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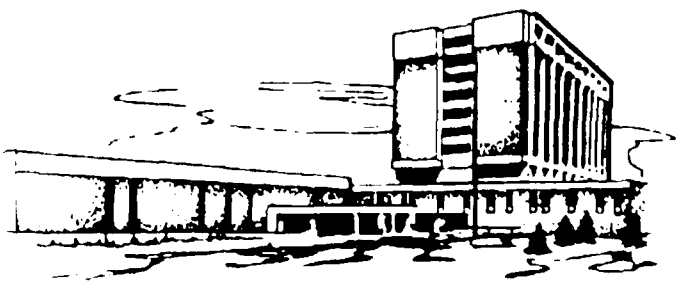
ANNUAL PROGRESS REPORT

Fiscal Year 1989



Department of Clinical Investigation
William Beaumont Army Medical Center
El Paso, Texas 79920-5001

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

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

Clinical Investigations
Publications, presentations
Detail Summary Sheets (~~Study Objective;~~ Technical Approach; ~~Progress, Status~~)

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

Subject report serves to identify the research activities conducted by William Beaumont Army Medical Center investigators who had protocols approved by the Clinical Investigation Committee, the Institutional Review Board, and the Animal Use Committee. This report includes all protocols registered with the Department of Clinical Investigation during FY 1989. All known presentations and Publications by the staff at William Beaumont Army Medical Center are also included.

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FY 89 Annual Progress Report

Headquarters
William Beaumont Army
Medical Center
El Paso, Texas 79920-5001

Clinical Investigation
Program
RCS MED-300 (R1)

This report was prepared under the direction of

Colonel Manuel Schydlower

Chief, Department of Clinical Investigation

William Beaumont Army Medical Center

El Paso, Texas 79920-5001

FORWARD

Fiscal year 1989 was another period of change and progress in Clinical Investigation at William Beaumont Army Medical Center.

The new Department Chief and Assistant Chief (Major Robert Martig) enjoyed the privilege of acquaintance with highly talented people, both in the department and in other areas of our medical center. While the material resources that support high quality research are outstanding, we are most impressed with the professionalism and dedication of our colleagues, to include researchers and support personnel.

The Biological Research Service was most active in participating and supporting physician-resident, field medic and paramedic training programs, and in furthering research projects in microsurgery, laser surgery, drug efficacy and immunology. The Chemistry Service made great strides in a project concerning gene sequence, conservation, control and intervention in the synthesis of mucin proteins. The Immunology/Microbiology Service advanced their studies of T cells in the peripheral blood circulation of patients with allergies and progressed in the development of an assay to measure epidermal growth factor in saliva and sera. The Human Performance and Physiology Laboratory finalized a fully funded joint Navy/Army agreement that aims to perform extensive sickle cell trait and asthma research.

This year we saw an increase in research directly related to the welfare of our soldiers, and several of these projects received USAMRDC funding. Additionally, numerous clinical and basic science research projects resulted in publications in major peer review journals and presentations (papers, posters, exhibits) at national medical meetings. These research activities were recognized as essential elements in the programs of several residencies that passed recent accreditation reviews.

Talented and dedicated professionals working together, collaboratively and cooperatively, are responsible for another year of accomplishments. We are proud to be members of this team and thank all our colleagues, military and civilian, for all their efforts.

Manuel Schydlower, M.D.

MANUEL SCHYDLOWER
Colonel, Medical Corps
Chief, Dept Clinical Investigation

Unit Summary FY 89

Objectives

The Department of Clinical Investigation is responsible for providing the facilities and atmosphere of inquiry necessary to support and stimulate basic and clinical medical investigation within William Beaumont Army Medical Center.

Technical Approach

The Department of Clinical Investigation provides support for staff, fellows and housestaff research projects under the guidelines of the Declaration of Helsinki, the Clinical Investigation Program (as described in AR 40-38 and HSC Reg 40-23), and the Use of Investigational Drugs in Humans and the Use of Scheduled Controlled Drug Substances (as described in AR 40-7). Research is conducted under protocols approved by the Research Committee (WBAMC HR 15-1), the Human Use Committee (WBAMC HR 15-1), and the Radioisotope Committee (WBAMC HR 15-1) where applicable. For research protocols utilizing laboratory animals, the Animal Use Committee (WBAMC HR 15-1) ensures that the investigators follow guidelines set forth in the "Guide for Laboratory Animal Facilities and Care", published by the National Academy of Sciences-National Research Council, and the criteria established by the American Association of Laboratory Animal Care.

MANPOWER: Listed below is the current strength of the Department of Clinical Investigation.

Description	Grade	MOS	Br	Req	Auth	Name	Rank
C, Dept Cl Inv	06	60P	MC	1	1	Schydlower	06
Dir, HP/SCT	05	60F	MC	1	1	Weisman	05
Immunologist	03	68E	MS	1	1	Martig	04
Biochemist	03	68C	MS	1	1	Smith	03
C, Bio Res Svc	03	64C	VC	1	1	O'Hair	04
Animal Care NCO	E6	91T	NC	2	1	Ribble	E5
Biol Sci NCO	E5	01H	NC	1	1	Fama	E6
Biol Sci Asst	E4	01H		1	1	Ezukanma	E5
Biol Sci Asst	E4	01H		0	0	Delgado	E4
Biol Sci Asst	E4	01H		0	0	Barlan	E4
Animal Care Sp	E4	91T		1	1	Kahn	E4
Animal Care Sp	E3	91T		2	1	Brown	E3
Supv Res Chem	12	1320	GS	1	1	Bhattacharyya	12
Microbiologist	12	403	GS	1	1	Veit	12
Chemist	09	1320	GS	1	1	Enriquez	09
Microbiologist	09	403	GS	1	1	Smiley	09
Med Technician	07	645	GS	2	1	Lund	07
Med Technician	07	645	GS	2	1	Mana	07
Med Technician	07	645	GS	2	1	McIntyre	07
Health Tech	07	640	GS	1	1	Revels	07
Cl Prot Coord	07	303	GS	1	1	McCollum	07
Edit Asst Typ	07	1087	GS	1	1	Lamonde	07
Sup Clk (Typ)	04	2005	GS	1	1	Turner	04
Anm Caretaker	04	5048	WG	1	1	Sigholz	04
Anm Caretaker	01	5048	WG	2	1	Burton	01

Civilian Personnel with Special Project Funding

Co-Director HP/SCT				Zeballos
Exer Physiol	09	413	GS	Connery
Med Technician	06	645	GS	Lopez
Edit Asst	05	1087	GS	Angerman
Res Proj Clerk	04	303	GS	Morillo
Data Transcriber	03	356	GS	Brungs

GRANTS:

USA Medical Research and Development Command

Prevention of Stress Fractures Through Modification of Basic Combat Training Physical Training Activities Based on Biodynamics. $72,000

Combat Trauma Surgery Using a Portable Contact Nd-(YAG) Laser in the Porcine and Ovine Models. $107,000

Rate of Spherulin Skin Test Conversion Among Basic Trainees Exposed to Desert Training at Ft Bliss, Texas. $8,000

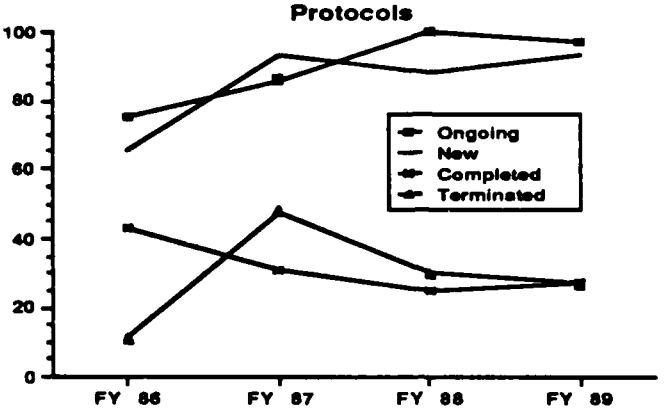
USN Medical Research and Development Command

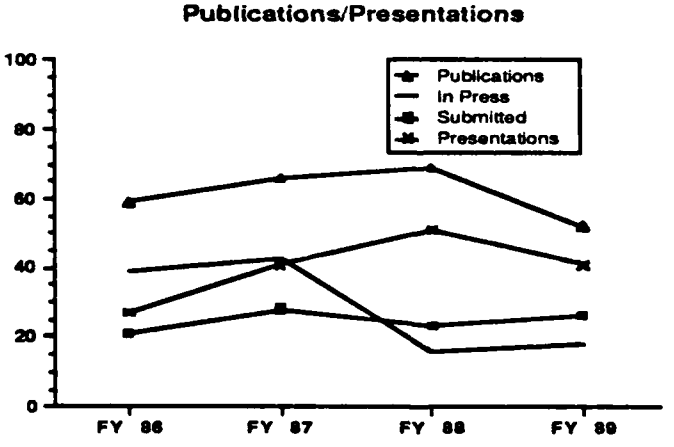
Joint Navy-Army Human Performance/Sickle Cell Trait Research Project at WBAMC. $60,000

PERSONNEL

	Required	Authorized	Assigned
Officers	7	5	5
Enlisted	7	5	7
Civilian	18	13	19*

* 6 civilians are funded through special projects





EXPENDITURES	**FY 86**	**FY 87**	**FY 88**	**FY 89**
Personnel (Civ)	307,120	363,094	375,197	405,498
Consumable Supplies	138,737	236,662	141,175	187,846
Capital Equipment	43,988	8,743	34,726	23,835
TDY	3,888	5,272	3,092	4,605
Printing and Publications	28,613	28,821	26,338	4,103
TOTAL	522,346	642,592	580,528	625,887
MEDCASE Equipment	161,839	89,105	434,064	361,427
Military Pay	237,754	457,879	417,265	510,814
TOTAL	921,939	1,189,576	1,431,857	1,498,128

PROGRESS FY 89

Biological Research Service

The Biological Research Facility is accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC). It has a total of 6,984 ft and during FY 89 has had an average daily inventory of 265 animals. A revised facility design is currently being prepared to conform with physical plant requirements of the pending USDA regulations which will implement the 1985 Animal Welfare Act Amendment and to enable increased capabilities.

The facility supports the total animal research and training mission for William Beaumont Army Medical Center and additionally, provides direct support to other MEDDAC's in this geographical region. The biomedical training utilizing animal models is primarily for the physician resident training programs. There are nine ongoing training protocols for physicians encompassing emergency trauma life support, general surgery, laser surgery, and microsurgery. In addition, there are two protocols for training field medics and paramedics in emergency trauma life support procedures. There are a total of 16 active research protocols including microsurgery, general surgery, therapy and techniques for the management of soft tissue and orthopedic trauma, laser surgery for visceral trauma repair, microstructural changes with stress reaction in bone, drug efficacy, and immunology.

This fiscal year there has been a substantial increase in research and training directed for the soldier. We are most pleased with the improvement in the quality of research design, equipment now available to complete the research or training, and a more automated and accurate means of data management. We implemented a computerized animal records management system. We now have the capability to quickly compile data from individual animals or from animals assigned to specific protocols. The system will also generate annual USDA reports, monthly workload summaries, animal inventories, protocol assignments, and assist in the management of recurring procedural requirements. The operating room equipment was upgraded to enable support of more involved surgery and allows support of two major surgeries simultaneously. An automatic x-ray film processor was procured which greatly enhances our efficiency for radiological procedures. A new cage wash unit and animal waste disposal system was procured to meet required sanitation standards and to limit animal diseases and protect personnel from occupational health hazards.

The residents and staff involved with these studies are extremely dedicated and we anticipate notable contributions to continue.

Chemistry Service

1989 was a very dynamic year for the Chemistry service of DCI. In addition to five presentations given to different scientific meetings, twelve papers were submitted, of which nine have been published. We are currently involved in six active protocols and are collaborating with the U.S. Army Institue of Surgical Research at Ft. Sam Houston, Texas on another protocol. Three of these protocols are concerned with the role of mucin in human respiratory diseases and the other three deal with the role of vitamin B6 in humans, both in the healthy and diseased states. The co-operative effort involves the examination of B6 levels in burn patients.

We have already established the structural entity of mucin macromolecules isolated from humans with different respiratory diseases and raised an antibody against the protein backbone of mucin. Our section has been successful in maintaining a tracheal epithelial culture cell line in the laboratory and have isolated mRNA from tracheal epithelia of different animals. Our long term goal is to study the control in the synthesis of mucin in the cellular as well as the gene level and intervene effectively with this hypersecretory process by utilizing different agents including therapeutic drugs.

The B6 projects continue to place us in the forefront of vitamin research and supply us with data and information concerning the role of B6 in both healthy and ill patients. Our long term goal is to continue examining B6 and its metabolites, and establish their relationship with other parameters such as albumin, LDH, cholesterol and others that govern good health as well as illness.

In our continuing effort to develop into one of the best analytically equipped laboratories in the DCI chain, this past year we have acquired two state of the art analytical instruments and upgraded a third. The instruments obtained were a Hewlett Packard liquid chromatographmass spectrometer and a Dionex carbohydrate/metal analyzer. Our existing Hewlett Packard 5995 gas chromatographmass spectrometer was upgraded with a new HP 9000 Series 300 data system.

HumanPerformance/SickleCell Trait Research Project

The Sickle Cell Research Project underwent a reorganization during the past year. A Memorandum of Agreement was signed between Health Services Command and Naval Medical Research and Development Command providing funding for personnel and supplies over a four year period to support their research efforts. The project is now entitled the Joint Navy-Army Human Performance/Sickle Cell Trait Research Project at WBAMC. The research itself has centered on the physiological responses of individuals with sickle cell trait to maximum exercise of short duration at various altitudes. Answers to the questions being asked in this lab will be useful to DA in setting quidelines for assignments of personnel with sickle cell trait. The Human Performance lab is also involved in clinical evaluations of patients refered from various Medical Center departments. The state-of-the-art equipment in the lab enables the investigators to analyze gases expired during exercise to assist in the evaluation of the causes of the decrease in performance. The Human Performance/Sickle Cell Trait lab is gaining national recognition (as determined by peer review, articles published, papers presented) for the work it is doing on exercise and sickle cell trait. This level of

expertise is expected to continue with continued funding of the project by Naval MRDC.

Immunology & Microbiology Section

Current research interests in this section are focused on five areas: immunoregulatory subsets of T cells in Bermuda grass allergy, epidermal growth factor production in peptic ulcer disease and colon carcinomas, B cell immunodeficiencies and production of regulatory lymphokines, allergic manifestations of Trichophyton disease, and immune responses to measles virus.

In studies of immunoregulatory subsets of T cells, use of triple-parameter flow cytometry has enabled us to identify specifically activated CD4 + (helper) T cells in patients with Bermuda grass allergy. Light scatter properties, as one parameter, isolates the lymphocyte population, anti-CD4 conjugated with FITC identifies only those lymphocytes which are CD4 + as the second parameter, and anti-IL-2R conjugated with phycoerythrin identifies those CD4 + cells which express IL-2 receptors as the third parameter. Since CD4 + cells may be functionally active as helper cells in inducing a suppressor cell population or, alternatively, as inducers of B cells which produce IgE, we are currently attempting to generate in vitro culture systems that allow for the testing of each of these possibilities. In an attempt to generate suppressor cells in vitro as described by others, we found that the resulting cell population enhanced rather than suppressed an immune response to Bermuda grass allergen. However, it is likely that the concentration of antigen used to stimulate T cells is critical in determining whether enhancement or suppression will occur. Studies now in progress are aimed at determining whether antigen concentration is a key factor in this immunoregulatory process. In associated studies, we have measured IgE- and IgG subclass-specific anti-Bermuda grass antibodies with ELISA. Results have indicated that allergy patients have significantly elevated levels of IgE antibodies with little (primarily of the IgG1 and IgG4 subclasses) or no IgG antibodies, as expected. By contrast, immunotherapy patients have very low or no specific IgE antibodies but do have elevated levels of IgG antibodies belonging to the IgG1 and IgG4 subclasses.

Epidermal growth factor (EGF) is a very potent stimulator of cell growth and, among various other biological activities, has been shown to inhibit the production and secretion of gastric acid. Because of this latter property, reduced levels of epidermal growth factor production may be one of the contributing events in the development of peptic ulcer disease. We have established a sensitive assay for measuring EGF in our laboratory. The assay utilizes competition between non-labeled and 125-Iodine-labeled EGF for the detection of nanogram quantities of EGF in saliva and serum samples. Results thus far have supported the concept described above and have shown that all patients with peptic ulcer disease tested have reduced levels of salivary EGF.

There are many causes for the development of immunodeficiency including hormone in-balance (stress-related production of ACTH), malignancies of the immune system, genetically-determined insufficiencies of or a congenital absence of various components of the immune system, or virus-induced deficiencies such as AIDS. Depending on the nature of the cause, immunodeficiencies may be primarily manifested in the functions of T cells or B cells or both. We have focued attention on B cell deficiencies which are primarily related to alterations in differentiation. Interleukin-4 (IL-4) is an essential growth factor for the differentiation of B cells into immunoglobulin-secreting cells. The system which we have established for the study of B cell function involves the activation of B cells from patients suspected of having a deficiency with anti-IgM-bound sepharose which cross-links IgM which is on the B cell surface. Once activated, the B cells undergo a process of differentiation that involves immunglobulin class switch from IgM to IgG and which requires the lymphokine, IL-4, that is provided exogenously to the cell culture. Following culture for several days, the culture supernatant is then analyzed for the presence of secreted IgM and IgG.

Trichophyton is a fungus which is responsible for variety of dermatophytic diseases including athlete's foot and ringworm. The finding that specific anti-Trichophyton antibodies of the IgE class appear in the sera of some patients suffering from these diseases, suggests that there may be allergic manifestations associated with these diseases. In support of this concept was the finding that treatment of asthmatic patients who also had athlete's foot with therapy for asthma, resulted in the amelioration of symptoms of dermatophytic disease. We have used an ELISA to measure anti-Trichophyton antibodies of the IgE isotype and of the four IgG subclasses in sera of patients with dermatophytoses. Of 37 patients tested, 13/37 had specific IgE, 36/37 had IgG1, 37/37 had IgG2, 27/37 had IgG3 and 14/37 had IgG4 anti-Trichophyton antibodies. Studies now underway are focused at determining whether any of the IgG subclass-specific antibodies have homocytotropic properties or blocking activity.

There is growing concern in the communicable disease field regarding the high incidence of measles epidemics in the US. The most recent documented outbreak in El Paso occurred in 1986 and we had the opportunity to study a military dependent population of students that received immunizations during the epidemic. Currently, WBAMC is engaged in a mass immunization program for school-aged children, 6 to 20 years of age which has been recommended by the American Academy of Pediatrics. Our laboratory has established as ELISA to measure IgG and IgM antibodies to the measles virus. We will obtaine pre- and post-immunization sera from these children and determine their status of immunity pre- and post-immunization. Currently, there is no clear explanation for why the immunity is not durable nor why there may have been an unusually high incidence of vaccine failures.

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Department of Clinical Investigation

Dental Service

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Psychology

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Social Work Service

Surgery

Fort Bliss, Texas

Darnall Army Community Hospital
Fort Hood, Texas

TRADOC

PUBLICATIONS FY 89

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Primary Care

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Surgery

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DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/17 STATUS: Ongoing

TITLE: Human Tracheal Mucin: Biochemical, Physical and Rheological Studies

START DATE: Mar 86 ESTIMATED COMPLETION DATE: Oct 90

PRINCIPAL INVESTIGATOR: PhD Sam Bhattacharyya

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Brigitta Manna, John Enriquez

KEY WORDS: Tracheal Mucin, Human

Study Objective: This proposal is concerned with isolation, purification and characterization of mucin glycoprotein components (mucins) from tracheal secretion of patients with asthma, chronic bronchitis and cystic fibrosis. The glycosylated and nonglycosylated peptides will be isolated, purified and sequenced (peptide portion) after subjecting the purified mucins with different proteolytic enzymes. Antibodies will be developed in rabbits against the nonglycosylated peptides which, in turn, will be used to follow the synthesis and secretion of these macromolecules in a tracheal (or bronchial) culture system. Finally, the viscoelastic properties of purified mucins will be investigated.

