cardiopulmonary Bypass.

WORK UNIT NO : 79/200

PRINCIPAL INVESTIGATORS: Douglas D. Pritchard, MAJ, MC
John Samuel Clark, COL, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
Judy A. Barber, MT, DAC

OBJECTIVES

1. To evaluate platelet function in patients undergoing cardiopulmonary bypass procedures.
2. To evaluate the effect of red cell hemolysis on circulating platelets.
3. To investigate the cause of platelet dysfunction in patients undergoing cardiopulmonary bypass - platelet activation vs. platelet refractoriness secondary to release of red blood cell ADP.
4. To attempt to correlate the degree of hemolysis with alterations of platelet function and clinical hemorrhage post-operatively.

TECHNICAL APPROACH

Twenty adult patients scheduled to undergo cardiopulmonary bypass procedures will be evaluated. All patients taking drugs; aspirin, persantin, (dipyridamole) or other agents known to alter platelet function, will be excluded from the study. Platelet function will be evaluated pre-operatively, in the operating room after anesthesia is induced and chest opened, hourly during the pump procedure, 10 min post protamine administration, and 1, 4, and 24 hours post-operatively.

The following laboratory procedures will be done, prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) after heparin reversal, fibrinogen, and aggregation to adenosine diphosphate (ADP), (2 and 5 μ m), collagen, epinephrine, (5.5 μ m) evaluation of circulating platelet aggregates according to method of Wu, evaluation of spontaneous aggregation of platelets in PRP, platelet counts, shape change estimated by electron microscopy, plasma hemoglobin, and RIA measurements of thromboxane B_2 , and nucleotide content of platelets and plasma. Platelets Cyclic AMP² (cAMP) and adenylyl cyclase measurements will

WORK UNIT 79/200

TECHNICAL APPROACH - continued

be performed on selected samples. All blood will be obtained through a central venous line which is normally placed in these patients at the time of surgery for clinical reasons.

Estimates of blood loss will be charted and compared with plasma hemoglobin levels. Alterations of platelet function tests vs. time will be analyzed using analysis of variance with intergroup comparisons.

Ten surgical patients meeting same criteria not undergoing cardio-pulmonary bypass will also be studied.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: 0.5

PROGRESS

Laboratory procedures for assay of adenine nucleotides by HPLC were developed. Ten patients were studied. Difficulties were encountered in interpreting laboratory data because of administration of drugs known to alter platelet function. In addition, enzymes present in plasma capable of breaking down ADP caused factious or spurious decreases in plasma levels. The initial principal investigator was separated from the Service. The protocol will be temporarily held in abeyance until the above-mentioned difficulties can be resolved.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Platelet Function in Disease States

WORK UNIT NO.: 79/201

PRINCIPAL INVESTIGATOR: Victor A. Ferraris, MAJ, MC

AS DEPUTY INVESTIGATORS: T. Phil O'Barr, Ph.D., DAC
Donald Corby, COL, MC
J. Bryan Smith, Ph.D., Consultant
Ellen Swanson, B.S., DAC

OBJECTIVES

- a. To develop and assess methods of measuring in vitro platelet function.
- b. To develop radioimmunoassays for the important metabolites of Arachidonic Acid, Thromboxane B_2 , and 6-keto prostaglandin $F_{1\alpha}$.
- c. To use the Thromboxane B_2 assay for measuring platelet survival.

TECHNICAL APPROACH

Alterations in Arachidonic Acid (AA) metabolism may be important in certain clinical entities, including coronary heart disease, stroke, hypercoagulable states and certain bleeding disorders. Two main human sources of Arachidonic Acid are platelets and vascular endothelium. The two measurable, important metabolites of Arachidonic Acid are Thromboxane B_2 (TXB₂) and 6-keto Prostaglandin $F_{1\alpha}$ and (PGF_{1 α}). The approach of this project is to develop radioimmunoassays for these two metabolites and then to use these assays in measuring alterations in AA metabolism in normal and in disease states.

manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 79: 1.5

PROGRESS

Between August 1979 and January 1980, radioimmunoassays for TXB₂ and PGF_{1 α} have been developed. The assay for TXB₂ has been used to measure platelet survival in human controls. Preliminary values on platelet survival have been obtained by intravenous aspirin poisoning of platelet AA metabolism.

WORK UNIT NO 79/201

PROGRESS - continued

compare favorably with published reports of platelet lifetime determined by CR⁵¹ isotope decay. In the coming years more control platelet survival measurements will be made and platelet lifetimes in certain disease states will be investigated.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 72/302

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATORS: T.P. O'Barr, Ph.D., DAC
Judy A. Barber, B.S., DAC
Ellen Swanson, DAC

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, 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: adenylyl cyclase, c-AMP, prostaglandin endoperoxides (thromboxanes A_2 and B_2), membrane glycoproteins, etc. In addition membrane receptors for epinephrine will be quantitatively evaluated using a new technique of binding with radioactive dihydroergocryptine. Other metabolic studies will be added as indicated.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)	FY 78:	3.0
	FY 79:	5.0

PROGRESS

During the past fiscal year, work on this project has concentrated in further investigation of the qualitative abnormality of platelets of newborn infants. In earlier studies (Corby & Schulman, J. Ped. 79:307, 1971) we showed that the platelets of newborn infants fail

WORK UNIT 72/302

PROGRESS - continued

to aggregate normally in response to a variety of inducers of platelet function which promote the release of adenosine diphosphate from the platelet. Data derived from FAMC Clinical Investigation Protocol 71/301 (completed in FY 75) suggested that this impairment of ADP release was due to a decreased sensitivity of newborn platelets to external stimuli (collagen and epinephrine). Since the importance of prostaglandin endoperoxides, prostaglandin G₂, (PGG₂) in mediating the release of ADP from the platelets has recently been established, it appeared necessary to determine if the metabolic pathway leading to the formation of these prostaglandin endoperoxides was functional in newborn platelets. The results of these studies, reported at the 6th International Congress on Thrombosis and Hemostasis in Philadelphia, Pennsylvania, June of 1977, are described in the following abstracts: Cyclooxygenase activity was evaluated in washed platelets from paired mother and cord blood samples by monitoring the incorporation of radioactivity into metabolites during incubation with (1-¹⁴C) arachidonic acid. Thin layer radiochromatograms of methylated incubation products were essentially identical. Three main peaks of radioactivity, which corresponded to identified arachidonic acid metabolites, were noted (Malmsten et al. Proc. Natl. Acad. Sci., USA, 72:1446-1450, 1975). Platelets from mothers and newborns incorporated similar amounts of radioactivity into 8-(1-hydroxy-3-oxopropyl)-9, 12L-dihydroxy-5-10-heptadecadienoic acid TBX₂, and 12L-hydroxy-5,8 10-heptadecatrienoic acid (HHT). Some variation in the extent of aggregation to arachidonic acid was observed in individual PRP samples from both mothers and infants. All infants studied exhibited aggregation in response to 50 ug of arachidonic acid. Aspirinated adult platelets, in which the conversion of arachidonic acid to prostaglandin endoperoxides is blocked, were mixed with an equal volume of newborn platelets which had been shown to be refractory to collagen and epinephrine. Although no correction was noted when epinephrine was used as the inducing agent, marked aggregation was observed following the addition of 0.1 mg/ml of soluble collagen.

The normal aggregation of newborn platelets, demonstration of the formation of prostaglandin endoperoxide metabolites, TBX₂ and HHT, indicate that the cyclo-oxygenase pathway is intact in newborn platelets. The demonstration of correction of second phase aggregation found after administration of soluble collagen in the mixtures of aspirinated adult and normal newborn platelets further suggest that the sufficient quantities of endogenous arachidonic acid can be made available by the action of phospholipase on membrane phospholipase on membrane phospholipids. The variability of this response as noted by the failure to form adequate amounts of prostaglandin G₂

WORK UNIT 72/302

PROGRESS - continued

after stimulation by epinephrine further suggests that the newborn platelet abnormality might reside in decreased sensitivity of its "Membrane Receptor Sites" to inducers of platelet function. We compared specific binding of the α -adrenergic antagonist ^3H -dihydroergocryptine (DHE), in intact washed platelets prepared from paired samples of maternal and cord platelet rich plasma. Platelets of newborn infants (NBP) demonstrated normal kinetics of ^3H -DHE binding and normal affinity for ^3H -DHE. Scatchard analysis of ^3H -DHE binding indicated the same class of binding sites that exhibited a high affinity for the radioligand ($k_d = 7.5 \text{ nM}$). Maternal platelets were found to bind approximately 2-fold more DHE than NBP ($3.70 \pm .28$ vs. $1.74 \pm 0.17 \text{ fmol}/10^7$ platelets) at saturation. This corresponds to 223 ± 17 vs. 105 ± 11 binding sites per platelet ($p < .001$). Repeat washing of NBP did not yield increased DHE binding suggesting the binding sites had not previously been masked by elevated circulating levels of E and/or-E in venous cord blood. When control platelets were incubated with concentrations of ^3H -DHE that half saturated the α -adrenergic receptors, diminution of platelet function comparable to that seen in NBP was observed. Since NBP and MP are similar size, it appears that a deficiency of α -adrenergic receptors may account for the diminished response of NBP to epinephrine. Work was presented at the VIIth International Congress of Hemostasis and Thrombosis; manuscript submitted to Developmental Pharmacology and Therapeutics.

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.
- (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.

WORK UNIT 72/302

Publications - continued

- (4) Corby, D.G., Preston, K.A., O'Barr, T.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, C.W., Greene, H.L.: Impaired Platelet Function in Glucose-6-Phosphatase Deficiency. The J. Ped., 85:71-76, July 1974.
- (6) Corby, D.G., and Zuck, T.F.: Newborn Platelet Dysfunction: A Storage Pool and Release Defect. Thrombosis and Haemostasis, 36:200-207, 1976.
- (7) Corby, D.G., Goad, W.C., Barber, J., and O'Barr, T.P.: Evaluation of Cyclo-Oxygenase Pathway in Platelets of the Newborn, Thrombosis and Haemostasis (Stuttgart), 38:35, 1977 (Abstract).
- (8) Corby, D.G., O'Barr, T.P.: Decrease in α -Adrenergic Binding Sites in Newborn Platelets: Cause of Abnormal Response to Epinephrine? Blood, 52:161, 1978.
- (9) Corby, D.G., O'Barr, T.P.: Decreased Alpha-Adrenergic Receptors in Newborn Platelets: Cause of Abnormal Response to Epinephrine. Pending publication.
- (10) Corby, D.G.: Aspirin in Pregnancy: Maternal and Fetal Effects. Pediatrics, 62:930, 1978.

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, California, 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 and 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.

WORK UNIT 72/302

Presentations - continued

- (4) Corby, D.G., Goad, W.C., Barber, J., and O'Barr, T.P.: Evaluation of Cyclo-Oxygenase Pathway in Platelets of the Newborn. Presented: Vith International Congress on Thrombosis and Haemostasis, Philadelphia, Pennsylvania, June 1977.
- (5) Corby, D.G. and O'Barr, T.P.: Decreased - Adrenergic Receptors in Newborn Platelets: Cause of Abnormal Response to Epinephrine? Presented: VIth Congress International Society of Thrombosis and Haemostasis, London, England, 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 73/305

PRINCIPAL INVESTIGATORS: George L. Brown, Ph.D., COL, MSC
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., 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 2641 patient records encompassing 59,269 messages 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 78: 1.5
FY 79: 1.0

PROGRESS

Between 1 Oct 78 and 30 Sep 79, 39 new patients' data encompassing 690 messages has been added to the data base. The data base now includes 2641 patients including 59,269 messages. During February 1979, a formal printout encompassing 108 patients with isolates other than M. Tuberculosis was retrieved for COL Ronald Nelson, C, Pul Disease. The intended use of this data was to determine the correlation between isolates and the current medical status of each patient. Work is

WORK UNIT 73/305

PROGRESS - continued

continuing to improve and expand the existing data base to improve retrieval and analysis methods.

Publications: none

Presentations:

- (1) Brown, G.L., and Rothlauf, M.V.: Computer File Analyses and Utilization of Mycobacteriology Laboratory Data. Presented: Colorado State University, May, 1978.
- (2) Brown, G.L. and Rothlauf, M.V.: Laboratory Management of the Tuberculous Patient. Computer File Analyses of Six Year Data, Society of Armed Forces Laboratory Officers, San Antonio, Texas, September 1976.
- (3) Brown, G.L., and Rothlauf, M.V.: Computer Utilization in the Laboratory. Colorado State Universtiy, Ft. Collins, Colorado, April, 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Microbiological Research in Tuberculosis.

WORK UNIT NO.: 74/300

PRINCIPAL INVESTIGATORS: George L. Brown, Ph.D., COL, MSC
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
Donald Paine, 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, in an effort to improve isolation of mycobacteria from clinical specimens; (II) Tests for identification of mycobacterial species; (III) Evaluation of drug susceptibility test medium; (IV) Characterization of non-mycobacterium tuberculosis species isolated from experimental medium; (V) characterization of contaminants growing on experimental medium; (VI) comparison of smears before and after decontamination to determine possible loss of staining characteristics and viability.

Manpower (in professional man years): 0.7/yr

Funding (in thousands)	FY 78:	1.8
	FY 79:	1.0

PROGRESS

Evaluation of a number of mucolytic agents is being conducted to determine if the current digestion process can be improved in terms

WORK UNIT 74/300

PROGRESS - continued

of cost as well as sensitivity. In addition the smear comparison study comparing smears data before and after decontamination is continuing. Both of the above areas of research should provide data which will improve current specimens processing methods.

