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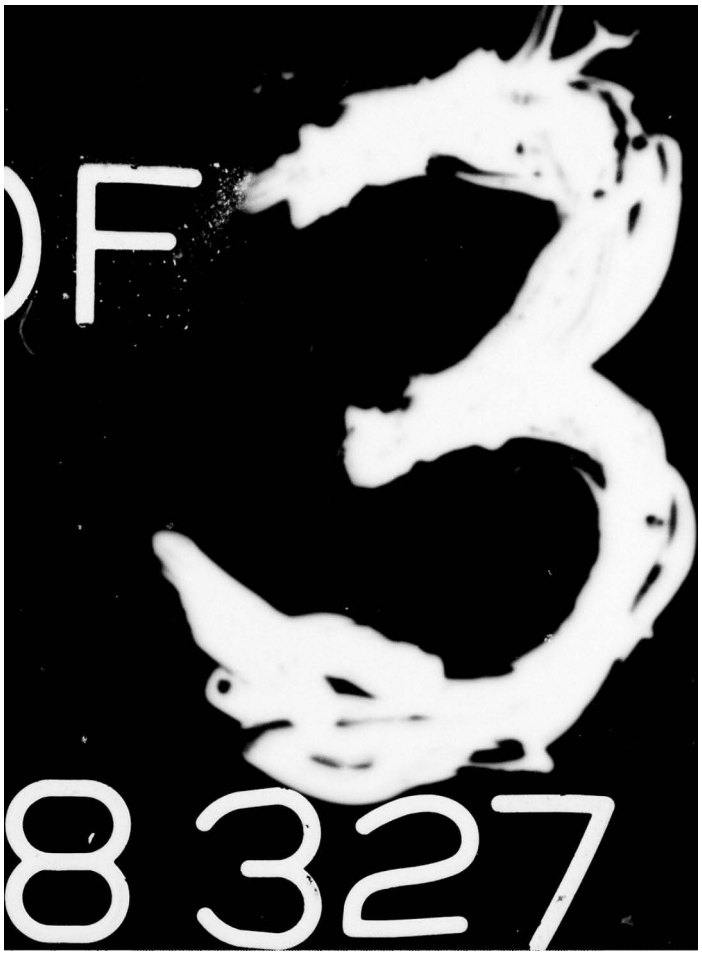
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30 June 1976

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Subject report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1976 and other known presentations and publications by the Fitzsimons Army Medical Center professional staff. The research protocols described were conducted under the provisions of AR 40-30, as amended, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans,
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30 JUNE 1976

CLINICAL INVESTIGATIONS (U)

FITZSIMONS ARMY MEDICAL CENTER

DENVER, COLORADO 80240

FOREWORD

This report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1976 and other known presentations and publications by FAMC professional staff.

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

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

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

Donald G. Corby

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

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

*Reference AR 40-38, para 6, and interim change thereto: DA Message R 151530 Z Jul, 75 -- DA (TSG) WASH DC // DASG-ZA SGRD-HR // and change thereto (DA message 122044Z Sep 75, ofc ref as cited), effective 1 Jan 76.

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Nelson, W. P.: Cardiac Arrhythmias - Concepts to Clarify High-Country Conference. Vail, CO, 23 January 1976.

Nelson, W. P.: Risk Factors in Coronary Heart Disease. Colorado Heart Assn. Meeting, Greeley, CO, 29 January 1976.

Nelson, W. P.: Interpretation of the Difficult Arrhythmia. Am. College of Cardiology, New Orleans, LA, 24 February 1976.

Nelson, W. P.: Interpretation of the Electrocardiogram and of Cardiac Arrhythmias. AMA Meeting, Denver, CO 28 February 1976.

Nelson, W. P.: Am. College of Physicians Course, Current Concepts of Cardiovascular Disease, (3 Lectures given) - Diagnosis and Management of Angina Pectoris; An Approach to Cardiac Arrhythmias, The Electro-Cardiogram and Ischemic Heart Disease. Tucson, AZ, 18-20 March 1976.

Nelson, W. P.: Three lectures given, Arrhythmias in Acute Myocardial Infarction; An Approach to Cardiac Arrhythmias; The Analysis of a Difficult Arrhythmia. Tulane University Post-Graduate Course in Cardiology, New Orleans, LA, 22-23-24 April 1976.

Nelson, W. P.: Cardiovascular Disease for Nurses, (3 Lectures given), The Electrocardiogram and Electrolyte Derangement; Confusing Confusin Phenomena; Deceptions in Electrocardiography. American College of Cardiology Post-Graduate Course, Clearwater, Florida, 25-27 April 1976.

Nelson, W. P.: Post-Graduate Program, (3 Lectures given), An Approach to Cardiac Arrhythmias; Aberrant Ventricular Conduction; Fusion Phenomena. University of Kansas School of Medicine, 6-8 May 1976.

Nelson, W. P.: Visiting Professorship, (3 Lectures given), The Interpretation of Cardiac Arrhythmias; The Significance and Treatment of Ventricular Conduction Disturbances; Cardiac Disease with Manifestations in Other Organ Systems. Tripler Army Medical Center, 1-11-12 June 1976.

Nelson, W. P.: Visiting Lectureship, Concealing Cancellations, Nefarious Normalization and Confusing Fusion, Queens Medical Center, Honolulu, Hawaii, 11 June 1976.

Williams. T. H.: Lecture. Non-Cardiac Surgery in the Cardiac Patient. Participant Vail ACC Course, January 1976.

Williams, T. H.: Lecture. Pseudo Infarction Patterns. Regional ACP Meeting, Colorado Springs, CO, January 1976.

Williams, T. H.: Lecture. Non-Cardiac Surgery in the Cardiac Patient. Durango Medical Program, Colorado Hospital Course, February 1976.

Williams, T. H.: Basic Electrocardiographic. AMA Regional Course, February 1976.

Williams, T. H.: Pseudo Infarction Patterns. Army Assoication of Cardiology Meeting, May 1976.

DERMATOLOGY

Dermatology

Aeling, J. L.: Localized Mycosis Fungoides. American Academy of Dermatology, San Francisco, CA, December 1975.

Aeling, J. L.: Histopathology of Viral Infections of Skin. Colorado Derm Society, Denver, CO, February 1976.

Dermatology - continued

Nuss, D. D.: Herpes Simplex - Herpex Zoster. University of Colorado Post Graduate Course in Dermatology, January and March 1976, Denver, CO. June 1976 at Estes Park, CO.

Aeling, J. L.: Treatment of Mycosis Fungoides. Tri-Service Seminar, San Francisco, CA, April 1976.

ENDOCRINOLOGY

Endocrinology

Plymate, S. R.: Chronic Lymphocytic Thyroiditis, Thyrotoxicosis and Low Radioactive Iodine Uptake. Regional ACP Meeting, Colorado Springs, CO, January 1976.

Plymate, S. R.: Endocrine Evaluation of the Testis. Regional ACP Meetings, Colorado Springs, CO, January 1976.

GENERAL MEDICINE

General Medicine

Bergin, J. J.: Platelets. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Platelet Hemostatic Levels and Major Surgery. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Platelet Factor 3 and Surgical Preparation. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Factor VIII Therapy. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Fibrinogen. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Reversal of Warfarin Toxicity. American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Disseminated Intravascular Thrombosis (DIT). American Association of Blood Banks, Chicago, Illinois, November 1975.

Bergin, J. J.: Coagulation Factors Influencing Thrombosis of Aorto-Coronary Bypass Grafts. Regional Meeting of the American College of Physicians, Colorado Springs, CO, January 1976.

General Medicine - continued

Bergin, J. J.: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome. Regional Meeting of the American College of Physicians, Colorado Springs, CO, January 1976.

Bergin, J. J.: Thromboembolism: When, Why, and How?. Colorado Heart Association High Country Cardiac Conference, Vail, CO, January 1976.

Bergin, J. J.: Is Thrombophlebitis a Clinical Diagnosis? Pulmonary Disease Symposium, FAMC, September 1975.

HEMATOLOGY

Hematology

DiBella, N. J.: Cellular and Humoral Immunity in the Myeloproliferative Diseases. American College of Physicians & American Society of Duternol Med Annual Joint Meeting. January 15, 1976, Colorado Springs, CO.

NEPHROLOGY

Nephrology

Ball, J. H.: Post Partum Nephrosclerosis. U.S. Army 3rd Annual Symposium in Nephrology, Presidio of San Francisco, San Francisco, CA, 23-24 October 1975.

Ball, J. H.: The Out-Patient Treatment of Refractory Hypertension with Minoxidil. Regional ACP Meeting, Colorado Springs, CO 15-17 January 1976.

PULMONARY DISEASE

Pulmonary Disease

Christensen, W. I.: Intermittent Mandatory Ventilation. American College of Chest Physicians 41st Annual Meeting, Anaheim, California, 28 October 1975.

Gerace, J.: Smoking and the Chest Physician. FGH Symposium, September 1975.

Hazlett, D. R.: Flows and Volumes Introduction to Basic Spirometry and Relationship of Flows and Volumes. Iowa Society for Respiratory Therapy 4th Annual Symposium on Pulmonary Function Testing, Adventure Land Inn, Des Moines, Iowa, 24-25 October 1975.

Pulmonary Disease - continued

Hazlett, D. R.: Acid-base Balance Diseases Causing Imbalance and the Role of Respiratory Therapy in its Treatment. Iowa Society for Respiratory Therapy 4th Annual Symposium on Pulmonary Function Testing, Adventure Land Inn, Des Moines, Iowa, 24-25 October 1975.

Hazlett, D. R.: New Modes of Pulmonary Function Testing, Flow Volume Loops, Closing Volumes and Others. Iowa Society for Respiratory Therapy 4th Annual Symposium on Pulmonary Function Testing. Adventure Land Inn, Des Moines, Iowa, 24-25 October 1975.

Hazlett, D. R.: Cardiopulmonary Exercise Stress Testing. Iowa Society for Respiratory Therapy 4th Annual Symposium on Pulmonary Function Testing, Adventure Land Inn, Des Moines, Iowa, 24-25 October 1975.

Zimmer, R. W., and Hazlett, D. R.: An Improved Non-Invasive Plethysmographic Measure of Transthoracic Pressure During Maximal Expiratory Maneuvers: Therapy. 41st Annual Meeting of the American College of Chest Physicians, Anaheim, CA, 26-30 October 1975.

Kindig, N. B., and Hazlett, D. R.: A New Measure of Anatomic Dead Space During Steady State Studies; Theory. 11th Annual Meeting of the Association for the Advancement of Medical Instrumentation, Hyatt Regency Hotel, Atlanta, GA, 21-25 March 1976.

Zimmerer, R. W., and Hazlett, D. R.: An Improved Non-Invasive Plethysmographic Measure of Transthoracic Pressure during Maximal Expiratory Maneuvers; Theory. 11th Annual Meeting of the Association for the Advancement of Medical Instrumentation, Hyatt Regency Hotel, Atlanta, GA, 21-25 March 1976.

Hazlett, D. R.: Chairman of Pulmonary Systems Session of the 11th Annual Meeting of the Association for the Advancement of Medical Instrumentation, Hyatt Regency Hotel, Atlanta, GA, 21-25 March 1976.

Kindig, N. B., and Hazlett, D. R.: Measurement of Anatomic Dead Space during Steady State Studies of Pulmonary Diffusing Capacity. 13th Annual Rocky Mountain Bioengineering Symposium and 13th Inter-National ISA Biomedical Science Instrumentation Symposium. University of Wyoming, Laramie, WY, 3-5 May 1976.

Nelson, R.: Extrapulmonary Tuberculosis. 28th Annual Symposium on Pulmonary Diseases, 8-11 September 1975.

Nelson, R.: Panel Discussion - Case Presentations - Ask The Experts. Co-Chairman - 28th Annual Symposium on Pulmonary Diseases.

Pulmonary Disease - continued

Nessan, V. J.: Review of Histoplasmosis. Pulmonary Disease Annual Symposium, September 1975.

Nessan, V. J.: Clinical Spectrum of Histoplasmosis. ACP Meeting, Colorado Springs, CO, January 1976.

SURGERY

Ophthalmology

Manson, R. A.: Common Eye Problems in Children. University of Colorado Family Practice Review.

Manson, R. A.: Immunofluorescence of Benign Mucous Membrane Pemphigoid. American Academy of Ophthalmology Annual Meeting.

Manson, R. A.: Experience with Soft Contact Therapeutic Lenses. Southern Medical Association Annual Meeting.

Manson, R. A.: A Year's Experience with Keratoplasty. Bascom Palmer Eye Institute Alumni Residents' Day.

Orthopedics

Ballard, A.: Traumatic Patellar Dislocation. Sport Medicine Society Meeting, New Orleans, La, July 1975.

Ballard, A.: Socpe of Children's Orthopedics. Post Graduate Medicine Symposium, University of Colorado, Denver, CO, August 1975.

Ballard, A.: Scoliosis Evaluation and Treatment. Post Graduate Medicine Symposium, University of Colorado, Denver, CO, August 1975.

Ballard, A.: Common Problems in the Lower Extremities in Children. Post Graduate Medicine Symposium University of Colorado, Denver, CO, August 1975.

Ballard, A.: Traumatic Patellar Dislocations. Childrens Symposium, FAMC, Denver, CO, December 1975.

Ballard, A.: Fractures of the Femur. Orthopedic Nurses Meeting AAOS, Denver, CO, December 1975.

Glancy, G.: Compartment Syndromes. Orthopedic Nursing, Atlanta, Ga, September 1975.

Orthopedics - continued

Glancy, G.: Pulmonary Embolism vs. Fat Embolism. Orthopedic Nursing, Atlanta, GA, September 1975.

Glancy, G.: Common Nerve Problems. Orthopedic Nursing, Atlanta, GA, December 1975.

Glancy, G.: Slipped Capital Femoral Epiphysis. Children's Symposium, FAMC, Denver, CO, December 1975.

Eversmann, W.: Management of Segmental Bone Loss of Forearm. Western Orthopedic Association Annual Meeting, San Francisco, CA, October 1975.

Eversmann, W.: Fracture of the Hand in Children. Western Orthopedic Association Annual Meeting, San Francisco, CA, October 1975.

Ballard, A.: Evaluation and Treatment of Scoliosis. Ogden Surgical Society Meeting, Ogden, Utah, May 1976.

Ballard, A.: Common Problems of Lower Extremities in Children. Ogden Surgical Society Meeting, Ogden, Utah, May 1976

Ballard, A.: The Congenital Dislocation of the Hip in Children and Adults. Ogden Surgical Society Meeting, Ogden, Utah, May 1976.

Sulkosky, J.: The Three Bone Forearm: A Salvage Procedure for Treatment of Ulnar Nonunion, Infection and Tumor. Rocky Mountain Orthopedic Association, Denver, CO, December 1975.

OTOLARYNOLOGY

Otolarynology

Krekorian, E. A.: Three Lectures given. Repair Combat Injured Facial Nerve; Laryngopharyngeal Injuries; Combined Craniofacial Approach to Extensive Tumors of the Nose and Paranasal Sinuses. Madigan Army Medical Center, panel member, Head and Neck Symposium, 5 December 1975.

Krekorian, E. A.: Surgical Management of Angiofibroma with Intracranial Extension. Middle Section, Triological Society, Minneapolis, Minnesota, 24 January 1976.

Hasbrouck, J. M. and Martin, R. R.: Modification of Normal Speech Disfrencies in Children. American Speech and Hearing Association Convention, Washington, D. C., 22 November 1975.

Otolarynology - continued

Hasbrouck, J. M.: Modern Techniques of Diagnosis and Treatment of Stuttering. Annual Wyoming Speech and Hearing Association Convention, four lectures, Casper, Wyoming 2-3 October 1975.

Hasbrouck, J. M.: Auditory Perceputal Disorders in Neurologically Damaged Adults. St. Thomas Moore Hospital, two lectures, Cannon City, Colorado 7 May 1976.

Plastic Surgery

LaRossa, D. D., et al: Use of Toluidine Blue as a Diagnostic Staining Technique for Malignant and Premalignant Lesions of the Skin and Oral Mucous Membranes. Proceedings of the Third International Symposium on the Detection & Prevention of Cancer, New York 1976.

Zbylski, J. R.: Eyelid Reconstruction with Ear and Nasal Cartilage Grafts. Symposium of Military Plastic Surgeons' Meeting, Washington D.C., January 1976.