Technical Approach: The following proposal will be undertaken in the Department of Clinical Investigation, WBAMC, regarding respiratory mucins:

(1) Collect sputum from patients (either male or female, any age) with asthma, chronic bronchitis and cystic fibrosis.

(2) Solubilize mucins with water and buffer.

(3) Establish the homogeneity of mucin glycoproteins isolated from sputum of patients with asthma, chronic bronchitis, and cystic fibrosis by molecular sieve and ion-exchange chromatography.

(4) Isolation and characterization of peptides (or glycopeptides) derived from digestion of mucins with different proteolytic enzymes (Column and HPLC);

(5) Amino acid sequence analysis of these peptides by sequenator and cDNA cloning procedure;

(6) Raise antibodies in rabbits against these peptides (preferably against nonglycosylated peptides); and finally,

(7) Establish a tracheal (or bronchial) culture system to examine the synthesis and control in secretion of these macromolecules by ELISA or radioimmunoassay (RIA) procedures using these antibodies.

In addition to the proposals cited above, the physical properties of mucins, particularly their interaction (in terms of viscosity) with other serum proteins (such as albumin, immunoglobulin, and fibronectin) will be studied.

Progress: Compositional analyses on the two deglycosylated peptides from human tracheobronchial mucin have been completed. antibodies have now been raised in rabbits (see protocol # 89/63) against these peptides. These antibodies will now be used to screen the human cDNA library for the purpose of sequencing these apoproteins. Also, these antibodies will be used to follow the production of mucin in different animal tracheal cell systems (protocol #89/16).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/14 STATUS: Completed

TITLE: Biochemical Properties of Colonic Mucin in Health and Disease

START DATE: Dec 87 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: PhD Sam Bhattacharyya

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. J.S. Ramirez, Ms. Brigitta Manna, Ms. Maxine Lund

KEY WORDS: Colonic Mucin, Human

Study Objective: This proposal is concerned with isolation, purification, and characterization of mucin glycoproteins from the human colon. The protein core of these mucins will be isolated by high pressure liquid chromatography after chemical deglycosylation procedure and amino acid sequence of these peptides will be determined either by sequanator or cDNA cloning procedure. Antibodies will be raised against these deglycosylated peptides which, in turn, will be used to follow the synthesis and secretion of these macromolecules in a colonic culture system.

Technical Approach:

1. Collect surgery specimens of colon from patients (either male or female of any age) with different bowel diseases with written permission from patients that these specimens will be used for research purposes only.
2. Solubilize mucins with water and buffer.
3. Establish purity of the preparation by molecular sieve and ion-exchange chromatography.
4. Deglycosylation of these mucins by chemical deglycosylation procedure (phenymethylsulfonyl fluoride method) and isolate the peptide(s) by high pressure liquid chromatography method.
5. Amino acid sequence analyses by sequanator and cDNA cloning procedure, and establish the homology of amino acid sequence of the colonic mucin peptides with those from respiratory sources.
6. Raise antibodies against these deglycosylated peptides and establish a clonic epithelium culture system to follow the synthesis of these macromolecules.

Progress: Human colonic mucin has been isolated from normal colonic mucosa by phenolwater extraction procedure and purified by Sepharose 2B column chromatography. The mucin was further purified by cesium bromide density gradient centrifugation. Sodium dodecyl sulfate-polyacrylamide gel (5%) electrophoresis of this material showed high molecular weight mucin component(s) at the top of the gel. chemical analyses of this preparation indicated a typical mucin profile of amino acids and carbohydrates. Ionexchange chromatography resulted in the separation of two major fractions, the one being more acidic than the other. Chemical deglycosylation of the purified preparation at 20°C for 3 1/2h showed loss of sialic acid, fucose, galactose, and N-acetylglucosamine, whereas traces of N-acetylgalactosamine were still detected. High pressure liquid chromatography of the deglycosylated material resulted in the purification of a major peptide, P_1, with high levels of threonine, serine, and proline, resembling, in most respects, the profile of native mucin. The molecular weight of the peptide was determined to be approximately 97 kDa and serine was the single NH_2-terminus. Further sequence analyses could not be done due to degradation of this protein by trifluoro acetic acid.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/16 STATUS: Ongoing

TITLE: Cellular Mechanism of Mucin Secretion: Studies Involving Rat and Rabbit Tracheal Culture System

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: PhD Sam Bhattacharyya

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: B. Manna, M. Lund, J.I. Enriquez

KEY WORDS: Mucin, animal

Study Objective: This proposal is concerned with the isolation and characterization of mucin glycoprotein components (mucin) from secretions of rat and rabbit tracheal epithelial cells in culture and establish their structural identity with those of the same components from human. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studies on the gene level.

Amendment August 1989: In addition to isolation of mucin proteins in the rat and rabbit models, it has become apparent that the isolation and characterization of mucin glycoprotein components from secretions of porcine (swine) tracheal epithelial cells in culture is also necessary. Once the mucin fraction is characterized at the structural level, it can be determined if it is comparable with the same components of human tracheal mucin. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studies on the gene level.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Rabbit tracheal epithelial cells have been successfully cultured in F-12 nutrient culture medium. At 7-8 day period, the cells were found to produce mucin as well as glycosaminoglycans. The secreted material was digested with hyluronidase and the mucin was separated by sepharose 2B column chromatography. The chemical composition of the purified mucin was similar to that of human. This culture system can be used now to study the regulation of mucin secretion on the gene level.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/63 STATUS: Ongoing

TITLE: Antibody Production Against Human Tracheal Mucin Apoportein in the Rabbit Model

START DATE: Jun 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: Ph.D. Sam Bhattacharyya

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce C. Veit, Ph.D.

KEY WORDS: Mucin, animal

Study Objective: To produce antibodies against human tracheal mucin apoproteins in the rabbit model and use these antibodies to study the control in mucin production on the gene level.

Technical Approach: The animals will be injected with a small volume of mucin protein emulsified in Complete Freund's Adjuvant. After 3-4 weeks the same rabbits will receive the mucin protein, except that it will be suspended in a normal saline carrier solution and injected subcutaneously. Three to five days following the second immunization, blood will be collected 2-3 times weekly from the ear veins of the rabbits while antibody titers are elevated or for a period not to exceed two consecutive weeks. Once blood collection has ceased, the rabbits will be rested a minimum of one month. If the hematocrit is normal at this time, they may be reimmunized with the mucin protein in a normal saline carrier solution, subcutaneously and the blood will be collected as stated below.

Mucin protein will be emulsified (water-in-oil) in Complete Freund's Adjuvant. Each of the three rabbits will be inoculated with a total volume of 0.25 mls divided among 4 intramuscular injection sites in the thigh muscles. No experimental manipulations will follow for at least 3-4 weeks. During this time the rabbits will continue to be housed and cared for as stated above. Following this period, the rabbits will be re-immunized with the mucin protein solubilized in normal saline 0.1 ml, subcutaneously. After 3-5 days, 10-20 mls of blood will be collected from each rabbit 2-3 times weekly during high antibody titers. They will not be bled for a period exceeding two consecutive weeks. A hematocrit will be measured prior to each blood collection to insure that excessive blood is not taken. Blood will not be collected if the hematocrit falls below 25 % unless the rabbit is to be euthanatized. Additional vitamin and mineral supplements will be administered during the blood collection period or as long as the hematocrit is below normal. Once blood collection has ceased, the rabbits will be rested a minimum of one month. If the hematocrit is normal at this time and additional antibody is required, they will be reimmunized with the mucin protein in a normal saline carrier solution, 0.1 ml subcutaneously and the blood will be collected on the same schedule as stated above. The procedure for collecting the blood specimens is as follows: the rabbits will be placed in a restraint cage for a few minutes during the procedure. The blood will be collected by placing a small needle in an ear vein and then allowing the blood to flow into a blood collection tube. If the rabbits become distressed or if adequate blood volumes can not be obtained without causing distress the rabbits will be anesthetized and euthanatized by exsanguination as stated in para 5. b.(1), above. Antibody will then be extracted from the blood.

Progress: The rabbits were injected with purified human mucin apoprotein. Two of the rabbits responded very well in producing antibody. We will now purify the antibody with non-exchange chromatography and use the antibody to screen human cDNA lung library for mucin gene.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #:** 82/60 **STATUS:** Ongoing

TITLE: Interactions Between Aminoglycoside Antibiotics and Vitamin B6 in Vitro and In Vivo

START DATE: Oct 82 **ESTIMATED COMPLETION DATE:** Jul 90

PRINCIPAL INVESTIGATOR: John Enriquez

DEPARTMENT: DCI **FACILITY:** William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: PFC Ismael Delgado

KEY WORDS: Pathology Aminoglycosides, Vitamin B6

Study Objective: To develop a method for isolating and quantitating aminoglycoside pyridoxal-5'-phosphate complexes. To isolate these complexes from the urine of patients receiving the aminoglycoside antibiotics. To determine if depletion of vitamin B6 occurs in patients receiving aminoglycoside antibiotics, and if so, how this depletion correlates with morbidity and mortality.

Technical Approach: Subjects will be patients who are to be given aminoglycoside antibiotics for clinical indications (sepsis, serious gram-negative infections, etc). These patients should also have SMAC 20 chemistry screens and monitoring of their aminoglycoside levels (procedures already routinely performed). The blood and urine samples from at least 30 patients will be examined.

Progress: In order to investigate the aminoglycoside - PLP complexation in vivo, we are now looking at PLP levels not only as free/unbound in plasma, but also looking at bound plasma PLP and total RBC PLP concentrations.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 85/52 STATUS: Ongoing

TITLE: Pyridoxine Effect in Aminophylline Toxicity in Rabbits

START DATE: Sep 85 ESTIMATED COMPLETION DATE: Jul 90

PRINCIPAL INVESTIGATOR: John Enriquez

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Raghave Charya, Ismael Delgado

KEY WORDS: Pyridoxine, Vitamin B6, Aminophylline toxicity

Study Objective: To determine the response of unsupplemented normal rabbits and B6 supplemented rabbits to theophylline administration.

Technical Approach: New Zealand rabbits were given single daily intraperitoneal injections of aminophylline in a dose of 17 mg/kg/day or increasing daily doses of theophylline for five days. Serum PLP levels were done every one to two days.

Progress: In the initial experiments, dramatic PLP concentration drops in rabbits treated with aminophylline was noted. At the time of these experiments, the investigators did not measure bound plasma PLP nor red blood cell PLP levels. The investigators would like to repeat two of the original experiments and look at free, bound and RBC PLP levels in order to try to develop a concentration equilibrium of PLP in the three states mentioned, as well as to correlate this with aminophylline levels and toxicity.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/28 STATUS: Ongoing

TITLE: Measurement of Plasma Pyridoxal 5'-Phosphate in Seriously Ill Patients and Effect of Supplementation of Pyridoxine HCL on Laboratory Tests (Monitor: COL Stephenson)

START DATE: Mar 86 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: John Enriquez

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Stephen Carey, MC., PFC Ismael Delgado

KEY WORDS: PLP

Study Objective: Gather evidence of vitamin B6 deficiency in hospitalized patients and determine if plasma pyridoxal 5' phosphate levels can be restored easily to normal. Determine effect of PLP level changes on other measured parameters.

Technical Approach: All surgical patients will have a plasma PLP, CBC and SMAC-20 drawn on admission or, in the case of elective surgeries, as part of the pre-admission lab work. Those patients found to have a plasma PLP of greater than 20 nM will not be entered into either the B6S or the NS group. If the initial or subsequent plasma PLP goes below 20 nM, the patient will be assigned the B6S or NS group on the basis of the last digit of their social security number. Me will be given 50 mg/day or 0 mg/day of PN:HCl if his plasma PLP is between 10 and 20nM, and 100 mg/day or 50 mg/day of PN:HCl if his plasma PLP is less than 10 nM. After one week of no supplementation (for those in the NS group) or one week of supplementation (for those in the B6S group), a repeat plasma PLP, CBC and SMAC-20 will be drawn. Whenever the plasma PLP exceeds 20 nM, supplementation with PN:HCl will stop and further plasma PLP levels will be drawn weekly and at pre-discharge.

Progress: Samples are still being received from the surgical ward and ICU. Samples are not delivered on a regular basis because of the unique qualifications the patients must meet in order for a blood sample to be valuable to the study. Data generated from this project has been invaluable in leading the investigators in the new direction of looking at only only unbound plasma PLP, but also bound plasma PLP and red blood cell PLP. This project has generated various publications and presentations.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/30 STATUS: Ongoing

TITLE: Vitamin B6 Status of Sergeant Major Candidates: Effect of Smoking on Vitamin B6 Levels and of Vitamin B6 Supplementation in Vitamin B6 Deficient Individuals

START DATE: Jul 86 ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: John Enriquez

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: John Enriquez, Ismael Delgado, Clent Aldridge, LTC Allister Morris, MC

KEY WORDS: Vitamin B6

Study Objective: To see if cigarette smokers are vitamin B6 deficient, and to determine if vitamin B6 supplementation of vitamin B6 deficient individuals alters serum chemistries (SMAC-20), CBC, and HDL cholesterol.

Technical Approach: Smoking-induced vitamin B6 deficiency may contribute to the altered biochemical measures. Increasing the plasma PLP of vitamin 86 deficient individuals may help to normalize these values. In particular, a relationship between plasma PLP levels and HDL cholesterol will be explored: this would have implications for the prevention and treatment of atherosclerosis. A performance measure effect of serum PLP will be explored. Subjects: All subjects will be Sergeant Major candidates, already enrolled in the Over 40-Sergeants Major Study (already scheduled to have blood drawn for a CBC, SMAC-20, and HDL cholesterol). Controls: These will be the nonsmokers and B6 deficient patients randomized to receive a placebo instead of vitamin B6. Design of the Experiment: (1) Initial Blood Draw - blood will be drawn for CBC, SMAC-20, HDL cholesterol, and plasma PLP. (2) Randomization and Supplementation Phase - subjects will be classified by smoking status, and assigned to vitamin B6 sufficient (B6+), intermediate vitamin B6 status (B6I), or vitamin B6 deficient (B6-) groups on the basis of the initial plasma PLP level (20 nM or greater, 10 to 20 nM, or less than 10 nM, respectively. The B6+ group will receive no PN:HCl supplementation; the B6- group will all receive 50 mg/day of PN:HCl; and the B6I group will be randomized to receive either 50 mg/day of PN:HCl or placebo. (3) Final Blood Draw - at the end of the Sergeants Major course, blood will be drawn for CBC, SMAC-20, HDL cholesterol, and plasma PLP.

Progress: 1200 samples have been received and approximately 750 have been processed. These samples should be finished by June 1990. At this time there are no plans to draw any more SGM classes. The data generated to date has resulted in various publications and presentations. The data has also attracted the interest of individuals who are working on redesigning the standard cardiac risk assessment techniques in use today.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 86/48** **STATUS: Completed**

TITLE: Alteration of Lymphomyelopoietic Cell Response and Treatment in Mice Following Burns and Radiation Trauma

START DATE: Jun 86 **ESTIMATED COMPLETION DATE: Nov 88**

PRINCIPAL INVESTIGATOR: MAJ Dennis A. Stewart

DEPARTMENT: DCI **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: G. David Ledney, PhD; Bruce Veit, PhD

KEY WORDS: Radiation trauma

Study Objective: The proposed study is designed to determine how the precursor stem cells are effected over a time course following injury, the initiating factors in the cellular response, and means of altering the response in vivo.

Technical Approach: Trauma Control - Previously established $LD_{50/30}$ survival curves for radiation exposure and combine radiation/burn will be verified in the B6D2 F_1 hybrid strain without administration of GM-CSF or other therapeutic agents except normal saline for burn trauma animals as described in the protocol. Recombinant muring GM-CSF will be tested in both normal and in animals subjected to trauma. In addition, CSF produced and purified utilizing high pressure liquid chromatography (HPLC) in our own laboratory will be tested in vivo in our trauma model (burn, physical skin injury, radiation, and combine radiation/burn).

Progress: Principal inves[illegible] PCS'd. Project was completed, however, no report is available.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/55 STATUS: Ongoing

TITLE: Development of a Hemophilus Influenza Anti-Idiotype Vaccine (In the Mice and Rabbit Models)

START DATE: May 87 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: PhD Bruce C. Veit

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ George McNamee, DVM; Becky Smiley, Susan McIntyre, Cambyses Darvish

KEY WORDS: Hemophilus influenzae, vaccine

Study Objective: Prepare an immunogenic vaccine that will establish effective immunity to Hemophilus influenzae in children under two years of age. Since the polysaccharide antigen (Hib) itself is only weakly immunogenic at best, we will attempt to develop an internal image anti-idiotype vaccine which, by virtue or its protein structure, should be highly immunogenic in this patient population. Although our ultimate goal is to develop such a vaccine for human use, our initial efforts will be focused on an animal model which will be used to establish the merit of this approach.

Technical Approach: Balb/c mice and New Zealand white rabbits will be immunized with Hemophilus influenzae type B polysaccharide (PRP). Since polysaccharides are poorly immunogenic in general, a protein conjugated form of PRP, namely polysaccharide-diphtheria toxoid, will be used in order to overcome this potential pitfall. At the time of peak, antibody synthesis, rabbits will be bled via the marginal ear vein or central artery in the ear and the anti-PRP antibodies will be affinity purified on PRP-Sepharose 4B columns. Spleens from immunized mice will be single-cell suspended and fused with the MAT-sensitive myeloma cells, SP2/0. Hybridomas secreting anti-PRP antibodies will be identified using ELIZA screening techniques.

Affinity-purified rabbit anti-PRP antibodies as well as mouse monoclonal antibodies will be used to immunize Balb/c for the production of monoclonal anti-idiotypic antibodies. Appropriate hybridomas secreting the desired antibodies will be selected by ELIZA screening. Those which bind to anti-PRP but not to pooled mouse immunoglobulins or to PRP antigen, will be further characterized for their ability to elicit an antibody response to PRP in rats (heterologous species with respect to the origin of the antibodies to be used).

Upon confirmation that the anti-idiotypic antibodies elicit a specific response to PRP, infant rats (1 to 2 weeks post-partum) will be immunized with the anti-idiotype vaccine and then challenged with virulent Hemophilus influenzae intranasally. Infected animals will be housed in isolation quarters so that other animals will not become infected.

Having established the efficacy of the anti-idiotype vaccine in protecting against infection, we will then submit an additional protocol which will describe the methodologies for generating hybrid molecules of the anti-idiotype antibodies so that the "V" regions are mouse and the "C" regions are human.

In initial studies that will focus on the immunogenic aspects of the anti-idiotype vaccine (immunization of rats), we will be able to ascertain whether heterologous proteins (mouse immunoglobulins into rat) will induce anti-mouse Ig and/or immune complexes. Then the hybrid immunoglobulins will be tested by comparison for elimination of any anti-mouse Ig response that may occur.