Improved method for conducting chromogenicity studies have been initiated and will hopefully reduce the time required to perform each tests.

Rapid methods for Arylsulfatase, niacin and nitrate reductase testing, are being explored and show promise for improving the current technology.

Extensive studies have been initiated to more rapidly identify Op IV rapid growers as well as provide important susceptibility data for patient treatment.

The evaluation of Mitchison's selective OA agar (PACT) has been completed and the data analyzed and submitted for publication. This media appears to have a definite benefit in reducing contamination rates and enhancing the recovery of mycobacteria species. In addition, studies utilizing a new temperature block procedure for determining temperature requirements of mycobacteria has been completed and data is undergoing analysis in preparation for publication.

Serotyping of Op III species is in the process of being implemented, facilitating the characterization and epidemiology of current isolates.

P-nitrophenyl-β-D glucose (PNPG) test is providing data which indicates that this new test may be used to separate various mycobacteria species. Extensive testing is underway to verify this preliminary finding.

Preliminary data illustrates that the PACT plate has promise for providing direct drug susceptibility data; however, additional data is required to fully develop this methodology.

Publications:

- (1) Rothlauf, Mary V., Brown, G.L., Blair, Eugene: Isolation of Mycobacteria from Undecontaminated Specimens Using Selective 7H10 Medium. Pending Publication.

WORK UNIT NO.: 74/300

Publications - continued

- (2) Kolb, J.G., Rothlauf, M.V., and Brown, G.L.: Isolation of Mycobacterium kansasii on Mitchison's Selective 7H11 medium. (Abyt.) American Society for Microbiology, C-69:47, 1977.

Presentations:

- (1) Damato, James J.: Rapid Methods for Differentiative Mycobacterial Species. Presented: University of Colorado, Greeley, CO, Oct 1979.
- (2) Kolb, J.G., Rothlauf, M.V., and Brown, G.L.: Isolation of Mycobacterium kansasii on Mitchison's Selective 7H11 Medium. American Society for Microbiology, New Orleans, Louisiana, May 1977.
- (3) Brown, G.L., and Rothlauf, M.V.: Effects of Alpha-tocopherol and/or Altitude Stress on BCG Vaccinated Mice. National Jewish Hospital, Dnever, CO, June 1978.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Mechanisms of Vitamin D Induced Calcium Transport.

WORK UNIT NO.: 76/300

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Futher characterization of vitamin D induced transcriptional event as it relates to calcium transport processes on polar cells.

TECHNICAL APPROACH

The isolation of mRNA involving proteins thought to be related in calcium transport by gel and chromatographic methods.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78: .0
FY 79: 0.1

PROGRESS

Because of manpower shortages this protocol has been unable to be continued, and since the principal investigator was released from active duty, this protocol has been terminated.

Publications:

- (1) Charles, M.A.: Regulation of CaBP Specific m-RNA by 1,25-D₃.
The Endocrine Society, 1978.

Presentations:

- (1) Charles, M.A.: Regulation of CaBP Specific m-RNA by 1,25-D₃.
Presented: 1978 National Endocrine Meetings.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Pancreatic Islet Transplantation in Diabetic Animals.

WORK UNIT NO.: 76/301

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Ed Dodson, MAJ, MC
Brahma Sharma, M.D., (Childrens Hospital)
Larry True, M.D., (University of Colorado Medical
Center)

OBJECTIVES

Information derived from islet transplantation experiments indicates that diabetes mellitus can be effectively treated in animals. For this treatment approach to become practical in humans it appears obligatory to achieve effective animal allograft islet transplants. This goal has not been realized and thus the current protocol directly attempts to perform allogeneic islet transplantation in diabetic animals.

TECHNICAL APPROACH

Rat colonies isolated at FAMC in three different strains: Lewis, Wistar Furth, and Fischer strains have been established at FAMC. The Lewis and Fischer strains share major rat histocompatibility antigens whereas Wistar Furth strains of rat does not share the major histocompatibility antigens with Lewis or Fischer. Pancreatic islets are isolated and purified from donor strain animals and under various conditions are transplanted to Lewis recipient animals. The assessment of transplantation success is made by measurement of daily urine volumes and 24-hour urine glucose excretion in addition to serum glucose values. Immunological studies of the transplantation are performed by immunization of rabbits by rat islet antigen from crude islet homogenates. Lymphocyte transformation studies were performed to assess cell mediated transplantation rejection phenomenon by isolating lymphocytes from transplant and control animals and incubating these lymphocytes with donor islet tissues as well as phytohemagglutinin as a control. Lymphocytes are also in the progress of being enriched for specific subpopulations including T-cells and B-cells. Macrophages have been also isolated by the principal investigator. Isolated rat islet B-cell preparations will be performed using a Danase technique.

WORK UNIT NO.: 76/301

TECHNICAL APPROACH - continued

Upon the completion of the above technology, lymphocyte cytotoxicity studies will be performed in animals after transplantation. The experiment is also in progress which involves isolation of Lewis lymphocytes and Wistar Furth lymphocytes for mixed lymphocyte culture. Purified T-cells will be used as responder cells and after optimum incubation of mixed lymphocyte cultures, lymphoblasts will be isolated by albumin gradient techniques. Lymphoblasts of the T-cell series will be used as an immunogen into potential islet recipients (Lewis). Rat livers transplanted with isografts (Lewis) and allografts (Wistar Furth) islets are being studied by immunohistochemical techniques to define humoral immunity factors involved in the rejection phenomena.

Manpower (in professional man years): 2.5/yr

Funding (in thousands)	FY 78:	8.0
	FY 79:	13.0

PROGRESS

Double transplants (syngeneic transplant on an already allogeneically transplanted animal) have been performed to discover if the rejection process has sensitized the recipient against his own (i.e. Lewis) islets. After testing 3 time periods post allograft (7 wk, 2 wk, 5 day), it appears autosensitization doesn't happen. However, as all the animals normalized at the 7 wk and 2 wk time period, only 50% normalized within the expected time (21 days) at the 5 day period; it appears some immediate but temporary sensitization may occur.

Publications:

- (1) Charles, Art, Noble, S., Ownbey, J., Brown, G., and O'Barr, T.P.: Mechanisms of Islet Allograft Rejection. (Abst.) Journal of the American Diabetes Association, 1979.
- (2) Charles, M.A.: Islet Allograft Transplantation in Diabetic Rats. Diabetes 26: 1978.

Presentations:

- (1) Charles, M.A.: Islet Allograft Transplantation in Diabetic Rats. Presented: American Diabetes Association National Meeting, 1978.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Calcium Metabolism in Diabetes Mellitus.

WORK UNIT NO.: 76/304

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Gary Treece, MAJ, MC
Fred Hofeldt, LTC, MC
T.P. O'Barr, Ph.D., DAC

OBJECTIVES

To determine if diabetes mellitus in humans is associated with renal unresponsiveness to parathyroid hormone. If this hypothesis is true, it could explain the bone demineralization associated with diabetes mellitus.

TECHNICAL APPROACH

Patients with diabetes but not on therapy will be assessed prior to being placed on therapy. If the assessment demonstrates no emergent need for diabetic control, the patient will be included into the study at which time the patient will be infused with thyroid hormone, and the patient's blood and urine will be analyzed for cyclic AMP, 125 Vitamins D₃ and in addition to other variables such as phosphate and calcium to prove or disprove whether diabetic kidneys are resistant to parathyroid hormone.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78:	0.1
FY 79:	0.1

PROGRESS

None. Protocol has been terminated since principal investigator has been released from active duty.

Publications and Presentations: none

STATUS:

Terminated.

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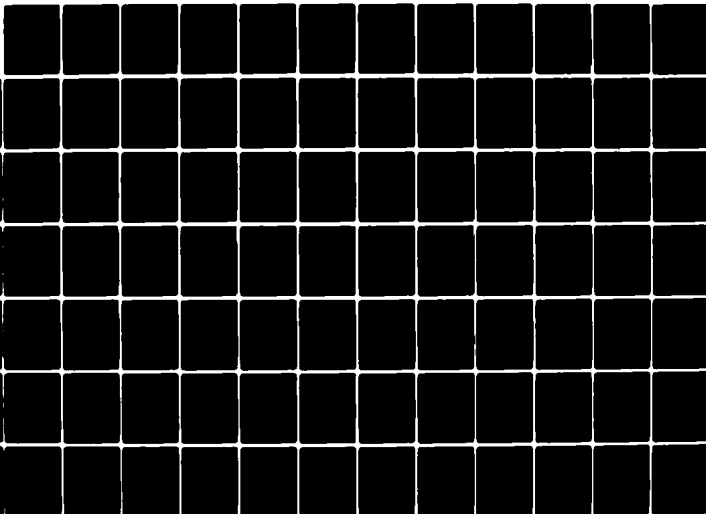
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CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Standardization of Hypoglycemic Criteria using a Physiological Stimulus.

WORK UNIT NO.: 76/305

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Fred Hofeldt, LTC, MC
Ed Dodson, MAJ, MC
Anna Lee Shackelford, M.T., DAC

OBJECTIVES

To establish criteria defining normal postprandial blood glucose and glucoregulatory hormone concentrations following a test meal which provides more physiologic stimulus than pure glucose and to compare these data with the traditional oral glucose tolerance test. Also to observe whether patients thought to have idiopathic reactive hypoglycemia do in fact have low postprandial blood glucose on altered levels of glucoregulatory hormones associated with clinical findings following the test meal.

TECHNICAL APPROACH

Patients and normals will be given a test meal consisting of figurines containing about a third of the daily caloric and protein carbohydrate and fat intake following which time multiple tests will be performed looking at glucose homeostasis.

Manpower (in professional man years): 0.20/yr

Funding (in thousands) FY 78:	0.20
FY 79:	0.5

PROGRESS

Eighteen patients presented to the FAMC Endocrine Clinic with a tentative diagnosis of reactive hypoglycemia have been evaluated using glucose tolerance testing and figurine tolerance testing. It is clear and there are no exceptions that patients having symptoms of post prandial reactive hypoglycemia episodes that have

WORK UNIT NO.: 76/305

PROGRESS - continued

been documented by glucose tolerance tests are not hypoglycemic during their similar symptoms after the test meal. Insulin, cortisol and glucagon levels will be compared with age, sex, and weight matched controls that are currently being performed. Approximately nine controls have been so studied. During the study of 18 patients it has become apparent that 4 of the 18 patients have elevated levels of immunoreactive glucagon that have been evaluated by gel filtration techniques. The elevated immunoreactive glucagon is not authentic 3500 mw glucagon but rather a large mw species exceeding 200,000 mw that has not been described in the literature and after conversations with various leaders in the field of glucagon physiology, including Dr. Roger Unger, it is apparent that the substance that we are measuring is unique.

Publications:

- (1) True, L., Charles, A., Lewis, H., Katz, F., Waldeck, N., and P. Nakane: A Pseudoglucagonoma Syndrome. (Abst.) Clinical Research, 1979.
- (2) Charles, M.A., Waldeck, Nancy, and O'Barr, T.P.: Excessive High Molecular Weight Immunoreactive Glucagon Levels in Patients with the Post Prandial Syndrome. (Abst.) Western Society for Clinical Research, 1979.
- (3) Charles, M.A.: The Absence of Hypoglycemia After a Test Meal in Patients with Idiopathic Reactive Hypoglycemia. Diabetes 26, 1978.

Presentations:

- (1) True, L., Charles, A., Lewis, H., Katz, F., Waldeck, N., and Nakane, P.: A Pseudoglucagonoma Syndrome. Presented: Western Society Meetings, American Federation for Clinical Research, February 1979.
- (2) Charles, M.A., Waldeck, Nancy and O'Barr, T.P.: Excessive High Molecular Weight Immunoreactive Glucagon Levels in Patients with the Post Prandial Syndrome. Presented: Western Society Meetings, Western Society for Clinical Research, February 1979.
- (3) Charles, M.A.: The Absence of Hypoglycemia After a Test Meal in Patients with Idiopathic Reactive Hypoglycemia. Presented: American Diabetes Association National Meeting, 1978.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Immunologic Disorders in Children and Adults: I. Correlation of Immune Functions in the Immunodeficiency State II. Correlation of Immune Functions of Leukemia and other Childhood Malignancies.

WORK UNIT NO.: 77/300

PRINCIPAL INVESTIGATORS: George L. Brown, Ph.D., COL, MSC
Donald G. Corby, COL, MC

OBJECTIVES

Existing specialized immuno-chemical procedures will be consolidated into a registered protocol for use, on a consultative basis, by the hospital staff.

TECHNICAL APPROACH

A clinical laboratory immunology consultation service has been established. Main emphasis is performance and evaluation of specialized immuno-chemical tests, for training house-staff personnel and consultative support of hospital. The major areas of studies include humoral and cellular immunity and leukocyte function evaluation. Patients are selected on the basis of severity of recurrent infections, clinical immunodeficiency state, lack of response to medical management and availability of clinical investigation service for laboratory evaluations for patient care.