LaRossa, D. D.: Correction of Facial Deformity from Frontal Sinus Mucocele. Symposium of Military Plastic Surgeons' Meeting, Washington, D.C., January 1976.

Rich, J. D.: Dermatofibrosarcoma Protuberans. Symposium of Military Plastic Surgeons' Meeting, Washington, D.C., January 1976.

Rich, J. D.: Dermatofibrosarcoma Protuberans of the Head and Neck. Senior Residents Meeting, New Orleans, March 1976.

Thoracic Surgery

Hamaker, W. R.: Valve Replacement in Bacterial Endocarditis. 5th Meeting of the Association of Army Cardiology, Denver, CO, May 1976.

Schuchmann, G. F.: Foreign Bodies of the Air Passages Requiring Surgical Management. 28th Annual Symposium on Pulmonary Disease, October 1975.

Zajtchuk, R., Hazlett, D. R., and Baugh, J. H.: Bioelectric Impedance Estimates of Heart Valve Cross-Sectional Areas. Fifth Annual Meeting of the Association of Army Cardiology, May 13-15, 1976. Current Trends in Cardiovascular Disease.

Urology

Weigel, J. W.: Abacterial Cystitis in Siblings. Kimbrough Urological Seminar, October 1975.

Urology - continued

Weigel, J. W.: Retroperitoneal Fibrosis. Kimbrough Urological Seminar, October 1975.

Dobbs, R. M.: Elemental Mapping of Renal Calculi Utilizing the Scanning Electron Microscope. Kimbrough Urological Seminar, October 1975.

Fauver, H. E.: Fat Necrosis in the Scrotum. Kimbrough Urological Seminar, October 1975.

Page, M. E.: Autotransplantation of the Canine Kidney with Proximal Vena Caval Ligation. Kimbrough Urological Seminar, October 1975.

Buntley, D. W.: Testis Tumors at FAMC. Kimbrough Urological Seminar, October 1975.

Weigel, J. W., and Page, M. E.: Renal Transplantation with Proximal Vena Caval. Scientific exhibit at the South Central Section Meeting in Urology, September 1975.

CLINICAL INVESTIGATION SERVICE

Rothlauf, M. V., and Kolb, J. G.: Laboratory Management of Mycobacterium Tuberculosis and Atypicals. Arapahoe Junior College, Denver, CO., 1976.

Calcagno, J. V., Brown, G. L., Tull, A. H., Yost, D. C., Jolly, D. J., and Cromwell, R. K.: Evaluation of Three Collections - Transport System for the Isolation of Group B Streptococcus from Prepartum Women and Neonates. American Society for Microbiology. Atlantic City, New Jersey, 1976.

Tull, A. H.: Mycoplasma and T-Strains. Laboratory Evaluation. Colorado Association for Continuing Medical Laboratory Education. Denver, CO., 1976.

Daniels, W. L., O'Barr, T. P., Miller, J. G., and Seab, J.: Circulatory and Hormonal Changes During Acute Pancreatitis. Federation Proceedings, April 1976.

Adler, R. A.: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Syndrome. Regional Meeting of the American College of Physicians, January 15, 1976.

Adler, R. A.: Prolactin, 1976. Endocrine Research Seminar, Dartmouth Medical School, April 9, 1976.

CIS - continued

Brown, G. L., DiBella, N., and Corby, D. G.: Immunologic Studies of IgE-IgM Kappa Gammopathy Associated with Lymphoma. Federation of American Societies for Experimental Biology. Anaheim, California, 1976.

Brown, G. L.: Serologic Evaluation of Mycoses. Medical College of Colorado. Denver, Colorado, 1976.

Brown, G. L.: Mycoplasmatales and T-Strains. Graduate Seminar, colorado State University, Ft. Collins, CO., 1976.

Brown, G. L.: Cellular Immunity. I. Lymphocyte Blast Transformation. II. Lymphokines. Graduate Seminar, Colorado State University. Ft. Collins, CO., 1976

Brown, G. L.: Cellular Immunity. I. Laboratory Evaluations. National Asthma Research Center, Denver, CO., 1976.

Brown, G. L.: Serum Gammopathies. I. Laboratory Parameters. St. Lukes Hospital, Milwakee, Wisc., 1976.

DiBella, N. J., and Brown, G. L.: Cellular and Humoral Immunity in Myeloproliferative Diseases. American College of Physicians and American Society of Internal Medicine. Colorado Springs, Colorado, 1976.

OB-GYN

OB-GYN

Llorens, A. S.: Control of Intractable Pain Secondary to Advanced Pelvic Cancer. ACOG, Armed Forces District Meeting, San Antonio, TX, 1975.

PEDIATRICS

Pediatrics

Merenstein, G. B.: Regionalization of Neonatal Intensive Care Units. Pediatric Seminar, U. S. AFA Hospital, Colorado Springs, CO, 31 March 1976.

Way, G.: Frequency, Incidence, and Etiology of Cardiac Malformations. Pediatric Seminar, U.S. AFA Hospital, Colorado Springs, CO, 31 March 1976.

Way. G.: Diagnostic Approach to Cardiac Disease in the Neonate. Pediatric Seminar, U.S. AFA Hospital, Colorado Springs, CO, March 1976.

Way, G.: Common Congenital Heart Disease. Pediatric Seminar, U. S. AFA Hospital, Colorado Springs, CO, March 1976.

OB-GYN - *continued*

Way, G.: Echocardiography. Pediatric Seminar, United States AFA Hospital, Colorado Springs, CO, March 1976.

Way, G.: Disorders of Heart Rate and Rhythm. Seminar, United States AFA Hospital, Colorado Springs, CO, March 1976.

Merenstein, G. B.: Audit of Paramedical Personnel in Emergency Air Transport. Emergency Medical Service, Hilton Inn, Denver, CO, March 1976.

Merenstein, G. B.: Recognition and Management of the High Risk Pregnant Female and Newborn Infant. Hilton Inn, Denver, CO, March 1976.

Merenstein, G. B., and Honeyfield, P.: Mechanisms of Ground and Air Transportation. Newborn Emergency Care, Denver Childrens Hospital, Denver, CO, June 1976.

Butterfield, L. J., Merenstein, G., and Honeyfield, P., et al: Standards of Inter-Hospital Care. Newborn Emergency Care, Denver Childrens Hospital, Denver, CO, June 1976.

Simons, D.: Colorado Conference on Teenage Pregnancy and Childbirth, Hilton Inn, Denver, CO, October 1975.

Spaulding, H.: Cataracts and Steroids in Asthmatic Children. Pulmonary Disease Symposium, FAMC, September 1975.

Sanders, J. M.: Chronic Illness in the Adolescent. First National Nurse Practitioner Symposium, Executive Tower Inn, Denver, CO, 3 June 1976.

DENTISTRY

Dentistry

Hoffman, W., Jr.: Practical Precision Paritals, Posterior Tooth Forms. Postgraduate Course in Removable Prosthodontics, Letterman Army Medical Center, San Francisco, California, 8-11 September 1975.

Snyder, A. J., and Vincent, J. A.: Enamel Projections & Furcation Involvements. Metropolitan Denver Dental Society-Midwinter Meeting, Denver, CO January 1976.

Snyder, A. J.: Biology of the Periodontium and Histopathology of Periodontitis. Postgraduate Course in Periodontics, Letterman Army Medical Center, San Francisco, CA, February 1976.

Physical Medicine

Scanlon, C.: Physical Therapy Section A New Look Through the Above Knee Prosthesis: Combined Midyear Section Meeting, APTA, Washington, D.C.; Southwest Region Education Section Meeting, APTA, Denver, CO.; Denver Orthopedic Meeting, Denver, CO.

Doctor, R. L.: Physical Therapy Section. Physical Therapy in Orthopedics. Orthopedic Nurses' Conference, Denver, CO.

Pfeiffer, V. R.: Physical Therapy Section. Special Interest Research Section. South Region Education Section Meeting of APTA.

Pfeiffer, V. R.: Acute and Traumatic Pulmonary Conditions. Continuing Education Program of School of Medicine, U. of Maryland, Baltimore, MD.

Schofield, G.: Current Trends in Sensory Integrative Development. Colorado Occupational Therapy Assn.

UNIT SUMMARY SHEET

UNIT SUMMARY SHEET

Clinical Investigation Program, FAMC

Clinical Investigation efforts by FAMC personnel in FY 76 culminated in the publication of 104 articles and 144 presentations and lectures at national, international, and regional scientific meetings. As of 30 June 1976, there were 96 research protocols on the CIS register. Of these 21 projects were completed and 10 terminated.

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

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

Manpower: Current and authorized strength is outlined.

Description	Grade	MOS	Br	Auth	Actual	Name
C, Clin Rsch	06	3116	MC	1	1	Corby
C, Immuno Sec	05	3311	MS	1	1	Brown
Internist	05	3139	MC	1	1	Charles
Lab Admin	03	3314	MS	1	1	Marsteller
C, Surg - Rsch Labs	03	3200	VC	1	1	Hoffman
C, Micro Sec	03	3307	MS	1	1	Calcagno
Physiologist-PhD	03	3327	MS	0	1	Daniels
Biochem	03	3309	MS	0	1	Yancy
NCOIC	E7	92B4R		1	1	Johnson
C. Med Lab NCO	E7	92B4R		1	1	Underhill
SR O.R. SP	E5	91D3R		1	1	Smith
Bio Sci Asst	E6	01H20		3	3	Turk

Description	Grade	MOS	Br	Auth	Actual	Name
Bio Sci Asst	E5	01H20				Andersen
Bio Sci Asst	E5	01H20				Glab
Bio Sci Asst	E4	01H20		1	1	Foster
Bio Sci Asst	E6	01H20		NTD	1	Jolly
Vet Sp	E5	91T2R		NTD	1	Rich
Vet Sp	E4	91T2R		NTD	1	Michelon
Microbiol-PhD	13	0403	GS	1	1	O'Barr
Microbiol	09	0403	GS	3	3	Lima Rothlauf Tull
Med Technol	09	0644	GS	1	1	Rush
Biochem	09	1320	GS	1	1	Goad
Microbiol	07	0403	GS	6	6	Cromwell Gray Kile Kolb Caigoy Paine
Rsch Chem	07	1320	GS	3	3	McNamara Noble Swanson
Bio Lab Tech	07	0404	GS	1	1	Hakes
Animal Tech	05	0404	GS	1	1	Roslan
Secy-DMT	05	0318	GS	1	1	McCrill
Animal Caretaker	05	7706	WG	2	2	Beltran Hitchcock
Clerk-Steno	04	0318	GS	1	1	Montoya
HSC Microbiol Interns	05	0403	GS	2	2	Bennett Fairley

	FY-75 Program	FY-76 Program
Civilian Pay	282,143	329,374
Travel	1,012	2,572
Supplies	109,972	115,000
Equipment	75,291	85,000
Contracts	15,300	29,000
Other (Military)	314,199	

PROGRESS:

In order to comply with the mission directives as outlined in AR 40-38, as amended, Clinical Investigation Program and FAMC 40-8, an aggressive and comprehensive program of expansion of the Clinical Investigation Service, FAMC, has been undertaken. The TDA was

redesigned to facilitate lines of command, coordination between sections, and better utilization of personnel and facilities. This reorganization has resulted in an integrated administrative section (Office of the Chief) and five independent functional laboratory sections: Immunology, Microbiology, Biochemistry, Surgical Research Laboratories and the Coagulation Laboratory. All sections are fully staffed, equipped and are presently providing technical support for registered protocols and teaching programs.

CIS, under the guidance of COL Donald G. Corby, MC, has completed a total activity relocation. The move from five widely scattered facilities located throughout the medical center into the laboratories formerly occupied by the US Army Medical Research and Nutrition Laboratories (now LAIR) has consolidated the physical facilities and resulted in a cohesive research organization offering support in: applied immunology, tissue culture, analytical chemistry, radioimmunoassays, medical microbiology, mycobacteriology, TB reference laboratory, surgical research, physiological monitoring and complete veterinary animal care.

CIS has justified and received from HSC two civilian microbiology intern training positions. This program brings in a qualified aspirant at the GS-05 entrance level and upon successful completion of a rigorous training program allows for non-competive promotions to GS-07 and finally the GS-09 journeyman level.

The constant turnover of enlisted personnel along with the competition between research and patient care activities for medical specialists forced CIS to consider alternative means of staffing those enlisted TDA positions. The solution was to convert the positions with the highest turnover rate in Science and Engineering slots (MOS 01H20) and utilize the Army's highly successful Stripes for Skills recruitment program. By doing this, CIS has recruited four individuals with backgrounds ranging from Bachelor of Science to Master of Science in: microbiology, biochemistry, and anatomy-physiology. These enlisted personnel are on stabilized assignments (SUE) and have enlisted specifically to work for our Ph.D. researchers.

Office of the Chief:

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

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

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

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

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

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

Immunology Section:

During FY 1976 the Microbiology Section, in addition to on-going research studies, provided consultative support services in two areas of specialization, to other federal agencies and medical civilian community of metropolitan Denver area. I. Mycobacteriology, approximately 960 specimens were processed for definitive identification/confirmation of M. tuberculosis, anti-tuberculous drug sensitivity patterns and identification of mycobacteria other than M. tuberculosis. II. Medical Microbiology, a total of 40 specimens were evaluated for mycoplatales and ureo-plasma (T-strain); specimens submitted originated from 11 infertility and 11 spontaneous abortion subjects.

During FY 76 the Immunology Section, in addition to on-going research investigations, studied 175 patients for a total of 419 consultative evaluations in the areas of applied immunology (cellular and humoral), hemoglobinapathy and gammopathy. Number of patients and specimens in area of specialization with indicated unusual findings are as follows: I. Hemoglobinapathy, 15 families studied, 36 evaluations. Hb species described: 2 Hbs, 1 HbH, 4 beta helasemia minor, 2 HbE and 1 Hb Lepore. II. Applied Immunology. Serum

protein profile evaluations - 94 patients, 127 evaluations: 1 Bruton's syndrome, 1 Waldenstrom's with polymerized IgM, 23 Gammopathies (2 IgA Kappa, w immune-complex of IgG + IgM, 1 light chain, 1 defective kappa chain, 1 IgG lambda, 1 IgE-IgM kappa complex, 1 IgG kappa, 12 suppressed IgG, IgM or IgG, 2 suppressed complement C'3 - C'4); b. Applied serology evaluations: 4 patients, 4 evaluations for infertility problems involving sperm immobilization by serum of wife and/or husband; c. Cellular immune evaluations - 62 patients, 252 evaluations: 20 patients with suppressed thymic derived lymphocytes, 1 patient with delayed sensitivity to aldomet.

Microbiology Section:

Two independent subsections of the Microbiology Section, CIS, provide technical support for on-going protocols, training and consultative services:

1. Medical Microbiology Subsection:

   Provides support for research studies requiring isolation and identification of pathogenic micro-organisms, development of new isolation media and culture collection systems. Current capabilities include: Isolation and identification of Group B and Group A Beta Hemolytic Streptococcus including definitive serologic grouping and sub-typing, pontential pathogens of the upper respiratory tract, mycoplasma, ureaplasma and L-forms.

2. Mycobacteriology Subsection:

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

Surgical Research Laboratories Section:

The newly re-organized Surgical Research Laboratory Section (formerly the Surgery/Physiology and Veterinary Sections) offers continued support in the areas of surgery, physiology, and veterinary care. A Veterinarian and Ph.D. Physiologist provide guidance in their respective areas of expertise. The section is currently supporting twenty-five protocols and associated training programs.

The relocation of the Section from Building 228 to Buildings 601 and 602 has resulted in a physical plant with more than three times the floor space. The acquisition of radiographic and electron microscopy equipment, an additional operating room, increased animal housing facilities and space for the performance of diagnostic laboratory procedures has greatly increased surgical research productivity. The Section's capabilities range from support in microvascular surgery, organ transplantation, to cardiac pulmonary by-pass procedures. The staff, equipment and facilities are varied enough to enable adaptation to new procedures with relative ease.

Our current facilities allow us to house and care for approximately 20 dogs, 25 cats, 8 monkeys, 1500 laboratory rodents, and miscellaneous small animals.

The training programs support ranges from exercises in endotracheal intubation, microsurgery, basic operating room techniques for Clinical Specialists (91C) to training in corneal transplantation techniques.

Proposed construction of an Animal Care Facility designed to meet American Association for Accreditation of Laboratory Animal Care has been disapproved by higher headquarters. Because current facilities do not comply with regulations of the AAALAC and Public Laws 89-544 and 91-479, failure to build the Animal Care Facility could result in the loss of research animal support and training previously outlined.