Progress: The principal investigator has been unsuccessful at obtaining monoclonal anti-rabbit anti-Hib (anti-idiotype). They will now attempt to purify human anti-Hib and immunize mice with the hope of producing monoclonal anti-human anti-Hib (anti-idiotype)

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/04 STATUS: Ongoing

TITLE: Activation of T-Cell Subsets in Bermuda Grass Allergy Patients

START DATE: Nov 87 ESTIMATED COMPLETION DATE: Nov 89

PRINCIPAL INVESTIGATOR: PhD Bruce C. Veit

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Stanislaus Ting, M.D.; LTC R.V. Charya, MC; Beck Smiley, B.S.; Susan McIntyre

KEY WORDS: Bermuda grass allergy, T-cell subsets, IL-2R, VLA, 2-color flow cytometry

Study Objective: To determine whether there are detectable changes in numbers and functions of manifestations of Bermuda grass allergy. Since T4+ cells are associated with helper/inducer functions and T8+ cells are associated with cytotoxic/suppressor functions, alterations in the numbers of T4+ or T8+ activated T cells may correlate with changes in the immunoregulatory processes involved in controlling the allergic state. Peripheral blood samples will be obtained from patients during active allergy, immunotherapy, and disease quiescence. Samples will be analyzed by 2-color flow cytometry and by immunohistochemical staining for the distribution of T4+ and T8+ cells and the percentage of activation antigen-positive cells within each of these subsets. T cell subsets will also be analyzed for their ability to increase or suppress the synthesis and/or secretion of IgE. Serum samples from these patients will be analyzed for the presence of soluble IL-2R (circulating IL-2 receptor). These studies should improve our understanding of the immunoregulatory processes involved in the control of IgE-mediated allergic responses.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Further analyses of peripheral blood lymphocytes (PBL) from Bermuda grass allergy (BGA) patients, long-term immunotherapy patients (those receiving BGA therapy) and normal individuals (those without clinical symptoms of allergy) were done by two-color immunofluorescence flow cytometry and tritiated thymidine incorporation following antigen stimulation. In an attempt to determine whether suppressor cells develop during immunotherapy treatment or whether allergy patients have the capacity to generate suppressor cells, peripheral blood lymphocytes were incubated for 2 days in the presence or absence of antigen and then treated with mitomycin C to eliminate any proliferating cells which might interfere with the subsequent assay. The putative suppressor cell population was mixed with a responsive population of cells from the same patient together with antigen (Bermuda grass extract) and co-cultured for 6 days and then pulsed for 24 hours with tritiated thymidine. Addition of mitomycin C treated cells resulted in a significant increase in the level of cell activation occurring in response to antigen stimulation suggesting that responsiveness was augmented rather than suppressed. The same finding was observed in allergy and immunotherapy patients as well as some normal individuals. These unexpected results remain unexplainable, however, experiments are now in progress to determine whether the subsets of cells which become activated to antigen are the same or are different in allergy, immunotherapy and normal individuals. IL-2 expression appeared to correlate with the increases in cell activation detected by thymidine incorporation and, as mentioned above with regard to determining which subsets of cells are responding in the three study groups, IL-2 expression is being analyzed for variability among these groups.

It appears that there is not 100% correlation of skin reactivity and responsiveness to antigen in lymphocyte transformation assays in vitro since several "normal individuals" were found to be skin test-negative and without clinical symptoms and yet were significantly reactive in lymphocyte transformation assays when their peripheral blood lymphocytes were stimulated in vitro with Bermuda antigen. Since specific IgE (anti-Bermuda IgE) is well recognized as a strong correlate of allergy and correlates well with skin test

reactivity, we are in the process of testing IgE and IgG antibodies to Bermuda to determine whether appearance of specific anti-Bermuda antibodies correlates with the augmentation effect of mitomycin-C treated cells in lymphocyte transformation responses.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 83/37 STATUS: Ongoing

TITLE: Cardiopulmonary Effects of Stressful Exercise at 4,000 Feet on SCT Individuals

START DATE: Jul 84 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sickle Cell Trait, Stress

Study Objective: To establish baseline pulmonary function data (spirometry, helium dilution lung volumes, maximum voluntary ventilation L/min (MVV), arterial blood gas analyses (ABG), single breath diffusing capacity DLCOSB (ml/min/mmHg) and steady state diffusing capacity DLCOSS (ml/min/mmMg) (Filley technique) as well as values for the partial pressure of oxygen at 50 saturation (mmHg) (P50) in HgbAS individuals and controls and to determine percent HgbS and percent HgbF in individuals heterozygous for sickle cell trait (HbgAS) at 4000 ft.

To carefully document cardiopulmonary response of individuals identified as having hemoglobin AS during both strenuous incremental and submaximal steady-state exercise at altitude with age, race, sex, smoking, matched non-HgbAS controls.

To correlate observed abnormalities (if any) in parameters of cardiopulmonary performance with levels of HgbS in individuals with sickle cell trait (i.e. are patients with 40 percent of HgbS more likely than controls to experience abnormalities during vigorous exercise. Also, to determine whether HgbF levels may be protective as they are in patients with sickle cell disease.

To determine whether conditioning (repeat studies after six weeks) is operative in modulating cardiopulmonary performance in both SCT individuals and controls.

Conclusive data is not anticipated from this protocol, but a preliminary statement or suggestion may be offered on the important question of occupational restriction of subjects with HgbAS. This is in keeping with the National Academy of Science - National Research Council Fs Report of 1973.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: 25 SCT individuals and 16 controls have been tested. No adverse effects have been noted. The hematologic and biochemical data from this study are bein g prepred for manuscript presentation.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/25 STATUS: Ongoing

TITLE: Axillary Venous Sickling in Individuals with Sickle Cell Trait During Upper Extremity Exercise in a Hypoxic Environment (Monitor: Dr. Ortiz)

START DATE: Mar 87 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Jorge Zeballos

KEY WORDS: Sickling, Armcrank Exercise

Study Objective: To determine the relationship between cardiopulmonary performance, blood gas and the degree of sickling in individuals with sickle cell trait during progressive armcrank exercise. To characterize the cardiopulmonary performance of individuals with sickle cell trait during progressive upper extremity exercise. To determine the effects of armcrank exercise on blood gases in individuals with sickle cell trait. To study the effects of environmental hypoxia on upper extremity exercise performance and venous blood gases at 1270 meters and during exposure to inspiratory hypoxia equivalent to 4000 meters on upper extremity exercise performance, venous blood gases and percent sickling.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: At 1,270 meters, axillary venous sickling increased significantly ($p < 0.05$) from (mean $\pm$ SD) 1.0 $\pm$ 1.0% at rest to 2.3 $\pm$ 2.6% during peak exercise. At simulated 4,000 meters, sickling increased significantly ($p < 0.001$) from 1.5 $\pm$ 1.2% to 8.5 $\pm$ 7.1%. A wide range of sickling during peak exercise was observed 1% to 25%). One minute after exercise at simulated 4,000 meters, venous sickling remained elevated (7.2 $\pm$ 7.8%) despite high levels of oxygen saturation. Arterial sickling (less than 1%) was present in only two subjects. There was no significant difference in oxygen consumption (29.4 $\pm$ 3 versus 30.7 $\pm$ 4 mL/kg/minute) between the subjects with SCT and the controls, nor was there a correlation between exercise performance and sickling ($r < 0.2$).

It was concluded that exercise at 1,270 meters slightly, albeit significantly, increased sickling in blood from an exercising limb and that simulated 4,000 meters dramatically potentiated this effect. Sickling in the effluent blood of an exercising limb does not appear to measurable affect overall maximal arm crank exercise performance.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/05 STATUS: Ongoing

TITLE: IND Janssen Pharmaceutica # R51,211 Treatment of Systemic Mycoses with Itraconazole (Monitor: MAJ Ortiz)

START DATE: Oct 87 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Itraconazole, Systemic mycoses

Study Objective: To assess the efficacy of Itraconazole therapy in fungal dissemination disease.

Technical Approach: The details are lengthy and specified in the Pharmaceutical Companies' protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This ongoing protocol is part of a multi-center evaluation of Itraconazole for the treatment of systemic mycoses. All patients todate have had disseminated cocci. all have had favorable responses to Itraconazole and appear to be stable.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/38 STATUS: Ongoing

TITLE: Comparison of Physiologic Responses to Prolonged Exercise Simulating Army Field Training in Sickle Cell Trait and Controls (Phase IVa) (Monitor: MAJ Ortiz)

START DATE: Jul 89 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R.J. Zeballos, M.D.; COL John Little, ADA; T.W. Martin, CPT, MC

KEY WORDS: Sickle Cell Trait, Endurance exercise

Study Objective:

1. To determine if submaximal (50-70% VO_2 max) prolonged treadmill exercise (1 hour 30 minutes) with a final maximum exercise (5 minutes), similar to Army field training conditions, would elicit differences in exercise performance between Sickle Cell Trait (SCT) and control volunteers.

2. To evaluate changes in Percent Sickling (%S) and blood viscosity with prolonged exercise in SCT volunteers and to analyze their relationship to venous oxygen saturation, hydration status and temperature.

3. To assess biochemical and enzymatic changes in blood and urine that would suggest muscle damage (rhabdomyolysis) during prolonged exercise.

4. To compare the effect of prolonged exercise on renal function in SCT and controls.

5. To determine whether subtle pulmonary microcirculatory abnormalities not present at rest would be detected during exercise in SCT compared to controls.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This protocol has only four people entered into it. The main testing will occur in May-Sep. It represents the major focus for the Joint Navy-Army Human Performance/SCT Research Lab.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/41 STATUS: Ongoing

TITLE: Itraconazole Drug Trial, Compassionate Clearance for One Person

START DATE: Apr 89 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Dissem. cocci, Itraconazole

Study Objective:

(1) To assess the efficacy of Itraconazole therapy in fungal dissemination disease.

(2) The study is a non-blinded, non-crossover study to assess drug efficacy.

(3) Medication used will be Itraconazole.

(4) Population studied will be those with disseminated fungal disease who have failed on standard drug therapy.

Technical Approach: The details are lengthy and specified in the protocol. duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Itraconazole has proven to be a life saving medication for this individual. He is a 10 gm amphoteria failure who nearly died in 1984. He is stable, although not cured. He will most probably be on medication for the rest of his life.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/68 STATUS: Ongoing

TITLE: In Vivo Sickling in Sickle Cell Trait (HbAs): Effect of Hypoxia, Exercise and Red Cell Sampling/Fixation Time

START DATE: Jul 89 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R. Jorge Zeballos, M.D.

KEY WORDS: Sickle Cell Trait

Study Objective: Recent discoveries in Hemoglobin S (HbS) polymerization kinetics make it imperative to re-examine the sickling phenomenon in vivo in order:

1. To corroborate, by using a new, specially designed blood drawing technique, that in vivo sickling is present in the blood of individuals with Sickle Cell Trait.

2. To determine the effect of hypoxia on the magnitude of sickling.

3. To compare the combined effect of hypoxia and exercise on sickling measured in effluent blood from an exercising limb and in arterial blood that has recirculated through the lungs during leg exercise.

4. To determine the effect of red cell sampling/fixation time on the measurement of percent sickling.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Eight individuals have participated in this protocol without any untoward effects. Important information is coming from this study, including the presence of in vivo sickling measured within 2 seconds of sampling.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/62 STATUS: Ongoing

TITLE: Armcrank and Cycle Exercise in the Evaluation of Dyspnea (Monitor: Dr. Wallingford)

START DATE: Jul 88 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: Dr. Jorge Zeballos

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Idelle M. Weisman, MC

KEY WORDS: Armcrank, cycle exercise

Study Objective: Compare the cardiopulmonary response to armcrank and cycle exercise in subjects with dyspnea on exertion.

Technical Approach: We will use 20 male or female patients, 18-65 years old, referred to the pulmonary department for evaluation of dyspnea on exertion. These patients routinely undergo cycle exercise testing with an arterial line in place. Subjects will be excluded if they have orthopaedic, neurologic, or vascular abnormalities which limit arm or leg exercise.

Subjects will perform both upper and lower extremity exercise on an electronically braked cycle ergometer. For the upper extremity test, the cycle will be placed on a table so that the crank shaft will be level with the seated patient's shoulders. The order of the tests will vary so that a similar number of subjects begin with either arm or leg exercise. Beginning with no added resistance or 0 watts, the work rate will increase 10-20 W/min until the subject is unable to maintain a 60 rpm crank rate. the test will also be discontinued if the subject has ventricular tachycardia, more than a 20 mm drop in systolic blood pressure, or > 3 mm ST depression.

While exercising, the subjects will breathe through a two-way valve. We will measure respiratory gases at the mouthpiece using a mass spectrometer (Perkin Elmer). Ventilation will be measured with a pneumotachometer (Hans Rudolph). An on-line computer (MGC 2001) will perform breath-by-breath calculation of 0_2 uptake (VO_2)m CO_2 production (VCO_2), minute ventilation (VE), and other measurements. We will monitor heart rhythm on an oscilloscope and measure heart rate from a rhythm strip obtained during the last five seconds of each minute.

One hour before the first exercise test, a 20 gauge catheter will be inserted in the patient's radial artery. A 25cm tube with a three-way stopcock will be attached to the catheter to permit anaerobic sampling while the subject exercises. Patency of the catheter and connecting tube will be maintained with a heparin solution (10 USP unit/ml).

We will draw blood samples with the subject at rest and every 2-4 minutes during exercise. We will measure PO_2, PCO_2, and pH with an automated blood gas analyzer (IL System 1303). Hemoglobin saturation and concentration will be measured with a spectrophotometric oximeter (IL 282 CO-Oximeter). The dead space-tidal volume ration and the alveolar-arterial oxygen difference will be calculated using standard equations.

Progress: Eleven additional patients will need to be added to the protocol before any meaningful statements can be made. No untoward events occurred in these four patients.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/48 STATUS: Ongoing

TITLE: Practical Value of Hyper-Reactive Airway Testing in the Assessment of Asthma in Army Recruits (Monitor: COL Ortiz)

START DATE: Aug 89 ESTIMATED COMPLETION DATE: 1993

PRINCIPAL INVESTIGATOR: M.D. R. Jorge Zeballos

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Idelle M. Weisman, MC

KEY WORDS: Asthma, EIB Army Recruits

Study Objective:

1. To determine whether a screening test for hyperreactive airways "asthma" should be established for individuals who, although having met entry requirements as specified in AR40-501-2-24d have allergic histories and/or a history of asthma in childhood (HAC), which would appear to increase their likelihood of exercise induced asthma and other asthma related problems during basic training.

2. To determine which of the currently available methodologies, for the diagnostic evaluation of hyperreactive airways, would be most accurate (high sensitivity, high specificity), practical, and cost effective for the screening of potential Army recruits.

3. To modify standard methods for the diagnosis of airway hyperresponsiveness so as to make them more suitable to the Military Entrance Processing Service (MEPS).

4. To propose modification for AR40-501-2-24d based on the results of this study and thereby reduce the number of Existing Prior to Service (EPTS) discharges secondary to asthma.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This protocol has just been initiated. Important information for the Army will result from this protocol, especially in the area of EPTS Army discharge.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/75 STATUS: Ongoing

TITLE: Comparison of Cranial and Iliac Autologous Bone Grafts and their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Minniature Swine

START DATE: 2 Feb 90 ESTIMATED COMPLETION DATE: Jan 91

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: Dentac FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Michael G. Donovan, DE; Jan Faulk, MAJ, DE

KEY WORDS: Cranial bone graft, Iliac bone graft

Study Objective:

PHASE I: Design surgical techniques for harvesting bilateral iliac corticocancellous bone grafts, and cranial bone and cranial-facial flap techniques.

(1) Study will provide knowledge for surgical techniques that will minimize morbidity (pain, muscular dysfunction, nerve damage) in swine for future studies.

(2) Phase I study will be performed on one (1) domestic swine prior to bone graft studies (Phase II and Phase III) on more expensive miniature swine.

PHASE II: Compare traditional reconstruction techniques, autologous iliac bone grafts, with autologous cranial bone grafts in maxillofacial reconstruction. Will verify if cranial bone is superior to iliac bone in maxillofacial reconstruction. Facial onlay bone grafts and continuity defect repairs are to be compared.

(1) Will compare rate of revascularization and magnitude of resorption at different time intervals for cranial and iliac bone grafts.

(2) Will evaluate need for donor bone graft to duplicate recipient site.

PHASE III: Will determine degree of osseointegration of pure titanium bone implants in cranial and iliac bone grafts in:

(1) Intraoral continuity defects

(2) Extraoral continuity defects

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Phase I, Test of Proposed Surgical Techniques on a Domestic Swine to Ensure Minimal Morbidity and Review of the Swine's Pelvic and Skull anatomy, was completed in December 1989. Objectives were met satisfactorily as the swine suffered no difficulty with ambulation from the dissection to harvest iliac bone, and the flap design gave good access to the surgical site. There was no noted disability from the cranial bone graft harvest, bicoronal flap, facial flaps or placement of bone grafts to nasal bones. There was sufficient bone from the ilium and frontal bones for bone grafting as proposed in the protocol for phases II and III. during necroscopy, dissection of mandibular dental alveolar ridge and infraorbital rim showed adequate width for bone grafts and osseointegrated implants of phases II and III.

Phase II, Cranial Bone Grafts and Iliac Bone Grafts to Facial Bones in Miniature Swine, as outlined in the protocol, is scheduled to begin 2 Feb 90.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/37 STATUS: Ongoing

TITLE: Bone-Anchored Craniofacial Prostheses Investigation

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: LTC Michael G. Donovan

DEPARTMENT: Dentac FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: John Gary, COL, MC

KEY WORDS: Craniofacial prostheses, Bone-anchored prostheses

Study Objective:

1. To evaluate the long term retention success rate for titanium implants anchoring craniofacial prostheses.

2. To evaluate the long term stability of the prostheses.

Technical Approach: Patients will be admitted to Ward 6W, and have the routine pre-surgery laboratory studies, to include blood work, x-rays and urinalysis, and any further tests required that would be dictated by their medical history. Appropriate referrals will be given to various medical specialties if indicated. The surgery to implant the prosthesis will be conducted in the operating room. Anesthetic will be given to minimize the pain that is associated with any surgical procedure. The doctor will cut the skin covering the area to be treated and then drill holes in the bones of the face, head, or both. Next, tiny titanium fixtures will be inserted into the holes, the skin will be replaced so that it covers the fixtures, and the skin stitched. The titanium fixtures will be left in place for 3-4 months to allow them to become integrated with the bone. During this time the patient will visit the doctor 2-3 more times so their condition can be monitored.

After 3-4 months, the patient will once again be admitted to the hospital, where they will undergo additional surgery. After the anesthetic is administered, the doctor will again cut the skin covering the area being treated. Some of the tissue under the skin will be removed and the skin will be stitched back together. The doctor will then puncture the skin directly over each implanted titanium fixture and will attach a small skin-penetrating abutment to each fixture. For 3-4 weeks, the treated area will be allowed to heal. During that time the patient will visit their physician 1-3 times so that their condition can be monitored.

After 3-4 weeks, a prosthesis will be made and will be attached to the anchors. After the prosthesis is in place, the patient will continue to visit their physician 3 times during the first year, then twice a year, so that their condition can be monitored, as well as their level of satisfaction.

Progress: Three patients have had a total of 10 implants placed. The integration phase takes six months. We are now awaiting the time when the implants can be uncovered to use. The patients that have had the implants placed will eventually require one ear prosthesis, one nasal prosthesis and one orbital prosthesis. The implants were placed without complications and all three patients are doing well.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/75 STATUS: Ongoing

TITLE: Comparison of Cranial and Iliac Autologous Bone Grafts and their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Minniature Swine

START DATE: 2 Feb 90 ESTIMATED COMPLETION DATE: Jan 91

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PRINCIPAL INVESTIGATOR: LTC Michael G. Donovan

DEPARTMENT: Dentac FACILITY: William Beaumont Army Medical Center

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Progress: Three patients have had a total of 10 implants placed. The integration phase takes six months. We are now awaiting the time when the implants can be uncovered to use. The patients that have had the implants placed will eventually require one ear prosthesis, one nasal prosthesis and one orbital prosthesis. The implants were placed without complications and all three patients are doing well.

DETAIL SUMMARY SHEET

DATE: 1 Octo' er 89 PROTOCOL #: 89/81 STATUS: Ongoing

TITLE: A Study to Assess the Training Needs of the Medical Staff for Transition to Diagnosis Related Groups

START DATE: Oct 89 ESTIMATED COMPLETION DATE: May 90

PRINCIPAL INVESTIGATOR: MAJ Henry Hernandez

DEPARTMENT: HQ FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: DRG's, Training

Study Objective: To assess the training needs of William Beaumont Army Medical Center's medical staff for transition to Diagnosis Related Groups (DRG's) and to determine a training program.

Technical Approach: Fifty physicians comprising the Department of Medicine and the Department of Surgery will be randomly selected and asked to respond to a questionnaire. The purpose of the questionnaire will be to assess the physician's current DRG knowledge level, as a method to determine transitional training requirements. The questionnaire will be a true/false type. Before the questioning begins, the respondents will be given directions and informed that their confidentiality and anonymity will be protected.

Descriptive statistics (item analysis) will be analyzed, and the alpha probability level will be established at .05 to evaluate the results of the study. A correlation matrix of all variables will be obtained. The r values for each variable will be compared to the Y sum to test for whole-part validity. Next, Randomized Blocks ANOVA will be evaluated, comparing individual test score against the domain Y (DRG knowledge). Each score will also be evaluated against each construct (general knowledge, impact issues, documentation issues, case-mix index issues, cost containment issues, and additional demographic data).