Manpower (in professional man years): 1.3/yr

Funding (in thousands) FY 78:	4.0
FY 79:	3.5

PROGRESS

A total of 202 patients were evaluated on consultative basis for immunologic disorders. During this period ten physician house-staff personnel were also trained in laboratory clinical immunology procedures (humoral and cellular). Patients studied: 119 in the area of serum protein gammopathies and 83 for special studies of cellular immunologic problems. Subjects with indicated major findings

WORK UNIT NO.: 77/300

PROGRESS - continued

were as follows: I. Humoral immunologic disorders - serum protein profile evaluations: 11 cryoglobulinemias, 69 serum protein gamma-pathies, 29 immunoglobulin disorders (heavy and light chain and benign spike), 16 hypogammaglobulinemias, 18 hypergammaglobulinemias, 4 C complement abnormalities; II. Cellular immunologic disorders - lymphocyte evaluations: 83 lymphocyte blast transformations (PHA, Con A, Pokeweed Mitogen), 81 T-lymphocyte enumeratives, of these 20, 10 and 6 patients were recorded suppressed post PHA, PWM and candida stimulations, respectively. III. Miscellaneous evaluations: 10 B-cell fluorescent tappings, 16 NBT evaluations, 13 neutrophil chemotactic studies, 7 monocyte chemiluminescence evaluations.

Publications: none

Presentations:

- (1) Brown, G.L. and Heggors, J.: Medical Mycology: Assessment of bacteriologic and serologic parameters of clinically-important mycoses normal and immunologic comprised host. Presented: American Medical Technologist Educational Seminars, Denver, CO, July 1979.
- (2) Brown, G.L. and Lima, J.: Assessment of Cell Medicated Immunity in Children and Adults: Pediatric Department Seminar, FAMC, Denver, Colorado, October 1978.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Thyroglobulin Levels in Patients with Thyroid Carcinoma.

WORK UNIT NO: 77/301

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Ed Dodson, MAJ, MC
Fred Hofeldt, LTC, MC
Phil Burstein, M.D. (University of Colorado
Medical Center)

OBJECTIVES

To determine if thyroglobulin serum levels reflect the occurrence of thyroid carcinoma metastases.

TECHNICAL APPROACH

A radioimmunoassay has been designed to measure circulating thyroglobulin levels in humans by isolating the thyroglobulin protein from human thyroid glands by column chromatographic techniques. Following the isolation of pure human thyroglobulin the protein was injected into rabbits on a pre-determined immunization schedule and rabbit serum was harvested for analysis of antihuman thyroglobulin antibodies. Radioactive Iodine 125 thyroglobulin is prepared by the chloramine T method. Following the development of the radioimmunoassay for serum thyroglobulin determination normals and patients were studied to determine various levels under different clinical situations. All patients studied with thyroid carcinoma had concomitant total body thyroid scanning procedures. Patients are studied in various stages of therapy following the diagnosis of thyroid carcinoma.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 78: 0.20
FY 79: 3.0

PROGRESS

The above immunoassay has been developed and has been shown to be sensitive to less than 1.25ng/ml of circulating thyroglobulin. Forty-nine normal volunteers have been evaluated with the normal range being 0-15ng/ml. Concomitant with all specimens run is a thyroglobulin

WORK UNIT NO.: 77/301

PROGRESS - continued

antibody technique and all patients with thyroglobulin binding greater than 10% are excluded from this study. Approximately 70 patients have been studied for serum thyroglobulin levels concomitantly with total body scanning procedures. By comparing the serum thyroglobulin level with total body thyroid scanning techniques it is apparent that the blood test is very efficient in predicting the result of the total body scan (chi square analysis highly significant less than 0.001).

Publications:

- (1) Dodson, E., Charles, A., Waldeck, N., O'Barr, T.P., Hofeldt, F., Ghaed, V. and Telepak, R.: Comparison of Total Body Thyroid Scans (TBS) with Serum Thyroglobulin Levels in Patients with Treated Thyroid Cancer. (Abst.) The Endocrine Society, Bethesda, MD, January 1979.

Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Regulation of 1,25-Dihydroxycholecalciferol (1,25-D₃)
in Humans.

WORK UNIT NO.: 77/302

PRINCIPAL INVESTIGATOR: M. Arthur Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Ed Dodson, MAJ, MC
Dave Zolock, CPT, MSC, PhD

OBJECTIVES

To determine if in vivo regulation of plasma 1,25-D₃ is mediated by calcium or parathyroid hormone (PTH).

TECHNICAL APPROACH

Measurement of serum 1,25-D₃ by techniques involving plasma extraction gel filtration, high pressure chromatography, and radioligand assay involving vitamin D binding protein isolated from rachitic chick gut.

Manpower (in professional man years): .2/yr

Funding (in thousands) FY 78: 4.0
FY 79: 0

PROGRESS

The 1,25-D₃ serum assay has been developed in this laboratory by the principal investigator and although this assay has required approximately 1.5 years to develop current manpower quality shortages have made this protocol impossible to perform. The techniques utilizing this protocol have been performed by the principal investigator, who has been discharged from military service.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Osteosarcoma.

WORK UNIT NO.: 77/304

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
William J. Zwartjes, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To increase survival and cure of patients with osteosarcoma.
- B. To preserve optimal function in the affected limb.
- C. To determine incidence, extent and duration of objective regressions of both localized and metastatic osteosarcoma to combined modality therapy.
- D. To compare incidence, extent and duration of objective response of localized tumors treated with immediate amputation, versus those treated with high-dose radiation with/without delayed amputation.
- E. To correlate degree of response to treatment with total time of tumor-free survival.
- F. To correlate degree of response with median survival in patients presented with metastases.
- G. To compare tumor-free survival and median survival on this protocol retrospectively with those described for other treatment protocols.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Childrens Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with osteosarcoma, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

WORK UNIT NO.: 77/304

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

As of 26 October 1979, no FAMC patients with osteosarcoma have been enrolled in this program. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Neuroblastoma (Stage III, IV) After Infancy.

WORK UNIT NO.: 77/305

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
Taru Hays, M.D., Children's Hospital
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
Lorrie Furman Odom, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To aggressively treat the child presenting after the age of one year with disseminated neuroblastoma with combination radiation therapy, multiple drug chemotherapy, and immunotherapy.
- B. To prospectively evaluate the efficacy of partial tumor resection in patients with known disseminated disease.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with neuroblastoma, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

As of 26 October 1979, no FAMC patients with neuroblastoma have been enrolled in this program. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

WORK UNIT NO.: 77/305

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Rhabdomyosarcoma Protocol.

WORK UNIT NO.: 77/306

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
William J. Zwartjes, M.D., Children's Hospital
Richard Heideman, M.D., Children's Hospital
David Tubergen, M.D., Children's Hospital

OBJECTIVES

1. To maintain good survival rates with best available therapy in Stage I disease by the use of chemotherapy following complete resection of the tumor.
2. To maintain good survival rates with best available therapy in Stage II and III disease by use of VAC therapy (vincristine, dactinomycin, cytoxan) following appropriate treatment to the local tumor. This may include either surgery before or after chemotherapy or the combination of surgery, chemotherapy and radiation.
3. To decrease morbidity of treatment in Stage II and III disease by avoiding mutilating surgery through the use of chemotherapy prior to the surgery to reduce bulk disease and make the surgical resection less destructive.
4. To determine the response rate of late stage rhabdomyosarcoma to a combination of chemotherapy including cytoxan, vincristine, dactinomycin, adriamycin and DTIC.
5. To determine host toxicity and tolerable levels of this five drug treatment in late stage disease.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the

WORK UNIT NO.: 77/306

TECHNICAL APPROACH - continued

auspices of the Denver Regional Cancer Center. Patients with Rhabdomyosarcoma, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

As of 26 October 1979, no FAMC patients with rhabdomyosarcoma have been enrolled in this program. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Protocol for the Treatment of Ewing's Sarcoma.

WORK UNIT NO.: 77/307

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: William Zwartjes, M.D., Children's Hospital
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To produce prolonged survivals and optimally, cures in Ewing's Sarcoma.
- B. To determine incidence, extent and duration of objective regressions of both localized and metastatic Ewing's Sarcoma to high-dose radiation and combined chemotherapy utilizing vincristine, cytoxan, adriamycin and dactinomycin in metastatic disease.
- C. To correlate response with tumor-free survival.
- D. To correlate response with median survival in patients presenting with metastases.
- E. To compare tumor-free survival and median survival on this regimen retrospectively with those described for other treatment methods.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with Ewing's Sarcoma, medium selection criteria, as outlined in the protocol were treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

WORK UNIT NO.: 77/307

PROGRESS

As of 26 October 1979, no FAMC patients with Ewing's Sarcoma have been enrolled in this program. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Non-Hodgkin's Lymphoma.

WORK UNIT NO.: 77/308

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
Taru Hays, M.D., Children's Hospital
Richard Heideman, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

The purpose of this study is to improve the chances of achieving a complete remission, as well as to hopefully prolong the duration of complete remission in children with non-Hodgkin's lymphoma.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with non-Hodgkin's Lymphoma, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

As of 26 October 1979, no FAMC patients with non-Hodgkins Lymphoma have been enrolled in this program. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: AL # 4 - Acute Lymphocytic Leukemia.

WORK UNIT NO.: 77/309

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
Lorrie Furman Odom, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To increase the number of long-term survivors of acute lymphogenous leukemia.
- B. To evaluate the clinical efficacy of immunological potentiation by BCG between 6-day courses of combination chemotherapy given every 3 weeks, with regard to remission duration and frequency of infections.
- C. To assess the effect of BCG on in vitro parameters of immunological function, such as numbers of T and B lymphocytes, lymphocyte cytotoxicity to autologous lymphoblasts, antibodies to BCG and tumor antigen, and monocyte-macrophage function.
- D. To determine if prolonged administration of BCG leads to antigenic competition by following sequential in vitro lymphocyte blastogenesis to diphtheria and tetanus antigens.
- E. To develop prognostic criteria based on histology with special stains (PAS, Sudan, Peroxidase, Alpha naphthal acetate esterase, Chloracetate esterase), electron microscopy, and T and B cell determination. •

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with AL #4 - Acute Lymphocytic Leukemia, medium selection criteria, as outlined in the protocol were treated with combined modality therapy.

WORK UNIT NO.: 77/309

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

As of 26 October 1979, two FAMC patients have been entered in the study.

December 1978: D.J., 14-year-old female who continues in remission on maintenance chemotherapy.

December 1978: J.C., 2-year-old male who continues in remission on maintenance chemotherapy.

Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Denver Children's Hospital has joined CCSG and will be entering their patients on CCSG protocols. Therefore, no new FAMC patients will be entered in this study.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Acute Non-Lymphogenous Leukemia.

WORK UNIT NO.: 77/310

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
Taru Hays, M.D., Children's Hospital
R. Eugene Lienert, M.D., Presbyterian Medical Center
David Tubergen, M.D., Children's Hospital
Lorrie Furman Odom, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To increase the duration of complete remission in children with ANLL.
- B. To determine whether administration of 2400 rads cranial irradiation and intrathecal Ara-C as soon as remission is achieved decreases the incidence of CNS leukemia when compared to historical controls.
- C. To determine the clinical efficacy of adding BCG applied by Heaf gun to aggressive intermittent combination chemotherapy in the treatment of children with ANLL.
- D. To follow in vitro parameters of immunological function, such as numbers of T and B lymphocytes, lymphocyte cytotoxicity to autologous blasts, antibodies to BCG and tumor antigen, and monocyte-macrophage function, and to determine if they correlate with remission or relapse.
- E. To determine if prolonged administration of BCG leads to antigenic competition by following sequential in vitro lymphocyte blastogenesis to diphtheria and tetanus antigens.
- F. To determine if cytochemical and ultrastructural features of the blast cells correlate with prognosis.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with Acute Non-Lymphogenous Leukemia, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

WORK UNIT NO.: 77/310

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

As of 26 October 1979, one FAMC patient, K.K., a 6-year-old male with AMML has been enrolled on the AMML treatment arm of the protocol on 16 June 1979. The patient failed to achieve initial remission after three courses of induction therapy according to this protocol, and was taken off the study on 4 October 1979. He was discharged home to Georgia with his parents to be treated with supportive care only by a private pediatrician. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Wilms' Tumor (Nephroblastoma).

WORK UNIT NO.: 77/311

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
David Tubergen, M.D., Children's Hospital
Taru Hays, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

- A. To produce prolonged disease-free survivals and cures of Wilms' tumor.
- B. To evaluate adriamycin in the treatment of Stages 3B and 4 of this disease.
- C. To compare disease-free survival and median survival on this protocol retrospectively and concurrently with treatment regimens used in other institutions.
- D. To monitor the toxicity and observe the incidence of long range side effects of our irradiation and chemotherapeutic treatments.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with Wilms' tumor, medium selection criteria, as outlined in the protocol will be treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

As of 26 October 1979, no FAMC patients with Wilms' tumor have been enrolled in this program. Denver Children's Hospital--the parent

WORK UNIT NO.: 77/311

PROGRESS - continued

institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: CNS Tumor Protocol for Study of Combined Surgery, Chemotherapy and Radiotherapy.

WORK UNIT NO.: 77/312

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
David Tubergen, M.D., Children's Hospital
Richard L. Heideman, M.D., Children's Hospital
Barbara Rose, Children's Hospital

OBJECTIVES

To determine the effects of combination surgery, chemotherapy and radiation in previously untreated or relapsing patients with central nervous system tumors. Data will be compared to historical controls obtained with surgery and radiation alone.