Coagulation Laboratory Section:

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

Biochemistry Section:

This section has made available a broad spectrum of laboratory support for protocols from the Departments of Medicine and Surgery. Generally, this involves the determination of drugs, biochemicals, metabolites and hormones through the application of radioimmunoassays, labeling with radioactive compounds, and a variety of spectrophotometric or fluorometric procedures. In examples of specific studies, complete endocrine profiles to include cortisol, compound-S, testosterone, aldosterone, insulin, growth hormone, TSH, FSH, LH, glucagon and prolactin, are furnished for groups of study patients, histamine released from sensitized leukocytes is monitored, and possible drug-induced changes in the serum content of free fatty acids are examined.

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DETAIL SHEETS

MEDICINE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Tuberculosis Research Follow-up Program.

WORK UNIT NO: 67/100

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years):	FY 75:	0.25/yr
	FY 76:	0.75/yr
Funding (in thousands)	FY 75:	0
	FY 76:	0

PROGRESS

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

PROGRESS - continued

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

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

Publications:

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

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

(3) Buchanan, B. D.: Atypical Tuberculosis Due to Type I and Type III Atypical Mycobacteria. (Submitted for Publication.)

(4) Gerace, J., Nelson, R. A.: Incidence of Drugs 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, FAMC, September 1972.

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

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

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

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

WORK UNIT 67/100

PROGRESS - continued

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

(7) Buchanan, B.: Atypical Tuberculosis. Presented: 28th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, September 1975.

(8) Nelson, R. A.: Extra Pulmonary Tuberculosis. Presented: Fitzsimons Army Medical Center, September 1975.

(9) Nelson, R. A.: Pleural and Lymph Node Tuberculosis. Presented: At the course, Clinical Management and Control of Tuberculosis, sponsored by National Jewish Hospital, Denver, Colorado, three times yearly.

(10) Christensen, W. I.: Genitourinary Tuberculosis. Presented: At the course, Clinical Management and Control of Tuberculosis. Sponsored by NJH, Denver, Colorado, three times yearly.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 71/107

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: George Brown, LTC, MSC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 75:	1.0
	FY 76:	1.0

PROGRESS

This cooperative VA-Armed Forces research project has been completed as far as patient input and data gathering. There is a tremendous amount of information which has accrued as a result of this research protocol.

WORK UNIT 71/107

PROGRESS - continued

Several preliminary reports, articles and presentations have already appeared usually authored and presented by Dr. James Raleigh, the chairman of this research committee whose home base is in the Houston, Texas VA Hospital. The main article to result from this project has been submitted for publication and will indicate the US Army's and specifically Fitzsimons's part in this project. There will no doubt be several other articles resulting from this data, which is all being analyzed at the West Haven VA Hospital, which is also the Eastern VA Research Center. We will still be asked to review and critique manuscripts prepared for publication.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Clinical Demonstration of Pulsus Alternans.

WORK UNIT NO.: 72/112

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 75:	0.5
	FY 76:	0.5

PROGRESS

Continued difficulty has been encountered with the recording apparatus and despite numerous efforts, satisfactory pulse recordings cannot be obtained with the transducer. The progress in the last year, therefore, has been nil and without the purchase of new equipment it is not anticipated that this project can be satisfactorily completed.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO: 73/115

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

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

WORK UNIT 73/115

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

The intra-cavity recording of sound events in the Cardiac Catheterization Laboratory remains unsatisfactory. Bedside observation, however, suggests that the notation of respiratory variation is a valid and valuable observation. Because of the departure of the principal investigator, the project will not be continued at this hospital.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/117

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 2.0
FY 76: 2.0

PROGRESS

Approximately thirty-six patients received daily injections of allergy extract to date. Blood is available prior to and following extract build-up in these individuals. Laboratory evaluation of these blood specimens plus those of previous years is presently underway.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Assessment of the Indoor Allergen Load in Colorado.

WORK UNIT NO.: 73/124

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

There were no further studies performed under this protocol during the current year.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/126

PRINCIPAL INVESTIGATOR: William P. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Material has now been accumulated for the completion of the report on this subject and awaits only the completion of adequate photographic illustrations of the illustrative material for publication.

WORK UNIT 73/126

PROGRESS - continued

Publications: None

Presentations:

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

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

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

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

(5) Nelson, W. P.: Dilemmas in Cardiac Diagnosis and Therapy: "Concealing Cancellations, Nefarious Normalization and Confusing Fusion". VA Hospital, KS, MO, September 1975; Univ. Of Arizona Sch of Medicine, Tucson, AZ, September 1975; Colorado University School of Med., January 1976; FAMC, March 1976; Cardiovascular Disease Course for Nurses, Clearwater, Florida, April 1976; Queens Hospital, Honolulu, Hawaii, June 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/132

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

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

Publications:

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

WORK UNIT 73/132

Publications - continued

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

(3) This was published in abstract form in the Journal of Allergy Vol. 57, page 259, 1976. The data has been submitted for publication to International Archives of Allergy and Clinical Immunology under the title: Beta-Adrenergic Subsensitivity Induced by Chronic Administration of Terbutaline.

Presentations:

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

(2) The data was presented in part at the 32nd Annual Meeting of The American Academy of Allergy by Harold S. Nelson, M.D., under the title of: Adrenergic Subsensitivity Induced by Chronic Administration of Terbutaline and Albuterol.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO. 73/133

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.01/yr

Funding (in thousands) FY 75: 0.5
FY 76: 1.0

PROGRESS

Nine individuals have been entered into the study and have either completed the anticipated course of injections or discontinued shots on their own volition. No patients received treatment under this protocol during this year. The laboratory studies are currently being completed.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Active Antigens in House Dust.

WORK UNIT NO.: 73/135

PRINCIPAL INVESTIGATOR: Leslie B. Branch, LTC, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

During this reporting period, no progress has been made on this project.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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 75: 0.0
FY 76: 0.0

PROGRESS

Two patients have been treated:

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

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

No toxicities were observed in these patients.
No patients have received this agent during FY 76.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/145

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.06/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Fifteen patients have completed therapy with CCNU:

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

WORK UNIT NO.: 73/145

PROGRESS - continued

(7) M. N. - Glioblastoma multiforme; no change.
(8) M. S. - Glioblastoma multiforme; 50% remission
(9) L. S. - Adenocarcinoma; subjective response then progression.
(10) J. H. - Bronchogenic carcinoma; (with hexamethylmelamine) progression.
(11) P. M. - Squamous cell ca of lung; no change for 5 months, then progression.
(12) G. P. - 30 y/o WF with Grade IV astrocytoma obtained a complete remission lasting 26 months before the tumor recurred; she had 19 courses of CCNU with only minimal neutropenia.
(13) J. H. - 54 y/o WM with metastatic melanoma to the CNS obtained no response to two courses of the drug.
(14) J. G. - 56 y/o WM with squamous cell Ca metastatic to pelvis, combined with mitomycin C and Vincristine; no response.
(15) L. F. - 50 y/o WF with thalamic glioma which responded >50%; response lasted 2 years prior to relapse; no significant toxicity.

Moderate thrombocytopenia at 3-5 weeks has been observed, without significant bleeding or other toxicity. Six patients are currently receiving CCNU.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/149

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

During FY 76 two patients have been treated with daunomycin. One is a 28-year-old WF (T.S.) with acute myelocytic leukemia who remains in complete remission after induction with daunomycin, plus cytosine arabinoside, 6 TG, vincristine and prednisone. During induction she experienced marked neutropenia but mild thrombocytopenia. Another patient (H.S.) was a 47-year-old WF who received only one dose of daunomycin and expired of intracranial hemorrhage without experiencing hematologic remission. One other patient is currently receiving this agent.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/150

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Eight patients were treated:

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

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

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

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

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

WORK UNIT 73/i50

PROGRESS - continued

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

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

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

During FY 76 two patients with metastatic melanoma have been treated with BCNU. One failed to respond objectively or subjectively. A second patient received BCNU plus ICDT and experienced stabilization of disease for 5 months prior to progression of the metastases. His only toxicity was moderately severe nausea and vomiting for up to 24 hours after receiving the drug. Six patients are currently receiving BCNU.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/158

PRINCIPAL INVESTIGATOR: Wendell E. Petty, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Original input in the study was terminated in March 1974 with a total of 80 patients being placed on Cromolyn Sodium, according to the protocol. Results of the initial response were analyzed during the current year. Follow-up data was obtained on 46 patients of the total of 80, and this data is currently being analyzed. No further work was done on this study during FY 76.

Publications: None

WORK UNIT 73/158

PROGRESS - continued

Presentations:

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

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Immuno-chemical Evaluation of Myeloproliferative and Plasmaproliferative Diseases.

WORK UNIT NO.: 74/101

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 1.5
FY 76: 1.5

PROGRESS

(1) Myeloproliferative Disorders: Thirty-six patients have been studied thoroughly since institution of this study. Isolated increases or decreases in the serum IgG, A and M were noted, but these immunoglobulins were normal in most patients. No monoclonal gammopathies were noted. Serum C'3 levels were decreased in 14 of 36 patients (39%) and normal in the remainder. Lymphocyte response to PHA was subnormal in 27 of 36 (75%) and to pokeweed mitogen in 18 of 27 (67%) of patients studied. Despite this only 2 of 29 (7%) were

PROGRESS - continued

anergic by intradermal skin testing. There was no association between depressed lymphocyte response to these mitogens and recent chemotherapy except in chronic myelogenous leukemia where 6 of 7 patients were receiving cytotoxic therapy when studied.

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.: Immune Dysfunction in the Myeloproliferative Disorders. Manuscript submitted to Ann. of Inter. Medicine, 1976.

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: Federation of American Societies for Experimental Biology, Anaheim, California, April 12, 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Immunologic Effects of Endocrine Manipulation in DMBA-Induced Rat Mammary Neoplasms.

WORK UNIT NO.: 74/106

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC

OBJECTIVES

To determine if the therapeutic efficacy of hormonal maneuvers in experimental rat mammary carcinoma is mediated by immunologic mechanisms.

TECHNICAL APPROACH

Immunologic parameters are being sequentially analyzed in rats prior to and following the induction of mammary tumors with DMBA, and again after oophorectomy-induced response.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 75: 3.0
FY 76: 2.0

PROGRESS

Phases I and II dealt primarily with a variety of technical problems in the experimental design. Experimentation with different dosages and routes of administration of the DMBA have led to the conclusion that 1.0 cc of the DMBA solution (5 mg/gm) given intraperitoneally yields optimum tumor development by day 50 to 70. Oophorectomy alone failed to control the progress of the tumor. It was also noted that frequent blood-letting in the test animals per se led to depression of lymphocyte transformation.

WORK UNIT 74/106

PROGRESS - continued

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

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

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

During FY 76 two hundred rats have been randomized to sham surgery vs adrenalectomy-oophorectomy following tumor development. We will be studying these animals for lymphocyte response to PHA and serologic response to sheep RBC's.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/107

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATORS: L. Bernard Branch, LTC, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.5
FY 76: 1.0

PROGRESS

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

Publications:

(1) Branch, L.B., Nelson, H.S., and Liptak, R.: Serum IgA and Delayed Hypersensitivity Skin Tests in Allergic Patients. Manuscript in preparation.

WORK UNIT NO. 74/107

PROGRESS - continued

Presentations:

(1) Branch, L.B., Nelson, H.S., and Liptak, R.: Serum IgA and Delayed Hypersensitivity Skin Tests in Allergic Patients. Presented: American Academy of Allergy, San Diego, CA, 1974.

STATUS

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Controlled Study of Dander Immunotherapy.

WORK UNIT NO.: 74/108

PRINCIPAL INVESTIGATOR: Melvin Hoffman, MAJ, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 75: .5
FY 76: 1.0

PROGRESS

Ten patients were observed for a total of two years. The supporting laboratory studies are now being performed and the data will be analyzed.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/109

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Dudley Raine, LTC, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Sixteen patients were entered into the study. This study is completed and the data has been fully analyzed.

Publications:

(1) Nelson, H.S., Raine, D: Adrenergic Subsensitivity Induced by Chronic Administration of Terbutaline and Albuterol. (Abst.) Journal of Allergy and Clinical Immunology. 57:259, 1976.

WORK UNIT 74/109

Publications - continued

(2) Nelson, H.S., Raine, D.: Long Term Double-blind Comparison of Oral Ephedrine and Albuterol in the Treatment of Bronchial Asthma. The Proceedings of the Fourth Annual Meeting Association of Military Allergists. Page 21, 1975.

Presentations:

(1) Raine, D.A.: "Long Term Double-blind Comparison of Oral Ephedrine and Albuterol" in the Treatment of Bronchial Asthma. Presented. Fitzsimons Army Medical Center Pulmonary Disease Symposium, Denver, CO., September, 1975.

(2) Nelson, H.S.: Long Term Double-blind Comparison of Oral Ephedrine and Albuterol" in the Treatment of Bronchial Asthma. Presented. The 32nd Annual Meeting of the American Academy of Allergy, March, 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/110

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, LTC, MC

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

OBJECTIVES

The objective of the hypoglycemic study is to continue to investigate in our large clinic population the glucose-insulin-glucagon interrelationship and the response of counter-regulatory hormones to hypoglycemic stress. For the first time, the pituitary hormone prolactin has been measured in this setting. This will determine whether the stress of hypoglycemia is a stimulus to prolactin secretion.

TECHNICAL APPROACH

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

WORK UNIT 74/110

TECHNICAL APPROACH - continued

sugar state sometime after glucose administrations and the clinical significance of a low blood glucose state is observed by recording appropriate adrenergic symptoms at the nadir of the glucose and determining if there is a counter hormonal responsiveness in defending the low blood glucose state as a manifest by timely rises in cortisol and growth hormone indicating hypothalamic-pituitary-end-organ stress.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 75: 4.0
FY 76: 6.0

PROGRESS

Approximately 200 oral glucose tolerance tests have been performed since inception of the study. The data derived have been applied to patient management. The data are presently being programmed into a computer at the University of North Dakota in preparation for the following future publications: Effect of Hypoglycemia on Prolactin Secretion, Secretion of Prolactin after Glucose Loading in Hypothyroidism, and Hypoglycemia, a Review.

Publications:

(1) Hofeldt, F. D.: Reactive Hypoglycemia, Metabolism 24:1193, 1975.

(2) Hofeldt, F. D., Adler, R. A., and Herman, R. H.: Postprandial Hypoglycemia, Fact or Fiction?, JAMA 233:1309, 1975.

(3) Hofeldt, F. D., Lufkin, E. G., Hall, S., Dippe, S., Davis, J. W., Levin, S., Forsham, P. H.: Alimentary Reactive Hypoglycemia: Effects of DBI and Dilantin on Insulin Secretion, Military Medicine. Volume, page number and year not available.

(Completed Papers Pending Publication):

(1) McCowen, K. D., Adler, R. A., O'Barr, T. P., and Hofeldt, F. D.: Clinical Implications of the Flat Oral Glucose Tolerance Test. Submitted for publication.

(2) Abrams, R., Adler, R. A., O'Barr, T. P., and Hofeldt, F. D.: Reactive Hypoglycemia in Hypothyroidism, submitted for publication.

(Published Abstracts):

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

WORK UNIT 74/110

Presentations:

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

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/111

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 4.0
FY 76: 4.0

PROGRESS

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

WORK UNIT NO.: 74/111

PROGRESS - Continued

most common methods. These are the Bohr (average steady state) Bates (end tidal) and the single breath methods. Our previous work has shown that one contribution to the discrepancy results from the usual lack of knowledge of the breathing patterns. The average partial pressure of CO in the lung and the CO uptake are required for the steady state estimates. However, the expired alveolar sample rarely represents the actual average alveolar partial pressure. The error arises in the effective sample time chosen by the experimental method. The correct alveolar sample occurs one half of a breathing period after the effective inspiration time (a reference time which was defined during this investigation). The time chosen by the experimental method also has a known relationship to the effective inspiration time. When these times are known the measured diffusing capacity can be corrected to the actual diffusing capacity by using a simple graphical technique.

Publications:

(1) Kindig, N.B., Hazlett, D.R.: Correcting Bates (End Tidal) Estimates of Pulmonary Diffusing Capacity for Breathing Pattern. Medical Instrumentation, 9:64, 1975.

(2) Kinding, N.B., Hazlett, D.R.: Time Delay Effects in the Estimation of Pulmonary Diffusing Capacity. Biomedical Sciences Instrumentation, 11:25-29, 1975.