The discussion will include a detailed explanation of the observed and statistical analysis. It is expected that military physicians will not score highly on the questionnaire because as a group they have not been exposed to working conditions under a prospective payment system. Appropriate descriptive statistics which represents demographic and summary data, will be displayed graphically. A recommendation for the most practical, simple and cost effective method for training for transition to DRG's will be made.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/49 STATUS: Ongoing

TITLE: The Natural History of HTLV-III Infection and Disease in a US Military Population

START DATE: May 86 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Charles E. Davis, Jr., MAJ Eugene Etzkorn

KEY WORDS: HIV Natural History

Study Objective: Study the epidemiology of HTLV-III infection in active duty and retired military personnel and their dependents.

Technical Approach: Standard evaluation will be routine medical evaluation, immunological evaluation, laboratory tests, tests for opportunistic infections, HTLV-III viral cultures on body fluids and organs whenever possible. Completion of HTLV-III clinical evaluation form. HTLV-III tests. Counselling, education, and referral of contacts. Follow-up of individuals in the study. Data analysis: disease progression will be studied, as defined by Walter Reed Staging Classification. The effect of variables, including but not limited to age, sex, ethnic background, risk factors, length of infection, and simultaneous viral infections, will be studied.

Progress: A total of 108 health care beneficiaries at WBAMC have been entered in this natural history study; 26 in the past year. There have been seven deaths. A total of 66 individuals have been lost to WBAMC followup either due to transfer to other posts, retirement or discharge from the Army and relocation (or in the case of a LaTuna person returned to local care and died). Eleven of the regularly followed 40-50 patients at WBAMC have shown a progression in WR Stage over the past year.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/06 STATUS: Ongoing

TITLE: A Prospective Double-Blind Study of Retrovir in the Treatment of Patients with Early HIV-Associated Immunodeficiency

START DATE: Dec 88 ESTIMATED COMPLETION DATE: Feb 91

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Shannon M. Harrison, Chief, Inf Dis Svc, FAMC

KEY WORDS: Zidovudine in Early HIV

Study Objective:

1. To evaluate the safety and tolerance of chronic administration of RETROVIR (zidovudine) to adult patients with early manifestation of ARC, including those presenting with only HIV-associated lymphadenopathy and a CD4 cell count < 500 cells/mm3.

2. To assess the efficacy of RETROVIR therapy in the treatment of HIV disease in these patients. Therapeutic efficacy will be determined by monitoring the following variables.

a. Changes in the incidence of progression of HIV disease to more advanced disease stages.

b. Changes in clinical manifestation of HIV disease as reflected in objective signs such as weight change, lymphadenopathy, Karnofsky score and performance on tests of neurologic function.

c. Prevention of the progressive deterioration of the immune response associated with HIV disease as reflected in changes in CD'4 cell number and skin test reactivity.

d. Changes in levels of HIV viremia/antigenemia in virus-positive patients.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: AT WBAMC, 10 patients entered, 1 withdrew. In early August this study's placebo arm was dropped and all individuals are now on Zidovudine, 200mg Q.6.h. and their parameters continue to be monitored.

The one patient who withdrew did so because his CD4 were < 200 and he was eligible for open-label Zidovudine. Emotionally he was having difficulty participating in a placebo controlled study and his varecella zoster, severe staph folliculitis was recurrent. He also had illusions of recurrent PLP, not found on clinical evaluation.

Five patients manifested megaloblastic RBC indices; one patient manifested nail bed discoloration; one patient manifested severe headache requiring short hospital admission; one patient manifested severe, transfusion dependent anemia. This occurred when Zidovudine was commenced after a bacteremic event of shegellosis. The Zidovudine was terminated for a month, then rechallenged and since then he has tolerated Zidovudine with normal hematocrit. It is felt he may have had RE block post his acute illness and Zidovudine treatment started too early.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 89/21** **STATUS: Terminated**

TITLE: Emergency Use of Itraconazole for Treatment of Pulmonary Coccidiomycosis

START DATE: Jan 89 **ESTIMATED COMPLETION DATE: -**

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS:

KEY WORDS: Itraconazole, Pulmonary cocci

Study Objective:

(1) To assess the efficacy of Itraconazole therapy in fungal disease.
(2) The study is a non-blinded, non-crossover study to assess drug efficacy.
(3) Medication used will be Itraconazole.
(4) Population studied will be those with fungal disease who have failed on standard drug therapy.

TECHNICAL APPROACH: **The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.**

PROGRESS: **This protocol is continued by protocol #89/66, "Use of Itraconazole for Treatment of Pulmonary Cocci". Patient, PGF, suffered no adverse reactions of itraconazole for her pulmonary cocci. After five months of continuous therapy her sputum cultures became sterile on therapy and her chest X-ray shows improvement; her symptoms of fever, hemoptysis, anorexia, and malaise have abated. Her cocci serologies, maximum at 1:256, have dropped on therapy to 1:32 consistent with her clinical improvement.**

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/22 STATUS: Ongoing

TITLE: Prospective Evaluation of Health Care Workers Exposed to the Blood of Human Immunodeficiency Virus (HIV)

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn McNicol, R.N.

KEY WORDS: HIV exposure in health care workers

Study Objective: The objectives of this prospective surveillance project are:

1) To estimate the risk of HIV infection in health care workers (HCWs) exposed via the parenteral or mucous membrane route to HIV infected blood, according to type of exposure.

2) Describe infection control precautions taken or not-taken to evaluate extent of preventable exposures.

3) To describe the clinical natural history and development of laboratory markers of HIV infection in health care workers enrolled in this project who seroconvert to HIV.

Technical Approach: The number of exposed health care workers is expected to be less than 30/year, but is dependent on the number of HIV infected individuals cared for at WBAMC, a population which is increasing in size.

Upon entry into the surveillance project, each exposed HCW will be interviewed and a questionnaire completed collecting the following data: demographic information, use of immunosuppressive drugs, circumstances of the blood exposure, type of infection control precautions used at the time of exposure, any past exposure prophylaxis and information on the source patient. The exposed HCW will be asked to complete a questionnaire concerning risk factors for HIV infection. This confidential report will be completed by the exposed HCW and mailed directly to CDC by the worker. Information collected on this form (CDC 57.42A) will not be released to personnel at WBAMC.

The exposed HCW will be prospectively followed by the investigators for one year with follow up data and specimen collection at 6 weeks, 3 months, 6 months, and one year post exposure. At each followup a questionnaire and 10 ml. serum will be sent to CDC. In addition to scheduled follow-ups the exposed HCW must report to the investigator any illness of at least one week duration which occurs in the 12 week period after exposure. If the symptoms are suggestive of an acute retroviral syndrome, the investigator will obtain whole blood for virus isolation + T cell subset (10 ml) and serum (10 ml) for antibody/antigen testing.

Baseline serum samples will be tested for HIV antibody, if negative, HIV antigen will also be evaluated. If a HCW seroconverts a 10 ml heparinized whole blood sample will be requested from the source patient with their informed consent. Viral isolates from the source patient and HCW will be compared using molecular techniques.

Exposed health care workers will be followed for one year post-exposure.

Progress: Two health care workers with HIV infected blood exposure have been enrolled in this CDC supervised study. No seroconversions noted to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/40 STATUS: Ongoing

TITLE: The Effect of Megestrol Acetate on the Cachexia of Human Immunodeficiency Virus Infection: A Randomized, Placebo-Controlled, Double-Blinded Study. (Monitor: Dr. Lundy)

START DATE: Aug 89 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Daniel Loube, MC; Ms. Lynn B. McNicol, RN; 1LT Melanie Freel, RD; Ms Janet Chilton, RD

KEY WORDS: Megace in HIV cachexia

Study Objective: Assess the efficacy of megestrol acetate in the treatment of the anorexia and weight loss associated with HIV infection. Conduct a longitudinal analysis of nutritional, biochemical, anthropomorphic and psychosocial parameters in HIV patients receiving megestrol acetate.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This protocol has enrolled one patient who is just completing an extensive entry evaluation and will start the protocol agent later this week.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 89/52** **STATUS: Terminated**

TITLE: A Treatment Protocol for the Use of Intravenous Ganciclovir in Aids Patients with Immediately Sight-Threatening CMV Retinitis (Emergency Use)

START DATE: May 89 **ESTIMATED COMPLETION DATE:**

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS:

KEY WORDS: Ganciclovir, CMV retinitis, HIV

Study Objective: To determine the safety and efficacy of intravenous ganciclovir induction and maintenance therapy in AIDS patients with sight-threatening CMV retinitis at standard doses of 10 mg/kg/day and 35 mg/kg/week, respectively. The primary endpoints will be (1) response to therapy after an initial course of ganciclovir induction therapy as determined by ophthalmologic examination and retinal mapping; and (2) response to and tolerance of maintenance therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Ganciclovir was approved by the FDA for use in AIDS patients with CMV retinitis. Protocol was terminated due to this drug no longer being considered an investigational agent. All data collected thus far will remain available for a minimum of 5 years.

Institution of ganciclovir therapy in patient on 22 May 1989 quieted the rapidly progressive CMV retinitis (bilateral). Patient has remained on maintenance therapy until this week when evidence of progressive infection was noted by ophthalmologist. He is now receiving a reinduction with full dose ganciclovir. His visual acuity remains 20/30 in both eyes, although visual field analysis documents multiple defects. I feel the institution of ganciclovir clearly preserved this patient's sight. His bone marrow suppression has been tolerable and has not required cessation of ganciclovir. He has required no more frequent transfusions than his usual 6 weeks.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/66 STATUS: Ongoing

TITLE: Use of Itraconazole for Treatment of Pulmonary Coccidiomycosis

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Itraconazole, Pulmonary Cocci

Study Objectives: To assess the efficacy of Itraconazole therapy in fungal disease. The study is a non-blinded, non-crossover study to assess drug efficacy. Medication used will be Itraconazole. Population studies will be those with fungal disease who have failed on standard drug therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This protocol is the continuaiton of WBAMC protocol 89/21, "Emergency Use of Itraconazole for Treatment of Pulnonary Cocci". The clinical response of the single patient enrolled is detailed in the "Progress" of protocol 89/21.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #:** 89/67 **STATUS:** Ongoing

TITLE: Investigational Prophylactic Use of Zidovudine in Health Care Workers Sustaining a Deep Percutaneous Occupational Exposure to Human Immunodeficiency Virus

START DATE: Jul 89 **ESTIMATED COMPLETION DATE:** Indefinite

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med **FACILITY:** William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn B. McNicol, RN

KEY WORDS: Retrovir prophylaxis for HIV needlesticks

Study Objective: To offer a defined course of zidovudine to HIV negative health care workers within 5 days of a significant exposure to HIV. To assess the safety and tolerance of 200mg zidovudine given orally every 6 hours for 42 days in otherwise healthy persons.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 87/85** **STATUS: Terminated**

TITLE: Evaluation of the Effectiveness of Reglan in Involuntary Movement Disorders (Monitor: COL Cuetter)

START DATE: Sep 87 **ESTIMATED COMPLETION DATE: Sep 89**

PRINCIPAL INVESTIGATOR: MAJ David Bartoszek

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: COL Jabbar, WRAMC Neurology Svc

KEY WORDS: Movement disorders, Metoclopramide, Torrette syndrome

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Study Objective: **To determine whether Metoclopramide at 120-240 mg/day in adults and up to 2 mg/kg/day in children can eliminate or significantly reduce the involuntary movements.**

Technical Approach: **Patients with involuntary movement disorders will be considered for the study. Patients will be admitted to the hospital and given increasing doses of Metoclopramide. In patients who achieve a complete remission at a lower dosage, the progressive increases will be held at the minimal effective dose. A videotape will be made of the patient before treatment is started and at the maximal effective dose. After a four-day observation period, a third videotape will be made. Those patients who improve on Metoclopramide and elect to continue the medication will be followed at four-month intervals by the investigators in the neurology clinic. The formal period of follow-up will be one year, in which the long-term effects will be monitored, including the development of adverse effects or decreased efficacy. A final tape will be made documenting the effects of the drug at the completion of the follow-up period.**

Progress: **Over the past two years there has been a lack of patients with appropriate movement disorders that meet entry criteria, i.e., refractory to other treamtnet modalities. This protocol was initiated at a large tertiery care center (WRAMC) that saw a different patient population. Therefore, I would suggest termination of this protocol, as insufficient patients present that qualify for entry.**

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 88/83** **STATUS: Completed**

TITLE: Assessment of the Clinical Value of Monitoring During Endoscopic Procedures

START DATE: Oct 88 **ESTIMATED COMPLETION DATE: Oct 88**

PRINCIPAL INVESTIGATOR: MAJ John C. Berg

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: MAJ David Macinni, MC; COL Edward Burkhalter, MC; MAJ Robert Miller, MC

KEY WORDS: Monitoring, Endoscopic procedures

Study Objective:

1. **To confirm or refute existing studies regarding the presence and degree of oxygen desaturation during endoscopy.**

2. **To identify the causes and/or variables as to when and in whom oxygen desaturation may occur.**

3. **To assess whether the performance of transcutaneous oxygen monitoring (tom), pulse, and blood pressure monitoring, even if abnormal, has any clinical correlation in detecting and/or preventing potential procedure complications.**

Technical Approach: **Prospective evaluation of all patients referred for any endoscopic procedures at WBAMC GI Service. No exclusion criteria other than patient refusal or contraindications for endoscopy. Transcutaneous oxygen monitoring with Physiocontrol Life Stat 1600 pulse oximeter, pulse, blood pressure, and Holter monitoring of patients undergoing endoscopy. Expected duration of study is six months to one year, with preliminary data evaluation expected after 250 patients. A complication shall be considered to have occurred if the oxygen saturation decreases more than 5% from the preprocedure values, reversal of narcotic sedation due to over sedation or excessive oxygen desaturation, bradycardia less than 50 beats per minute, development of a malignant cardiac dysrhythmia (eg. ventricular tachycardia, bigeminy, 3rd degree atrioventricular block), or any other observed significant cardiopulmonary event.**

Progress: **Two-hundred-sixty-six patients entered in this study, with no withdrawals or adverse reactions. Data collection and tabulation has been completed. Statistical analysis ongoing with projected finalization of the initial study October 1989. Further investigation of specific points of interest possible pending the above.**

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 89/60** **STATUS: Ongoing**

TITLE: Cholesterol and Lipid Profiles of Male Soldiers During U.S. Army Basic Training

START DATE: Sep 89 **ESTIMATED COMPLETION DATE: Dec 89**

PRINCIPAL INVESTIGATOR: MAJ Joseph Caravalho, Jr.

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: CW2 Margaret A. Kinney, PA; CPT John D. MacDonald, MC; MAJ Thomas E. Martyak, MC

KEY WORDS: Cholesterol, Lipid profile, U.S. Army, Basic trainee

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Study Objective:

1. **Determine the plasma total cholesterol (TC); triglyceride (TG); high density lipoprotein (HDL-C); low density lipoprotein (LDL-C); and very low density lipoprotein cholesterol (VLDL-C) levels of healthy young adult males from the general population as they enter the Army for Basic Training (BT).**

2. **Determine the background demographic data of these soldiers in order to assess dietary, smoking, and alcohol consumption habits, as well as previous physical activity and educational levels attained.**

3. **Determine the effect of eight weeks of continuous BT (i.e., without administrative or medical breaks in training) on these soldiers' serum TC, TG, HDL-C, LDL-C, and VLDL-C.**

4. **Determine if there is any significant change in demographic data (to include diet, physical activity and perceived level of stress) at the conclusion of BT.**

5. **Determine if there is any significant change in lipid profile following BT attributable to a change in diet or other factor.**

Technical Approach: **The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.**

Progress: **Initial questionnaires and lipid profiles were obtained from Basic Trainee volunters without problems. Anticipate no difficulties in obtaining post-BT results from those still in the study.**

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 85/47** **STATUS: Terminated**

TITLE: Effect of Vitamin B-6 on Asthma

START DATE: Mar 89 **ESTIMATED COMPLETION DATE: Jul 89**

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: Ruth Hulse, LPN

KEY WORDS: Vitamin B6, Asthma

Study Objective: To investigate whether asthmatic patients will benefit from oral vitamin B6 supplementation.

Technical Approach: Fifty stable, asthmatic adult patients attending the Allergy Clinic will be invited to be participants in this study. Baseline spirometry, plasma histamine, B6 level and skin response to histamine DMH and allergens will be recorded. Oral vitamin B6, 50mg b.i.d., will be given for 3 weeks. The patient will be advised not to add supplemental "over-the-counter" type vitamins to their diet during the testing period. Similar laboratory testing and skin testing will be repeated. Various data points obtained pre- and post-B6 treatment will be analyzed by paired student's t-test.

Progress: Principal investigator left the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/07 STATUS: Terminated

TITLE: Evaluation of Specific IgE Level, IgG Blocking Antibody Level and Skin Test Reactions with Plasma Histamine Levels in Patients with Adverse Reaction to Allergen Immunotherapy

START DATE: Jan 1987 ESTIMATED COMPLETION DATE: Oct 1989

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ruth Hulse, LVN; Robert Haverly, DAC

KEY WORDS: Allergy immunotherapy

Study Objective: To determine the effect of nicotine on serum theophylline in nonsmokers and in asthmatics.

Technical Approach: Approximately ten nonsmokers, who do not have asthma, and ten nonsmoker asthmatics will be invited to participate in this study.

The nonsmoker subjects will be given a theophylline preparation of Theo-Dur, 10mg/kg/day in divided doses, and a baseline theophylline level will be obtained on the sixth day. A baseline, four and eight hours after a dose of theophylline, blood samples will be drawn.

Nicotine chewing gum will be prescribed for a total of 10 sticks per day for three days. At the end of three days, three serum theophylline levels will be obtained, baseline, four hours and eight hours post-dose.

The asthmatic subjects will continue to take their prescribed theophylline, and serum theophylline level will be obtained, pre-dose and four hours and eight hours after the dose. The nicotine gum will be prescribed if theophylline levels are within therapeutic range. Otherwise the dose of theophylline is adjusted prior to prescribing the nicotine gum. Serum theophylline levels will be drawn three days after being on nicotine chewing gum. Blood samples will be drawn also, before and after administration of nicotine chewing gum, for the following:

a. Vitamin B6
b. Plasma histamine level.

Progress: Principal investigator left the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/24 STATUS: Terminated

TITLE: Effect of Auranofin on Skin Test Response to Histamine, Codeine, Dextromethorphan on 24-Hour Histamine Levels

START DATE: Apr 1987 ESTIMATED COMPLETION DATE: Oct 1989

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ D.R. Hough, MC

KEY WORDS: Auranofin, Skin test response

Study Objective: Investigate in vivo effect of the oral gold preparation (auranofin) on the skin test response to histamine, codeine phosphate, and dextromethorphan and 24-hour urinary histamine levels.

Technical Approach: Adult patients requiring treatment with triethylphosphine gold (auranofin) as determined by their rheumatologist will be invited to participate in this study. Baseline urinary histamine levels will be measured by assay in DCI or referred to a laboratory where the assay is established. Skin tests will be performed with histamine phosphate 0.1 mg/ml, codeine phosphate 1 mg/ml, and dextromethorphan 1 mg/ml injected in a dose of 0.02 ml. The wheal and flare reaction will be measured after 15 minutes. The patient will be instructed to begin therapy with auranofin per prescribed schedule. After a two-week treatment with auranofin, and after with-holding any antihistamine drug, the urinary histamine levels will be determined. Skin testing will be repeated with histamine phosphate, codeine, and dextromethorphan as described above. Data will be analyzed by repeated measures ANOVA.

Progress: Principal investigator left the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 87/45** **STATUS: Terminated**

TITLE: Comparison of Prick and Intradermal Skin Test

START DATE: May 1987 **ESTIMATED COMPLETION DATE: Oct 1989**

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: M. Wells, Juan Cruz, Helen Villegas

KEY WORDS: Skin testing

Study Objective: To investigate the correlation between prick and intradermal skin test with serial concentrations of extracts.