TECHNICAL APPROACH

The University of Colorado Medical Center, Denver Children's Hospital and FAMC are cooperating in the study of this protocol as a group under the auspices of the Denver Regional Cancer Center. Patients with CNS Tumor, medium selection criteria, as outlined in the protocol were treated with combined modality therapy.

Manpower (in professional man years): 0.05/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

As of 26 October 1979, no new patients have been admitted to this protocol since November 1978 when patient RR, a 3-year-old male with Glioblastoma Multiforme was enrolled in this study. In February 1979, this patient relapsed while on the protocol and was taken off the study. He subsequently responded to MDPP chemotherapy but relapsed again in October 1979. Denver Children's Hospital--the parent institution sponsoring this protocol--has decided to discontinue this program for new patients because Children's Hospital has entered CCSG and will be using CCSG protocols.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Radiometric Methods for the Rapid Detection, Identification and Susceptibility Testing of Mycobacterium Species.

WORK UNIT NO.: 78/301

PRINCIPAL INVESTIGATORS: James J. Damato, MAJ, MSC
George L. Brown, Ph.D., COL, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
Kenneth McClatchy, Ph.D., National Jewish
Hospital, Denver (Consultant)

OBJECTIVES

To develop radiometric methodology for rapid detection, identification and susceptibility testing of mycobacteria isolated from patients' specimens.

TECHNICAL APPROACH

C¹⁴ substrates are employed to detect the early growth of mycobacteria in various medium bases. In addition, various chemical agents are being evaluated and incorporated in these bases in order to attempt to differentiate the various mycobacterial species and provide early susceptibility data.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 79: 3

PROGRESS

Current data illustrates that the Bactec detection system is at least as sensitive as standard methods for detecting mycobacteria and that a number of chemical agents appear capable of rapidly separating the M. tuberculosis bovis group from mycobacterium other than tuberculosis. In addition, four-day drug susceptibility testing is feasible and is undergoing additional testing. In addition, a number of standard biochemical tests have been improved to provide test data much earlier.

WORK UNIT 78/301

Publications: none

Presentations:

- (1) Damato, James J.: Rapid Methods for Differentiating Mycobacterium Species. Presented: University of Northern Colorado, Greeley, CO, October 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Adsorption of Propoxyphene by Activated Charcoal.

WORK UNIT NO.: 78/302

PRINCIPAL INVESTIGATOR: W: Nicholas Glab, Sp6, B.S.

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
Walter J. Decker, Ph.D., Department of Pharmacology/
Toxicology, University of Texas Medical Branch,
Galveston, Texas

OBJECTIVES

To determine the efficacy of activated charcoal in the emergency management of propoxyphene overdosage.

TECHNICAL APPROACH

Rats received, by group, propoxyphene HCl and propoxyphene napsylate at a by weight dosage that exceeded the LD50. These groups were countered by rats receiving activated charcoal at a rate 10 times their respective dosages of propoxyphene. These four groups are compared to a control group receiving only placebo dosages. At intervals over a twenty-four hour period, representative animals were sacrificed. The kidneys, liver, and brain were excised, weighed, lyophilized, and submitted for gas-liquid chromatography.

Manpower (in professional man years): 0.6/yr

Funding (in thousands): FY 78: 0.7
FY 79: 0.5

PROGRESS

The animal portion of the study has been completed and tissues submitted for analysis. Preliminary findings show a 50% decrease in mortality of rats receiving activated charcoal versus unmodified, propoxyphene-dosed animals. Results of propoxyphene assay are pending.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of Humic Substances as Potential Gastro-intestinal Decontaminants in the Emergency Management of the Poisoned Patient.

WORK UNIT NO.: 78/303

PRINCIPAL INVESTIGATORS: Donald G. Corby, COL, MC
T.P. O'Barr, Ph.D., DAC
Walter J. Decker, Ph.D., Department of
Pharmacology/Toxicology, Univ. of
Texas Med. Br., Galveston, Texas

ASSOCIATE INVESTIGATORS: R. L. Wershaw and
Ronald L. Malcolm, US Geological Survey
Denver, CO

OBJECTIVE

To prepare and evaluate in vitro the ability of humic substances to bind a large variety of potentially toxic drugs and household poisons.

TECHNICAL APPROACH

Approximately 100 pounds of soil known to contain large amounts of humic substances will be obtained from Florida State University through the assistance of the U.S. Geological Survey. Humic and fulvic acids will be extracted from the soil specimens using the method of Malcolm (5) (App A). Elemental analysis of lyophilized humic and fulvic acid preparations will be performed by Huffman Laboratories, Wheat Ridge, Colorado.

Once sufficient quantities of low ash content humic and fulvic acids are prepared, in vitro studies will be performed to determine the relative complexing or adsorptive activities of these substances to amphetamine, primaquine, chlorpheniramine, colchicine, diphenylhydantoin, aspirin, probenecid, quinacrine, chlorpromazine, meprobamate, chloroquine, quinidine, quinine, ferrous sulfate, iodine, phenol, methylsalicylate, 2,4-D (20%), malathion (50%), DDT, N-methyl carbamate, boric acid (3%), d-propoxyphene hydrochloride, mineral acids, sodium and potassium hydroxides, sodium metasilicate, and tolbutamide using the method of Decker, Combs and Corby (5) (App B). Percent of drug or household poisons adsorbed or complexed with humic substances will be compared for drugs listed with that adsorbed by activated charcoal.

WORK UNIT NO 78/303

TECHNICAL APPROACH - continued

Test dose of solid drugs will be based on numbers of tablets or capsules rather than a weight basis. Liquid and household products will be analyzed on an millimeter basis.

Manpower (in professional man years): 0.75/yr

Funding (in thousands) FY 79: 2

PROGRESS

Experiments on the ability of humic acid prepared from lake soil by an external agency and by this organization were conducted from February 1979 to November 1979 with the following conclusions:

1. Humic acid does complex iron (Fe^{++}).
2. The amount of complex formed depends on iron concentration, ph, temp, time, and concentration of other cations in solution. (Max of 64% Fe by wt. at 1.5 mg/ml Fe^{++} added.)
3. From an antidotal standpoint the complexation reaction does not appear to be practical in the presence of stomach contents primarily due to the fact that a very high concentration of free iron exists in equilibrium with the complex.

Key parametric data to illustrate these conclusions are presented in the attached chart.

Publications and Presentations: none

STATUS:

Ongoing.

Expt #	Fe ⁺⁺ added	Humic Acid Added	Fe ⁺⁺ Remaining	Remarks
17	4.93 mg/ml	10 mg/ml	4.9 mg/ml	With Stomach Contents ph=1.5
18	5 mg/ml	10 mg/ml	5 mg/ml	With Stomach Contents ph=1.5
68-69	1.5 mg/ml	1 mg/ml	.9 mg/ml	With Stomach Contents ph=3
73S	3.17 mg/ml	.732 mg/ml	2.13 mg/ml	With Stomach Contents ph=6.67
73C	3.17 mg/ml	none	2.67 mg/ml	w/Stomach Contents Fe ⁺⁺ Precipitates
75	4.64 mg/ml	2.85 mg/ml	3.16 mg/ml	w/Stomach Contents ph=6.8

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Treatment of Iron-deficiency Anemia I: Comparison of
Hematologic Parameters following Treatment with Carbonyl
Iron of Ferrous Sulfate in Wistar Rats.

WORK UNIT NO.: 78/304

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATORS: Walter J. Decker, Ph.D., Dir., Department
of Pharmacology/Toxicology, Univ. of
Texas Med. Br., Galveston, Texas
Penelope D. Rich, SSG, B.S.
Lawrence E. Jones, M.T., DAC
Troy Engle, SFC

OBJECTIVES

To evaluate carbonyl iron in the treatment of experimentally induced
iron deficiency in the rat.

TECHNICAL APPROACH

This will be a comparative study of hematocrit values using an animal
model. In addition, this study will evaluate CBS indices, serum
iron, unsaturated iron-binding capacity, free erythrocyte protoporphyrin
levels, ferritin levels, and stainable bone marrow iron. This experiment
will be conducted in three phases in which the first two phases will be
identical due to time, space, and personnel limitations to minimize
temporal changes.

Manpower (in professional man years): 0

Funding (in thousands) FY 79: 2.0

PROGRESS

This study has not yet begun.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A Study of the Hormone-Dependent Growth of Human Mammary
Tumors In Vitro.

WORK UNIT NO.: 79/300

PRINCIPAL INVESTIGATOR: John W. Harbell, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATOR: Donald Mercill, B.S., DAC

OBJECTIVES

To examine the hormone requirements for the growth of human mammary tumors using explant organ culture.

TECHNICAL APPROACH

Tissue samples are obtained from biopsy or mastectomy specimens. Each sample is cut into many small pieces and distributed, for culture, in a battery of hormone combinations. At the initiation of the culture and at specific intervals throughout its duration, replicate samples from each hormone combination are subjected to the appropriate radiolabelled precursor to determine DNA, RNA, and protein synthesis. The tissue is then processed for autoradiography and the relative efficacy of the hormonal stimulus to cell replication and/or maintenance determined.

Manpower (in professional man years): 0.6/yr

Funding (in thousands) FY 79: 3.0

PROGRESS

In order to begin this protocol, a histology and tissue culture facility was equipped and technical staff trained. To date, samples from twenty women have been carried in culture; 3 of normal breast, 9 of benign disease, and 8 carcinomas. Having now determined some of the basic parameters for culturing this tissue (basic medium, proper gas phase, and length of culture period), quantitation of the resulting autoradiographs is in progress. Preliminary results indicate a marked insulin requirement,

WORK UNIT NO 79/300

PROGRESS - continued

in conjunction with known mammatrophic hormones, for maximal epithelium which is lost in some carcinomas.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Basic Studies to Hasten Recovery From or Help Prevent
Bone Injury.

WORK UNIT NO.: 79/301

PRINCIPAL INVESTIGATOR: David T. Zolock, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To reduce the incidence of fracture wounds and to reduce the time involved to heal fracture wounds by increasing the absorption and retention of calcium and phosphorus through nutritional and medical therapeutic improvements.

TECHNICAL APPROACH

Since bone mineralization is indirectly regulated by intestinal absorption, the bone as well as the intestinal responses to various therapeutic measures, will be studied. In general the animal of choice will be checked, which will be fed a vitamin D deficient diet containing 0.43% phosphorus for approximately three weeks.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 79: 3.0

PROGRESS

The correct conditions have been established for obtaining checks in a rachitogenic state. Studies have indicated the intestinal calcium binding protein or protein synthesis is not necessary for vitamin D mediated calcium transport across the lumen or mucosal calcium accumulation. The calcium binding protein is necessary in protecting the cell from high levels of calcium during the mediated absorption process. Protein synthesis is necessary for bone calcium uptake.

WORK UNIT NO 79/301

Publications:

- (1) Zolock, David T., Morrissey, Robert L., and Bikle, Daniel D.:
Meaning of Non-parallel $1,25(\text{OH})_2 \text{D}_3$ Mediated Response Relationships
in Intestine and Bone to Dose and Time in Vitamin D; Biochemical,
Chemical and Clinical Aspects Related to Calcium Metabolism.
Walter DeGruyter, Inc., New York, 1979.

Presentations:

- (1) Zolock, David T., Morrissey, Robert L., and Bikle, Daniel D.:
Meaning of Non-parallel $1,25(\text{OH})_2 \text{D}_3$ Mediated Response Relationships
in Intestine and Bone to Dose and Time. Presented: Berlin (West),
Germany, February 1979.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Investigation of the Effects of Temperature, Humidity, Air Flow, and Method of Breathing on Airway Diameter.

WORK UNIT NO: 79/302

PRINCIPAL INVESTIGATOR: Peter Hameister, LTC, MC

ASSOCIATE INVESTIGATORS: Lyndon E. Mansfield, LTC, MC
Nigel J. Smith, E6
Nicholas Glab, E6, B.S.

OBJECTIVES

To assess the importance of nasal versus oral breathing at different air flows, and with variations of temperature and humidity.

TECHNICAL APPROACH

The upper airways of 10 dogs were mechanically isolated, (mouth, oropharynx, and nasopharynx).

Various air temperatures and flow rates were directed to each of the areas. At each step functional residual capacity (Frc) and total respiratory resistance (Rrs) were measured.

An additional 5 dogs were utilized as a control group.

Manpower (in professional man years): 0.8/yr

Funding (in thousands) FY 79: 3.0

PROGRESS

All animal work has been completed and data is presently being examined.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Investigation of the Association Between Sinusitis
and Asthma.

WORK UNIT NO: 79/303

PRINCIPAL INVESTIGATOR: Peter Hameister, LTC, MC

ASSOCIATE INVESTIGATORS: Lyndon E. Mansfield, LTC, MC
Nigel J. Smith, E6
Nicholas Glab, E6, B.S.

OBJECTIVES

To demonstrate if sinus congestion and obstruction can lead to the
development of bronchoconstriction.

TECHNICAL APPROACH

Ten dogs were anesthetized and intubated. The maxillary sinus was entered
and a catheter placed. The balloon was inflated to obstruct the sinus,
then deflated. Acetic Acid, 10%, was instilled in the sinus cavity. It
was also nebulized down the endotracheal tube. At each of these steps
forced residual capacity (Frc) and respiratory resistance (Rrs) were
measured to determine total respiratory resistance. An additional 5
dogs were run as a control group.