(3) Kindig, N.B., Hazlett, D.R.: Time Delay Effects in the Estimation of Pulmonary Diffusing Capacity. Instrument Society of American Transactions, 15:81-85, 1976, in press.

Presentations:

(1) Kinding, N.B., Hazlett, D.R.: Dorrecting Bates (End Tidal) Estimates of Pulmonary Diffusing Capacity for Breathing Pattern, Annual Conference AAMI, Boston, 1975.

(2) Kindig, N.B., Hazlett, D.R.: Time Delay Effects in the Estimation of Pulmonary Diffusing Capacity, 12th Annual Rocky Mountain Bioengineering Symposium, Denver, 1975.

(3) Kinding, N.B., Hazlett, D.R.: A Comparison of Estimation Methods for Steady State DLCO in Normal Subjects, Biomedical Engineering Society, 6th Annual Meeting, New Orleans, 1975.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Effect of Terbutaline on the Response of Normal Individuals to Exercise and Methacholine Inhalation.

WORK UNIT NO.: 74/112

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVE

To determine whether moderately long term ingestion of terbutaline significantly alters the normal responses to exercise in methacholine aerosol inhalation.

TECHNICAL APPROACH

Normal volunteers were tested on a treadmill employing either slow, prolonged or rapid vigorous exercise. They then received one week of terbutaline, 5 mg four times a day and studies were repeated. The same was done with methacholine inhalation before and following a week of terbutaline.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Six patients were studied and the study is completed.

Publications:

(1) Nelson, H. S.: Adrenergic Subsensitivity Induced by the Chronic Administration of Terbutaline and Albuterol. (Abst.) Journal of Allergy and Clinical Immunology, 56:259, 1976.

(2) Nelson, H. S.: Beta Adrenergic Subsensitivity Induced by Chronic Administration of Terbutaline. International Archives of Allergy and Clinical Immunology. Submitted for publication.

WORK UNIT NO. 74/112

Presentations:

(1) Nelson, H. S.: Adrenergic Subsensitivity Induced by the Chronic Administration of Terbutaline and Albuterol. Presented. 32nd Annual Meeting of the American Academy of Allergy, March, 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: A Controlled Trial of Intranasal Cromolyn Sodium in the Prevention of Seasonal Allergic Rhinitis.

WORK UNIT NO.: 75/100

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

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

OBJECTIVE

To evaluate the efficacy of intranasal installation of 4% sodium cromolyn in the treatment of allergic rhinitis.

TECHNICAL APPROACH

Double-blind evaluation of 4% sodium cromolyn solution and placebo to be administered four times daily throughout the weed season in patients with allergic rhinitis produced by weed pollen.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0.0
FY 76: 0.0

PROGRESS

This study is completed.

Publications and Presentations:

The material was presented at the annual meeting of the American College of Allergy and is currently being finalized for presentation for publication.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/101

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

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

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands)		
	FY 75:	4.0
	FY 76:	5.0

PROGRESS

Ten smokers and ten nonsmokers have been studied. Frequency dependence of compliance (dynamic compliance/static compliance ratio) is abnormal

WORK UNIT NO.: 75/101

PROGRESS - Continued

in all of the smokers averaging 53% at 100 breaths per minute and normal in the nonsmokers averaging 98.2% at 100 breaths per minute. Sixty percent of the smokers had a poorly formed notch in the first portion of the spirogram and 70% of the smokers had a roughening in the mid-portion of the curve whereas none of these findings were present in the normal nonsmoker. Eighty percent of the smokers had an abnormal increase in the functional residual capacity during the maximal voluntary ventilation maneuver whereas none of the normal nonsmokers had an increase in the functional residual capacity of more than 200 cc. By definition both groups had a normal vital capacity, forced expiratory volume in one second and a FEV_1%. The maximum mid-expiratory flow rate was abnormal in only one smoker and normal in all of the nonsmokers. The critical flow of the flow volume loop was less than 80% of predicted in 60% of the smokers and was within normal limits in all of the nonsmokers.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/102

PRINCIPAL INVESTIGATOR: John H. Ball, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.0
FY 76: 0.0

PROGRESS

Since the last progress report, 4 more patients have been treated with Minoxidil to make a total of 15. Sufficient clinical data has been

WORK UNIT 75/102

PROGRESS - continued

accumulated for presentation to clinical meetings. Along these lines, a presentation entitled "The Out Patient Treatment of Refractory Hypertension with Minoxidil" was presented at the Regional American College of Physicians Meeting in Colorado Springs in January 1976. A manuscript entitled "Out Patient Therapy of Refractory Hypertension with Minoxidil" has been submitted for publication. An additional manuscript entitled "Treatment of Minoxidil Induced Hypertrichosis with Calcium Thioglycolate" has been submitted for publication.

Publications:

(1) Kleiner, J., Ball, J.H., and Nelson, W. A.: The Out Patient Treatment of Refractory Hypertension with Minoxidil. Abstracts. Colorado Regional ACP Meeting Rocky Mountain Medical Journal, pg. 534, December 1975.

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, CO, 15-17 January 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/103

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: L. Bernard Branch, LTC, MC

OBJECTIVE

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 75: 0.0
FY 76: 0.0

PROGRESS

PK testing is currently being performed on four Macque monkeys. Completion is anticipated within a few months.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/104

PRINCIPAL INVESTIGATOR: John P. Kleiner, MAJ, MC

ASSOCIATE INVESTIGATOR: Bruce H. Brundage, LTC, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0.0
FY 76: 0.0

PROGRESS

One apparent conclusion is that such a study can be performed only with the aid of a computerized electrocardiographic system. As a result, the study has been terminated until such support becomes available.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO: 75/105

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Dudley A. Raine, LTC, MC

OBJECTIVE

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Approximately twenty-five patients have been studied. The results in the first twenty patients were presented at the 32nd Annual Meeting of the American Academy of Allergy in March, 1976 and published in abstract form.

Publications:

(1) Hoffman, M.: Challenges with Aspirin, F.D. & C. Dyes, and Preservatives in Asthma. (Abst.) Journal Allergy & Clinical Immunology, 57:206, 1976.

WORK UNIT NO. 75/105

Presentations:

(1) Hoffman, M.: challenges with Aspirin, F.D. & C. Dyes, and Preservatives in Asthma. Presented. 32nd Annual Meeting of the American Academy of Allergy, March, 1976.

STATUS:

Ongoing.

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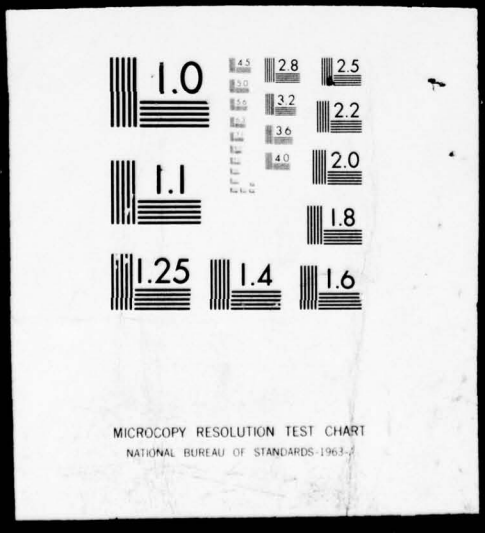

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/106

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

ASSOCIATE INVESTIGATOR: None

OBJECTIVE

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.0
FY 76: 1.5

PROGRESS

Approximately thirty patients were studied. The laboratory procedures are partially completed.

Publications: None

Presentations:

(1) Posey, W.C.: Controlled Trials with 4% Cromolyn Nasal Spray in Seasonal Allergic Rhinitis. Presented. Hugh Mahon Lectureship Award Competition, 12 June 1976, Fitzsimons Army Medical Center, Denver, CO.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/107

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVE

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

No new patients have been enrolled during FY 76. Those 70 patients who continue in the study are entering their second year of observation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/108

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Wendell E. Petty, MAJ, MC

OBJECTIVE

To evaluate two aspects of aerosol terbutaline response.

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

The study has been completed. Twelve patients were entered into the study. All data has been analyzed. It was submitted in competition for the Hugh Mahon award by Dr. Petty and is presently being prepared for publication.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Bioelectric Impedance Estimates of Heart Valve Cross-Sectional Areas: II.

WORK UNIT NO.: 75/109

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: Russ Zajtchuk, LTC, MC

OBJECTIVES

To improve heart valve cross-sectional area measurement using bioelectrical impedance.

TECHNICAL APPROACH

a. Fourteen mongrel dogs weighing 23-35 Kg will be anesthetized with a 4% Thiamylal Sodium solution and Atropine. Paralytic, vasoconstrictor and vasodilator drugs will not be used. A Bird Mark VIII respirator will maintain anesthesia and artificial respiration with air-Halothane mixture through a cuffed endotracheal tube.

b. Thoracic cavity was entered through a left fifth intercostal space and a dual electrode catheter was inserted through the apex of the heart. The catheter was positioned so that the distal electrode lay above the valve and the proximal electrode below the valve. Bioelectrical impedance measurements between the electrode pair were made with an instrument designed to operate at 500 cps and 10 microamperes.

c. The dog's heart will be rapidly removed and carefully opened upon completion of the impedance measurements.

d. Three or more observers will accurately measure the width of each leaflet at its base and calculate the anatomic cross-sectional area.

e. Before sacrificing the animal, 20 cc of left ventricular blood will be drawn into a heparinized syringe. A 10 cc graduated cylinder of precisely known cross-sectional area will be filled with this blood and placed in a water bath maintained at 37^{o}. The dual electrode catheter used in the intracardiac impedance measurements will be immersed in the blood and impedance determined.

WORK UNIT NO.: 75/109

Technical Approach - continued

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 4.0

PROGRESS

Impedance estimates and anatomic measurements of the cross-sectional area of pulmonic and/or aortic valves were made in 14 mixed-breed dogs. Over 90% of the observations showed an absolute difference of 0.3 cm^2 or less between the anatomically measured heart valve cross-sectional area and that determined by bioelectrical impedance. In 70% of the normotensive animals the electrical impedance estimates of heart valve cross-sectional area was larger than that measured anatomically. This probably is due to the "shunt" effect of heart walls. Hypotensive animals tend to have a smaller heart valve cross-sectional area by bioelectrical impedance estimates than that determined anatomically. This implies that heart valve cross-sectional area may be smaller during hypotensive episodes. These studies show that bioelectrical impedance measurements are an accurate and convenient means of determining heart valve cross-sectional areas.

Publications: None

Presentations:

(1) Hazlett, D. R., Zajtchuk, R., and Nessan, V. J.: Measuring Heart Valve Cross-Sectional Areas by an Electrical Impedance Technique. Presented at the Annual Meeting of the Biomedical Engineering Society, April 1975.

(2) Bioelectrical Impedance Estimates of Heart Valve Cross-Sectional Areas: II, Association of Army Cardiology, Denver, Colorado, May 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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, MAJ, MC

OBJECTIVES

To treat patients with advanced solid neoplasms, 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 75: 0.0
FY 76: 0.0

PROGRESS

Two patients have been treated:

1) K.A. - 18-year-old WM with metastatic embryonal Ca. of the testis, experienced no improvement.

2) R.G. - 32-year-old WM with metastatic embryonal Ca. of the testis, experienced a transient 50% reduction in tumor mass.

Currently one patient (D.M.) with embryonal Ca. of the testis is on the protocol and he has experienced a 25% response to date.

The primary toxicity has been a transient rise in serum creatinine & BUN.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: An Evaluation of Treatment with Oral Albuterol in Children with Bronchial Asthma.

WORK UNIT NO.: 75/111

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: H. C. Doner, MAJ, MC (USAF)

OBJECTIVE

To determine the efficacy, safety and tolerance of oral albuterol syrup and tablets in the treatment of asthma in children between the ages of 6 and 14.

To compare the efficacy of albuterol tablets and syrup.

TECHNICAL APPROACH

Twenty patients received increasing doses of albuterol, 2, 4, and 6 mg., QID to test their tolerance, then when all proved able to tolerate the drug without difficulty, a four-week double-blind cross-over study was performed with 4 mg. albuterol, liquid and tablets, and placebo, liquid and tablets administered four times daily. The patients reported to the clinic one day each week and their pulmonary functions response was followed for six hours to the medication which they were ingesting.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

All twenty patients were studied and the study is completed.

Publications: None

Presentations:

(1) Doner, H. C.: A Double Blind Study of Oral Albuterol in Children. Presented. Southwest Allergy Forum, San Antonio, Texas, May 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: An Evaluation of the Role of Adrenergic Bronchodilators in Patients with Bronchial Asthma on Optimal Doses of Theophylline.

WORK UNIT NO.: 75/112

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: L. Bernard Branch, LTC, MC

OBJECTIVES

To determine whether in patients with bronchial asthma who have optimal doses of oral theophylline, the addition of beta adrenergic bronchodilators would produce any significant further improvement of pulmonary function.

TECHNICAL APPROACH

Optimal theophylline dosage will be determined for individual based on theophylline blood levels. The patients response to sympathomimetic bronchodilators in a double-blind and placebo controlled study will then be determined.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)		
	FY 75:	0.0
	FY 76:	9.0

PROGRESS

No patients have entered this study. The equipment has been obtained to perform serum theophylline blood levels but is thus far non-functional.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Study of the Impaired Water Excretion in Primary Hypothyroidism.

WORK UNIT NO.: 75/113

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: Fred D. Hofeldt. M.D.
Paul D. Miller, M.D.
Robert J. Anderson, M.D.
Robert W. Schrier, M.D.
Gary Robertson, M.D.
Peter Steele, M.D.

OBJECTIVE

The study is assessing the role of thyroid hormone in relation to the development of hyponatremia and impaired free water clearance as observed in clinical hypothyroid states.

TECHNICAL APPROACH

Before and after thyroid replacement, hypothyroid patients undergo PAH and inulin clearances, response to a water load and mannitol infusion. Blood and urine are analyzed for osmolality, electrolytes, and creatinine. Plasma ADH and prolactin response to these maneuvers are also measured. Cardiac output is measured by Indium ^{131}.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 76: 2.0

PROGRESS

During the past fiscal year, seven patients with mild hypothyroidism and three patients with moderate to severe hypothyroidism have been studied as outlined above. All procedures have worked well without complications. Patients with mild hypothyroidism are able to excrete approximately 2/3 of a water load, whereas the more severely hypothyroid can only excrete about 1/4 of this. Normals and these patients after thyroid hormone replacement excrete 100% of the water load. There seems to be a change in glomerular filtration rate (GFR) causing this. This decreased GFR is not due to decreased cardiac output. Preliminary data suggest no change in ADH or prolactin accounting for the inability to excrete a water load.

WORK UNIT NO. 75/113

PROGRESS - continued

The data will be analyzed again after studies are performed in two patients now in the euthyroid state. If statistical significance is achieved, the paper will be submitted to the Journal of Clinical Investigation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: A Phase III Study of Adriamycin/5-Fluorouracil/Methotrexate/ Cyclophosphamide and Prednisone Administered in Different Schedules for the Treatment of Inoperable Primary or Metastatic Breast Cancer.

WORK UNIT NO.: 75/114

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To test the efficacy of two different schedules of the above listed five drugs in the treatment of inoperable primary or metastatic breast cancer.

TECHNICAL APPROACH

The two different schedules of drug treatment are described in detail in the protocol.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)		
	FY 75:	0
	FY 76:	0

PROGRESS

Two patients were treated with this combination:

1) M.L. - 68 y/o WF received 7 weeks of regimen A with complete resolution of a metastatic node lesion but no change in a sternal lesion; after 7 weeks she experienced progression of disease and was removed from the study.

2) E.R. - 56 y/o WF received regimen B and obtained an 80-90% improvement in her lung and bone metastases, but no improvement in a lymph node metastasis; no significant toxicity was experienced and she remains on this drug combination.

Protocol has been terminated due to closure of the Western Cancer Study Group.

WORK UNIT NO. 75/114

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: A Phase I Study of Combination Chemotherapy for Advanced Hodgkin's and Non-Hodgkin's Lymphomas with Adriamycin (NSC 123127), Bleomycin (NSC 125066) and ICRF-159 (NSC 129943).

WORK UNIT NO.: 75/115

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

1. To determine the efficacy of bleomycin, adriamycin and ICRF-159 in advanced Hodgkin's and non-Hodgkin's lymphomas.

2. To define the schedule and dosage of these drugs which is best tolerated for a subsequent Phase II study.

3. To determine whether ICRF-159 in combination with adriamycin diminished the cumulative cardiotoxicity due to adriamycin.