Technical Approach: Fifty patients with various allergies will be invited to participate in this study. In patients being evaluated for various allergies, routine skin testing will be performed. If the prick skin test is negative, intradermal skin testing is performed with selected antigens such as Bermuda, Mulberry, Russian Thistle, and Ragweed, starting with 1:50,000, 1:5000, 1:500 dilutions, i.e., a patient may have a positive reaction only with 1:500 extract. If the skin test is positive, the size of the reactions is marked with a ballpoint pen and a clear scotch tape impression is obtained and will be transferred to the patient fs record. A blood sample will be obtained to determine RAST specific IgE for the tested antigens. The first positive reaction (the weakest positive test) for each patient for his most reactive skin test will be compared with RAST using paired t-test.

Progress: Principal investigator left the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/62 STATUS: Terminated

TITLE: ACTH and Beta-Endorphin Levels in Patients with Urticaria

START DATE: Feb 88 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Arun Thyagarajan, M.B., B.S., Laboratory of Clinical Sciences, National Institute of Health, Bethesda, Maryland

KEY WORDS: Beta-endorphin, Urticaria, ACTH

Study Objective: To investigate the levels of Beta-endorphin, histamine and ACTH in patients during acute episodes of urticaria and during asymptomatic state.

Technical Approach: Twenty adult patients with chronic urticaria without any obvious cause will be given State-Straight Anxiety Inventory, a standard questionnaire to evaluate psychological stress. ACTH and Beta-endorphin levels will be obtained at various points, baseline (asymptomatic state and on no medication), during the episode of acute urticaria and during asymptomatic phase while patients are receiving antihistamine therapy. In addition to the above, blood samples will be obtained to measure plasma histamine levels, along with ACTH and Beta-endorphin. Plasma ACTH and Beta-endorphin assays will be performed by the co-investigator in the Laboratory of Clinical Sciences, National Institutes of Health. Stress levels will be evaluated with the use of the questionnaire during different phases; i.e., asymptomatic state, urticarial phase. Patients will be instructed to avoid medications containing opioids. Statistical analysis: repeated measure ANOVA will be utilized.

Progress: The study is terminated due to the lack of accurate Beta-endorphin assay. The principal investigator has separated from active duty Army.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/11 STATUS: Terminated

TITLE: Skin Test Response to Histamine. DMH and Aeroallergen and Plasma Histamine Levels in Patients Undergoing Hemodialysis and Peritoneal Dialysis (Monitor: MAJ Grant Greely)

START DATE: Feb 88 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Maxine Lund, John Enriquez, MAJ Richard Keniston, MC; MAJ Clifford Ferguson, MC; MAJ Don Hammonds, MC

KEY WORDS: Histamine, hemodialysis, peritoneal dialysis

Study Objective: Histamine levels will be determined in plasma and dialysate fluids in renal failure patients before and after peritoneal/hemodialysis. Skin test response to a panel of aeroallergen histamine and Dextromethorphan to determine the atopic nature.

Technical Approach: Fifteen patients who undergo hemo/peritoneal dialysis for chronic renal failure will be invited to participate in this study. History of allergic disease will be evaluated through an allergy survey questionnaire. Antihistamines will be withheld 5 days prior to allergy skin testing and prior to obtaining plasma samples for histamine level. Baseline plasma histamine levels will be collected prior to the patients' routine dialysis procedure. Throughout the dialysis period, 5 ml samples from the dialysate fluid will be collected and stored at -70 degrees. Immediately following the hemo/peritoneal dialysis, a second blood sample will be obtained. Plasma is separated from the cells by centrifugation at 4 degrees and the samples are stored at -70 degrees until assayed. In addition to the above, BUN, creatine, and creatine clearance will be obtained pre and post dialysis. Prick and intradermal skin testing will be performed with histamine (0.1mg/ml for prick and 1mg/ml for intradermal) and Dextromethorphan (0.1mg/ml prick and 1.0mg/ml intradermal) prick skin testing will also be performed with a standard panel of aeroallergens (1:20 w/v extracts) which includes grass, tree, weeds, and mold extracts. Total IgE in blood will be determined and correlated with skin tests.

Progress: This study is terminated due to the lack of adequate number of subjects to arrive at meaningful data; the lack of accurate histamine assay for dialysate fluid and urine. The principal investigator is separating form active duty Army.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/25 STATUS: Terminated

TITLE: Immediate and Delayed Hypersensitivity with Correlation of Specific IgE and IgG to Trichophyton Antigen

START DATE: Jun 1988 ESTIMATED COMPLETION DATE: Oct 1989

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: *Specific IgE, Trichophyton, Delayed hypersensitivity*

Study Objective: To determine the incidence of immediate type reaction, IgE and IgG antibodies to Trichophytin during routine delayed hypersensitivity skin testing.

Technical Approach: Sixty patients who require anergy screen with standard anergy panel that includes Trichophytin antigen, will be invited to participate. Any reaction that occurs at 20 minutes will be recorded. Serum samples will be obtained for specific IgE and IgG antibodies. Skin test response will be recorded at 24 and 48 hour intervals and the size of the reaction will be noted.

The data will be analyzed to find:

1. The incidence of positive reaction at 20 minutes and Trichophytin antigen.
2. Correlation between positive skin tests and specific IgE for Trichophytin.
3. Incidence of positive delayed hypersensitivity skin tests at 24 and 48 hours with Trichophyton in patients who react in 20 minutes.

Progress: Principal investigator left the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/31 STATUS: Completed

TITLE: Comparison of Intradermal and Multitest (CIM) DHS Skin Tests and Correlation with CD4 Cells in HIV Patients

START DATE: May 88 ESTIMATED COMPLETION DATE: Mar 89

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Joan Cruz, Helen Villegas, C. Davis, M.D.

KEY WORDS: CD4 cells, Multitest-CMI^{R}, Mantoux technique

Study Objective: To compare standard intradermal (Mantoux) DHS skin tests with Multitest CMI anergy screen.

Technical Approach: It is planned to investigate DHS with simultaneous application of multitest CMI and a panel of antigens that are present in multitest intradermally on a different site. Multitest CMI has 8 areas loaded with various antigens and the device is applied on the forearm after cleaning with 70% alcohol to the site. Gentle pressure and side to side motion is applied to introduce the antigens into the skin. Intradermal technique (Mantoux) consists of injection of 0.1 ml of antigen intradermally. Tetanus (1:100), Trichophyton (1:30), Monila at 20 minutes, 24- and 48-hour intervals. A blood sample is obtained to determine CD4 helper-inducer cells as part of staging and follow-up of disease status.

Progress: Project was completed with 38 subjects being entered and no adverse reactions. Principal investigator separated from the Army. No progress to report.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/34 STATUS: Terminated

TITLE: Correlation of 24- and 48-Hour Skin Test Reaction with In Vitro Lymphocyte Transformation with Spherulin

START DATE: Feb 89 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Maurice Wells, Bruce Veit, Ph.D.

KEY WORDS: *Lymphocyte transformation, Spherulin*

Study Objective: To evaluate the significance of 24-hour and 48-hour skin test reactions with spherulin and correlate with in vitro lymphocyte transformation in patients undergoing anergy screen.

Technical Approach: Forty patients referred for anergy screen as part of their medical evaluation will be invited to participate in the study. DTH skin tests will be placed with a panel of antigens including spherulin. 0.1ml of antigen will be injected intradermally after cleaning the area with 70% alcohol. Patients will be observed in the clinic for 20 minutes to record any positive reactions. The reaction size is measured at 24- and 48-hours. Dr. Veit and personnel in DCI will perform in vitro lymphocyte transformation studies per standard protocol. If any of the study patients have had serological studies for cocci, the results will be utilized in the study. Repeated measure ANOVA will be utilized.

Progress: This project was terminated. Principal investigator was separated from the Army.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/37 STATUS: Terminated

TITLE: Role of Endogenous Opioids in Acute Bronchospasm, Urticaria, and Anaphylactic Reactions

START DATE: Aug 88 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Charles C. Eaves, Jr.; MAJ Thomas P. Giberson; Arun Thyagarajan, M.B., B.S.

KEY WORDS: Beta endorphin, acute bronchospasm, endogenous opioids

Study Objective: To determine the significance of endogenous opioids in acute asthma, acute urticaria, and anaphylactic reactions where mast cell degranulation may play a key role.

Technical Approach: Twenty asthmatics visiting the Emergency Room for treatment of bronchospasm will be asked to participate in the study. Seven ml of blood sample will be obtained by venipuncture for beta-endorphin and ACTH level. Twenty patients with acute urticaria will be recruited for 7ml venous blood sample for determination of beta-endorphin and ACTH level. Similarly, twenty patients who are evaluated and treated for acute anaphylactic/anaphylactoid reaction will be asked for a 7ml venous blood sample for beta-endorphin and plasma ACTH level. The patients will be followed in the Allergy Clinic. A second blood sample of 7ml venous blood will be obtained during a stable/asymptomatic stage of the disease. ACTH and beta-endorphin assay will be performed by the co-investigator, Dr. Thyagarajan, at the National Institute of Health.

Progress: This project was terminated. Principal investigator was separated from the Army

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/75 STATUS: Terminated

TITLE: Effect of B^6 Supplementation on the DHS Skin Test and T-Lymphocytes in Anergic Patients

START DATE: ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: LTC Raghava V. Charya

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Richard C. Keniston, M.D., Bruce Veit, Ph.D., John Enriquez

KEY WORDS: Anergy-lack of reactivity, DHS-delayed hypersensitivity, PLP-Pryidoxal 5' phosphate, T-Lymphocytes, Cell Mediated Immunity, Antigen

Study Objective: To study the effect of B^6 supplementation on the delayed hypersensitivity skin tests in anergic patients who do not respond to a battery of standard DHS skin test antigens.

Technical Approach: We plan to investigate the effect of vitamin B^6 supplementation on the delayed hypersensitivity response to a battery of antigens that include mumps, monilia, tetanus, trichophyton, PPD, and spherulin. Thirty individuals, age 18 and above, both male and female, will be studies. Military active duty, retired and their dependents are included in the study. No civilians will participate in the study. Individuals who were anergic to standard anergy panel (monilia, trichophyton, tetanus, PPD, and coccidioidomycosis) will be invited to participate in the study. Patients will be asked to withhold any vitamin supplements for 3 weeks prior to the study. Baseline DHS skin tests will be performed as described below. Volar surface of both forearms will be cleaned with 70% alcohol. The individual antigens will be injected intradermally 0.1ml with tuberculin syringes with 27 gauge needle. Patients will be asked to wait for 20 minutes to record any reactions. The skin reaction will be recorded either negative or induration in 2 opposite planes in millimeters in 24- and 48-hour intervals. If the patient continues to be anergic (negative reaction to skin test antigens), pyridoxine Hcl 50mg will be given P.O. daily for 4 weeks and the anergy screen will be repeated. In addition to the above, plasma PLP levels will be measured before and after supplementation. Lymphocyte transformation with PHA will be studies by Dr. Veit in the DCI Immunology Laboratory. Briefly, lymphocytes will be obtained by density centrifugation and cultured with and without PHA. Transformation will be evaluated by tritiated thymidine uptake, before and after supplementation of vitamin B^6. The blood samples will be drawn before placing the skin tests.

Progress: Principal investigator was separated from the Army; project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/46 STATUS: Ongoing

TITLE: Rate of Spherulin Skin Test Conversion Among Basic Trainees Exposed to Desert Training at Fort Bliss, Texas

START DATE: Sep 88 ESTIMATED COMPLETION DATE: Nov 90

PRINCIPAL INVESTIGATOR: MAJ Robert B. Ellis

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT B.L. Martin, MC

KEY WORDS: Spherulin, Skin test to C. immitis.

Study Objective: To establish the rate of spherulin skin test conversion among active duty basic trainees who are exposed to desert training at Fort Bliss, Texas. To attempt to define the morbidity associated with Coccidioides immitis in terms of time lost from basic training due to acute Coccidioidal infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: While this was initially a one year study which was to have been completed in Oct 89, events have transpired which have caused the investigators to request a second year for data acquisition. Additional administrative requirements by MRDC caused the investigators to lose the ability to gather information during some of the months in which the weather was optimal for the spread of the Coccidiodomycosis spores. The study is ongoing at this time. The revised Informed has been approved by MRDC and the project will re-start in Dec 89.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/03 STATUS: Ongoing

TITLE: Malignancy Associated Changes in Peripheral Blood Smears

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: MAJ Robert B. Ellis

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Bryan L. Martin, MC; MAJ I.L. Levey, MC

KEY WORDS: Cancer; blood cells

Study Objective: Analyze leukocytes from patients with non-hematologic cancer searching for patterns of cellular structure identifiable with the light microscope and indicative of underlying malignancy.

Technical Approach: Each individual will fill out a basic data sheet listing past medical history, past surgical history, past and present medications, and allergies. A known diagnosis of malignancy will be noted with histologic type and clinical stage if possible.

Three smears will be obtained from capillary blood of each patient along with 7cc of blood collected from the antecubital vein form which 3 smears will be made. The cytomorphological features described by Johnston et al. were noted in smears from earlobe blood and finger tip blood. To confirm their findings and determine if these features can also be found in the antecubital vein blood, both sources will be collected form patients with known malignancy. If early results indicate there is a good correlation between antecubital vein blood and fingerstick or ear lobe capillary blood, then only venous antecubital blood will be used, as this is the method of routine collection and judged less painful than fingertip collection.

Smears will be stained and examined as follows: blood will be collected four hours after meals, preferable in the morning to control possible variables in a similar method as Johnston et al. There should be nor surgery or transfusion of blood 2 months prior to the test. Fingertip and ear lobe blood will be obtained by scrubbing the area with 70% alcohol which is allowed to dry. Blood will be expressed with lancet and small drop placed on a slide. This smear will be prepared by either mechanical smear maker or manual "spreader slide" technique. The slides will be allowed to air dry for 5-10 minutes and fixed with anhydrous acetone free methanol for 30 minutes.

Smears will be stained with a modified Wright-Giemsa stain as per Johnston et al: Undiluted Wright's for 3 minutes, then Wright's diluted with equal amount of distilled water for 3 minutes. the slide will then be rinsed with water and stained with 1:10 diluted Giemsa for 13 minutes followed by water rinse and air dry.

The smears will be examined with the 100x oil immersion objective of a Zeiss photomicroscope III. A standard manual differential count will be performed on each specimen and representative photomicrographs will be taken. The leukocytes will be examined for two hematologic parameters: (1) the polymorphonuclear leukocytes will be inspected for the presence of excrescences, which are thread-like, thin, non-pedunculated projections from the nucleus, and the percent with excrescences will be calculated, (2) the cytoplasm of large mononuclear cells will be examined for the presence of small inclusion bodies surrounded by lightly stained areas or halos. One hundred mononuclear cells will be examined to estimate the percent haloed bodies.

Progress: There have been no enrollees in the study at this time. Current work involves standardization of the stains to be used on the peripheral smears. It is projected that the standardization will be completed in approximately 2-3 weeks and data acquisition with volunteers will begin in mid-December.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/32 STATUS: Terminated

TITLE: The Frequency of Campylobacter pylori Infection in Primary Care Outpatient Clinics as Determined by Serologic Test

START DATE: Apr 89 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: CPT Jesus A. Hernandez

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Edward Burkhalter, COL, MC; David Y. Graham, MD

KEY WORDS: Campylobacter pylori, serology

Study Objective: A serologic test has been developed that appears to be as good as the breath test in identifying the presence of C. pylori infection. We will use this test to determine the prevalence of C. pylori infection in asymptomatic, apparently healthy individuals from ages 20-80. This data will provide a baseline to which age matched patient population groups such as those with gastroesophageal reflux, Barrett's esophagus, and other groups could be compared. At the present time the prevalence of C. pylori in the general population is unknown. The results of this study will be analyzed for publication.

Technical Approach: Asymptomatic persons visiting the Ft Bliss CTMC and WBAMC outpatient clinics (Adult Medicine Clinic) for health maintenance purposes will be offered the opportunity to participate in the study. We will obtain approximately 50 blood samples per decade (groups 20-29, 30-39, 40-49, 50-59, 60-69, 70-79) for a total of approximately 300 specimens. Each participating subject will fill a brief questionnaire which accompanies this form. The samples will have to be spun and frozen at WBAMC laboratory and sent to Dr. Graham for serologic testing for C. pylori.

Progress: This study was terminated due to the difficulty of finding volunteers who would give blood.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/30 STATUS: Ongoing

TITLE: Impact of Serum Iron from the Routine Multiphasic Biochemical Panel in the Detection of Iron Overload States

START DATE: Apr 89 ESTIMATED COMPLETION DATE: Nov 89

PRINCIPAL INVESTIGATOR: CPT Lawrence Lepler

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Jesus A. Hernandez, CPT, MC; Robert M. Miller, MAJ, MC; Edward L. Burkhalter, COL, MC

KEY WORDS: Serum iron, Screening test

Study Objective: Evaluating the yield in detecting iron overload states by prospectively evaluating chem-20 panels over a period of 6 months.

Technical Approach: All patients with abnormally elevated serum iron levels on chem-20 panels ordered at WBAMC during a 6 month period will be identified. Those individuals older than 21 years old will be invited to participate in the study. After a preliminary discussion to evaluate for the possibility of recent or repeated blood transfusions, supplemental iron therapy or known hematologic disease, the chem-20 will be repeated and at that time formal determinations of serum iron, transferrin saturation and serum ferritin will be requested. Those patients with normal studies will receive no further evaluation. However, if these test results are abnormal (elevated serum ferritin and/or transferrin saturation greater or equal than 60%) a formal interview and physical examination will be obtained to assess for hematologic or liver disease. complete blood count, prothrombin time and partial thromboplastin time will be obtained at that time. Those patients with platelet count greater or equal than 100,000 and prothrombin time not prolonged more than 2 seconds percutaneously or by laparoscopic guidance. Liver tissue will be submitted for routine histology, iron staining and quantitative iron measurement. The diagnosis of homozygous genetic hemochromatosis will be made by determination of the hepatic iron index. If genetic hemochromatosis is diagnosed, the subjects will be offered treatment with weekly phlebotomies of approximately 500cc of blood with the goal of achieving iron depletion (ferritin less than 20 mg/dl). All diagnostic and therapeutic maneuvers described in this protocol are in accordance with our routine management of patients with suspected iron overload.

Progress: Data is currently being analyzed. Preliminary data appears to substantiate SMA iron as a useful screening test for iron overload states.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/20 STATUS: Terminated

TITLE: Ifosfamide/Mesna, Emergency One-time Use, Ind. #123-999-672

START DATE: Dec 88 ESTIMATED COMPLETION DATE: Feb 89

PRINCIPAL INVESTIGATOR: MAJ Irwin L. Levey

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Ifosfamide/Mesna

Study Objective: To attempt to treat advanced sarcoma. Ifosfamide is an experimental drug that has been reported to be useful in treatment of sarcoma.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in Department of Clinical Investigation and are available upon request.

Progress: On 12 December 1988, cytotoxic chemotherapy using the investigational drug Ifosfamide was initiated in a patient with advanced soft tissue sarcoma. The drug was supplied by the Bristol-Myers Company under compassionate IND #123-999-672.