Manpower (in professional man years): 0.7/yr

Funding (in thousands) FY 79: 6.5

PROGRESS

All animal work has been completed and data is presently being collected
and analyzed.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Quantitation of Steroid Hormone Receptors in Tissue Sections
Using Quantitative Autoradiography.

WORK UNIT NO: 79/304

PRINCIPAL INVESTIGATOR: John W. Harbell, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To provide a means to quantify cellular steroid receptors (i.e., estrogen, progesterone and glucocorticoids) on a cell by cell basis in both normal and transformed tissue samples.

TECHNICAL APPROACH

The original protocol plan has been modified to assess both steroid receptor binding and nuclear translocation. Viable tissue samples are pulse labelled, in vitro, with ³H-labelled steroids, further incubated in culture medium to allow translocation to the nucleus, and finally quick frozen. Frozen sections are placed on emulsion-coated slides and exposed at -15°C. Microscopic quantitation of specific (total-background) silver grains over the cell nucleus is used to indicate a responsive cell.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: 0.5

PROGRESS

Several parameters of the technique have been established by using mouse and guinea pig uterus. These include the labelling procedure, concentration of isotope during the pulse, freezing procedure and autoradiographic technique. The optimum post pulse label incubation is yet to be determined, to allow maximum translocation without metabolic breakdown of the steroid, and minimum emulsion exposure time for sufficient silver grain development.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Field Trial of New Techniques for Isolation, Identification
and Susceptibility Testing of Mycobacteria.

WORK UNIT NO.: 79/305

PRINCIPAL INVESTIGATORS: James L. Owmbey, MAJ, MC
Mary V. Rothlauf, MS, DAC
James D. Hakes, DAC

ASSOCIATE INVESTIGATORS: James J. Damato, MAJ, MSC
J. Kenneth McClatchy, Ph.D., Consultant

OBJECTIVES

1. To set up a field trial of Mitchison's selective medium.
2. To develop and evaluate the use of a *transport medium* for clinical specimens for mycobacteriology sent to reference laboratories for processing.
3. To determine primary antituberculosis drug resistance of T.B. infected US personnel stationed in Korea.

TECHNICAL APPROACH

The 121st Evacuation Hospital, Korea, will collect TB sputum specimens, prepare smears, inoculate S7H10 directly and split remaining specimens. They will process one aliquot as usual and, after adding an equal volume to holding medium to the remaining portion, send that portion to Mycobacteriology, Clinical Investigation Service, Fitzsimons Army Medical Center, for isolation and susceptibility testing. Drug susceptibility *M. tuberculosis* isolated will be correlated with the incidence of resistant disease in Korea.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 79: 0.5

WORK UNIT NO 79/305

PROGRESS

Dr. Owmbey has been reassigned from Korea to Fort Carson Army Hospital. He has been contacted and is interested in continuing as a principal investigator and liaison between Clinical Investigation Service, Fitzsimons Army Medical Center and the 121st Evacuation Hospital, Korea.

Between Sep 77 and Sep 79, 78 new patient records have been initiated and 1379 messages entered relative to these patient records. The file now contains a total of 2602 patient records encompassing 57,151 messages. On 4 Feb 79 a formatted file print of all patients (180), having identified mycobacteria isolates other than M.tuberculosis, was pulled for use by COL Roald Nelson, Chief, Pulmonary Disease Service. The intended use is to determine correlation between the isolate and the medical status of each patient.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Adenohypophyseal-thyroid Interrelationships in Dehydration.

WORK UNIT NO.: 79/306

PRINCIPAL INVESTIGATOR: W. Nicholas Glab, SP6, B.S.

ASSOCIATE INVESTIGATOR: John W. Harbell, Ph.D., CPT, MSC

OBJECTIVES

To examine the activity of the thyroid and thyroid stimulating hormone (TSH) producing cells of the anterior pituitary gland during dehydration, utilizing light and electron microscopy. This data will be correlated with circulating T_3 - T_4 levels.

TECHNICAL APPROACH

Sacrifice periods, totaling 8 days, will include members of three groups of rats: controlled, water-deprived, and water-deprived with daily injections of TSH, and body weights and urine output monitored. Upon sacrifice, blood serum will be collected for radioimmunoassay for T_3 - T_4 . Pituitary, thyroid, and adrenals will be processed for light and electron microscopy. Cell morphology, counts of both TSH cell numbers, and secretion granule size versus number per cell will be evaluated.

Manpower (in professional man years): 0.7/yr

Funding (in thousands) FY 79: 0.4

PROGRESS

The animal phase has been completed and samples collected. Tissues and serum are presently being processed for study. Significant weight loss, in water-deprived versus controlled animals, verifies dehydration.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE Use of In Vitro Cytotoxicity Assay in Diabetic Patients for
the Evaluation of Immune Mechanisms in Diabetes Mellitus.

WORK UNIT NO.: 79/307

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

1. To determine which types of diabetic patients have immune mechanisms that kill rat islet B-cells.
2. To attempt to suppress these immune phenomena with immunosuppressant agents.
3. To determine if immune suppression is associated with improved endogenous B-cell function, such as improved B-cell secretion.

TECHNICAL APPROACH

This protocol is specifically designed to answer two questions: a) what classes of patients have cytotoxic immune mechanisms active in their disease? and b) will immunosuppressive treatment affect endogenous islet B-cell activity?

Manpower (in professional man years): 2/yr

Funding (in thousands) FY 79: 3.0

PROGRESS

The technique for cytotoxicity was improved to the point of adequacy and reproducibility. The tests indicated heterogeneity of immune

WORK UNIT NO 79/307

PROGRESS - continued

killing mechanisms with 4 of 5 patients having at least 1 active mechanism. The mechanisms evaluated were cell mediated cytotoxicity (CMC), antibody dependent cell mediated cytotoxicity (ADCC), and complement-dependent antibody mediated cytotoxicity (AC). AC occurs but may be unusual. CMC was found in 4 of 5 patients. ADCC was suppressed in 2 patients, unchanged in 3 (may suggest T-cell activity in some diabetics). These results, along with some found in histology studies, suggest rejection is due to histocompatibility barriers, not islet specific antigens.

The major mechanism of islet destruction appears to be mediated by spleen or blood lymphocytes. Studies on killing these lymphocytes by culturing was begun but not carried far enough for conclusions. Islets have been kept alive in sterile, 23°, high O₂ condition and successfully syngeneically transplanted but no studies have been done on an allogeneic basis.

Technique for cytotoxicity: Lewis diabetic rats receive 500 Lewis or Wistar-Furth islets intraportally 5 days prior to lymphocyte and plasma harvesting. Either lymphocytes alone (CMC), lymphocytes plus heat inactivated plasma (ADCC) or fresh plasma (AC) are incubated with single cell suspensions of Cr⁵¹ labelled rat islet target cells. Specific cytotoxicity equals the % Cr⁵¹ release above the spontaneous target cell release (normal controls). These results were double checked by means of an insulin assay on pellets of islets and supernatants.

CMC = cell mediated cytotoxicity

ADCC = antibody dependent cell mediated cytotoxicity

AC = complement-dependent antibody mediated cytotoxicity

Publications:

- (1) Charles, M. Arthur, Sharma, B., Waldeck, N., Dodson, E., Noble, S.: Use of an In Vitro Cytotoxicity Assay for the Direct Evaluation of Immune Mechanisms in Diabetic Patients. (Abst.) Journal of the American Diabetes Association, New York, N.Y., 1979.

Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE

Surgical Research Section

Training Support Summary

During the year, 112 students from the practical nurse (91C) course were trained in suturing techniques. Training was conducted on 28 days, using 28 dogs, and consisted of a slide lecture and movie, introduction to the operating room, including aseptic technique, scrub, gowning and gloving, and hands-on experience in the dry and wet labs. 336 hours were expended by Surgical Research Labs personnel in providing this training.

The Department of Pediatrics trained 66 nurses and medical students in the placement of endotracheal tubes and chest tubes, using 32 cats in 11 visits of approximately 3 hours duration. 88 hours were required of Surgical Research Labs personnel for initial anesthetic induction, maintenance and monitoring.

Orthopedic Service, Department of Surgery, utilized 51 rabbits in 73 visits to train one staff surgeon and seven surgical residents in microvascular surgery using the operating microscope. A total of 219 hours was spent to accomplish this training, requiring 365 hours of support by Surgical Research Labs personnel in pre-operative anesthetic induction, surgical preps, anesthesia monitoring, post-operative recovery and angiography.

Fifteen physicians from Department of Obstetrics and Gynecology received consultant training in tubal anastomosis using the operating microscope. Training was accomplished in 3 visits totalling 6 hours, requiring 3 hours of support (set-up and instrument care).

CIS-SRL Training Support Summary - continued

General Surgery Service, Department of Surgery, used three dogs in training 18 surgeons in the use of staple guns. A total of 90 hours of training was received, requiring 36 hours of support (pre-op anesthetic induction, surgical prep, anesthesia monitoring, circulating and clean-up).

Cost of training, 91C students:	\$78.82/session x 28 days =	\$2,206.96
Pediatric nurses, et. al.:	12.48/animal x 32 cats =	399.36
Orthopedic Surgery Service:	68.86/animal x 51 =	3,511.86
OB/Gyn:	NA	
General Surgery Service:	66.18/session x 3 dogs =	198.54

OB-GYN

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 67/351

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To evaluate the Pereyra method of urethro-vesical suspension as a means of treatment for patients with true 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 questionnaires on a six-month 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 78: 0
FY 79: 0

WORK UNIT 67/351

PROGRESS

This study has been terminated as Dr. Deubler (principal investigator) is no longer in the Service.

Publications: None

Presentations:

- (1) Buffone, D.: 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, Nevada, October 1970.
- (2) Woods, W.M.: Evaluation of the "Pereyra-Harer" Procedure in the Treatment of Urinary Stress Incontinence. Accepted for Presentation. Armed Forces District Meeting of the American College of OB-GYN, Washington, D.C., November 1975.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 73/353

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: Durell A. Hiller, CPT, MC

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 78:	0
FY 79:	0

WORK UNIT 73/353

PROGRESS

This study has been terminated as Dr. Deubler is no longer in the Service.

Publications: none

Presentations:

- (1) Hiller, D.A., Elliott, J.P.: Tubal Ligation Syndrome Myth or Reality. Presented: Armed Forces Division of ACOG, New Orleans, Louisiana, October 1977.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: A Comparison of Serum Estriol Levels and Human Placenta
Lactogen (HPL) Levels in the Management of Hypertensive
and Vascular Disease in Pregnancy.

WORK UNIT NO.: 75/352

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

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

OBJECTIVES

The object of this study is to determine if HPL level obtained after the 30th week of gestation will be as effective in managing the outcome for mother and fetus as serum estriols which are currently being utilized at Fitzsimons Army Medical Center.

TECHNICAL APPROACH

During the 12 months from initiation of this study, all patients seen in the clinic or hospitalized with the diagnosis of hypertension in pregnancy, preeclampsia, glomerulonephritis, systemic lupus erythematosus, or other vascular diseases will be studied. Each patient will be studied from onset of clinical findings or 30 weeks' gestation until delivery.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 78:	2.5
FY 79:	0

PROGRESS

This study has been terminated as Dr. Deubler is no longer in the Service.

Publications: None

Presentations:

- (1) Edward J. Lazarus, MAJ, MC, is presenting the preliminary results at the Annual Armed Forces Seminar and 16th Annual District Meeting, American College of Obstetrics and Gynecology, October 1977.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of Ibuprofen (Motrin) in Dysmenorrhea.

WORK UNIT NO.: 76/350

PRINCIPAL INVESTIGATOR: Gordon S. Park, CPT, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To compare the relief of dysmenorrhea pain by Ibuprofen.

TECHNICAL APPROACH

Patients have been taken into the study and evaluated on either aspirin, placebo, or motrin for three consecutive cycles on each drug. The patients are filling our report cards with each cycle as to the amount of relief they have obtained and the amount of medication taken. These are returned after each set of three cycles and new drugs are obtained through the pharmacy.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

Since the onset of the study, there have been 54 women enrolled in the study and the study is now closed to new enrollment. Eleven women have completed three cycles on all three medications. Eighteen have dropped out of the study due to moving from the area, pregnancy or desire to stop the study. There are 25 patients currently ongoing in the study. Results will be tabulated at the end of the study which is anticipated by May 1980.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of the Role of Unrecognized Intrauterine Infection
in Premature Labor and Premature Rupture of Membranes.

WORK UNIT NO.: 77/350

PRINCIPAL INVESTIGATORS: J.R. Bobitt, LTC, MC
G.L. Brown, COL, PhD, MSC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the presence, number and frequency of bacteria and mycoplasmatales in the amniotic fluid of patients presenting with premature labor and/or premature rupture of membranes.

TECHNICAL APPROACH

This study is a coordinated investigation between Department of Obstetrics and Gynecology and Clinical Investigation Service, Fitzsimons Army Medical Center. All administrative and professional care, including specimen collection and distribution to the Clinical Investigation Service, will be the responsibility of OB-GYN. The management and methodology for microbiological evaluation of specimens will be the responsibility of CIS, Microbiology Section.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 78: 0.0
FY 79: 0.0

PROGRESS

This study has been modified and replaced by Study 78/352.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Inhibition of Premature Labor with Terbutaline.

WORK UNIT NO.: 78/350

PRINCIPAL INVESTIGATORS: D.D. Riston, CPT, MC
J.R. Bobitt, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To study inhibitory effects of Terbutaline on premature labor.