TECHNICAL APPROACH

A combination of the above agents is to be used in the treatment of advanced lymphomas.

Treatment schedule is as follows:

Drug	Dose	Route	Schedule
Bleomycin	8 mg/M^2	IM	Days 1, 4, 8 and 11
ICRF-159	500 mg/M^2	P.O.	Days 3 and 4
Adriamycin	60 mg/M^2	I.V.*	Day 4 (with ICRF)

*through running I.V.

Rest Period.....Days 12 to 21

ICRD doses will be escalated according to marrow tolerance.

WORK UNIT NO.: 75/115

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

A 58 y/o WF with diffuse histiocytic lymphoma has been treated with this protocol. She experienced complete resolution of adenopathy and >50% of a bone lesion. Response lasted seven months prior to CNS relapse. Moderately severe marrow toxicity was experienced (neutropenia and thrombocytopenia) necessitating a marked dose reduction. There also was possible cardiotoxicity (change in STI)

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/116

PRINCIPAL INVESTIGATOR: Mark R. Stein, MAJ, MC

ASSOCIATE INVESTIGATORS: Harold S. Nelson, COL, MC
Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

This study is designed to extract raw kochia pollen 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. Further work on this project must await delivery from Pharmacia Fine Chemicals, Inc. of RAST assay discs for kochia. These 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.

Manpower (in professional man years): 0.01/yr

Funding (in thousands) FY 76: 0.5

PROGRESS

Raw kochia has been extracted. A rabbit antisera has been prepared. Allergic human sera and monkeys are available. Column fractionation equipment is available. Once the RAST materials arrive further progress will be achieved.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Evaluation of Inhaled Cromolyn Sodium in the Treatment of Seasonal Asthma.

WORK UNIT NO.: 75/117

PRINCIPAL INVESTIGATOR: Dudley A. Raine, Jr., LTC, MC

ASSOCIATE INVESTIGATORS: L. Bernard Branch, LTC, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To determine the efficacy of inhaled sodium cromolyn in the treatment of ongoing seasonal allergic bronchial asthma, and to attempt to define parameters which would assist in the future in selection of patients for this treatment.

TECHNICAL APPROACH

Suitable patients from the Allergy Clinic at Fitzsimons Army Medical Center with fall seasonal asthma or perennial asthma with fall exacerbations are screened for selected criteria. If they are interested in participating in the study, written informed consent is obtained on initial history and physical examination is obtained. Appropriate skin testing for weed sensitivity is done if recent skin test results are not in their records. Baseline pulmonary function tests, chest x-ray, CBC, UA and 12 chemistries are obtained. The patient is then given a supply of medication which is double blinded, a spin haler for administration, a daily record sheet, a Wright Peak Flow Meter and written instructions as well as on oral review on how to participate in the study. At the onset of the symptoms of asthma for that fall season, the patient will begin the study, carefully recording daily his symptoms, the amount of medication he is using and twice daily peak flow readings. They will be followed by a clinic visit every two weeks with a history, physical exam and pulmonary functions. Blood will be obtained at the beginning and the end of study, and analyzed by RAST for levels of specific IgE antibodies directed toward ragweed, Russian thistle and sage.

WORK UNIT NO.: 75/117

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.01/yr

Funding (in thousands) FY 76: 0.0

PROGRESS

Eleven patients have begun and completed this study. Another 9-29 patients are being sought to participate in this study for this coming Fall.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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 albumen 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): 0.1/yr

Funding (in thousands) FY 76: 0

PROGRESS

The first set of extracts is currently set up and further lots will be set up at three month intervals. No patients will be tested until the completion of one year from the initial dilutions.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Fluoridated Tooth Paste as the Possible Agent Responsible for Perioral Dermatitis.

WORK UNIT NO.: 75/119

PRINCIPAL INVESTIGATOR: J. Ramsey Mellette, Jr., MAJ, MC

ASSOCIATE INVESTIGATORS: John L. Aeling, COL, MC
Donald D. Nuss, COL, MC

OBJECTIVES

To determine if fluoridated tooth paste causes or greatly enhances the development of perioral dermatitis.

TECHNICAL APPROACH

Patients have been entered into a randomized double-blind cross-over study with tooth pastes that are identical except that one contains 0.5% stannous fluoride. The patients are to be crossed over after two months use of the tooth paste if no dermatitis develops. If a significant perioral dermatitis develops, they may be crossed over earlier.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FT 76: 0

PROGRESS

The patients have been issued the tooth paste in a double-blind fashion. After approximately six (6) weeks, two patients have developed perioral dermatitis and have been crossed over. The remaining patients are still on the first tooth paste. All patients were photographed at the onset and the required consent forms obtained.

Publications:

(1) Mellette, J. R., Aeling, J. L. and Nuss, D. D.: Fluoride Tooth Paste: A Cause of Perioral Dermatitis. Arch of Derm, Vol. 112, No. 5, 1976.

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Study of ICRF-159 (NSC 129943) Given Orally Plus Radiation Therapy for the Treatment of Bronchogenic Carcinoma.

WORK UNIT NO.: 75/120

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: Kenneth D. Herbst, MAJ, MC

OBJECTIVES

To assess the toxicity and tolerance to a regimen of ICRF-159 combined with conventional radiation therapy in patients with unresectable non-oat cell bronchogenic carcinoma.

TECHNICAL APPROACH

Patients who met criteria for selection and who agreed to enter onto the protocol were treated with ICRF-159 in combination with radiation therapy as outlined in the protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 75:	0.0
	FY 76:	0.0

PROGRESS

Two patients have been treated with this therapeutic regimen. One patient withdrew from the study because of toxicity (radiation esophagitis) after six weeks of therapy. The second patient had distant recurrence of his bronchogenic carcinoma after five months of therapy.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Prolactin Response to Water Loading in Hypothyroidism.

WORK UNIT NO.: 75/121

PRINCIPAL INVESTIGATOR: Stephen R. Plymate, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To define the prolactin response to water loading in the hypothyroid state.

TECHNICAL APPROACH

Ten adult patients with primary hypothyroidism or all patients presenting to the Endocrine Clinic with primary hypothyroidism in a period of 60 days from acceptance of this protocol will receive a water load p.o. of 20 m./kg body weight within 15 minutes. Prior to this water load for a period of two hours, baseline serum samples will be drawn for prolactin, sodium, potassium, chloride, CO_2, osmolality. These studies will be conducted after an overnight fasting. A 2 hour urine specimen will also be collected for osmolality, creatinine, sodium, potassium and chloride. Over a period of 15 minutes, each patient will then drink the allotted water following which counting from the beginning of the water drinking as time 0, the patient will have q 30 minute serum samples drawn for prolactin, sodium, potassium, chloride, CO_2 and osmolality for a total of 3 hours. Urine samples will be collected q 2 hours X 6 hours for osmolality, sodium, potassium, chloride and creatinine. These patients will then be treated with L-thyroxine, prolactin levels being drawn every other day for the first week of treatment then two times a week for 3 weeks. When the patients are clinically euthyroid, the water loading studies will be repeated. All results will be subject to appropriate statistical analysis.

Manpower (in professional man years): 0.2/yr

Funding (in thousands): 2.0

WORK UNIT NO.: 75/121

PROGRESS

A total of 9 patients have been completed on this protocol with an increase or no change in prolactin levels found following water loading. Prolactin levels tended to increase as the severity of hypothyroidism increased.

Publications:

(1) Plymate, S. R.: Prolactin Response to Water Loading in Hypothyroidism. Abstract Rocky Mountain Medical Journal, June 1976.

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Blocking Effect of SCH 1000 and/or Isoproterenol Upon the Bronchoconstrictive Action of Antigen Inhalation Challenge.

WORK UNIT NO.: 75/122

PRINCIPAL INVESTIGATORS: Mark R. Stein, MAJ, MC
Sheldon L. Spector, M.D.

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

This study is designed to determine the blocking effect on antigen induced bronchospasm of: SCH 1000, an atropine-like medication, isoproterenol and the combination of SCH 1000 and isoproterenol. It is also designed to evaluate the systemic effects, if any, and side effects of these blocking agents.

TECHNICAL APPROACH

At Fitzsimons Army Medical Center, Allergy Clinic, suitable patients with reagin mediated asthma are screened for selection criteria. If they are interested in participating in this study, informed consent is obtained to perform a history and physical exam and an isoproterenol inhalation test. Patients who are acceptable by study criteria are then referred to National Jewish Hospital, Denver, Colorado. There they must meet criteria of stability of asthma and a positive antigen bronchial challenge, before they are eligible to enter the double-blind study using placebo, SCH 1000, isoproterenol, or the combination of SCH 1000 and isoproterenol.

Manpower (in professional man years): 0.01/yr

Funding (in thousands) FY 76: 0

PROGRESS

Of the 10 patients found to meet the study criteria and referred to National Jewish Hospital, only one patient has successfully completed the study. Since the study requires 20 patients, additional patients are being screened.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: A Long-Term Efficacy and Safety Study of Albuterol Tablets and Syrup in Children 6-14 Years Old.

WORK UNIT NO.: 75/123

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

(1) To determine the efficacy, safety, and tolerance of albuterol tablets and syrup when administered for periods of up to 12 months in children 6-14 years of age.

(2) To determine the spectrum and frequency of side effects which may be associated with chronic treatment with albuterol tablets or syrup.

(3) To determine the potential for diminished therapeutic response when albuterol tablets or syrup are administered regularly for periods of up to 12 months.

TECHNICAL APPROACH

Patients will be placed on a dose of albuterol, either four milligrams q.i.d. or six milligrams q.i.d., guided by their demonstrated tolerance for these dosages in the previous study. Patients will keep a twice daily symptom diary and record twice daily peak flows for the first two months of the study. Thereafter, they will not record symptoms or pulmonary function.

Patients will have their response to albuterol measured at three-month intervals, at which time they will report to the Allergy Clinic at 8:00 o'clock for at least six hours prior to the visit. After baseline pulmonary function, pulse and blood pressure measurements have been obtained, they will receive either four or six milligrams of albuterol and their response will be monitored for the succeeding six hours.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

WORK UNIT NO.: 75/123

PROGRESS

Patients will continue to be evaluated until the code is broken. No data will be available until code is broken. It is anticipated that the study will be completed during calendar year 1977 and a progress report for this project will be included as part of the FY 77 Annual Progress Report.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 76/100

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, 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

A theory of the experiment will be developed using digital computer analysis and simulation on a lung model that consists of a single cylindrical dead space volume in which no mixing occurs and a single alveolar compartment in which perfect mixing occurs. The "actual" and "predicted" dead space will be compared. Significant sources of error and fundamental limitations of the method will be identified. Three steps are anticipated in the experimental valve design problem. First, an existing solenoid valve system that was designed for single breath helium measurement will be tried. Second, a commercial valve will be sought with the required control capabilities and capacity. Third, simultaneously with the search for a commercial valve, a study will be made of the flow capacity, port capability and switching speed required for a programmable pulmonary function valve. Several preliminary approaches to valve design including programmable flop and programmable rotary head will be considered. Design specifications for a valve will be proposed.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 5.0

PROGRESS

The theoretical two breath experiment was simulated by digital computer. This proved the correctness of the basic concept,

WORK UNIT NO.: 76/100

PROGRESS - continued

identified potential sources of error and limitations. The error in the estimate was found to increase with increasing tidal volume and with inequality of the tidal volumes of the successive breaths. The error was found to vary with the square of the alveolar dilution ratio $[(Vt - Vd)/(Va + Vt)]^2$ remaining relatively small for ratios up to about 30%. Preliminary theoretical work has been started on an approach to the dead space estimate when successive tidal volumes are unequal. A limited number of experiments have been carried out on the programmed solenoid valve system. The results were encouraging but there are many limitations in this system. Regular breathing is difficult because of the noise and resistance of the valves. Pressure waves created by opening and closing of the valves probably cause errors in the flow and volume measurements. Electrical delay and noise produce erratic timing of the opening and closing of the valves. Work will now proceed on improved valve specifications.

Publications:

(1) Kindig, N.B., Hazlett, D.R.: A New Measurement of Anatomic Dead Space During Steady State Studies: Theory. Medical Instrumentation, 10:69, 1976.

(2) Kindig, N.B., Hazlett, D.R.: Measurement of Anatomic Dead Space During Steady State Studies of Pulmonary Diffusing Capacity. Biomedical Sciences Instrumentation, 12:89-92, 1976.

Presentations:

(1) Kindig, N.B.: A New Measure of Anatomic Dead Space During Steady State Studies. Theory. Presented. 11th Annual Meeting, Association for the Advancement of Medical Instrumentation, Atlanta, 1976.

(2) Kindig, N.B.: Measurement of Anatomic Dead Space During Steady State Studies of Pulmonary Diffusing Capacity. Presented. 13th Annual Rocky Mountain Bioengineering Symposium, Laramie, 1976.

STATUS:

Ongoing.

SURGERY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 71/202

PRINCIPAL INVESTIGATOR: Anthony Ballard, COL, MC

ASSOCIATE INVESTIGATOR: William W. Eversmann, Jr., LTC, MC

OBJECTIVES

The purpose of this study is to evaluate the functional recovery, sensory and motor, of these upper extremity peripheral nerve injuries. This will be carried out by visits to the individual patients by the responsible investigator and his assistant to determine the status of motor recovery and sensory recovery following treatment. Not since WW II has any number of peripheral nerve injuries been examined as long as 2 years following the injury and in no situation has it ever been possible to examine these peripheral nerves utilizing a limited number of investigators. As a consequence, this long postoperative followup averaging five to seven years of peripheral nerve injuries and the eventual outcome of these injuries is vital to our knowledge and understanding of the long term results of nerve injuries in humans.

TECHNICAL APPROACH

To determine the functional recovery, both motor and sensory, following neurolysis and/or neurorrhaphy at Fitzsimons Army Medical Center in a group of patients that were treated from 1966 through 1971 at Fitzsimons Army Medical Center individual followup examinations by the investigator and his assistant are necessary to maintain adequate records of prolonged followup.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

WORK UNIT NO.: 71/202

PROGRESS

The increasing number of peripheral nerve injuries seen at Fitzsimons Army Medical Center continue to be followed through a tumor registry technique, through which periodic reports of the patients on their status and the return of function of their peripheral nerve injury can be maintained. As a result of this detailed questionnaire followup, names and addresses of approximately 500 patients involved in upper nerve, peripheral nerve injury cases have been maintained. The majority of these patients currently reside in the Midwest, roughly from Chicago toward Denver and as far South as Kansas City. The initial investigator, Dr. William E. Burkhalter, who has since departed this station, originated this continuing project and supervised the Annual Reports received through the tumor registry at Fitzsimons from the various patients who have sustained peripheral nerve injuries. The reports continue to be correlated but the questionnaire technique is found to be less than desirable and often inadequate to supply detailed clinical information concerning the followup of these nerves, particularly critical, sensory and motor testing. Therefore, at this time we are inviting as many of these patients as possible, all of whom have been retired under medical disability and continue to be eligible for care, for individual followup examination here at Fitzsimons. The response thus far to these invitations has been gratifying but thus far the information is insufficient on the group as a whole to judge a more definite statement regarding the status of these nerve injuries. Throughout the forthcoming fiscal year, continued, more complete, and more detailed motor and sensory evaluation will be necessary for this group of patients. It is entirely possible after we have exhausted the followup technique here at Fitzsimons that outlying clinics at Federal institutions, by the principal investigators, or possibly monetary subsidy for individual patients to come to Denver, may be necessary to complete the detailed study of these peripheral nerve injuries. The funding implications of this cannot be estimated at this time.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: External Rotation Contractures in the Above Knee Amputee.

WORK UNIT NO.: 72/209

PRINCIPAL INVESTIGATOR: Anthony Ballard, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine whether or not external rotation deformities of the proximal femur in above knee amputations create a prosthetic and ambulatory problem for the amputee.

TECHNICAL APPROACH

Plans are to study the abductor weakness created in the above knee amputee with internal and external rotation position of the hip. It is known that the intact individual external rotation weakens the abductors. The resulting gluteus medius gait is inefficient and causes increased energy expenditure.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

We sincerely regret that our initial requests and followup for a progress report for the project indicated above have not been acknowledged to date.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/219

PRINCIPAL INVESTIGATOR: James B. Haden, MAJ, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC
Howard E. Fauver, LTC, MC
David W. Buntley, MAJ, MC
Torrence M. Wilson, MAJ, MC

OBJECTIVES

The ongoing objective of this study concerns development of technique in auto-transplantation of the canine kidney following trauma. The parameters studied thus far include auto-transplantation following partial nephrectomy, following damage to the venous system including venal caval ligation and most recently following central renal injury. Various parameters have been measured including flow studies and survival of the renal unit.