In May 1988, a 28-year-old caucasian man, active duty USAF, was received in transfer for management of advanced neurogenic sarcoma arising in the colon. He had been treated by right hemicolectomy and primary re-anastamosis on 24 Mar 88. Liver biopsy at surgery revealed metastatic tumor. Upon arrival at WBAMC, staging evaluation disclosed extensive intra-abdominal and hepatic tumor. Medical Board proceedings were initiated, and following Tumor Board recommendations palliative chemotherapy was begun using standard chemotherapeutic agents. Progressive disease was noted despite three courses of aggressive therapy, and the National Cancer Institute was subsequently contacted regarding the availability of salvage therapy. Dr. Claude Nicaise at Bristol-Myers agreed to enter the patient into a Phase II trial of ifosfamide with mesna uroprotection. Chemotherapy was initiated with the first course given 12-16 December 1988, and a second course administered 23-27 January 1989. The patient tolerated treatment well, suffering only mild hemorrhagic cystitis. Although hepatic enzyme levels improved slightly, nomeasurable response could be documented by CT scanning. The patient subsequently expired. Limited autopsy was performed and reportedly disclosed extensive intra-abdominal and intra-thoracic metastases.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 84/35** **STATUS: Ongoing**

TITLE: Adjuvant Chemotherapy with 5-FU, Adriamycin and Mitomycin-C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma (SWOG 7804)

START DATE: Mar 1978 **ESTIMATED COMPLETION DATE: Indefinite**

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS:

KEY WORDS: Adenocarcinoma, Stomach, Adjuvant chemotherapy vs surgery

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Study Objective: **To determine the efficacy of adjuvant chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.**

Technical Approach: **The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.**

Progress: **Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).**

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 85/07 STATUS: Ongoing

TITLE: Treatment of Limited Non-Small Cell Lung Ca Radiation vs Radiation & Chemotherapy (SWOG 8300)

START DATE: Jul 1984 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Lung Carcinoma

Study Objective: To compare combination chemotherapy (FOMI/CAP: 5-Fluorouracil, Vincristine and Mitomycin-C alternating with Cyclophosphamide, Adriamycin and Cis-platinum) plus radiotherapy to radiotherapy alone for patients with limited, non-small cell lung cancer (NSCLC) in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration and survival duration. To determine the toxicity of radiotherapy plus FOMI/CAP relative to radiotherapy alone for patients with limited NSCLC. To evaluate the responsiveness of smaller tumor burdens to FOMI/CAP (i.e., less than metastatic disease). To determine the pattern of relapsing disease in each treatment arm and in subgroups of patients determined by histology and response to FOMI/CAP. To determine if prophylactic brain irradiation will decrease the chances for brain metastases and influence toxicity of survival.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 85/10 STATUS: Ongoing

TITLE: Evaluation of Tamoxifen in Unresectable and Refractory Meningioma (SWOG 8415)

START DATE: Jul 1984 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Meningioma

Study Objective: To determine the antitumor activity of Tamoxifen in meningiomas not amenable to surgery or radiotherapy. To estimate the response rate and response duration experienced by these patients.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/32 STATUS: Ongoing

TITLE: SWOG 8313 Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Carcinoma of the Breast

START DATE: Apr 1984 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Breast carcinoma

Study Objective: To compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses. To compare a multiple item questionnaire to a single item questionnaire for assessing quality of life.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/40 STATUS: Ongoing

TITLE: SWOG 8590 Effect of combining chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of Head and Neck

START DATE: Feb 1985 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Squamous Cell Carcinoma

Study Objective: Case identification and data collection.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/41 STATUS: Ongoing

TITLE: SWOG 8600 Randomized Investigation of High Dose vs Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Nonlymphocyte Leukemia

START DATE: Nov 1986 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Nonlymphocyte leukemia

Study Objective: To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high dose cytosine arabinoside and daunorubicin. To compare the duration of complete remission and of disease-free survival among patients who each receive one of three combinations of induction and consolidation regimens: Standard dose cytosine arabinoside and daunorubicin for both induction and consolidation. Standard dose cytosine arabinoside and daunorubicin for induction followed by high dose cytosine arabinoside and daunorubicin for consolidation. High dose cytosine arabinoside and daunorubicin for both induction and consolidation.

To determine the comparative toxicities of these three programs of induction and consolidation.

To determine the feasibility of implementing a predetermined approach to supportive care within a multi-institutional cooperative group setting for patients receiving intensive chemotherapy for acute nonlymphocytic leukemia.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/47 STATUS: Ongoing

TITLE: SWOG 8598 Prospective Trial for Localized Cancer of the Esophagus

START DATE: Oct 1986 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Cancer, esophagus

Study Objective: Determine the role of chemotherapy for a potentially curable subset of patients with squamous cell cancer of the esophagus. Specifically to determine if the combination of chemotherapy and radiation will add to the overall survival and cure of patients treated with the combination when compared to patients treated by radiation alone. Determine if the patterns of recurrence for patients treated with the combination of chemotherapy and radiation differs from those patients treated with radiation alone.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/48 STATUS: Ongoing

TITLE: SWOG 8691 A Randomized Comparison of Deoxycoformycin vs Alpha Interferon in Previously Treated Patients with Hairy Cell Leukemia

START DATE: Dec 1986 ESTIMATED COMPLETION DATE: *Indefinite*

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Leukemia

Study Objective: Compare deoxycoformycin and alpha-interferon with respect to frequency of response, time to response, and duration of relapse-free survival among unsplenectomized patients with hairy cell leukemia.

Compare deoxycoformyhcin and alpha-interferon with respect to improvement in specific patient characteristics including hematologic parameters, size of the spleen, performance status, frequency of documented infections, and number of red blood cell and platelet transfusions.

Estimate the rate of response for each treatment when used among patients who have failed to respond to or had unresolvable toxicity from the other treatment.

Determine the impact of a complete versus a partial remission on remission duration and survival.

Compare toxicities of administration of interferon versus deoxycoformycin to patients with hairy cell leukemia.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients entered in this study. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/74 STATUS: Ongoing

TITLE: SWOG 8693 Adjuvant Therapy of Primary Osteosarcoma: A Phase III Randomized Intergroup Study

START DATE: Mar 1987 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Osteosarcoma

Study Objective: Determine whether the intensity of adjuvant chemotherapy affects its success in terms of local recurrence, disease-free survival and overall survival in patients who have primary osteosarcoma of the extremities and who are randomized to either surgery followed by adjuvant chemotherapy with three drugs or surgery followed by adjuvant chemotherapy with six drugs. Determine the influence of clinical prognostic variables on disease outcome. Determine the influence of histopathology on disease outcome. Determine the influence of clinical prognostic variables on disease-free survival and survival after resection of pulmonary metastases in patients who relapse after being treated as above.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered into this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/75 STATUS: Ongoing

TITLE: SWOG 8694 A Comparison of Pentostatin (NSC-218321) and Alpha-Interferon (NSC-377523) in Splenectomized Patients with Active Hairy Cell Leukemia

START DATE: Feb 1987 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Hairy Cell Leukemia

Study Objective: To compare the frequency of response between pentostatin and a-IFN treatment in patients with hairy cell leukemia who following splenectomy manifest active or progressive disease. To compare time to response between these two treatments. To compare the response duration of these two treatments.

To determine whether pentostatin salvages nonresponders to a-IFN treatment and whether a-IFN salvages nonresponders to pentostatin treatment. To compare the toxicity of the two treatments.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered into this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/77 STATUS: Ongoing

TITLE: SWOG 8792 Phase III Study of Alfa-nl (Wellferon) as Adjuvant Treatment for Resectable Renal Cell Carcinoma

START DATE: Jun 1987 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Renal Cell Carcinoma

Study Objective: To assess in a controlled fashion the effectiveness of interon alfa-nl (Wellferon) as a surgical adjuvant in patients with renal cell carcinoma. Study endpoints will consist of patient survival and time to recurrence.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered into this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/26 STATUS: Ongoing

TITLE: A Randomized, Double-Blind, Placebo-Controlled Dose Range Evaluation of Oral GR 38032F in the Prevention of Nausea and Vomiting Associated with Non-Cisplatin Chemotherapy

START DATE: Feb 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Irwin L. Levey, MC; MAJ Ruben D. Sierra, MC; LTC Marcia L. Carle, AN; Karlyn K. Pearl, RN; CPT Ricke J. Weickum, MS

KEY WORDS:

Study Objective: To determine the antiemetic efficacy of three different doses of oral GR 38032F in patients receiving a cyclophosphamide based regimen of chemotherapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered into this protocol. We have had a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/29 STATUS: Ongoing

TITLE: SWOG 8624: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma. Comparison of (1) VMCP/VBAP to VAD or VMCPP/VBAPP for Induction; (2) Alpha-2b Interferon or No Therapy for Maintenance; and (3) Alpha-2b Interferon + Dexamethasone for Incomplete or Non-Responders

START DATE: 1986 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Multiple myeloma, Chemotherapy, Interferon

Study Objective: To compare the effectiveness of three chemotherapy induction schedules for the induction of remission in previously untreated patients with multiple myeloma. The three schedules are:

1) VMCP/VBAP;
2) VAD (a four day infusion schedule);
3) VMCPP/VBAPP,

To compare the value of Intron-A (alpha-2b interferon) maintenance versus no maintenance for patients proven to achieve remission (at least 75% tumor regression after induction).

For patients who achieve only improvement (50-74% tumor regression) or are non-responders with chemotherapy induction, to determine whether dexamethasone plus alpha-2b Interferon (INTRON-A) will increase the remission rate and survival duration.

D. To determine prognostic applicability to multiple myeloma of serum beta-2 microglobulin level, plasma cell LI%, using the BU-1 monoclonal antibody, bone marrow plasma cell morphologic characteristics, and histochemical staining for acid phosphatase and beta-glucuronidase content.

E. Nationwide, the study group desires to accrue 450 evaluable patients in the induction phase of approximately 3.3 years, and expects to have 130 patients in the maintenance phase, and 230 patients in the dexamethasone plus interferon trial. We expect no more than 2O patients will be enrolled at WBAMC.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in Department of Clinical Investigation and are available upon request.

Progress: Zero patients have been entered in this protocol. We have ha[illegible] a critical shortage of resources, i.e. physicians, and lack of a data manager which has made it difficult in the last year to register patients on these protocols (SWOGs).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/82 STATUS: Completed

TITLE: Emergency Use of Misoprostol (Cytotec)

START DATE: Sep 88 ESTIMATED COMPLETION DATE: Jan 89

PRINCIPAL INVESTIGATOR: MAJ David M. Maccine

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Misoprostol

Study Objective: To allow licensed physicians in the USA to treat patients they consider in need of the prostaglandin analogue, misoprostol (Cytotec) in a timely and appropriate manner e.g., (patients with a resistant peptic ulcer with or without concomitant NSAID usage).

Technical Approach: Patients considered suitable for the study, by their treating physician, should receive misoprostol 200mg 4 times daily for 4-8 weeks. completed CRF (case report form), patient informed consent, and a copy of local IRB approval should be returned to the Searle clinical monitor within 4 weeks of completion of the study. Pre and post treatment routine biochemical and hematological screening are advised.

Progress: A request for emergency use of Misoprostol was submitted for use in two patients. Both patients had peptic ulcer disease refractory to currently available medical therapy.

The nature of the illness was not emergent in either of these patients. However, at that time a supply of the medication had been received and one of the patients was hospitalized at our institution from Ft. Huachuca, and was due to be released. In order to give him the available medication, approval for use was sought from the Consultant to the Surgeon General and our Acting Hospital Commander, and this was approved verbally by both parties, although the patient did not strictly meet criteria of emergency need.

The medication was Misoprostol (Cytotec), received form GD Searle and Co. Two bottles of 100 tablets were received from the company and the patient was administered one bottle. Subsequently the second bottle was returned to GD Searle because the patient discontinued the medication after two weeks due to diarrhea.

The second patient was not administered the drug until local approval of the compassionate use protocol was approved. This was due to the fact that the medication was not available. This patient completed a two month course of the medication with improvement in her symptoms. Two 100 tablet bottles were received for this patient and subsequently dispersed one at a time.

Misoprostol has subsequently been approved by the FDA for general use and is expected to be available in March of 1989. The compassionate use program has been terminated. Future use of the drug at our institution will be through routine channels.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/82.5 STATUS: Completed

TITLE: Compassionate Use of Misoprostol (Cytotec)

START DATE: Sep 88 ESTIMATED COMPLETION DATE: Jan 89

PRINCIPAL INVESTIGATOR: MAJ David M. Maccine

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Misoprostol

Study Objective: The purpose of this compassionate use program is to allow licensed physicians in the USA to treat patients they consider in need of the prostaglandin analogue, misoprostol (Cytotec) in a timely and appropriate manner e.g., (patients with a resistant peptic ulcer with or without concomitant NSAID usage).

Technical Approach: This is an open compassionate use program through Searle Laboratories. Patients considered suitable for the study, by their treating physician, should receive misoprostol 200mg 4 times daily for 4-8 weeks. completed CRF (case report form), patient informed consent, and a copy of local IRB approval should be returned to the Searle clinical monitor within 4 weeks of completion of the study. Pre and post treatment routine biochemical and hematological screening are advised.

Progress: A request for emergency use of Misoprostol was submitted for use in two patients. Both patients had peptic ulcer disease refractory to currently available medical therapy.

The nature of the illness was not emergent in either of these patients. However, at that time a supply of the medication had been received and one of the patients was hospitalized at our institution from Ft. Huachuca, and was due to be released. In order to give him the available medication, approval for use was sought from the Consultant to the Surgeon General and our Acting Hospital Commander, and this was approved verbally by both parties, although the patient did not strictly meet criteria of emergency need.

The medication was Misoprostol (Cytotec), received form GD Searle and Co. Two bottles of 100 tablets were received from the company and the patient was administered one bottle. Subsequently the second bottle was returned to GD Searle because the patient discontinued the medication after two weeks due to diarrhea.

The second patient was not administered the drug until local approval of the compassionate use protocol was approved. This was due to the fact that the medication was not available. This patient completed a two month course of the medication with improvement in her symptoms. Two 100 tablet bottles were received for this patient and subsequently dispersed one at a time.

Misoprostol has subsequently been approved by the FDA for general use and is expected to be available in March of 1989. The compassionate use program has been terminated. Future use of the drug at our institution will be through routine channels.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/04 STATUS: Ongoing

TITLE: Salivary Immunoreactive Human Epidermal Growth Factor (IR-hEGF) and Bicarbonate in Patients with Peptic Ulcers

START DATE: Feb 89 ESTIMATED COMPLETION DATE: Feb 90

PRINCIPAL INVESTIGATOR: MAJ David Maccini

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Allan L. Parker, MC

KEY WORDS: Epidermal growth factor; peptic ulcers

Study Objective: To determine if there exists a significant difference between the levels of salivary and serum Ir-hEGF and bicarbonate found in patients with documented peptic ulcer disease and a control group without peptic ulcers.

Technical Approach: Serum and salivary samples will be collected from patients prior to their undergoing esophagogastroduodenoscopy (EGD). Patients who are found to have active peptic ulcers will serve as the study group. Patients with no ulcers by EGD or past history of PUD will serve as the control group. All patients (male and female) over the age of eighteen will be eligible to participate in the study. Levels of IR-hEGF will be tested in both saliva and serum, while HCO3 will be measured in saliva, of study patients and controls.

Salivary samples will be collected by spit technique. Approximately 3.0cc of saliva will be obtained by having the patient spit into a sterile container. The samples will be frozen and stored until the assay is performed in the Department of Clinical Investigations. Using a one-way analysis of variance, the salivary and serum IR-hEGF activity in each group will be compared. A p value of <0.05 will be considered to be statistically significant. Twenty patients will be studies in each group. Statistical support will be obtained from the Department of Clinical Investigations following collection of all the data.

Progress: Specimens have been collected for some time (110 subjects have been entered into the study), but logistical problems setting up assay for EGF have not yet been overcome. Awaiting assay before proceeding with study.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/51 STATUS: Completed

TITLE: The Yield of Routine Pre-Operative Barium Enema in Patients Undergoing Total Abdominal Hysterectomy and Inguinal Hernia Repair

START DATE: Dec 88 ESTIMATED COMPLETION DATE: --

PRINCIPAL INVESTIGATOR: MAJ David M. Maccini

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Robert M. Miller, MC

KEY WORDS: Barium enema; Hysterectomy; Inguinal hernia

Study Objective: The purpose of this study is to determine the findings on pre-operative barium enema performed prior to total abdominal hysterectomy (TAH) and inguinal hernia repair. Additionally, a cost analysis of the procedure will be performed.

Technical Approach: Retrospective review of all TAH and IHR performed at WBAMC during 1986 and 1987 to determine how many had pre-operative BE. The results of the BE and any subsequent colonoscopies will be noted. Additionally, the tumor registry charts of patients with colorectal carcinoma discovered during 1986 and 1987 will be reviewed to determine if any tumors had been diagnosed during the workup for gynecological surgery or inguinal hernia repair. A cost analysis will be performed.

Progress: It is the practice of some gynecologists and general surgeons to pre-operatively evaluate the colon with a barium enema (BE) examination to exclude potential bowel involvement or coexistent disease in patients undergoing pelvic or hernia surgery respectively. This practice appears based on anecdotal data with few studies specifically evaluating its usefulness. We retrospectively evaluated the records of 190 patients at WBAMC during the period 1986-87 who received a pre-operative BE prior to total abdominal hysterectomy (TAH) or inguinal hernia repair (IHR). The tumor registry charts of 59 patients diagnosed with colorectal carcinoma during the same period were also cross-checked to determine if any were detected during pre-operative evaluation for TAH or IHR. BE findings were considered significant if they altered surgical management or asymptomatic carcinoma was detected. Of 86 pre-TAH BEs, 8 (9.2%) were abnormal with subsequent colonoscopy revealing 4 with adenomatous polyps one of which required surgical resection. Of 104 pre-IHR BEs, 15 (15%) were abnormal with subsequent colonoscopy revealing 5 patients with adenomatous polyps and 2 with adenocarcinoma. Screening pre-operative BE had a low (1.2%) yield of clinically significant findings which was even lower in the sub-group with carcinoma (0.5%). There was no apparent relationship between findings and age in our study. Our results suggest that the use of routine pre-operative BE has a low yield, and should be performed only if clinical symptoms or findings suggest a need for its performance.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/71 STATUS: Ongoing

TITLE: Iron Levels in Hair of Patients With Anemia of Chronic Inflammatory Disease, Iron Deficiency Anemia and Normals

START DATE: Sep 89 ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: MAJ David Maccini

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Allan L. Parker, MC; MAJ James M. Baunchalk, MC

KEY WORDS: Iron, hair

Study Objective: This study is to determine if measurement of iron levels in the hair of patients with anemia and chronic inflammatory disease can be used to exclude iron deficiency as a cause of their anemia.

Technical Approach: Twenty patients will be studied in each of three groups. Group one will be patients with anemia and chronic inflammatory disease. These patients will be recruited from the Rheumatology Clinic. Group two will be patients with iron deficiency anemia and no evidence of any inflammatory disease. These patients will be selected from patients evaluated by the Gastroenterology, Hematology and Gynecology Services for iron deficiency anemia and also from screening results of complete blood counts (CBC) performed in the laboratory. Group three will consist of normal volunteers who have no evidence of anemia or chronic inflammatory condition. These patients will consist of hospital staff and patients seen in the GI Clinic.

After obtaining informed consent, 14 milliliters of blood will be drawn for the following studies: CBC, reticulocyte count, sedimentation rate, serum iron and ferritin levels. Additionally, three scalp hairs will be plucked and submitted for measurement of iron content. Levels of iron in hair and blood will be compared between the three groups.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/73 STATUS: Ongoing

TITLE: Serum Gastrin and Epidermal Growth Factor Levels in Patients with Adenomatous Polyps and Carcinoma of the Colon

START DATE: Sep 89 ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: MAJ David M. Maccini

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Edward L. Burkhalter, MC

KEY WORDS: Epidermal growth factor; Colon cancer; adenomatous

Study Objective: The purpose of this study is to determine if there is a significant elevation of the serum levels of gastrin and EGF in patients with colon carcinoma and colonic adenomatous polyps when compared to a control population (patients with a normal colonoscopy).

Technical Approach: Measurement of serum gastrin and epidermal growth factor will be performed in three groups of patients. Group one will be patients who are found to have polyps (adenomatous or hyperplastic) at colonoscopy. Group two will consist of patients who are found to have colorectal carcinoma at colonscopy or surgery. And group three will include patients who have undergone colonscopy and had a normal examination (no piror history of colonic polyps or cancer). patients will be between the ages of 18 and 99 (male and female) and have no history of other malignancies or peptic ulcer disease. It is expected that most patients will be recruited prior to or after undergoing colonoscopy in the GI Clinic at WBAMC. Indications for colonoscopy will be independent of this study. Twenty patients will be included in each group.