TECHNICAL APPROACH

Patients at less than 36 weeks of gestation, with no contra-indicating condition such as ruptured BOW, intrauterine sepsis, or abruptio placentis, will be treated for premature labor with either Terbutaline or a placebo. The presence of labor and absence of fetal distress will be confirmed by electronic monitor. Entrance to the study will be approved by a member of the attending staff prior to obtaining permission from the patient.

Manpower (in professional man years): 0.01/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

Twenty-seven patients were entered in the study: 3 primiparae and 24 multiparae. All 27 received at least one course of terbutaline I.V. In addition, 20 received terbutaline SQ and 10 were given terbutaline P.O. There were no unsuspected side effects on any form of the drug. Side effects were as follows for I.V., SQ and P.O., respectively: Tachycardia-14,9,6; Nervousness-7,2,0; Tremor-2,1,0; Palpitation-2,0,0; Dizziness-3,0,1; Headache-1,0,0; Nausea-3,0,0; Vomiting-2,0,0; Anxiety-4,0,0.

The majority of patients required only 1 course of I.V. terbutaline before contractions stopped. I.V. and SQ efficacy were almost the same. On P.O. terbutaline, 6 patients were readmitted with contractions (22.2%). As compared to ETOH, terbutaline was at least as effective with far less potentially dangerous side effects. To this date, there has been no

WORK UNIT NO 78/350

PROGRESS - continued

neonatal morbidity or mortality attributable to terbutaline. On or about 6 June 1979, the Office of the Surgeon General ordered discontinuance of I.V.-administered terbutaline.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Evaluation of the Effect of Suction Drainage on Infectious Morbidity in Patients Undergoing Cesarean Section.

WORK UNIT NO.: 78/351

PRINCIPAL INVESTIGATOR: J.R. Bobitt, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine if the incidence and severity of pelvic infections in patients undergoing cesarean section is significantly decreased through the use of retroperitoneal suction drainage of the uterine operative site.

TECHNICAL APPROACH

We plan to compare the frequency and severity of pelvic infections among 50 patients undergoing cesarean section with suction drainage of the operative site, with a similar group of 50 patients without drainage. Patients considered infected at the time of cesarean section will not be included in the study. Patients on antibiotic medications will also be excluded. Any patient who will have had two hours of labor at the time of cesarean section or has ruptured membranes at the time of cesarean section is a candidate for the study. The study group will be drained by a hemovac suction apparatus whereas this technique will not be available to those patients in the control group. The suction catheter will be placed beneath the vesico-uterine fold and brought out through the lower abdomen remaining extraperitoneal. Study and control patients will be selected by a table of random numbers prepared prior to the study.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	0.0
	FY 79:	0.0

PROGRESS

To date 90 patients have been entered into the study. Analyses as to the number of those placed in the group receiving a retroperitoneal hemovac drain at the time of cesarean section and those randomized

WORK UNIT NO.: 78/351

PROGRESS - continued

into the control group is presently being compiled. At this point in the study no conclusions can be drawn as to whether postoperative drainage decreases febrile morbidity following cesarean section. No complications have arisen as the result of drainage. The patients' records are currently being studied for information as to the amount of drainage obtained and to the culture findings done on the drainage fluid.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of the Role of Unrecognized Intrauterine Infection
in Premature Labor.

WORK UNIT NO.: 78/352

PRINCIPAL INVESTIGATORS: J. R. Bobitt, COL, MC
James J. Damato, MAJ, MSC
C. Hayslip, CPT, MC

OBJECTIVES

To determine the presence, number and frequency of bacteria in the amniotic fluid of patients in premature labor with intact membranes.

TECHNICAL APPROACH

Patients in premature labor with intact membranes will have an amniocentesis if they consent to participate in the study. Amniotic fluid will be analysed for the following infectious parameters: 1) Quantitative cultures, 2) Viral cultures, 3) Polymorphonuclear count, 4) Lactic dehydrogenase, and 5) Gram stain.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 79: 0.5

PROGRESS

Amniocentesis was initially restricted to patients who were clearly going to deliver. This approach resulted in only five study patients in seven months. In October 1979 we returned to our original plan. The first patient was afebrile, intact membranes and delivered a 28 week infant. Amniotic fluid cultures grew C. albicans 950 cal/ml, PMN 600/ml, LDH 2,000. The same organism was in the infant's gastric aspirate, and pathology reported histologic signs of chorioamnionitis. The mother remained afebrile and received no antibiotic. This project should now show progress.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Prenatal evaluation of Quantitative Cervical and Vaginal Cultures for the Group B Streptococcus and Their Relationship to Maternal and Neonatal Infectious Morbidity.

WORK UNIT NO.: 78/353

PRINCIPAL INVESTIGATORS: J. R. Bobitt, COL, MC
George L. Brown, Ph.D., COL, MSC
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To determine the incidence and clinical significance of group B Streptococcus colonization in the cervix and vagina of prenatal women after 24 weeks gestation.

TECHNICAL APPROACH

Antepartum vaginal cultures are collected by the clinical personnel in the Department of OB-GYN at weekly intervals and at delivery. Plates are streaked and growth quantitated by the Clinical Investigation Service, Department of Microbiology. Results are blinded. Mother and newborn records are reviewed for infectious morbidity.

Manpower (in professional man years): 1.75/yr

Funding (in thousands)	FY 78:	2.7
	FY 79:	2.0

PROGRESS

Study was begun in February 1979. 190 patients have been followed through pregnancy and delivered. Almost all of our entire antepartum population is now in the study. No clinical correlations have yet been studied.

Publications and Presentations: none

STATUS:

Ongoing.

PEDIATRICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effect of Prophylactic Antibiotic Therapy on Gravid Group
B Beta Hemolytic Streptococcus Carriers.

WORK UNIT NO.: 75/401

PRINCIPAL INVESTIGATORS: Gerald B. Merenstein, LTC, MC
George L. Brown, Ph.D., COL, MSC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To evaluate several selective culture media for the isolation of Group B Beta Hemolytic Streptococcus (GBHS) and the use of prophylactic antibiotic therapy in antepartum GBHS carriers with regard to colonization of the infant.

TECHNICAL APPROACH

Endocervical cultures are obtained from all obstetrical patients at FAMC at the initial obstetrical visits and at delivery. Those positive are re-evaluated for GBHS at the 30th and 38th week visits. In addition, "positives" are placed in a control or a treatment group; those in the treatment group are placed on oral penicillin or erythromycin, if allergic. Ear, umbilical and cord cultures are obtained from each infant for GBHS evaluation. Numerous media incorporating inhibitory substances are evaluated for GBHS isolation. Isolated GBHS are studied for type specific antigen composition.

Manpower (in professional man years): 1.5/yr

Funding (in thousands)	FY 78:	4.0
	FY 79:	0

PROGRESS

The actual study has been temporarily halted while reevaluation of technique of evaluating mothers prior to term is being studied by members of the Department of Obstetrics and Gynecology. In addition methods of more rapidly identifying protein GBHS carriers are being considered.

WORK UNIT NO. 75/401

Publications:

- (1) Yost, C.C., Calcagno, J.V., Merenstein, G.B., Todd, W.A., Dashow, E.E., Brown, G.L., Tull, A.H., and Kile, D.E.: Group B Beta Hemolytic Streptococcus: Improved Culture Detection and a Controlled Treatment Trial. Clinical Research, 24:186A, 1976.
- (2) Luzier, T.L., Merenstein, G.B., Todd, W.A., Yost, C.C. and Brown, G.L.: The Treatment of Gravid Females at Term Colonized with Group B Streptococcus: A Randomized Controlled Study. Clinical Research 26:200A, 1978.

Presentations:

- (1) Calcagno, J.V., Brown, G.L., Tull, A.H., Yost, C.C., Jolly, D.J., and Cromwell, R.K.: Evaluation of Three Collection - Transport Systems for the Isolation of Group B Streptococcus from Pre-Partum Women and Neonates: American Society for Microbiology, Atlantic City, New Jersey, 1976.
- (2) Luzier, T.L.: The Treatment of Gravid Females at Term Colonized with Group B Beta Hemolytic Streptococcus: A Randomized Study. Accepted for presentation Military Section, American Academy of Pediatrics, November 1977.
- (3) Luzier, T.L.: The Treatment of Gravid Females at Term Colonized with Group B Beta Hemolytic Streptococcus: A Randomized Study. Second prize Hugh Mahon Award, Fitzsimons Army Medical Center, Denver, Colorado, June 1977.
- (4) Luzier, T.L.: The Treatment of Gravid Females Colonized with Group B Beta Hemolytic Streptococcus: A Randomized Controlled Study. Military Section, American Academy of Pediatrics, New York City, November 1977.
- (5) Luzier, T.L.: The Treatment of Gravid Females at Term Colonized with Group B Streptococcus. Western Society for Pediatric Research, Carmel, California, 2 February 1978.
- (6) Pierce, J.: Streptococcal Sudden Unexpected Death Syndrome. Aspen, Colorado, July 1978. Aspen Conference on Perinatal Research.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Early Digitalization in Premature Infants with Idiopathic Respiratory Distress (IRDS) Who Have Echocardiographic Evidence of Left Atrial Enlargement.

WORK UNIT NO.: 75/402

PRINCIPAL INVESTIGATOR: Gerald L. Way, MAJ, MC

ASSOCIATE INVESTIGATORS: Gerald B. Merenstein, LTC, MC
John R. Pierce, MAJ, MC

OBJECTIVES

To determine the usefulness of early digitalization in altering the progression of congestive heart failure and left-to-right shunting through the PDA in premature infants with IRDS.

TECHNICAL APPROACH

Infants with RDS and left atrial aortic diameter ratio of greater than 1.0 by echocardiograph will be included in the two study groups. The two study groups will be Group A-infants who will be digitalized with 40 mcg/kg dose of digoxin and maintained at 10 mcg/kg/day. Group B-infants who will not receive digoxin unless they clinically demonstrate overt congestive heart failure. Echocardiograms will be repeated every other day throughout the respirator course, and subsequently only if abnormal findings remain. Additional echocardiograms will be obtained if the clinical situation deteriorates. Echocardiograms will be evaluated with coinciding arterial blood gases, chest x-rays, EKG's, and laboratory data which will be done as needed for clinical management.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 78:	1.0
FY 79:	0.5

PROGRESS

During the past year an additional eight patients were added to this study. Interestingly, there has been an apparent decrease in the incidence of patent ductus arteriosus and subsequent left atrial

WORK UNIT NO.: 75/402

PROGRESS - continued

enlargement in premature infants cared for in the nursery at FAMC.
In the next few months, the data from the study will be analyzed and
hopefully some useful conclusions will be reached.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of High Intensity Fiberoptic Transillumination
in Infants.

WORK UNIT NO.: 76/400

PRINCIPAL INVESTIGATOR:

ASSOCIATE INVESTIGATORS: Gerard Breitzer, CPT, MC
Gerald B. Merenstein, LTC, MC

OBJECTIVES

To establish a new set of normal values of transillumination distances of infants' skulls using a 5,000 foot-candle fiberoptic light; to determine the efficacy of high intensity light in diagnosing pneumothoraces.

TECHNICAL APPROACH

All children in the normal newborn nursery and pediatric outpatient clinic and well child clinics for routine visits will have their skulls transilluminated using 3,000, 4,000, and 5,000 foot-candles of light from a fiberoptic source. Areas transilluminated will be the anterior fontanelle, posterior fontanelle, left parietal bone above the pinna midway on a line from the external air canal to the left eye on the frontal bone. Measurements of transillumination will be made from the center of the beam as outlined by Cheldelin et.al. and will be compared with previous study results. Infants in the nursery with respiratory distress will be examined using the fiberoptic light as discussed by Kuhns, et.al. to see if a pneumothorax or pneumomediastinum can be diagnosed by transillumination.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

No new investigator has taken over this study, therefore, no patients have been added.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Purulent Nasopharyngitis: Double Blind Treatment Protocol.

WORK UNIT NO.: 77/401

PRINCIPAL INVESTIGATORS: Warren A. Todd, LTC, MC
James K. Todd, M.D., Children's Hospital,
Denver, Colorado
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine which is the most effective treatment of children with purulent rhinitis and if the effective therapy is free of side effects. In addition data will be collected to determine the etiologic agent of purulent rhinitis.

TECHNICAL APPROACH

Children between the ages of 6 months and 6 years seen in the General Pediatric Clinic with a diagnosis of purulent rhinitis and with no other treatable disease receive a nasal culture and/or placed on the protocol regimen. This regimen consists of four different packages: One containing Placebo-Actifed, one containing Placebo-Keflex, one containing Actifed-Keflex, one containing Placebo-Placebo. The child is seen for followup four days later where a repeat culture is done, physical examination is done, and a record is obtained from the mother as to whether or not there was improvement in the nasal discharge.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)	FY 78:	0.5
	FY 79:	0.5

PROGRESS

The study has been completed but the data has not been completely analyzed. It is anticipated that this will be accomplished during FY 80.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 78

TITLE: Evaluation of Ventricular Function and Pulmonary Vascular Resistance in Asphyxiated Infants.

WORK UNIT NO.: 77/402

PRINCIPAL INVESTIGATORS: Gerald L. Way, MAJ, MC
John R. Pierce, MAJ, MC
Gerald B. Merenstein, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To serially measure left ventricular (LV) function in asphyxiated infants. To determine if all asphyxiated infants have decreased ventricular function or only those who have severe symptomatology of congestive failure. To evaluate the course of the decreased ventricular function. To serially estimate pulmonary pressures, and to define the change in pulmonary vascular resistance in asphyxiated infants.