TECHNICAL APPROACH

Through a midline abdominal incision the studies during the past fiscal year have revolved around ligation and reanastomosis of the venous drainage in the transplanted kidney as well as the kidney left insitu. During the second portion of the past fiscal year, a study utilizing auto-transplantation with central renal resection and repair have been performed in approximately thirty dogs. Survival rate of these re-implanted auto-transplanted kidneys has been tabulated. This portion of the study is still in progress.

Manpower (in professional man years): 0.4/yr

Funding (in thousands) FY 75: 6.0
FY 76: 6.0

PROGRESS

Evaluation revolving around venous injury has been terminated with presentation of the results to the Kimbrough Urological Seminar in October 1975 and to the South Central Section of the American Urologic Association in September 1975. In addition, the presentation was

WORK UNIT 73/219

PROGRESS - continued

written to enter the Residents Research Competition at FAMC. The study concerning central renal injury is continuing and the results will be presented to the Kimbrough Urologic Seminar in November 1976.

Publications:

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

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

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

Presentations:

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

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

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

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

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

(6) Page, M. E., and Weigel, J. W.: Exhibit-Renal Transplantation with Proximal Vena Caval. Presented: South Central Section Meeting in Urology, Sep 75.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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 acalulous biliary tract disease; (c) Evaluation of radiomanometry with pressures in the gallbladder and common duct in acalulous biliary tract disease.

TECHNICAL APPROACH

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

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

WORK UNIT 73/221

TECHNICAL APPROACH - continued

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

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 1.0
FY 76: 0.0

PROGRESS

There has been absolutely no progress in this project during the past year. No one has taken this project over since the departure of Dr. Steyskal on 1 July 1975. This project still has merit, and should be continued. However, continuation of and completion of this project will be contingent upon the General Surgery Service being supplied with an adequate staff to meet its clinical responsibilities, residency training responsibilities, and administrative responsibilities before efforts can be expended in the area of clinical investigation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/201

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 3.0/yr

Funding (in thousands) FY 75: 2.0
FY 76: 2.0

PROGRESS

Human erythrocytes (RBC) were lysed in a hypotonic solution of phosphate buffer (20 ideal milliosmolar, pH 7.4). The stroma component was isolated by centrifugation of the hemolysate at 20,000 x G and it was stored as a lyophilized preparation. Rabbits were immunized with the Hb stroma emulsified in Freund's incomplete adjuvant. Rabbit globulin, serologically active for Hb stroma (RASG), was isolated with DEAE ion exchange chromatography. Microdouble diffusion precipitin reactions were utilized to assay the anti-stroma globulin. Serologically competent RASG

WORK UNIT NO.: 74/201

PROGRESS - continued

was adsorbed on Bio-Rad Affi Gel 10 and the gel was evaluated for efficiency by florescent quenching. A Hb hemolysate was prepared from lysed RBCs; particulate matter was removed by centrifugation at 100,000 x G. The Hb solution containing residual stroma components was subjected to affinity chromatography with the bed gel matrix coupled to RASG. Hb samples before and after chromatographic elution were assayed for stromal content. In a modification, purified RASG was eluted from RASG agglutinated RBCs using glycine-HCl buffer at pH 3.0 and it was coupled to Affi-Gel 10. A 3-fold efficiency increase for removal of Hb stroma was recorded after a single cycle with the Affi-Gel ligant coupled to purified RASG. In post affinity chromatographic cycled Hb, microdiffusion precipitin and biochemical tests indicated a 50% elimination of stroma and 20-25% removal of phospholipids and cholesteral, respectively.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Treatment of Digoxin Toxicity with Activated Charcoal.

WORK UNIT NO.: 74/202

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

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

OBJECTIVES

Evaluate activated charcoal in the treatment of digoxin toxicity.

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 75: 1.2
FY 76: 0.5

PROGRESS

The first phase of the project has been terminated and the second phase is being carried out under the direction of COL Corby.

Publications:

(1) Zajtchuk, R.: Treatment of Digoxin Toxicity with Activated Charcoal. American Journal of Cardiology, Volume 35, February 1975.

Presentations:

(1) Zajtchuk, R.: Treatment of Digoxin Toxicity with Activated Charcoal. Presented. American College of Cardiology, Houston, Texas, February 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/203

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

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

OBJECTIVES

To improve heart valve cross-sectional area measurement.

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.35
FY 76: 0.35

PROGRESS

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

Publications: None

Presentations:

(1) Zajtchuk, R., Hazlett, D.R., and Baugh, J.H.: Bioelectric Impedance Estimates of Heart Valve Cross-Sectional Areas. Presented: Fifth Meeting of the Association of Army Cardiology, May 13-15, 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 82040

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Role of Hypercoagulability in Patients Undergoing Myocardial Revascularization.

WORK UNIT NO.: 75/200

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 3.0
FY 76: 3.0

PROGRESS

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

Publications: None

WORK UNIT NO.: 75/200

PROGRESS - continued

Presentations:

Zajtchuk, Russ: Rose of Hypercoagulability in Patients Undergoing Myocardial Revascularization. Presented at American College of Chest Physicians 21 October 1975, Anaheim, California.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Microbial Penicillinase Antagonism to Therapy in Chronic Tonsillitis.

WORK UNIT NO.: 75/201

PRINCIPAL INVESTIGATORS: Joan E. Zajtchuk, LTC, MC
George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: William H. Falor Jr., MAJ, MC

OBJECTIVES

To determine whether refractoriness in penicillin therapy in chronic tonsillitis is due to local penicillinase production or whether this is an anatomic basis.

TECHNICAL APPROACH

The following study was undertaken in patients with chronic tonsillitis to determine if local penicillinase production occurred within the tonsillar crypts, or if an anatomic nucleus for the proliferation of bacteria existed.

Crypt and surface cultures of patients who have chronic tonsillitis and are scheduled for tonsillectomy are studied for microbial flora including bioassays for penicillinase. Patients who are treated with penicillin for clinical reasons will be compared with the non-treated group. Tonsil homogenates will also be studied.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 2.5
FY 76: 2.5

PROGRESS

Since the inception of the project 15 months ago, 26 patients have been enrolled in the study which is considerably short of the original number of 80 predicted for a protocol of approximately 1 year duration. It is apparent that in this small number, there is no local penicillinase produced within the tonsil. It does appear that there is a higher

WORK UNIT NO.: 75/201

PROGRESS - continued

incidence of culture positive pathogens within the crypts which may act as a reservoir and account for the repeated recurrences of acute episodes of tonsillitis.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Wet Lung 1: Solubility of Inert Gases in Lung Tissue and Blood.

WORK UNIT NO.: 75/202

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: David Hazlett, COL, MC
Robert E. Yancy, CPT, MSC

OBJECTIVES

To determine the solubility of certain inert gases in lung tissue and blood.

TECHNICAL APPROACH

Tissue homogenate or blood will be deaerated in a manometric Van Slyke chamber and then transferred anaerobically to a tonometer through which the desired inert gas is flowing. After equilibration the solubility of gas will be determined with Van Slyke apparatus. The Bunsen solubility coefficient will be calculated.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 1.0

PROGRESS

Technique has been worked out and data collection begun.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Systemic Vascular Performance in Endotoxic Shock.

WORK UNIT NO.: 76/200

PRINCIPAL INVESTIGATOR: Alan E. Seyfer, MAJ, MC

ASSOCIATE INVESTIGATORS: David R. Hazlett, COL, MC
Russ Zajtchuk, LTC, MC

OBJECTIVES

To investigate patterns of systemic pressure, systemic vascular resistance, and oxygen consumption in endotoxic shock, so that logical treatment plans can be formulated in the future.

TECHNICAL APPROACH

Sixteen mongrel dogs were studied in an effort to investigate systemic and pulmonary vascular resistance, oxygen consumption, extraction ratios, and oxygen availability in endotoxic shock. Twelve of the animals were placed on total cardiopulmonary bypass in order to study these parameters at constant circulatory flow rates.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 76: 4.0

PROGRESS

During the past fiscal year, the entire project was completed. From these studies, it appears that endotoxin is capable of initiating profound hemodynamic changes. Initially, cardiac output and arterial pressure drop precipitously, despite a transient rise in systemic vascular resistance. After this, peripheral arterial pressures and systemic vascular resistance continue to decline, even when arterial blood flow remains at constant levels. Oxygen extraction by peripheral tissues decreases after endotoxin injection, despite adequate oxygen availability and constant levels of hemoglobin. In addition, post-mortem studies indicate that endotoxin administration results in abnormal translocation of significant quantities of clear fluid (i.e., ascites and severe edema of all intraperitoneal organs),

WORK UNIT NO.: 76/200

PROGRESS - continued

suggesting impairment of capillary permeability.

Publications:

(1) Seyfer, A. E., Hazlett, D. R., and Zajtchuk, R.: Systemic Vascular Performance in Endotoxic Shock - submitted for publication.

Presentations:

(1) Seyfer, A. E.: Systemic Vascular Performance in Endotoxic Shock. Presented: Hugh Mahon Lectureship Award Competition, Fitzsimons Army Medical Center, 12 June 1976 - 1st place.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Treatment of Renal Trauma in Laboratory Animals.

WORK UNIT NO.: 76/201

PRINCIPAL INVESTIGATOR: Torrence M. Wilson, MAJ, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC
Howard E. Fauver, LTC, MC

OBJECTIVES

Investigation of treatment of central renal trauma with extracorporeal surgery and autotransplantation of the repaired kidney.

TECHNICAL APPROACH

Mongrel dogs will have the central portion of a kidney resected segmentally using microdissection extracorporeally. The kidney will be perfused with cooled perfudex during microdissection. Renal autotransplantation to the animal's pelvis will then be done, anastomosing the renal vessels to the iliac vessels: renal artery end to end to iliac artery, and renal vein end to side to iliac vein. Spot urine and blood creatinine, urea, and sodium will be collected preoperative. At sacrifice, selective urine samples for above chemistries will be collected, as well as blood chemistries. Flow studies will be done on the renal artery prior to autotransplant, and again at sacrifice.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 2.0

PROGRESS

To date 24 operations have been performed. Limited success has been encountered, with two dogs cancelled for multiple renal vessels. Six operations have been successful. The study will be continued in FY 1977.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: An Experimental Dog Model for the Study of Coronary Artery Spasm.

WORK UNIT NO.: 76/202

PRINCIPAL INVESTIGATOR: George F. Schuchmann, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To establish an animal model for the study of coronary artery spasm and to study the effects of various drugs on coronary artery blood flow.

TECHNICAL APPROACH

The technical approach to this project involved establishing a dog coronary artery model which could be easily used for monitoring and experimental purposes. For this purpose seven dogs underwent end-to-side anastomoses between the right internal mammary artery and the right coronary artery. Because of arterial spasms during operative procedures, it was elected to allow these dogs to convalesce and to return them to the operating room in a well-healed and stable state for determining the status of various drugs on coronary artery blood flow. To date, the second portion of this experiment has not been satisfactorily completed because of inadequate flow probe measurements. The second portion of the procedure involves creation of a denervated heart specimen. For this purpose autotransplantation was undertaken, although autotransplantation of the dog heart has been fraught with difficulties in controlling hemorrhage. It is anticipated that we can complete this portion of the procedure without difficulty. It is then planned to perform the flow measurements as outlined in the protocol as a second portion of this procedure.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 1.0

PROGRESS

During the past fiscal year the surgical aspects of this research

Work Unit No.: 76/202

Progress - continued

project have been fairly well worked out. The first part of the experiment called for right internal mammary artery to right coronary artery grafts. Seven dogs underwent this operative procedure. Six dogs have been long-term survivors. One dog was inadvertently sacrificed by laboratory personnel. However, the grafts were proven patent at the time of autopsy. This left five dogs for study. All dogs have received angiograms and have patent grafts. One dog was re-operated in an attempt to establish flow criteria and to measure drug effects on flow. However, at the time of surgery it was found that the flow probes were not functioning properly and the dog had to be sacrificed without obtaining any worthwhile information other than that the graft was widely patent with an excellent flow. Four dogs remain awaiting completion of this portion of the experiment pending adequate flow probe function.

The second portion of this experiment revolves upon obtaining the effects of various drugs on coronary flow in the denervated heart. For this purpose autotransplantation of the heart was performed. The technical details of this operation have now been well worked out. Two dogs were operated on with this intent and while neither dog was a long-term survivor, it is thought that this portion of the experiment can be completed. Again, an adequate flow measurement system is necessary for completion of this portion of the experiment. It is my intent to restudy the dogs currently in a study prior to performing any more surgical procedures to determine whether our current flowmeter system is sensitive enough to measure changes in cardiac output and coronary blood flow in anesthetized dog. Once this has been established I intend to perform similar experiments in approximately 10 additional dogs prior to completion of experiment.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 75: 0.5
FY 76: 0.5

WORK UNIT 72/302

PROGRESS

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

Publications:

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

WORK UNIT 72/302

Publications - continued

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

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

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

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

Presentations:

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

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

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

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/305

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
Al Bell, DAC

OBJECTIVES

To estabiish 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 2250 patient records encompassing 52,500 bits of information have been accumulated in the computer file. Patient data include: smear and culture results, drug susceptibilities of mycobacterial isolates, initial drug therapy data, serum tests, data on special study patients, and experimental data on methodology studies.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 75: .5
FY 76: 1.5

PROGRESS

Since December 1973 all computer capability provided by USAMRNL was terminated. Between September 1974 and September 1975, with the assistance of personnel from MISO, update of the mycobacteriology file to MISO storage was completed. Data input to the present is current. Since September 1975, 200 new patients encompassing 4000 messages have been added to the file.

WORK UNIT 73/305

PROGRESS - continued

As of June 1976 the following programs have been shown to be operational:

1. PATIENT ID AND NAME
2. ENTIRE MASTER FILE
3. SELECTED FILE PRINT
4. SPECIMEN CALCULATION (CONTAMINATION RATE DATA)

The program for a formated file print with the orders and code translation is available for evaluation. A number of options to this program can be executed by input of specific control cards which have been developed by MISO personnel.

After input for June 1976 has been updated, an entire master file print through June 1976 will be reviewed and corrected as needed and a formated file print will be called for. This will be updated every six months. A formated file print of all oriental female patient files will test one of the program options.

Publications:

(1) Blair, E. B., Brown, G. L. and Tull, A. H.: Computer Files and Analyses of Laboratory Data from Tuberculosis Patients. II. Analyses of Six Years Data on Sputum Specimens. Amer. Rev. Resp. Dis., 1976, 113, 426-432.

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Microbiological Research in Tuberculosis.

WORK UNIT NO.: 74/300

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years) 0.5/yr

Funding (in thousands) FY 75: 1.6
FY 76: 1.6

PROGRESS

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

WORK UNIT 74/300

PROGRESS - continued

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

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

Use of "Dri-Blocks" for determination of temperature growth range of Mott has been incorporated as a routine procedure for identification of these organisms. A description of the method has been included in CIS Manual "Mycobacteriology Laboratory Methods".

Methods of determining enzymatic activity were evaluated to develop rapid, reproducible, routine tests for MOTT identification. Tests for urease and pyrazin-amidase have been evaluated and are included in CIS T.B. Manual. Procedure for nicotin-amidase is ongoing.

Publications: Brown, G. L., Calcagno, J. V., Rothlauf, M. V., and Kolb, J. G.: Mycobacteriology Laboratory Methods, Laboratory Report No. 1, Clinical Investigation Service, FAMC, 1976.

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Depletion of Liver Glycogen During Endotoxemia.

WORK UNIT NO.: 74/303

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

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To examine the possibility that the hypoglycemic state present in endotoxin-poisoned animals results from the over production of insulin.