Patients will have ten milliliters of blood drawn at the time their IV is being started for colonoscopy. This will end the patient's participation in the study. Findings at colonoscopy will be noted on the usual endoscopic record used by the clinic (WBAMC form 524). Blood will be take to Clinical Investigation where it will be centrifuged and the serum frozen. Measurement of epidermal growth factor levels will be performed by RIA by an assay previously set up in Clinical Investigations. Gastrin levels will be processed through the Nuclear Medicine Service. Statistical analysis of the data in each group will be performed and compared. A p value < 0.05 will be considered statistically significant.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/77 STATUS: Ongoing

TITLE: In Vitro Qualitative ELISA Testing as a Screening Tool for Significant Allergy

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: LTC David L. Michaels

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Allergy, ELISA

Study Objective: Evaluate the sensitivity and specificity of the new flipSCREEN™ in vitro diagnostic test for allergy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/78 STATUS: Ongoing

TITLE: Food Sensitivity and Inhalant Allergy: Effect of Immunotherapy

START DATE: Sep 89 ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: LTC David L. Michaels

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Allergy, food sensitivity, immunotherapy

Study Objective: This project will investigate the incidence of allergy to various foods in patients being treated for inhalant allergy. Change in reported food allergy symptoms following inhalant immunotherapy will be investigated to determine whether the food symptoms represent cross reactivity with IgE antibody to inhalant allergens.

Technical Approach: The first phase of this study will employ a questionnaire to evaluate the frequency of adverse reactions to various ingestants including foods, preservatives, food colors, alcohol, and aspirin. This questionnaire will be distributed to all patients currently being treated with immunotherapy at WBAMC Allergy Clinic. Patients who agree to participate in the study will also be queried whether any of the ingestant symptoms have changed following inhalant immunotherapy. responses will be correlated with skin test results, antigens contained in immunotherapy mix, and duration of immunotherapy.

Where possible correlations between food and inhalant allergen are found, repeat skin testing with both antigens will be performed using the skin prick test titration method to measure degree of sensitivity. RAST assays will also be performed to highly reactive foods to determine correlation with skin prick test results. Selected patients may also be asked to participate in double blind food challenges to confirm the relationship of food ingestion to symptoms. A second phase of this study will use information obtained from the questionnaire. New patients being evaluated for inhalant allergy at WBAMC Allergy Clinic will be questioned about possible food sensitivities. Skin prick tests to the most commonly implicated foods will routinely be done in patients having positive skin tests to inhalant allergens. The food skin test results will be compared with the pattern of inhalant skin test reactivity and the presence of symptoms recorded on the history form. Testing of 200 patients in this manner should determine whether a particular positive food skin test in an inhalant sensitive person is of any clinical significance or merely represents antibody cross reactivity.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/53 STATUS: Terminated

TITLE: IND - Single Patient Emergency Administration of Dipentum in Patients with Active Ulcerative Colitis Disease for Whom Sulfasalazine is Contraindicated (Monitor: COL Burkhalter)

START DATE: Aug 1988 ESTIMATED COMPLETION DATE: --

PRINCIPAL INVESTIGATOR: MAJ Robert Miller

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Greg Schlepp, MC

KEY WORDS: Dipentum, ulcerative colitis

Study Objective: To ascertain the efficacy of Dipentum in the treatment of active ulcerative colitis in emergency instances of individual patients for whom sulfasalazine is contraindicated. To ascertain the potential of Dipentum to produce side effects in such patients.

Technical Approach: The details are lengthy and specified in the Pharmaceutical Companies' protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Principal investigator ETS'ed in June 1989. The patient was sent to surgery.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/34 STATUS: Ongoing

TITLE: The Effects of Verapamil and Diltiazem on Gastric Emptying

START DATE: Dec 87 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Albert J. Moreno

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Morakinyo A. Oyewole Toney

KEY WORDS: Gastric Emptying

Study Objective: Calcium channel blockers are currently indicated in the treatment of several medical problems. Data on the effects of calcium channel blockers on gastric emptying currently is sparse, but potentially important. This study is to determine the effects of verapamil and diltiazem on gastric emptying in normal human volunteers.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Volunteers are being pre-medicated with diltiazem, 60 mg, p.o., 30 minutes prior to a standard meal including the radionuclide, Tc-99m SCOL. Stomach half-empty rates are being determined. Likewise, stomach half-empty rates are being determined on the same patients when they are not on diltiazem. Very early preliminary data, shows no significant difference in half-empty rates. Progress in project has been impeded by lack of volunteers.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 88/40** **STATUS: Completed**

TITLE: IND Janssen Pharmaceutica # R51,619 - Use of IND Cisapride (Monitor: COL Burkhalter)

START DATE: Jun 1988 **ESTIMATED COMPLETION DATE: May 89**

PRINCIPAL INVESTIGATOR: LTC Allan L. Parker

DEPARTMENT: Med **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: CPT Jesus A. Hernandez, MC

KEY WORDS: Cisapride

Study Objective: To determine the effect of cisapride on the symptoms of unexplained upper abdominal pain, nausea, vomiting, early satiety, bloating/distension in patients with gastroparesis and/or gastrointestinal motor dysfunction.

Technical Approach: The details are lengthy and specified in the Pharmaceutical Companies' protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Cisapride was found to have no beneficial effect in this patient. No adverse effects were noted.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/43 STATUS: Completed

TITLE: Effect of Sclerotherapy on Gastric Emptying

START DATE: Apr 88 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Allan L. Parker

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Albert Moreno, MD

KEY WORDS: Sclerotherapy, gastric emptying

Study Objective: Sclerotherapy of esophageal varices to control upper gastrointestinal bleeding is now commonly done. This procedure has been shown to cause extensive periesophageal inflammation and eventually fibrosis which may lead to stricture formation. Since the vagus nerves are in this immediate area it is possible that they are injured as a result of the inflammatory response. A readily measurable effect of vagal activity is gastric motility. The objective of this study will be to use gastric emptying time as a measure of vagal integrity in post sclerotherapy patients.

Technical Approach: Patients seen in the GI Service for sclerotherapy will be asked to obtain a gastric emptying study (Nuclear Medicine). If agreed the study will be performed in the usual manner. These results will be compared with normal values (standard) as well as with other patients with cirrhosis who have not undergone sclerotherapy. The number of sclerotherapy sessions, amount of sclerosant injected, and time from last therapy will also be studied.

No equipment or special materials will be required above those used normally in the above procedures.

The number of patients to be involved will be approximately 15-20 sclerotherapy patients and as many controls as available up to a comparable number.

The only risks of the study are those associated with a minuscule dose of radiotracer for the gastric emptying study. To date, no adverse effects have been reported with this study and any risks are theoretical only. The expected survival for these patients is less than five years, further minimizing the radiation risk.

Progress: Three (50%) of the studies were normal with a T 1/2 less than 90 minutes.
Three (50%) were abnormal with a T 1/2 greater than 90 minutes. The average T 1/2 for normal patients was 50 minutes versus 187 minutes for the abnormals. All patients had at least three sclerotherapy sessions with no notable difference in the number or amount of injections. The time elapsing from the last sclerotherapy session to gastric emptying study averaged 1.1 month for abnormals versus 10.1 month for the normals.

Conclusions: 1. Sclerotherapy for bleeding esophageal varices may be associated with significant prolongation of gastric emptying possibly secondary to vagal injury.

2. This effect is probably transient resolving over time.

The slowed gastric emptying is not associated with symptoms.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/23 STATUS: Completed

TITLE: Magnetocardiography in the Evaluation of Left Ventricular Hypertrophy

START DATE: Feb 86 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Ho, Dept of Physics, UT El Paso

KEY WORDS: Magnetocardiography

Study Objective: Superconducting Quantum Interface Device (SQUID) Magnetocardiography has proven a reliable noninvasive method of studying the human heart. The objective of the present study is to define changes from normal in the magnetocardiogram in left ventricular hypertrophy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: In order to establish the effectiveness of magnetocardiography in detecting heart disease, we have measured the resting magnetocardiogram and simultaneous electrocardiogram in 30 subjects. An electrocardiogram was not recorded in the earliest subjects. Subjects were evaluated before exercising on a bicycle ergometer. We have found that there are statistically significant differences between normal and abnormal subjects. In most normal subjects, the magnetic and electrical T-wave vectors point in opposite directions, whereas in the abnormal subjects that generally point to the same direction. We have also demonstrated that the time lag between the electrocardiogram and the magnetic cardiogram after exercise is significantly greater in subjects with heart disease than in normal subjects.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/74 STATUS: Ongoing

TITLE: Echocardiographic Standards for Adolescents Based on Tanner Staging

START DATE: Aug 88 ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Maatinko and Dr. Stafford, Dept of Pediatrics

KEY WORDS: Echocardiography

Study Objective: To establish echocardiographic standard for healthy adolescents based on Tanner staging, which measures biologic age rather than chronologic age. The new standards will allow a more narrow definition of normal.

Technical Approach: We propose to obtain an echocardiogram on consenting patients presenting to the Pediatric and Adolescent Clinic for school or sport physicals, between 10 and 17 years of age. Tanner staging will be assessed by examiners, which is part of the normal physical examination. Complete physical examinations will be performed and subjects with evidence of chronic illness or heart or lung disease will be excluded. Furthermore, a questionnaire is to be completed by each subject which elicits additional information on athletic activities and health. The patient will be sent to the Cardiology Clinic upon completion of the physical examination for an echocardiogram to be performed by a trained technician.

Echocardiographic data will be measured by computer analysis and reviewed by a pediatric cardiologist. Measurements will include the thickness of the right free ventricular wall, interventricular septum, left ventricular free wall, aortic root, left atrium, aortic valve opening, and each of the identifiable portions of the mitral valve motion. From the data collected, mean values and standard deviations will be determined for males and females in each of the five Tanner stages. Additional data to be collected on each subject will include height, weight, race, and body surface area.

Progress: We are performing echocardiograms on normal adolescents presenting for routine physical examinations. Various measurements are made from the electrocardiograms, and these are correlated with physical maturation (Tanner stage). We have currently accumulated data on 242 subjects. This information is being evaluated and a determination will be made of whether we need additional data.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 85/21 STATUS: Terminated

TITLE: Treatment of Graves' Ophthalmopathy With Cyclosporin: A Multicenter Study (Sandoz IND 24761) (Monitor: Dr. Amegin)

START DATE: Nov 1985 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: MAJ Leonard Sanders,

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Cyclosporin, Grave's Ophthalmopathy

Study Objective: To assess the efficacy of cyclosporin treatment on the ophthalmopathy of Grave's Disease.

Technical Approach: Approval to undertake this project was first requested at WRAMC with collaborative studies in Endocrinology Services at other MEDCENs on a slightly more limited basis in order to enroll as many patients as possible with this relatively rare problem and attain an earlier completion date. The study will be composed of a random cross-over design comparing Cyclosporin treatment to the most commonly employed current therapy, high dose oral prednisone. Due to the nature of these drugs and their potential side-effects, a double-blind design is not feasible. Since responses tend to be seen rapidly (if they occur at all) with steroids, and the favorable responses to Cyclosporin in the recent reports by both Weetman et al., and Nussenblatt et al., were seen within seven to ten days, we plan to administer each drug for three weeks. Each patient's response to one drug will be compared to their own response to the other drug. A total of 20 patients will be initially evaluated with random alternating allocation to either: Group A (1) Prednisone 40 mg t.i.d. x three weeks, (2) full evaluation of response, and (3) cyclosporin 5-10 mg/kg/day x three weeks; Group B Reverse order of Group A.

Progress: Principal investigator is no longer at WBAMC. Medical Monitor recommended termination of project.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/84 STATUS: Ongoing

TITLE: Induction of Tumor Necrosis Factor Alpha (TNF-alpha) in Human Infection with Coccidioides immitis

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Matthew J. Dolan, MC, USAF; Rebecca A. Cox, Ph.D.; MAJ J. William Kelly, MC; MAJ Robert A. Zajac, MC, USAF; MAJ Gregory P. Melcher, MC, USAF

KEY WORDS: Coccidioides immitis, Tumor necrosis factor alpha

Study Objective: To determine if human infection with the dimorphic fungus Coccidioides immitis induces the production of cytokine TNF-alpha/cachectin as part of the overall host immunologic response to infection.

Technical Approach: Patients and controls (staff volunteers) from each facility will be phlebotomized on one occasion; approximately 50 ml of blood by peripheral venipuncture will be required. Antigen stimulation will be performed at WBAMC by MAJ Slagle, using the facilities of the Department of Clinical Investigation. Supernatants from this portion of the assay will be frozen at -70°C, batched and transported at a future date to the San Antonio Sate Chest Hospital (SASCH). The TNF-alpha RIA will be performed by the Research Immunology Laboratory at SASCH.

Patients suitable for inclusion in this study include individuals 18 years of age or old or older having documented active infection with C. immitis, as evidenced by:

1. Acute pneumonitis with positive sputum culture.

2. Disseminated disease within the thorax, with pulmonary parenchymal involvement as shown by biopsy stain or culture.

3. Extrathoracic disseminated disease, with demonstration of C. immitis on biopsy stain or culture of involved tissue or biologic fluid.

Exclusion criteria for patients and controls include the presence of concurrent infection or underlying malignancy. Patient controls will be matched for age (± 10 years), sex, and race.

Risks to patients and controls are limited to those risks associated with phlebotomy (bruising, infection, or thrombophlebitis at the venipuncture site). The study is designed to begin in October 1989 upon IRB approval, with an anticipated duration of two years. It is anticipated that 5-10 patients from WBAMC will be eligible for enrollment in each year of the study.

PBM from each patient and control will be stimulated in vivo with Formalin-killed spheres (test antigen), lipopolysaccharide (LPS) from E. coli serotype 055:B5 (positive control), and tissue culture media (negative control). thus, TNF-alpha levels will be analyzed using two-factor analysis of variance (factors of infected/not infected and stimulated/not stimulated).

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/55 STATUS: Ongoing

TITLE: Nursing Implications for Determining the Differences in Paternal-Infant Attachment Behaviors Exhibited in the Intensive Care Nursery and the Term Nursery

START DATE: Jun 89 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: MAJ Lorna Chatmon

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Carol Fox, AN

KEY WORDS: Paternal and infant bonding

Study Objective: The purpose of this observational study is to determine if paternal-infant attachment behaviors differ between father's experiencing a normal term infant delivery and those experiencing a preterm infant delivery. The following questions will be addressed: 1) Does the altered ability of the preterm infant to interact with the father effect the attachment behaviors exhibited by the father? 2) Do the variables of infant gender, father's presence at delivery, father's early contact with infant, pleasure or pain value placed on the pregnancy by the father, and whether the pregnancy was planned or unplanned predict attachment behaviors?

Technical Approach: Subjects for the study would be recruited during initial obstetrical orientation or during preadmission to the labor and delivery unit. Couples would be approached and if the selection criteria met, would be asked to participate in a study of "how first-time fathers get to know their infants". A sample of 20 fathers, 10 of which have experienced a preterm delivery and 10 which have experienced a term delivery would be selected. The sample size is felt adequate to pilot test the use of the assessment inventory tool with fathers of preterm infants as well as term infants. Randomization of study participants is not possible due to the differentiation of participants into groups experiencing preterm deliveries versus term deliveries. Four criteria for sample selection exist; 1) This is the fathers' first child, 2) Study participants are married, 3) Fathers are present at delivery, 4) The infant is born alive, whether term or preterm. A term infant is defined as any infant greater than 36 weeks gestation and 2500 grams. A preterm infant is defined as less than 36 weeks gestation and 1500-2500. The exclusion of preterm infants less than 1500 grams is felt to be necessary due to their often precarious initial medical course and the inability of this study to adequately research them at this time.

The inventory is used during 3 observational periods of father-infant interaction. Each observational period is 10 minutes long. during that time the nurse observer would check each item or behavior on the inventory with a plus (+) if the behavior was observed; if a behavior was not observed it would be indicated with a minus (-). The paternal behaviors are scored on an item-by-item basis and analyzed individually. Observation periods occur during father-infant interaction in delivery, recovery, nursery and neonatal-intensive care unit, as well as when the fathers are visiting in the room with their infants. The first observational period would occur during delivery if the infant is handed to the father and/or in recovery. The second and third observational periods would then occur during subsequent visit and interaction between the father and his infant.

Progress: Continuing to accept subjects for the three observations periods. No data to report at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/41 STATUS: Terminated

TITLE: 25-Hour Prospective Concurrent Acuity Determination vs Unpredicted Patient Acuity Determination on Evening and Night Shifts, Critical Care Areas

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: LTC Ruth Cheney

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Acuity, nursing workload

Study Objective: To ascertain whether or not significant nursing workload is lost in critical care areas by categorizing unpredicted patients arriving on the evening and/or the night shifts. The evening and night shifts would complete the patient acuity worksheet only if a new admission or transfer in occurs on their shift; or, in the case of the night shift, to further capture the direct nursing care requirements of a patient received on the evening shift. Data obtained will be analyzed to determine if workload lost is significant enough to negatively affect the manpower requirements of the specific unit.

Technical Approach: The patient acuity worksheet will continue to be filled out, and data entered into UCAPERS, on a propective concurrent basis. There will be no change to this aspect of the existing system. Data required by OTSG and HSC will continue to be generated and be available in accordance with OTSG, HSC, and WMSN instructions.

The study design requires the patient acuity worksheet also be filled out by the ANC/RN on both the evening and night shift, with these two shifts reflecting only their unanticipated workload created by the admission of new patients or transfer in of patients another area of the hospital. The study will not address the hours between 1200 and 1500, after acuity has been entered into UCAPERS and prior to the beginning of the evening shift.

The ANCs/RNs responsible for completing the patient acuity worksheet on the evening and night shifts will be trained on the system by the principal investigator in accordance with WMSN guidelines. All nursing personnel are routinely taught to document to support acuity.

At the conclusion of training, a 10-20 day pilot study will be conducted to elicit problem areas, clarify instructions/procedures, and implement correcitons/improvements in the study design. (The actual length of the pilot study will be determined by the number of unpredicted patients arriving on the evening and night shifts.) The tools used to elicit problems will be:

a. communication with the participants in data collection
b. conduct of inter-rater reliability

Inter-rater reliability will be perforemd by the principal investigator on a daily basis on each ANC/RN assigned to the evening and night shifts who will be filling out the patient acuity worksheet. All 8 factors will be evaluated on each patient in each unit. An inter-rater reliability score below 80% will determine the need for retraining of the specific individual(s).

Once the principal investigator is confident that data obtained on the evening and night shifts is valid and reliable, a 6-month period of data collection will commence. (Confidence is inherent on inter-rater reliability scores consistently 80% or greater.) During the 6-month study period, inter-rater reliability will be performed by the performed by the principal investigator on a monthly basis on ANCs/RNs on the evening and night shifts who are filling out the patient acuity worksheet.

Progress: No progress was made during this year. Principal investigator requested project be terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 88/18** **STATUS: Completed**

TITLE: Community Health Needs Assessment

START DATE: Jan 88 **ESTIMATED COMPLETION DATE: Jun 89**

PRINCIPAL INVESTIGATOR: LTC Rita Hadersbeck

DEPARTMENT: Nsg **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: Ms. Cheryl Aldridge, MN, RN; Ms. Carin McCoy, RN

KEY WORDS: Community health needs

Study Objective: A Community Health Needs Assessment will be utilized to assess the knowledge, attitudes, and beliefs regarding several health related subjects of a sample of the military community that uses Ft. Bliss and WBAMC Services. Future health promotion programs will be developed based in results of the survey.

Technical Approach: Surveys will be sent to a random sample of each military beneficiary group represented in the community. Demographic information plus questions addressing attitudes, knowledge, and beliefs will be used in the survey. Participants will be asked to return the surveys in the self-addressed, stamped envelopes that will be provided. Surveys will be sent to approximately 10,000 individuals (10% of the military community) of all ages and will include Department of the Army Civilians (DAC), military (active duty and retired), and dependents. The University of Texas at El Paso (UTEP), College of Nursing and Allied Health, has designed the questionnaire and will analyze the results.

Progress: Interim report on individuals was received and was used to help develop the DAC Fitness Program. Final reports for adults (1977) and children under 11 (89) were received June 1989. Results will be used to help develop specific health promotion programs. An additional correlational analysis is being requested. Publications are in progress and requests to present parts of data at OTSG Fitness Facilitators Conference in San Antonio, Texas in September 1989, and the Fifth Annual Conference on Military Medicine, Bethesda, Maryland in October 1989.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/57 STATUS: Terminated

TITLE: Differences in Prenatal and Postpartum Anxiety Levels Due to Childbirth Preparation

START DATE: Jun 89 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: DAC Adela Hernandez

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: This study has been discontinued as a result of lack of subjects.
Susan G. Ferree, RN

KEY WORDS: Anxiety, Prenatal, Postpartum

Study Objective: To show that women who attend childbirth preparation classes have a lower anxiety level than those who do not.