TECHNICAL APPROACH

All infants with the diagnosis of asphyxia neonatorum are to be entered into the study. Ventricular function and pulmonary vascular resistance will be evaluated.

Manpower (in professional man years): 1.0/yr

Funding (in thousands): FY 78: 0
FY 79: 0

PROGRESS

This project received a low priority. Along with this was the problem of lack of a skilled technician to perform the echocardiograms thus leading to no patients being enrolled in this study. Due to these problems and the recent illness and medical retirement of the pediatric cardiologist involved, the study has been temporarily suspended. It is hoped that this study can be re-instituted when another pediatric cardiologist joins the staff.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Determination of Pulmonary Vascular Resistance in Newborn
Infants at 5,280 feet using Right-Sided Systolic Time Intervals.

WORK UNIT NO.: 77/403

PRINCIPAL INVESTIGATORS: Gerald L. Way, MAJ, MC
John R. Pierce, MAJ, MC
Gerald B. Merenstein, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

We hope to determine the normal range of pulmonary vascular resistance in babies and the decline of increased pulmonary vascular resistance at this altitude and then compare it to the other altitudes mentioned.

TECHNICAL APPROACH

The babies are evaluated within 12 hr of delivery with complete echocardiograms being done. Repeat echo is done daily until discharge. If the echocardiograms are abnormal on discharge, the babies are reappointed to come back to Cardiology Clinic for repeat echocardiograms and evaluations.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)	FY 78	0
	FY 79	0

PROGRESS

As indicated in last year's report, slow progress was expected due to lack of manpower in obtaining echocardiograms. This has indeed been the case and no new patients have been added to the study. Since the illness and subsequent medical retirement of the cardiologist involved, the study has been temporarily suspended. It is hoped that it can be re-instituted when another pediatric cardiologist joins the staff.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Perceptions of Discipline: A Comparison of Mothers of School Age Children with Asthma and Children without Asthma.

WORK UNIT NO.: 78/400

PRINCIPAL INVESTIGATORS: Linda Kerscher, CPT, ANC (M/RET)
PNP, Student MS in Nursing (UCMC)
Jean Robidoux, CPT, ANC (M/RET)
PNP, Student MS in Nursing (UCMC)

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

The purpose of this study is to find out whether mothers of school age children with chronic asthma are more permissive in their approach to discipline as compared to mothers of school age children without asthma or any chronic illness.

TECHNICAL APPROACH

Fifteen mothers of children with chronic asthma who require daily doses of a bronchodilator will be selected randomly and interviewed using a tool on discipline techniques developed at the National Institute of Mental Health. They will return for follow-up care at the Allergy Clinic of Fitzsimons Army Medical Center. The asthmatic children will then be matched with children without any chronic diseases by age, sex, and race. Mothers of the non-asthmatic children will be interviewed at the Pediatric Clinic at Fitzsimons. With this interview tool it is possible to obtain summed standardized scores for overall restrictiveness severity of punishment, the child's compliance and dependent behaviors by summing the ratings of these behaviors in specific situations. Each interview which is recorded on tape, will be independently coded by two raters to give a measure of reliability to the resulting scores. The means of the summed standardized scores will be compared between the asthmatic and non-asthmatic groups. A T-test will be used to determine the significance of the difference between the means.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 78: 0
FY 79: 0

WORK UNIT NO.: 78/400

PROGRESS

Twenty Six patients were surveyed during the course of this study in accordance with signed consent forms received in Clinical Investigation Service. The study is presumed completed since no further report on progress has been received from the principal investigator.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Influence of Body Positioning on Gastric Residuals in
Premature Infants.

WORK UNIT NO.: 78/402

PRINCIPAL INVESTIGATOR: Barbara S. Turner, CPT, ANC, RN, MS, MA

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To compare the amount of gastric residuals in the premature infant's stomach three hours after feeding in relation to the body position of the infant.

TECHNICAL APPROACH

Premature infants requiring gavage feedings who were less than 35 weeks gestation were examined. Infants meeting outlined criteria were fed the same formula, at the same time and in the same manner as previously used. Gastric residuals were measured and recorded with body position. Positions used are right side, left side and stomach.

Manpower (in professional man years): 0

Funding (in thousands) FY 78: 0
 FY 79: 0

PROGRESS

Data collection began in July 1978. To date, 7 subjects have been studied. Data have been recorded on gastric residuals, body positions as well as the extraneous variables of gestational age, sex, race and type of formula. Data analysis will begin when target subject population of 20 has been studied.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Influence of Body Positioning on Gastric Residuals in
Premature Infants Requiring Ventilatory Assistance.

WORK UNIT NO.: 78/403

PRINCIPAL INVESTIGATOR: Barbara S. Turner, CPT, ANC, RN, MS, MA

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To compare the amount of gastric residuals in the premature infant's stomach three hours after feeding in relation to the body position of the infant.

TECHNICAL APPROACH

Premature infants requiring ventilatory assistance and gavage feedings who were less than 35 weeks gestation were examined. Infants meeting outlined criteria were fed the same formula, at the same time, and in the same manner as previously used. Gastric residuals were measured and recorded with body position. Positions used are left side, right side and back.

Manpower (in professional man years): 0

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Data collection began in July 1978. To date, 7 subjects have been studied. Data have been recorded on gastric residuals, body positions as well as the extraneous variables of gestational age, sex, race, and type of formula. Data analysis will begin when target subject population of 20 has been studied.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Assessment of the Relationship of Serum Amino Acid Levels
to Episodes of Apparent Sepsis.

WORK UNIT NO.: 78/404

PRINCIPAL INVESTIGATORS: John R. Pierce, MAJ, MC
Thomas P. O'Barr, Ph.D., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the relationship between possible abnormal serum amino acid levels and clinical episodes of apparent sepsis in premature infants.

TECHNICAL APPROACH

Blood samples will be taken from each premature infant (26-36 weeks gestation) who is suspected of having sepsis. These samples will be examined by thin-layer chromatography for the amino acids: tyrosine, phenylalanine, cystine and methionine. A relationship between elevated levels of these amino acids and episodes of clinical sepsis (signs consistent with sepsis but negative cultures) is being sought.

Manpower (in professional man years): 0

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Numerous samples were sent to the Clinical Investigation lab for evaluation of serum amino acids. The lab technique was found to be acceptable. Other projects received higher priority, however, and no patients were enrolled. It is anticipated that with the conclusion of other projects this particular one will receive more attention.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Use of Aspirin as a Prostaglandin Synthetase Inhibitor in
Dysmenorrhea -- A Crossover Double-Blind Clinical Trial

WORK UNIT NO.: 78/405

PRINCIPAL INVESTIGATORS: Christine L. Lawlor, CHA, PA-C
Ann M. Davis, CHA Intern
Joe M. Sanders, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

This study shall attempt to show that aspirin, a known prostaglandin synthetase inhibitor, taken before the onset of symptoms of primary dysmenorrhea is therapeutically more beneficial than placebo in minimizing the pain of primary dysmenorrhea.

TECHNICAL APPROACH

Subjects included in this study were 90 female adolescents between the ages of 13 and 21; randomly selected from Adolescent Clinic at Fitzsimons Army Medical Center. Each subject was administered either placebo, acetaminophen, or aspirin for a period of 6 months beginning 7 days before date of expected onset of menses until onset of menses. Each patient was placed on a schedule for the different medications and arranged in a manner blind to investigator and subjects. Pain experienced by patients was evaluated at the end of each 6 menstrual periods.

The study was conducted through 7 encounters with each subject. An attempt to monitor compliance was made by obtaining a urine sample at home on day one of each period, sample frozen and tested at the upcoming encounter. A master worksheet was utilized to record each month's scores. The statistical analysis was conducted under guidance of the University of Colorado Medical Center, Department of Biometrics.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 78: 0
FY 79: 0

WORK UNIT NO.: 78/405

PROGRESS

No progress report has been received; neither is one anticipated since the principal investigator resigned her position in June 1979.

Publications and Presentations: none

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: The Outpatient Management of Simple Gastroenteritis.

WORK UNIT NO.: 78/406

PRINCIPAL INVESTIGATOR: Warren Todd, LTC, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To determine the effects of the addition of sucrose, glucose, or fructose to an elemental formula (CHO-Free^R) on the resolution of uncomplicated gastroenteritis.

TECHNICAL APPROACH

Approximately 90 infants, who presented to Fitzsimons Army Medical Center Pediatric OPC with a chief complaint of diarrhea, were entered in a double-blind study. Smears, cultures, and P.H. were obtained at initial visit and forwarded to Clinical Investigation Service lab for evaluation and results. Instructions were given for appropriate medication and care to be administered at planned intervals over a period of 72 hours. Data were collected from clinical summary and follow-up sheets to be analyzed in determining end result in the use of glucose-electrolyte solution and formula.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 78:	0
	FY 79:	0

PROGRESS

This project has been terminated since the elemental formula (CHO-Free^R) has been removed from the market.

Publications and Presentations: none

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of New Criteria in the Diagnosis of Acute Renal Failure in the Full-Term and Premature Newborn.

WORK UNIT NO.: 78/407

PRINCIPAL INVESTIGATOR: John Moore, CPT, MC

ASSOCIATE INVESTIGATOR: none

OBJECTIVES

To determine the normal values of urine and serum urea nitrogen, creatinine, sodium, potassium, and chloride in full-term and premature infants of various gestational ages on a fixed oral or I.V. sodium load. The infants to be included may be healthy or ill.

Using these normal values, the usefulness of the urine-to-plasma urea, urine-to-plasma creatinine ratios, and the fractional excretion of sodium in the differential diagnosis of pre-renal versus renal failure in the newborn can be determined. Their usefulness in the differential diagnosis of polyuria in the newborn can also be evaluated. These criteria will be tested in addition to those already established in adults and older children. If the established criteria do not apply to newborn infants, new criteria will be established from this data.

TECHNICAL APPROACH

Since July 1979, randomly selected, well, full-term newborns of consenting parents, have been studied. Serum and urine BUN, creatinine, sodium, potassium and chloride have been obtained on days 1,3,7, and 14 of life. Urine analysis has been obtained on day one. Detailed feeding histories have been obtained regarding the first week of life.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 78:	0
FY 79:	0

WORK UNIT NO.: 78/407

PROGRESS

Between July 1979 and September 1979, seven well, full-term newborns have been studied. The data regarding these infants has not yet been analyzed as this represents a statistically insignificant sample.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Effect of Adriamycin on Platelet Function

WORK UNIT NO.: 79/400

PRINCIPAL INVESTIGATOR: Askold D. Mosijczuk, MAJ, MC

ASSOCIATE INVESTIGATORS: T. Philip O'Barr, Ph.D., DAC
Ellen Swanson, M.S., DAC

OBJECTIVES

To determine and measure possible effect of adriamycin on platelet function.

TECHNICAL APPROACH

Forty ml of blood are drawn from a healthy adult volunteer. The blood is centrifuged and PRP and PPP are drawn off. In a platelet aggregometer, 20 ml of adriamycin are added to the PRP in one cuvette, with the other cuvette with PRP serving as a control. After one minute, aggregating agents--ADP, Epinephrine, collagen--are added to each cuvette and the percent aggregation compared in the two samples. Aliquots of PRP are removed at certain times to measure the amount of thromboxane released.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 79: \$400.00

PROGRESS

To date, 21 donors have been studied; in five of these a slight to moderate degree of inhibition of platelet aggregation has been found, which was also reflected by decreased levels of thromboxane.

Additional donors are being tested, as well as repeating initial studies on the donors whose platelet aggregation was affected by adriamycin. Once this observation can be verified, attempts will be made to determine this possible mechanism(s) by which adriamycin decreases platelet function in these persons.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: An Investigation of the Effects of Aminoglycosides and Lasix
upon the Inner Ear of the Guinea Pig

WORK UNIT NO.: 79/401

PRINCIPAL INVESTIGATORS: John D. Daigh, Jr., CPT, MC
Patrick Glasow, CPT, MC
John W. Harbell, Ph.D., CPT, MSC
W. Nicholas Glab, B.S., SP6

OBJECTIVES

The objective is to establish the effect upon the cochlea of the Guinea pig of aminoglycosides and lasix.

TECHNICAL APPROACH

Guinea pigs are to be given various amounts of aminoglycosides and lasix. The animals will be sacrificed and their cochlea examined under light and electron microscopy.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: \$975.00

PROGRESS

The animals are at Fitzsimons Army Medical Center and the major portion of the work will be completed by 1 Dec 79.

Publications and Presentations: none

STATUS:

Ongoing.

PATHOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Role of Complement Activation in the Pathogenesis of Juvenile Onset Diabetes Mellitus and its Subsequent Effects on the Coagulation Status and Peripheral Vascular Complications in Diabetic Patients.

WORK UNIT NO.: 79/450

PRINCIPAL INVESTIGATOR: Patricia L. Stranghan, MAJ, MC

ASSOCIATE INVESTIGATORS: Paul Nakane, Ph.D.
Judy Barber, MT (ASCP)
Patricia Rush, MT(ASCP)

OBJECTIVES

Clq is present on human platelets. 1) It is known that Clq displaces collagen with respect to collagen dependent platelet aggregation. 2) It is also known that Clq specifically binds to Beta cell membranes. 3) The objective of this study is to compare the levels of Clq in normal patients with juvenile onset diabetes mellitus.