TECHNICAL APPROACH

Two hundred gram Holtzman rats, which were injected eighteen hours prior to use with saline or 100 ug of Salmonella Typhimurium endotoxin, were anesthetized with pentobarbital, and the pancreas prepared for perfusion accouding to the technique of Sussman et al. (Metabolism 13:No. 5, May, 466-476, 1966). Various concentration of glucose were perfused through the organ and the effulent examined for immunoreactive insulin.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.5
FY 76: 0.5

PROGRESS

Under these conditions, the pancreas from our endotoxemic animal consistently produced more immunoreactive insulin than controls. With greater refinement of the technique an attempt will be made to examine the kinetics of insulin production by control and endotoxin preparations.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Effect of the Addition of Artificial Flavoring Agents on the Adsorptive Capacity of Activated Charcoal.

WORK UNIT NO.: 74/304

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

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

OBJECTIVES

To determine whether the adsorptive capacity of an "activated charcoal slurry" is significantly altered when artificial flavoring agents are added to improve palatability.

TECHNICAL APPROACH

a. *In vitro* Studies:

320 mg of sodium salicylate will be added to each of three flasks containing 100 ml of simulated gastric juices and incubated with shaking for 30 minutes at 37° C (1). Individual flasks will then receive one of the following test solutions:

(1) 5 gms of Norit-A (American Norit Co.) in 50 ml of distilled water or

(2) 5 gms Norit-A plus 2 ml of artificial cherry flavoring agent in 50 ml distilled water or

(3) 50 ml water.

After an additional 20 minutes of shaking, samples of the incubation mixtures will be centrifuged and the supernatant solutions assayed for salicylate.

b. *In vivo* Studies (Rat):

In this portion of the study the procedure described by Decker, et al. (2) will be used. Test animals will consist of 250 g Holtzman rats which are fasted overnight and treated in the following manner:

(1) A control group of 15 rats will be fed by nasal gastric tube 0.25 ml of a sodium salicylate solution containing 640 mg/ml.

WORK UNIT 74/304

In vivo Studies (Rat) - continued

(2) A second group of 15 rats will receive 0.25 ml of sodium salicylate solution (640 mg/ml). After 30 min. 1.5 g of Norite A suspended in 5 ml of water will be administered by gastric tube.

(3) The third group of 15 rats will be treated identically to the second group except the charcoal slurry will contain 1.5 ml of cherry flavoring syrup.

At 60 minutes, all rats will be sacrificed and blood drawn for plasma salicylate determinations.

Manpower (in professional man years):

Funding (in thousands)	FY 75:	0.5
	FY 76:	0.5

PROGRESS

All studies have been completed. Analysis of data indicates no significant decrease in adsorptive capacity of activated charcoal after addition of cherry flavoring.

Publications:

Yancy, R. E., et al: Evaluation of the Effect of Cherry Flavoring on the Antidotal Capacity of Activated Charcoal. Veterinary Toxicology. Accepted for publication, November 1976.

Presentations:

Corby, D.G.: Metalling with Charcoal. 1st American, Canadian, French International Conference of Clinical and Analytical Toxicology. Montreal, Quebec, Canada, August 1974.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Clinical Application of TSH Radioimmunoassay.

WORK UNIT NO.: 74/305

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

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

OBJECTIVES

To establish a specific homologous radioimmunoassay for thyrotropin, TSH.

TECHNICAL APPROACH

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

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

Funding (in thousands) FY 75: 2.0
FY 76: 4.0

PROGRESS

This radioimmunoassay has been developed and has turned out to be a sensitive and specific assay. The serum from many patients have been studied and has had important clinical implications. TSH has been found to be elevated in several patients with the low thyroid reserve syndrome. These patients have symptoms of hypothyroidism, low normal thyronine levels, and TSH levels in the hypothyroid range. After thyroid hormone replacement, the symptoms disappear, the thyroxine levels rise but remain in the normal range, and TSH levels fall to normal.

Publications:

(1) Adler, R. A., Bergin, J. J. and O'Barr, T. P.: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome, (in preparation).

WORK UNIT NO.: 74/305

Presentations:

(1) Adler, R. A., Bergin, J. J. and O'Barr, T. P: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome, Regional Meeting of the American College of Physicians, Colorado Springs, Colorado, 15 January 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Effect of Oral Water Loading on Plasma Prolactin.

WORK UNIT NO.: 75/300

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

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

OBJECTIVES

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

TECHNICAL APPROACH

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

Prolactin is measured by radioimmunoassay.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 3.0

PROGRESS

This test has been performed in several patients. The radioimmunoassay for plasma prolactin is sensitive, specific and reproducible. Interassay variability in about 15%.

Publications:

(1) Adler, R.A., Noel, G.L., Wartofsky, L., Frantz, A.G.: Failure of All Water Loading and Intravenous Hypotonicsaline to Suppress Plasma Prolactin in Man, J. of Clin. Endocrinol. 41:383, 1975.

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

WORK UNIT 75/300

Publications - continued

(3) Adler, R. A.: The Evaluation of Galactorrhea (submitted for publication)

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FTIZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Circulatory and Homoral Changes In Dogs During Acute Pancreatitis.

WORK UNIT NO.: 75/301

PRINCIPAL INVESTIGATOR: William L. Daniels, CPT, MSC

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

OBJECTIVES

To determine changes that occur in heart rate, blood pressure, plasma glucagon, plasma insulin, blood glucose and serum amylase during the development of acute pancreatitis. To determine the effect of drugs, suggested for use in treatment of acute pancreatitis, on the above parameters and on the development of acute pancreatitis.

TECHNICAL APPROACH

a) Acute pancreatitis is induced by injection of 10 cc. of autologous bile into the dorsal pancreatic duct.

b) 5-fluoruracil and Aprotinin will be given in two groups of dogs at the time of induction of pancreatitis.

c) Blood pressures and electrocardiograms will be recorded.

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 2.0

PROGRESS

Three groups of animals have been studied so far. One group consisted of anesthetized controls. In the second group, the effects of acute pancreatitis were studied. In the third group,

WORK UNIT NO.: 75/301

PROGRESS - continued

the effects of 5-fluorouracil on the development of pancreatitis were determined. A fourth group of animals is now being studied to determine the effects of aprotinin on the development of pancreatitis. All animals were studied for an eight hour period.

Publications:

(1) Daniels, W. L., O'Barr, T. P., Miller, J. G., and Seab, J.: Circulatory and Hormonal Changes During Acute Pancreatitis. Fed. Proc., Vol. 35, No. 3, 1976. Abstract No. 1035.

Presentations:

(1) Daniels, W. L., O'Barr, T. P., Miller, J. G., and Seab, J.: Circulatory and Hormonal Changes During Acute Pancreatitis. Federation Proceedings, April 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Use of L-Dopa as a Measure of Pituitary Function.

WORK UNIT NO.: 75/302

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

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

OBJECTIVES

This study will attempt to assess the efficacy of L-Dopa as a stimulus of growth hormone secretion in patients suspected of pituitary abnormalities.

TECHNICAL APPROACH

After 500 mg of L-Dopa po, blood samples for growth hormone and prolactin are drawn at 30 minute intervals. These hormones are measured by specific radioimmunoassays.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0.1
FY 76: 0

PROGRESS

No progress has been made on this protocol because of an apparent delay in paperwork. The FDA informed AIDRB (OTSG) that an IND application was necessary. It is not known whether this was furnished them by the principal investigator, and since he has now departed this station, the protocol has been terminated

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Immuno-Surveillance Monitoring in Post Surgery Cancer Patients as Means of Evaluating Anti-Tumor Response.

WORK UNIT NO.: 75/303

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Joseph H. Baugh, COL, MC
Richard M. Hirata, COL, MC
Russ Zajtchuk, LTC, MC

OBJECTIVES

To evaluate tumor cell-mediated immunity and immuno-surveillance mechanisms in breast and colorectal cancer patients post-operative at different stages of disease.

TECHNICAL APPROACH

A piece of tissue from excised tumor and 10-20 cc heparinized and clotted blood samples are obtained at the time of surgery. Additional heparinized and clotted blood samples are obtained at monthly intervals. Soluable tumor components are extracted from tumor by standard technique and are used as stimulants on lymphocytes. Serum samples are evaluated for immunoglobulin content (i.e., IgG, IgM, IgA, alpha 1 glyco-protein), serum protein electrophoretic profiles, and carcinoembryonic antigen. Cellular immuno mechanism is also evaluated monthly after surgery by lymphocyte blast transformation technique using mitogenic stimulation with phytohemogglutinin, conconavalin A and pokeweed mitogen. Peripheral lymphocytes are quantitated as to percent thymic derived lymphocyte population with SRBC "rosette" test.

Manpower (in professional man years): 1.5/yr

Funding (in thousands) FY 76: 2.0

PROGRESS

Thirteen (13) patients encompassing five (5) breast and eight (8) colon cancer types were studied for periods of two to eleven months. Period of evaluation started on date of surgery with monthly follow-up intervals. Approximately 50% of the patients,

WORK UNIT NO.: 75/303

PROGRESS - continued

of the patients, in addition to indicated surgical procedures, were also placed on selected chemotherapy. Serum evaluations for IgG, IgM, IgA, complement C'3 and C'4, and electrophoretic profile showed no abnormal results. Concentration of serum alpha 1 acid glycoprotein in 70-75% of subjects were elevated on the initial sample with normalization within two (2) months post surgery. On two (2) patients with clinical metastatic symptoms the alpha 1 acid glycoprotein was noted to be abnormally light with no normalization. Lymphocyte blast transformation post mitogenic stimulation was markedly suppressed on the initial samples, date of surgery, with normalization within two months. No differences in lymphocyte blast transformation was noted in the non-chemotherapeutic treated and treated groups.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: 24-Hour Prolactin Patterns in Patients with Galactorrhea and/or Pituitary Tumors.

WORK UNIT NO.: 75/304

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: Stephen R. Plymate, MAJ, MC
T. Philip O'Barr, Ph.D., DAC

OBJECTIVES

This study attempts to find a new tool for differentiating functional from tumor-induced galactorrhea and for assessing pituitary function in patients with pituitary tumors and/or hypogonadism.

TECHNICAL APPROACH

Samples for hormones are drawn every 20 minutes through an indwelling catheter via a constant withdrawal pump connected to a fraction collector. The following hormones are measured by sensitive and specific radioimmunoassays: prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone (T). The assay for Estradiol (E_2) is under development.

Manpower (in professional man years): 2/yr

Funding (in thousands)		
	FT 75:	4.0
	FY 76:	4.0

PROGRESS

Approximately 10 patients have now been studied via this technique. The preliminary results are very exciting. One patient with primary hypothyroidism and galactorrhea had elevated prolactin levels without normal diurnal variation. After treatment with thyroid hormone, galactorrhea has all but disappeared and basal prolactin has returned to normal. However, diurnal variation has not appeared. This has never been reported. Studies will continue in the next few months on patients with pituitary abnormalities at various stages of diagnosis and treatment.

WORK UNIT NO.: 75/304

Publications:

(1) Adler, R. A.: The Evaluation of Galactorrhea (submitted for publication)

Presentations:

(1) Adler, R. A.: Prolactin, 1976, Endocrine Grand Rounds, University of Colorado Medical Shcool, 15 January 1976.

(2) Adler, R. A.: Prolactin, 1976, Endocrine Research Seminar, Dartmouth Medical School, 9 April 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Effect of Colestipol in Patients with Hyperlipoproteinemia, Type II.

WORK UNIT NO.: 75/305

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

The purpose of this study is to detect the efficacy of a new cholesterol lowering agent.

TECHNICAL APPROACH

Ten patients with hyperlipoproteinemia Type IIA will be studied in this experiment. Baseline fasting cholesterol and triglyceride will be drawn as well as any other blood tests that are indicated in the particular individuals. Then the patients will begin taking colestipol at the dose of 10 grams twice a day. They will receive Colestid® in the form of two packets for each dose to be taken with water twice a day. Each patient will be seen once a month to note any side effects. Blood for cholesterol and triglycerides will be drawn monthly. The test is to last three months.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

By the time final approval was received, the study was no longer feasible. One patient was tried on the medication with success, but other patients could not wait for approval of this therapy.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: An Evaluation of the Medical Treatment of Thyroid Cancers Using Various Radioablative Approaches.

WORK UNIT NO.: 75/600

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: K. David McCowen, MAJ, MC
Stephen R. Plymate, LTC, MC
Nasser Ghaed, LTC, MC
Fred Hofeldt, M.D.

OBJECTIVES

This study will assess the long-term efficacy of treatment with 29 mCi I^{131} doses for ablating residual thyroid tissue in post-thyroidectomy thyroid cancer patients versus the larger treatment doses of 100 mCi. The study is to be both a prospective and retrospective assessment of these varying treatment schedules.

TECHNICAL APPROACH

After total thyroidectomy, patients are treated with 29 mCi of ^{131}I, after informed consent, to ablate remaining thyroid tissue. Patients are scanned just after surgery, 3 to 6 months after treatment, and as needed thereafter.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 75: 0.5
FY 76: 1.0

PROGRESS

Project has been completed with final publication in the American Journal of Medicine, July 1976.

WORK UNIT NO.: 75/600

Publications:

(1) McCowen, K. D., Adler, R. A., Ghaed, N., Verdon, T., and Hofeldt, F. D.: Low Dose Radio-iodine Treatment of Post-Surgical patients with Thyroid Carcinoma, in press, American Journal of Medicine, July 1976.

Presentations: None

STATUS:

Completed.

OB-GYN

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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: Alfred S. Llorens, COL, MC

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 questionnaire on a six monthly basis. This will ultimately give sufficient data to define the relative merits of different surgical approaches in our treatment of this clinical problem.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 75: 0
FY 76: 0

WORK UNIT 67/351

PROGRESS

The project is continuing as outlined with accumulation of patients and follow-up information. There are currently over 200 patients in this study with approximately 90 of them being followed after a "Pereyra" procedure.

Publications: None

Presentations:

(1) Deubler, K.F.: 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, October 1973.

(2) Deubler, K.F.: 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 1974.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/353

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

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

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

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

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 75:	0
	FY 76:	0

WORK UNIT 73/353

PROGRESS

Data collection only, at present. Material collected has not been reviewed as yet. The three-year collection of cases is to be followed for five years and is to be maintained on these patients by questionnaire.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Microplasma and Infertility - Therapeutic Result of Doxycycline Therapy.

WORK UNIT NO.: 74/301

PRINCIPAL INVESTIGATOR: Larry B. Norfleet, MAJ, MC (for Dr. J.S. Powers)

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

a. Couples with no demonstrable cause for infertility will be treated with doxycycline to determine whether subsequent pregnancy rates of these patients are significantly higher than couples treated with placebo.

b. Husband and wife will be cultured for the presence of mycoplasma and/or ureoplasma (T-strains) to determine the role (if any) of each organism in infertility; and to determine if eradication of these organisms affects pregnancy rates in these patients as compared with a treated control group who do not harbor these organisms.

TECHNICAL APPROACH

If it can be established that mycoplasma organisms contribute significantly to infertility problems and if the organism can be eradicated with appropriate therapy, then successful pregnancies can be achieved by proper evaluation and examination. The data will also serve as a sound basis for further research in mycoplasma microbiological studies.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 1.5
FY 76: .5

PROGRESS

Principal Investigator has left the U.S. Army and no replacement has been assigned for this project.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: A Comparison of Oxytocin and Oral Prostaglandin E_2 in the Induction of Labor

WORK UNIT NO.: 75/350

PRINCIPAL INVESTIGATOR: John P. Elliott, MAJ, MC

ASSOCIATE INVESTIGATOR: William P. Byars, Jr., CPT, MC

OBJECTIVES

To determine the effectiveness of Prostaglandin E_2 orally as an inducing drug in pregnancies which are to be terminated by medical means.

TECHNICAL APPROACH

Patients selected for induction of labor will be divided into two random groups which contain three subgroups each based on the Bishop's Score for evaluating ease of induction. Either oral Prostaglandin E_2 or intravenous oxytocin is administered until delivery or the method is termed failure after eight hours of no progress.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0

PROGRESS

No progress has been made on this protocol to date since approval for the protocol arrived during the departure of the original Investigator. Approval of a new Investigator will be sent to OTSG pending certain requested modifications to the protocol by OTSG.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Prevention of Radiation Induced Diarrhea.

WORK UNIT NO.: 75/351

PRINCIPAL INVESTIGATOR: Alfred S. Llorens, COL, MC

ASSOCIATE INVESTIGATOR: Robert Hesselgesser, MAJ, MC

OBJECTIVE

To determine if administration of aspirin to patients undergoing abdominal or pelvic radiation will influence gastrointestinal toxicity.