TECHNICAL APPROACH

We have developed a rocket immunoelectrophoresis procedure for quantitation of Clq. Previous methods used for determining Clq levels take up to ten days. With our procedure overnight results are obtained. Presently we are reporting our results in % of normal as we currently have no purified Clq to quantitate ug levels.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: 0.5

PROGRESS

In the past six months we have run serum on several normal patients, two diabetic patients and several patients with known auto-immune disease. At present we are attempting to correlate our levels with those obtained by others who use radial immunodiffusion.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 80

TITLE: Efficacy of Freeze Preservation of Platelets for Human
Utilization - In Vitro and In Vivo Functional Capabilities
after Freeze Preservation with Hydroxyethylstarch (HES).

WORK UNIT NO.: 79/451

PRINCIPAL INVESTIGATOR: Patricia L. Stranahan, MAJ, MC

ASSOCIATE INVESTIGATORS: Rick Martinez, ASCP
John C. Michalak, LTC, MC

OBJECTIVES

To compare the differences between fresh platelets and freeze preserved (HES) platelets for use in thrombocytopenic leukemic patients.

TECHNICAL APPROACH

In the past six months, platelets have been frozen in HES and tested for in vitro function. These studies have been carried out both before freezing and after thawing. Suitable controls with room temperature incubation have also been studied.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 79: 0.5

PROGRESS

The frozen platelets do not survive. Work is underway to determine if this is due to the HES or the freezing process, and to determine if this method of preservation is feasible.

Publications and Presentations: none

STATUS:

Ongoing.

RADIOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 74/600

PRINCIPAL INVESTIGATOR: Peter W. Blue, LTC, MC

ASSOCIATE INVESTIGATOR: Nasser Ghaed, COL, MC

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 performed. 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 NO.: 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): 0.05/yr

Funding (in thousands) FY 78:	0
FY 79:	0

PROGRESS

There were no Indium-111 Chloride studies during fiscal year 1979. It is anticipated that some of these scans will be done in the coming year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 74/602

PRINCIPAL INVESTIGATOR: Peter W. Blue, LTC, MC

ASSOCIATE INVESTIGATOR: Nasser Ghaed, COL, MC

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): 0.1/yr

Funding (in thousands) FY 78:	0
FY 79:	0

PROGRESS

Seven studies using Indium 111 DTPA for evaluation of patients with cerebral spinal fluid pathways pathology have been done in the last year since 30 September 1978. 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
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Non-Invasive Real-Time Ultrasonic Evaluation of Carotid Occlusive Vascular Disease.

WORK UNIT NO.: 79/600

PRINCIPAL INVESTIGATORS: Stanley F. Smazal, Jr., M.D., DAC
Lewis Mologne, COL, MC

ASSOCIATE INVESTIGATORS: John Buscemi, LTC, MC
John Eielson, LTC, MC
Nasser Ghaed, COL, MC

OBJECTIVES

To objectively evaluate the patency of the carotid artery; to evaluate the presence and extent of thrombus and/or ulcerative plaque in the carotid artery; and to employ a full pulsed doppler to measure bi-directional flow in the carotid artery.

TECHNICAL APPROACH

Approximately 120 patients will be evaluated. Patients will be divided into 4 groups as follows (with approximately 30 patients in each group): 1) Control population; 2) Patients with asymptomatic carotid bruits; 3) Symptomatic patients with or without carotids bruits; 4) Patients who have experienced a previous stroke within the last 12 months. This entire patient population will be evaluated by a non-invasive real-time technique.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 79: 0

PROGRESS

Special MEDCASE funding for real-timer ultrasound not available during the fiscal year.

Publications and Presentations: none

STATUS:

Ongoing.

HOSPITAL CLINICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

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

WORK UNIT NO.: 74/651

PRINCIPAL INVESTIGATOR: Nicholas C. Bethlenfalvay, M.D., DAC

ASSOCIATE INVESTIGATOR: George L. Brown, Ph.D., COL, 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 exist-
ing 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 78:	2.5
FY 79:	0.3

WORK UNIT 74/651

PROGRESS

Since September 1978 the following new methodology was acquired: The addition of Nonidet P40 to the urea-isoelectric focus system now enables the investigator to separate and thus quantitate the two non-allelic gamma globin chains, i.e., G-gamma and A-gamma. The presence or absence of either one of these genes is of crucial importance in the understanding of genetic mechanisms that govern the fetal to adult switch of human hemoglobins. Efforts are under way to add, in FY 81, an oxygen dissociation curve analyzer to the capabilities of the hemoglobin effort.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Evaluation of Thalassemia as Cause of Hypochromic Microcytic Anemia or in Interaction with Hemoglobin Variants.

WORK UNIT NO.: 78/650

PRINCIPAL INVESTIGATORS: Nicholas C. Bethlenfalvay, M.D., DAC
Donald G. Corby, COL, MC
George L. Brown, Ph.D., COL, MSC
John C. Michalak, LTC, MC
Philip O'Barr, Ph.D., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To demonstrate that thalassemia may be one of the causes of hypochromic-microcytic anemia and a factor that modified the amount of hemoglobin variants with which it interacts.

TECHNICAL APPROACH

Patients with (a) hypochromic-microcytic anemia the cause of which could not be determined by routine clinical laboratory methods and (b) patients whose hemoglobin electrophoregram reveals a variant hemoglobin in amounts greater than 50 or less than 40% will be evaluated in this study by means of hemoglobin electrophoresis in diverse media and column chromatography. To determine the globin polypeptide chain synthetic ratios peripheral blood will be incubated with ¹⁴C leucine. The red cell lysate will be transformed into globin and the individual polypeptide chains separated on CM cellulose columns. Alpha/beta ratios will be calculated as total radioactivity or specific activity ratios. Synthetic ratios of alpha to non-alpha chains deviating from unity indicate non-balanced chain synthesis and establish the diagnosis of thalassemia.

Manpower (in professional man years): 0.5/yr

Funding (in thousands)	FY 78:	1.0
	FY 79:	1.5

WORK UNIT NO.: 78/650

PROGRESS

In FY 79, 20 patients have been found eligible to enter the study after routine screening. In the six families comprising these 20 patients; the following conditions have been identified: HbC/alpha thalassemia, HbS/beta plus thalassemia, HbS/beta 0 thalassemia, hemoglobin H disease, alpha thalassemia 1, the silent carrier state of alpha thalassemia and beta 0 thalassemia trait.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME

30 SEP 79

TITLE: Evaluation and Structural Identification of Unusual Human Hemoglobin Variants.

WORK UNIT NO.: 78/651

PRINCIPAL INVESTIGATORS: Nicholas C. Bethlenfalvay, M.D., DAC
Donald G. Corby, COL, MC
George L. Brown, Ph.D., COL, MC
John C. Michalak, LTC, MC
Philip O'Barr, Ph.D., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To demonstrate that variation at critical sites in hemoglobin structure is one of the reasons for anemia, polycythemia or a hemolytic state in man.

TECHNICAL APPROACH

Documented cases of chronic hemolytic anemia, erythrocytosis with a demonstrably left shifted oxygen dissociation curve, cases of anemia with a definite right shift of the hemoglobin oxygen dissociation curve, and cases who on routine screening are recognized to have hemoglobins C, D, E, G or J will be studied. Special electrophoretic techniques (cellulose, agar or polyacrylamide media with IEF as applicable) and column chromatography will be employed. Localization of the structure of the modification(s) within the polypeptide chain will be made following enzymatic digestion of the affected polypeptide chain following electrophoretic and chromatographic separation and staining of the individual peptides.

Manpower (in professional man years): 0.5/yr

Funding (in thousands)	FY 78:	2.0
	FY 79:	1.0

WORK UNIT NO.: 78/651

PROGRESS

In FY 79, two patients entered the study. One of these was identified to have double heterozygosity for the hereditary persistence of fetal hemoglobin (the common Black A-gamma/G-gamma) variety. The second patient's hemoglobin was sent in from the AMIC Clinic, Fort Dix, of a man with marked erythrocytosis for which no etiology was found on extensive workup. A high oxygen affinity, electrophoretically silent hemoglobin was suspected. Isoelectric focusing of the patient's hemolysate indeed revealed an abnormal band anodal to HBA. The oxygen dissociation curve of the hemolysate was found to be left shifted. Amino acid analysis of the beta chain (Dr. E. Schwartz, University of Pennsylvania, Department of Pediatrics, Division of Hematology) revealed a substitution of proline to threonine at beta 100. This abnormality has not been previously described, and thus represents a new high oxygen affinity hemoglobin variant.

Publications and Presentations: none

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Alpha Thalassemia: Evaluation of the Significance of Hemoglobin Bart's in the Black Neonate.

WORK UNIT NO.: 78/652

PRINCIPAL INVESTIGATORS: Nicholas C. Bethlenfalvay, M.D., DAC
Askold P. Mosijczuk, MAJ, MC

ASSOCIATE INVESTIGATORS: George L. Brown, Ph.D., COL, MC
Thomas P. O'Barr, Ph.D., DAC
Donald G. Corby, COL, MC

OBJECTIVES

To confirm the presence and assess the severity of alpha thalassemia in Black neonates who have Hemoglobin Bart's by means of in vitro globin polypeptide chain synthesis and calculation of alpha-beta radioactivity ratios.

TECHNICAL APPROACH

Black neonates will be screened by means of electrophoresis for the absence or presence of Hemoglobin Bart's. Quantitation of Hemoglobin Bart's will be done by column chromatography. Those cases who present with detectable amounts of Hemoglobin Bart's at birth will be again studied at one year of age for the presence or absence of "free" alpha chain pool by incubating their peripheral blood with ¹⁴C leucine in vitro and separation of globin chains on CM cellulose columns. At that time alpha/beta chain synthetic ratios will be determined.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 78: 1.0
FY 79: 1.0

PROGRESS

Since the inception of this protocol in FY 78, Black neonates with Hemoglobin Bart's, ranging between 11 and 0%, were studied. Most of these neonates are now over one year of age. The Pediatric Hematologist, who has been recently assigned and one who will be collaborating in this

WORK UNIT NO 78/652

PROGRESS - continued

study, will continue ascertaining the alpha/beta globin synthetic ratios to determine to what extent the presence and amount of Hemoglobin Bart's appears at birth and if there is a reflection of alpha thalassemia in this ethnic group.

Publications and Presentations: none

STATUS:

Ongoing.

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CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: Gamma Thalassemia in the Newborn.

WORK UNIT NO.: 78/653

PRINCIPAL INVESTIGATORS: Nicholas C. Bethlenfalvay, M.D., DAC
Askold P. Mosijczuk, MAJ, MC

ASSOCIATE INVESTIGATORS: George L. Brown, Ph.D., COL, MC
Thomas P. O'Barr, Ph.D., DAC
Donald G. Corby, COL, MC

OBJECTIVES

To demonstrate that suppression of gamma polypeptide chain synthesis is one of the mechanisms that causes microcytic-hypochromic (hemolytic) anemia in the newborn.

TECHNICAL APPROACH

Reticulocyte enriched peripheral blood of newborn having microcytic-hypochromic anemia of unknown etiology will be incubated with ^{14}C leucine in vitro. Globin will be prepared by the acid acetone technique and fractionated into alpha, beta and gamma chains on CM cellulose columns. Radioactivity and specific activity ratios of gamma/alpha and gamma plus beta/alpha chains will be calculated.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)	FY 78:	0.8
	FY 79:	1.0

PROGRESS

In FY 79 no newborn met the selection criteria to enter into the study.

Publications and Presentations: None

STATUS:

Ongoing.

SOCIAL WORK SERVICE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Aurora, Colorado 80045

RESEARCH PROJECT RESUME
30 SEP 79

TITLE: The Gravity of Child Care and Maltreatment Acts: An Assessment of Opinions of U.S. Army Child Protection and Case Management Team Members.

WORK UNIT NO.: 78/755

PRINCIPAL INVESTIGATOR: Theodore P. Furukawa, CPT(P), MSC, M.S.W.

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Through written questionnaire survey of selected U.S. Army Child Protection and Case Management Team (CPCMT) members assigned to continental United States (CONUS) medical treatment facilities, the study will: (1) clarify the types of acts toward children which are considered acceptable child care vs. maltreatment, (2) ascertain the way in which specific features of the child care incident affect the judgement of seriousness, and (3) consider the extent to which seriousness judgements are determined by characteristics of those making the assessments.

TECHNICAL APPROACH

Since 1976, all CONUS Army installations with 2,000 or more dependents are mandated to establish a multidisciplinary CPCMT to identify, protect, and treat the maltreated child and his/her family (AR 600-48). Two written questionnaires were developed for the study: (1) a survey of the installations' senior social workers for organizational data and (2) a survey of CPCMT members for personal/professional data and for their ratings on a standard set of vignettes (for seriousness and predicted level of intervention by their CPCMTs).

Manpower (in professional years): 0.25/yr

Funding (in thousands) FY 78: 0
FY 79: 0

PROGRESS

Between July and September 1978, questionnaires were developed and sent to forty-two installation senior social workers and to 469 CPCMT members (dated 1 October 1978). A suspense date of 1 November 1978 was established for the return of all questionnaires.

Publications and Presentations: None

STATUS:

Completed.

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