TECHNICAL APPROACH

A double-blind study will be carried out administering aspirin, .93 gm, daily and placebo to patients undergoing pelvic or abdominal radiation. Parameters to be evaluated are subjective assessment of gastrointestinal toxicity and also objective levels of prostaglandin F2α breakdown products.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 1.5

PROGRESS

This study was just recently approved by HSRRB OTSG and has not commenced in FY 76, but should start approximately 1 July 1976.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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: Edward J. Lazarus, MAJ, 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 (FAMC).

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 75:	0.5
	FY 76:	0.5

PROGRESS

As of 15 July 1976, there are currently 30 patients that have taken part in the investigation and to this date the results of the HPL levels are still blind. It is anticipated that by the time there are 50 patients in the study, and the pregnancies on these 50 patients have been completed, that the results will be examined. It is postulated at this time that it will be September or October of 1976 by the time this point has been reached. The serum estriols are still being obtained through the Department of Pathology and the serum human lactogen levels are obtained through the Clinical Investigation Serivce, Biochemistry Section, Dr. O'Barr assisting.

WORK UNIT NO.: 75/352

Publications and Presentations: None

STATUS:

Ongoing.

PEDIATRICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 73/413

PRINCIPAL INVESTIGATOR: William H. Parry, LTC, MC

ASSOCIATE INVESTIGATOR: Gerald B. Merenstein, LTC, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

The major problem at present is adapting the equipment to recording equipment in order to register valid tracings and thus useful data. The equipment itself is working well and the study is in progress. Several trials on infants have been performed. One interesting spinoff of the primary experiment is that the equipment has been

WORK UNIT 73/413

PROGRESS - continued

used on two (2) infants with unexplained apnea who were thought to be at risk for developing Sudden Infant Death Syndrome (SIDS). This equipment was used to prove that these infants had normal chemoreceptor responses to hypercarbia.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Posterior Polar Cataracts and Steroid Therapy in Children.

WORK UNIT NO.: 74/406

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

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

OBJECTIVES

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

TECHNICAL APPROACH

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

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

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

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

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 75: 0
FY 76: 0

WORK UNIT 74/406

PROGRESS

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

Publications:

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

Presentations:

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

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

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Computer Assisted Diagnosis in a Military Hospital.

WORK UNIT NO.: 74/407

PRINCIPAL INVESTIGATOR: Warren A. Todd, LTC, MC

ASSOCIATE INVESTIGATOR: Gary Pettet, MAJ, MC

OBJECTIVE

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Unfortunately the project was terminated approximately 10 months ago due to the fact that the Meditel Corporation went bankrupt. At the time of termination of the project, approximately 45 patients were enrolled in the study. It is felt by the principal investigator, myself, and the associate investigator that these numbers do not justify submission of statistical data to see if there was a decrease in hospitalization cost and time.

WORK UNIT 74/407

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 75/400

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

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

OBJECTIVES

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

TECHNICAL APPROACH

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

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

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

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 75: 1.0
FY 76: 0.0

PROGRESS

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

WORK UNIT 75/400

PROGRESS - continued

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

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

Two additonal infants have been added to the study at FAMC and additional infants at the University of Colorado Medical Center under a separate protocol have also been entered. These infants have continued to provide the spectrum of the myocardiopathy of infants of diabetic mothers.

Publications:

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

Presentations:

Way, G.: The Spectrum of Myocardiopathy in Infants of Diabetic Mothers. Annual Meeting of American Academy of Pediatrics, Cardiology Section, Washington, D.C., Oct. 75.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Effect of Prophylactic Antibiotic Therapy on Gravid Group B Beta Hemolytic Streptococcus Carriers.

WORK UNIT NO.: 75/401

PRINCIPAL INVESTIGATORS: Christian C. Yost, CPT, MC
George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Edward E. Dashow, CPT, MC
John V. Calcagno, CPT, MSC
Ann H. Tull, DAC, GS-9

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 75: 1.0
FY 76: 4.0

PROGRESS

Three collection-transport systems (CTS) were studied for optimum isolation of Group B Streptococcus (GBS) among 1626 multiple prepartum endocervical and 610 infant ear impression specimens. At the time of specimen collection, one swab was placed in Todd-Hewitt broth containing neomycin, naladixic acid, and sheep

WORK UNIT NO. 75/401

PROGRESS - continued

erythrocytes (THB); a second was maintained in the Duo-Trans-Cul system (Wampole); a third was left dry (DRY). All specimens were inoculated on sheep blood agar (SBA) and on Columbia agar containing neomycin and naladixic acid (CHN); all were again replated within 24 to 48 hours for GBS. SBA were maintained in an atmosphere of 5% CO_2, and CHN under 5% H_2 - 95% CO_2. Biochemical and serological tests were used for definitive identification. GBS carrier rates of 9.47 and 3.11% were recorded for prepartum women and neonates, respectively. Evaluation of 44 positive cultures from 771 specimens showed significant differences among the three CTS and the two time intervals of specimen inoculation. GBS recovery in these modalities was as follows: THB, 63.64% initial plating, 93.18% replating; Duo-Trans-Cul, 63.64% initial, 77.27% replating; DRY, 45.45% initial, 34.09% replating. The data support a concept that recorded carrier rates based on laboratory results are influenced by the initial specimen management.

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.

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, N.J., 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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
Bruce H. Brundage, LTC, MC
Stephen Golden, LCDR, 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): .25/yr

Funding (in thousands) FY 76: 1.0

PROGRESS

While awaiting permission to randomly treat or not treat with digitalis those patients who had echocardiographic evidence of left atrial enlargement, it was decided that it was clinically warranted to treat all partients with digitalis. The patients treated with digitalis during

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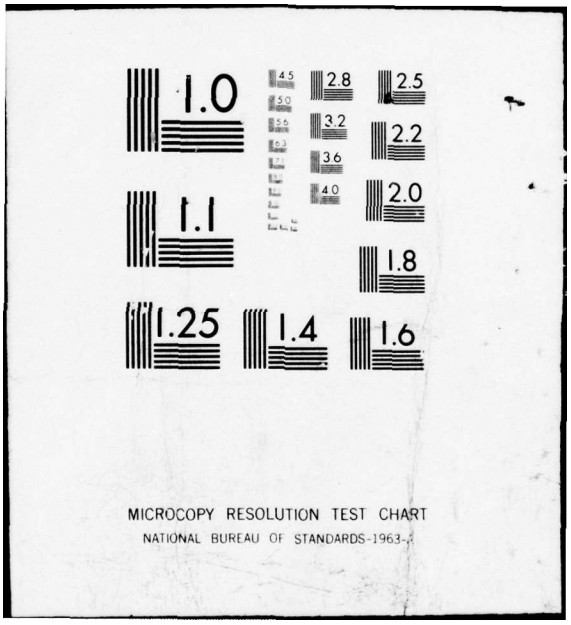
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MICROCOPY RESOLUTION TEST CHART
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WORK UNIT NO.: 75/402

PROGRESS - continued

the 9-month period prior to permission for randomization have been analyzed, and a paper is being prepared for submission for publication. The permission to randomly treat or not treat with digitalis has been received, and the protocol is being implemented. No patients have been entered on a random basis to this date.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Efficacy of a New Combined Measles-Mumps-Rubella Vaccine.

WORK UNIT NO.: 75/403

PRINCIPAL INVESTIGATOR: Frances A. Ennis, M.D., Dir., Div. of Virology, Bureau of Biologics, UCMC
Richard B. Krugman, M.D., Dept. of Med., UCMC
Warren A. Todd, LTC, MC, FAMC

ASSOCIATE INVESTIGATORS: Paul D. Partman, M.D., Dep. Dir., Bureau of Biologics, UCMC
Harry M. Meyer, Jr., M.D., Dir., Bureau of Biologics, UCMC

TECHNICAL APPROACH

Approciamtely 250 children between the ages of 12 and 24 months of age will be included in the study with the following considerations: (1) Informed parental consent will be obtained; (2) There is no contraindication to vaccination; (3) There would be no previous clinical history of mumps, rubella or rubeola; (4) Neither measles, mumps, nor rubella vaccines have been previously given to the children. A 10 ml venous blood specimen will be collected and then the triple vaccine will be administered. The parent will be instructed to telephone the FAMC, Pediatric Clinic, should the child develop any illness (other than low grade fever for a brief duration the second week after vaccination). A prompt clinical and epidemiologic evaluation will be carried out for all such reports. Sixty days after vaccination, the child will return to the clinic for a second 10 ml blood specimen.

Manpower (in professional man years): .10/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Although this project was submitted to the Fitzsimons Clinical Investigation Service as well as to OTSG, Washington, D.C., and approval to

WORK UNIT NO. 75/403

PROGRESS - continued

commence study was subsequently obtained, the project was never initiated because of problems encountered in release of the vaccine from the Bureau of Biologics. Therefore, no work was ever done on this project.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Early Discharge of Low Birth Weight Infants.

WORK UNIT NO.: 75/404

PRINCIPAL INVESTIGATOR: John B. Woodall, MAJ, MC

ASSOCIATE INVESTIGATOR: Gerald B. Merenstein, LTC, MC

OBJECTIVES

To determine the following:

a. Criteria most useful in judging the safety of discharging a low birth weight infant.

b. The growth and development patterns of low birth weight infants who are discharged prior to attaining the customary discharge rate of 2268 grams or more.

c. The incidence and type of medical and/or psychiatric illness occurring in the first 1-2 years after discharge.

d. Whether a prospective study would be meaningful.

TECHNICAL APPROACH

A retrospective review of infants weighing less than 2500 gm to evaluate the children's physical and mental development using a general physical examination, serial Denver Developmental Screening Tests, hospital admissions, and clinically treated illnesses was undertaken.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 75:	0
	FY 76:	0

PROGRESS

During this past Fiscal Year, review of the charts of the infants weighing less than 2500 gm at birth and controls of full-term infants has been completed, and the results compiled into a report submitted for publication.

WORK UNIT NO. 75/404

Publications:

Woodall, J. B., Merenstein, G. B., Merchant, M.: Early Discharge of Low Birth Weight Infants. Clin Res 24:196A, 1976 (Abstract).

Presentations: None

STATUS:

Completed.

PATHOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Relationship of Estrogenic Hormones to the Coagulation Balance.

WORK UNIT NO.: 71/450

PRINCIPAL INVESTIGATOR: Paul W. Holley, MAJ, MC

ASSOCIATE INVESTIGATORS: James J. Bergin, COL, MC
Donald G. Corby, COL, MC

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 75: 5.0
FY 76: 5.0

WORK UNIT 71/450

PROGRESS

The thrombin generation test and the functional serum antithrombin-III determination have been discussed in previous Research Project Resumes. Studies indicate that in all patients taking estrogens, either alone or in an oral contraceptive preparation, there is a significant depression of serum functional antithrombin-III and an acceleration of thrombin generation to a somewhat lesser degree. Plasma antithrombin III is mildly depressed, also, indicating probable *in vivo* catabolism. Studies indicate that the degree of drop in serum antithrombin-III activity is not related to the amount of estrogen in oral contraceptive medication or to the dose of exogenous estrogens (Premarin) taken.

In males with prostatic carcinoma treated with estrogens serum functional antithrombin-III activity is decreased significantly.

Current studies are being conducted as follows:

(1) In a group of females prior to castration, after castration but prior to estrogen replacement, and then after several months of estrogen replacement, determination of estrogen levels, thrombin generation index (TGI), and antithrombin-III depression.

(2) Two hundred patient studies will be undertaken using the Sonoclot, an electro-mechanical device which evaluates and records *in vitro* clotting by assessing changes in clot impedance. Sonoclot tracings will be compared with the thrombin generation curve and the thrombin generation index (TGI) to determine if any useful correlation exists.

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

Publications:

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

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

WORK UNIT 71/450

Publications - continued

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

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

(5) Holley, P. W., Bergin, J. J., Powers, J. S., Barber, J. A., Rush, P. A., and Zuck, T. F.: Antithrombin-III Depression in REsponse to Estrogen Dose in Oral Contraceptives. (In preparation for publication).

(6) Bergin, J. J., Holley, P. W., Dobbs, R. M., Barber, J. A., and Rush, P. A.: Depression of Antithrombin-III in Patients with Prostatic Carcinoma Receiving Estrogen Therapy. (In preparation for publication).

(7) Holley, P. W., Bergin, J. J., Barber, J. A., Rush, P. A., and Zuck, T. F.: Alteration of Thrombin Generation and Antithrombin-III Level with Respect to Dose of Conjugated Equine Estrogens. (In preparation for publication).

Presentations:

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

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

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

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

WORK UNIT NO.: 71/450

Presentations - continued

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

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: Treatment of Hemophilia A or B with Inhibitors Using Auto-Factor IX Concentrate (Human).

WORK UNIT NO.: 75/450

PRINCIPAL INVESTIGATOR: Paul W. Holley, MAJ, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To evaluate treatment of hemorrhagic episodes in Factor VIII or IX deficient patients with inhibitor activity using the activated prothrombin complex concentrate Auto-Factor IX Concentrate (Human).

TECHNICAL APPROACH

Hemophilia A or B patients with inhibitor activity requiring treatment for significant hemorrhage will be evaluated clinically and with laboratory coagulation testing (APTT, PT, platelet count, fibrinogen, FDP, Factor VIII activity) prior to and after treatment with Auto-Factor IX Concentrate.

Manpower (in professional man years): 0

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

No patients with Hemophilia A or B and inhibitor activity have required transfusion therapy for hemorrhage.

Publications and Presentations: None

STATUS:

Ongoing.

RADIOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO: 73/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

WORK UNIT 73/600

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Thirteen studies using I-123 (Sodium Iodide) for evaluation of patients suspected of having thyroid disease. The I-123 studies were resumed as of 21 June 1976.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

WORK UNIT 74/600

TECHNICAL APPROACH- continued

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

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

Patients have now become available, and there have been three Indium-111 Chloride studies to date.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/601

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

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

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/602

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

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

TECHNICAL APPROACH

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

Manpower (in professional man hours): 0.1/yr

Funding (in thousands) FY 75: 0
FY 76: 0

PROGRESS

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

Publications and Presentations: None

STATUS:

Ongoing.

HOSPITAL CLINICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

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

WORK UNIT NO.: 74/651

PRINCIPAL INVESTIGATOR: Nicholas C. Bethlenfalvay, COL, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC

OBJECTIVES

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

TECHNICAL APPROACH

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

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

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 75:	4.0
	FY 76:	2.5

WORK UNIT 74/651

PROGRESS

The following procedures can now be performed: Preparation and preservation and storage of hemoglobin and globin. Zone electrophoresis of hemoglobin in various media and electrophoresis in polyacrylamide gel with isoelectric focusing. Quantitiation of Hb F. Quantitation of Hb A_2 by microcromatography. Hb stability testing by the isopropanol technique. Electrophoresis of urea dissociated globin, and qualitative and quantitative recovery of hemoglobin and its sub units using column chromatography.

Since 30 June 1975 the following in new methodology was acquired: Hybridization procedures to delineate alpha vs. beta chain variant hemoglobins. Separation of hemoglobins into alpha and beta chains by reaction with PMB or PCMB. Globin chain synthesis studies using either ^{3}H leucine or ^{14}C leucine have commenced and, at this stage are aimed at establishing a range of normal control values. High voltage electrophoresis equipment for use in peptide mapping is nearly complete. Preliminary mapping of globin peptides should be commencing soon.

Publications and Presentations: None

STATUS:

Ongoing.

NURSING

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 JUN 76

TITLE: The Impact of Pediatric Nurse Practitioner Programs: An Exploratory Methodology Study.

WORK UNIT NO.: 75/700

PRINCIPAL INVESTIGATOR: American Nurses' Association, Inc.

ASSOCIATE INVESTIGATOR: Marian J. I. Walls, LTC, ANC

OBJECTIVES

(1) To select a representative sample of pediatric nurse practitioner programs to be included in the study based upon selected program characteristics and a listed universe of goals.

(2) To operationalize the universe of goals for pediatric nurse practitioner programs.

(3) To determine congruence between goals of selected PNP programs and their curricula utilizing the criteria of emphasis and thoroughness.

TECHNICAL APPROACH

Much of the study has been curtailed due to lack of funding. The only aspect will be the collection of data, involves questionnaires which will be completed by program directors.

Manpower - N/A

Funding - The American Nurses' Association is seeking funding.

PROGRESS

This is the first four months of the investigation. Data questionnaire is in the process of being completed for the American Nurses' Association. FAMC is one of 20 Nurse Clinician Pediatric courses being studied.

Publications and Presentations: None

STATUS:

Ongoing.

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