Technical Approach: A convenience sample of 20 subjects will be utilized upon their consent to participate in the study. The sample population to be assessed will meet the following criteria: All English-speaking primiparous women the ages of 18 through 35 years who have had an uncomplicated pregnancy as determined by the medical records. Those mothers who have not attended, as well as those who have attended childbirth preparation classes are to be included. Those potential participants who have attended the childbirth preparation classes taught by the investigator will be eliminated. Subject recruitment will take place in the obstetric clinic. Those women who are between 37 and 40 weeks gestation will be invited to participate. The number of subjects anticipated for the study within each group will be limited to 10, however, 15 participants per group will try to be recruited. The exceptions will include those who had a delivery by Cesarean Section, infant admission to the NICU, and those who decide they no longer wish to participate.

The mothers will be approached during a routine clinic visit by the investigator. A description of the study will be provided to the potential subjects. After their verbal agreement to participate in the study is obtained, they will then have the opportunity to sign the written consent and complete the Trait Anxiety Inventory (Form Y-2), the first State Anxiety Inventory (Form Y-1) as well as the demographic sheet. A manual blood pressure reading will then be taken by the investigator using the mother's non-dominant arm which she is in a seated position. Provisions will be made at that time for a visit by the investigator for the completion of the second State Anxiety Inventory (Form Y-1) as well as the information on the measurements of blood pressure in the first 24-48 hours after delivery.

Progress: Primiparous mothers who were experiencing an uncomplicated pregnancy were approached as potential subjects for this study. Those who agreed to participate were then asked to complete the State Trait Anxiety Inventory Forms Y-1 and Y-2, a demongraphic sheet, and to have their blood pressures taken by the investigator. Followup was made in the first 24-48 hours of the postpartum period for a repeat of the Strait Anxiety Inventory Form Y-1 and a repeat blood pressure. A total of 20 subjects were anticipated for the study. In the time alloted, only 1 subject completed the study.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 88/68** **STATUS: Terminated**

TITLE: Perceived Learning Needs and Quality of Life of Patients with Ventricular Arrhythmias

START DATE: Jul 1988 **ESTIMATED COMPLETION DATE: Jun 1989**

PRINCIPAL INVESTIGATOR: MAJ Diane Kessler

DEPARTMENT: Nsg **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: Ann E. Sossong, MSN Candidate

KEY WORDS: Arrhythmias, quality of life, knowledge

Study Objective:

1. To describe the learning needs of patients with ventricular arrhythmias.
2. To describe what the quality of life is for patients with ventricular arrhythmias.
3. To describe what the relationships are between patient's learning needs and their perceptions of quality of life.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Principal investigator PCS'd to Korea, leaving no data to be reported.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/33 STATUS: Terminated

TITLE: What Heart Valve Replacement Patients Know (and Don't Know) About Preventing Infective Endocarditis (IE)

START DATE: Apr 89 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: MAJ Diane L. Kessler

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Francis R. Grzejka, LTC, DC

KEY WORDS: Endocarditis

Study Objective: To determine what patients with heart valve replacements know about prevention of infective endocarditis (importance of oral hygiene, frequency of dental examinations, and requirements for antibiotic therapy before and after dental procedures).

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Principal investigator PCS'd to Korea, leaving no data to be reported.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/56 STATUS: Ongoing

TITLE: Follow-up Support for Breastfeeding Mothers: Mothers' Perceptions of and Outcome of the Breastfeeding Experience

START DATE: Jun 89 ESTIMATED COMPLETION DATE: Nov 89

PRINCIPAL INVESTIGATOR: LTC Marcia L. Kossman

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Elizabeth E. Cook, RN

KEY WORDS: Follow-up support, Breastfeeding mothers

Study Objective: The purpose of this study is to evaluate the effectiveness of extending nursing care for breastfeeding mothers past the post-partal discharge. This study will determine what, if any, differences occur over a three month period in the breastfeeding experience of mothers who receive follow-up support in addition to routine breastfeeding education, versus mothers who receive only routine breastfeeding education. The following questions will be addressed:

1. What, if any, relationship exists between the length of time mothers continue to breastfeed and the availability of follow-up support?
2. What, if any, relationship exists between the number and type of breastfeeding problems experienced and the availability of follow-up support?
3. What, if any, relationship exists between the ability of mothers to resolve breastfeeding problems and the availability of follow-up support?
4. What, if any, relationship exists between mother's feelings of satisfaction with the breastfeeding experience and the availability of follow-up care?

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: During June and July 1989, 22 mothers volunteered to participate in this study. All mothers have been contacted by phone at 1, 2, 4, 6, 8 and 12 weeks post-partum to identify difficulties/concerns with breastfeeding, and to establish whether the mother is still breastfeeding. The researcher has assisted mothers in the experimental group (11) in problem-solving, answering questions, and utilizing available resources which support her effort to successfully brestfeed. Follow-up calls will be completed in October.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/62 STATUS: Ongoing

TITLE: The Effects of Psychodrama, Large Groups and Small Groups, on Head Nurses' Burnout, Anxiety, and Work Satisfaction

START DATE: Jun 89 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: CPT B.J. Thomas

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Conrad Silvani, AN; CPT Danny Davison, AN; Mariva Barajas, DAC

KEY WORDS: Burnout, anxiety, work satisfaction

Study Objective: To empirically validate the use of the psychiatric techniques of using psychodrama, small group, and large group interventions by measuring the changes in burnout, anxiety, and work satisfaction.

Technical Approach: The subjects for this study will be the convenience sample of all the head nurses that attend the work shop "Stress and Burnout for Head Nurses".

Three instruments will be used in this study: The Tedium Measure, Spielberger's State-Trait Anxiety Self Evaluation Questionnaire, and Stamps-Piedmonte Index of Work Satisfaction.

Data will be collected using all three instruments at the beginning of the work shop after a brief welcome, introduction, and signing of the consent form. Demographic data will also be collected at this time. Only the Tedium Measure and STAI will be self-scored at this time. The results of these scores will be discussed in a large group atmosphere for the rest of the first hour.

The second hour will consist of psychodrama vignettes that all of the participants will have the opportunity to participate in using scripts that have been developed to portray typical difficulties on the nursing units. The scripts have been designed to demonstrate different leadership styles and attitudes that may be encountered on nursing units.

The third hour of the work shop will be small groups that will focus on the feelings and attitudes that the participants had when they were placed in the roles of the vignettes in positions other than the head nurse such as ward clerk, LPN, staff nurse, patient, etc.

The fourth hour will be a large group problem-solving discussion on how to improve attitudes, and decrease burnout and stressors by the inclusion of positive attitudes and conditions in the work place. All three of the instruments will then be re-administered at the end of the fourth hour.

Two weeks after the work shop each of the head nurses will again be administered each of the three instruments by the primary investigator.

The control group, which will consist of the head nurses that do not participate in the workshop , will be contacted on an individual basis and be administered the three instruments after signing a consent form and filling in the demographic data. The second administration of the instruments will take place approximately four hours after the first administration. The third administration of the instruments will take place approximately two weeks after the first two. No intervention will take place between the administration of the instruments.

All data sheets will be coded to protect the privacy of the participant. Only the primary investigator will have a master list of participant names and codes that will be secured at all times.

Progress: The workshop was held and the measurement tools administered to the experimental group. Data is being collected on the control group at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/24 STATUS: Ongoing

TITLE: The Effect of Relaxation Therapy on Patients with Asthma

START DATE: Jan 87 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: RN Helen Villegas

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Raghava Charya, MC

KEY WORDS: Asthma

Study Objective: To measure the effects of relaxation therapy on asthma symptoms, frequency of prn medications, and emergency medical care.

Technical Approach: Fifty intrinsic asthma patients, 20-40 years of age, followed daily in the Allergy clinic, will be involved in participating in this pilot study for 6 weeks. History and biographical data will confirm the diagnosis of intrinsic asthma. Pulmonary function tests (PFT) will be measured on the first visit. PFT will also be recorded on the second and last visit. Patients will keep an asthma diary which will document daily peak expiratory flow rate, asthma symptoms, assessment of mood and use of prn medications and medical care. After 3 weeks, subjects will return to the Allergy Clinic with their completed diaries. Their PFT will be recorded. They will be instructed in the use of a relaxation tape to use each morning upon awakening and each night after retiring. This relaxation tape will include facial muscle exercises and positive thoughts and imaging. Medical news in the Journal of the Medical Association reported in 1983 that the imagination can be used to relieve asthma symptoms while Connors has concluded that tension changes in the facial musculature reliably influences the PEFR. The patient will be given a new asthma diary to record the next 3 weeks. The hypothesis is that the relaxation therapy component of the patient's multifactorial therapy will improved asthma symptoms and decrease medication intake and the need for emergency medical care.

Progress: Nine subjects were enrolled in the study in January 1989. Due to an unusually severe pollen season in the spring, the principal investigator decided the balance of patients and control group would be recruited in September 1989.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/10 STATUS: Completed

TITLE: Areas of Job Satisfaction and Dissatisfaction for Army Nurse Corps Officers at William Beaumont Army Medical Center

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: MAJ Cindy L. Wesso

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Job satisfaction, Army Nurse Corps Officers

Study Objective: The purpose of this study is to identify organizational activities with the Department of Nursing at WBAMC which are satisfying and dissatisfying to Army Nurse Corps Officers.

Technical Approach: The sample will be a convenience sample identified from the WBAMC rating scheme. This ample represents all ranks, clinical specialties, service agreement and time in active federal service.

The tool is a self designed questionnaire drawn from literature, experience and the conceptual framework discussed. There are serial sections, the first being an introduction to the survey and biographical data. The second section is a 35 item factor response on a 7 point scale with 1 (highly satisfied) to 7 (highly dissatisfied) in the same format used by Robert C. Preziosi. The final section is comprised of open-ended questions in which subjects are encouraged to offer comments and suggestions.

There is no preestablished reliability. Content validity was established by a panel of Army Nurse Corps Officers representing different ranks, clinical specialties and service agreement. The survey tool was critiqued by several tool construction experts.

The survey will be distributed to each ANC Officer identified on the rating scheme. A self-addressed stamped envelope will be provided and participants will be encouraged to complete the survey within two days. One week after initial distribution of the survey, each participant will receive a note card reminder encouraging them to return the survey if they have not already done so or thanking them if they have.

Progress: The purpose of this study was to identify organizational activities at William Beaumont Army Medical Center which are satisfying and dissatisfying to Army Nurse Corps Officers. A convenience sample of 118 male and female officers representing all ranks, job positions, and service agreement was received. The research tool was a self-designed satisfaction questionnaire based on the conceptual framework of Wiesbord's Six-Box Organizational Model and Robert C. Preziosi's Organizational Diagnosis Questionnaire. Statistical procedures used for data analysis included descriptive statistics, oneway analysis of variance, and Pearson Product-Moment correlations. The research hypothesis; significant correlation exists between the number of years active federal service and job satisfaction at WBAMC and personal satisfaction varies with rank, duty position, and service agreement was supported. Low satisfaction levels were seen in ANC officers with less time in service. Staff nurses, lieutenants, and those fulfilling their initial service commitment were most dissatisfied. Salary, patient/staff ratio management, rotating shifts, and lack of shift and overtime compensation, and the reward system were dissatisfying in all groups. The most commonly cited satisfiers were patriotism, professionalism, and autonomy. Seggestions offered for improving recruitment and retention were increase salary, decrease or eliminate rotating shifts, and improve management.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/39 STATUS: Completed

TITLE: Biorhythms and Deaths from Heart Disease Among Hospitalized Patients

START DATE: May 89 ESTIMATED COMPLETION DATE: --

PRINCIPAL INVESTIGATOR: MAJ Carolyn R. Wier

DEPARTMENT: Nsg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Irvin L. Brown, BSN, RN, CNA

KEY WORDS: Birohythms

Study Objective: The purpose of this pilot study is: 1) Study the relationships of biorhythms and deaths from heart disease among hospitalized patients, and b) to analyze any relationships found for possible nursing intervention.

Technical Approach: The sample for this study will be male or female patients with heart disease between the ages of 25 and 75 who have expired in a hospital. A sample size of 30 patients is desired.

The data gathered for this study will be based on retrospective mortality data from patients' medical records in a southwest community. The patients' confidentiality will be protected by the researcher. The only data taken from the patient's medical records will be: (a) date of admission, (b) date of birth, (c) date of death, and (d) time of death. This data will be gathered from a local hospital by obtaining permission through the appropriate administrative channels and medical records.

The tool used for determining biorhythmical critical days will be a computer software program which calculates a patient's biorhythm (Public Brand Software). The information needed for this process are the patients' date of birth and date of death. Once this information is calculated, the critical days can be compared with the patient date of death.

Progress: To determine whether an association exists between deaths among hospitalized patients with heart disease and a critical day of their biorhythm. The sample for the study consisted of 60 hospitalized patients' who died from heart disease. The data was gathered from the patients' medical records. A computer software program was utilized to calculate the patients' biorhythms. The researcher analyzed the data by comparing the patients' date of death with his critical day. The findings of this pilot study did not identify a significant number of deaths occurring on a patients' critical day. Only 9 (14.9%) of the subjects died on a critical. However, there was some suggestive association between deaths and critical days when one considers deaths one day before or one day after the critical day (32 [53.2%] of the patients died in this category). If these two categories are combined, a total of 41 (68.1%) of the subjects died on a critical day or one day before or after a critical day. further studies need to be designed to explore the relationship between biorhythms and death in order to develop nursing interventions pertinent to the findings.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/87 STATUS: Completed

TITLE: The Male Dysplasia Clinic: Clinical, Colposcopic, and Histologic Findings in the Partners of Patients with Evidence of Human Papilloma Virus on Papanicolaou Smear (Monitor: MAJ Andrew Robertson)

START DATE: Nov 88 ESTIMATED COMPLETION DATE: Mar 89

PRINCIPAL INVESTIGATOR: CPT Rebecca C. Cavazos

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Jay Carlson, CPT, MC; Pamela S. Hill, MAJ, MC

KEY WORDS: Male dysplasia, Human Papillomavirus

Study Objective: Assess the colposcopic, histologic, and clinical features of the male partners of patients identified as having evidence of human papilloma virus (HPV) on pap smear, and evaluate their response to therapeutic intervention.

Technical Approach: Male partners of dysplasia patients identified as having evidence of human papilloma virus on pap smear are now being referred to the Male Dysplasia Clinic. All male partners who desire evaluation presently undergo colposcopy of the genital area using a 3% acetic acid solution and document any abnormal areas. Biopsy of appropriate acetowhite lesions are done using both topical and infiltration local anesthetics.
Specimens for cytologic examination are obtained using a Q-tip and a cytobrush placed in the distal urethra. Urethral chlamydia cultures are obtained using standard chlamydiazyme assays for male patients.
Patients will be followed longitudinally and treated for any positive findings with standard treatment regimens. All patients will be included in the study group after informed consent for collection of data has been obtained. Patients will be excluded if they do not desire their data be used in a study project. Evaluation, diagnosis, and treatment will not be altered by participation or non-participation.
The study will be ongoing with no set number of patients entered, but will be reviewed on a 3 month basis to correlate the following data:

1. Incidence of condyloma in the male partners of patients with evidence of HPV on Pap smear.
2. Colposcopic findings of same patients.
3. Correlation of colposcopic findings with histologic diagnosis.
4. Cytologic findings with regards to sensitivity and specificity of Q-tip and cytobrush in diagnosing HPV.
5. Incidence of associated chlamydia infections in patients with evidence of HPV.

Progress: The male partners of 62 women with evidence of Human Papilloma Virus (HPV) infections were evaluated by colposcopy, histology, and urethral cytology. Forty-three men (69%) had gross or colposcopically detected HPV lesions. Eighteen men (29%) had abnormal urethral cytology, two of which were dysplastic. In three cases (5%), the only evidence of HPV infection was found on urethral cytology. These findings suggest that the male urethra may be a reservoir for the virus. Emphasis should be placed on the evaluation of the male in an attempt to reduce the viral reservoir from which condyloma and dysplasia may arise in their partners.

Out of the sixty-two patients entered into the study, there was one reportable complication when an active duty male had a biopsy taken, had a syncopal episode (vasovagal) which cumulated in a 24-hour admission for admission.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/46 STATUS: Ongoing

TITLE: The Effect of Intraperitoneal Administration of Tissue Plasminogen Activator on Adhesion Formation in a New Zealand Rabbit Model

START DATE: Aug 89 ESTIMATED COMPLETION DATE: Mar 90

PRINCIPAL INVESTIGATOR: CPT Dan Gehlbach

DEPARTMENT: OB/GYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MC

KEY WORDS: Adhesions, Tissue plasminogen activator

Study Objective: To investigate whether the intraperitoneal administration of tissue plasminogen activator can prevent adhesion formation following an abdominal operation for lysis of pelvic adhesions.

Technical Approach: 60 New Zealand white rabbits will be randomly assigned to 4 treatment groups. All animals will undergo laparotomy and standardized peritoneal injury to induce adhesion formation. Three weeks later the rabbits will undergo a second laparotomy with lysis of adhesions, using the operating microscope and microsurgical technique, with intraperitoneal adjunctive treatment as follows: Group 1 will serve as controls with no further treatment; Group 2 will have 20 ml of 2% sodium carboxymethylcellulose added; Group 3 will have 20 mg rt-PA combined with 20 ml 2% sodium carboxymethylcellulose added; and Group 4 will have 20 ml of 32% dextran 70 added. All animals will have a hematocrit drawn intraoperatively and one day after surgery. Three weeks later the animals, blinded to the surgeons, will be sacrificed and undergo adhesion scoring individually by each author, using two separate scoring systems. system 1: the summation of adhesion location (0 = no adhesions, 1 = adhesions on 25% of traumatized area, 2 = adhesions on 50% of traumatized area, and 3 = total adhesion involvement) and tenacity (0 = no resistance to separation, 0.5 = some resistance required, and 1 = sharp dissection required), with range 0-4. system 2: 0 = no adhesions; 1 = localized, filmy adhesions; 2 = localized, dense adhesions; 3 = widespread, filmy adhesions; and 4 = widespread, dense adhesions.

Progress: One group of 10 rabbits has completed the first abdominal operation to create adhesions and will undergo their second procedure in the next 1-2 weeks.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/08 STATUS: Ongoing

TITLE: OBGYN Bowel Training Utilizing the Pig Model

START DATE: Jul 86 ESTIMATED COMPLETION DATE: Open-ended

PRINCIPAL INVESTIGATOR: CPT Pamela S. Hill

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Carla Hawley-Bowland, MC

KEY WORDS: OBGYN Training

Study Objective: This training is designed to teach physicians the basic knowledge and operative skills required to perform basic small and large bowel surgery.

Technical Approach: Through a midline incision in the abdomen, the abdominal cavity will be opened and explored. Small bowel lacerations and anastomosis procedures will be performed as outlined in the surgical texts. Procedures will be performed every 3 weeks and at the time of the third procedure, a colostomy procedure will be performed as outlined in texts.

Progress: Bowel training utilizing the pig model continues to be a valuable asset in the training of OB/GYN residents. GYN pathology often involves the GI tract, and it is advantageous to have prior training before being confronted with an actual bowel injury. It also trains the gynecologist for his war time role.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/33 STATUS: Ongoing

TITLE: OB/GYN Microsurgical Tubal Re-Anastomosis Training Utilizing A Rabbit Model

START DATE: Mar 86 ESTIMATED COMPLETION DATE: Open-ended

PRINCIPAL INVESTIGATOR: MAJ Pamela S. Hill

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MC

KEY WORDS: Tubal Re-anastomosis

Study Objective: To teach resident physicians the basic knowledge and operative skills required to perform microscopic tubal surgery.

Technical Approach: This laboratory exercise will concentrate on developing the surgeon's confidence in utilizing the operating microscope and microsurgical instruments as well as planning and accomplishing the operative procedures.

Progress: OB/GYN microsurgical tubal reanastomosis training utilizing a rabbit model continues to be a valuable asset to our OB/GYN residency training program. Our residents only get three months of infertility surgery during their PGY 4 year. The rabbit model allows mastering of technique before their exposure to human patients and, thus, allows maximal utilization of their limited time on the Infertility Service.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/64 STATUS: On-going

TITLE: Genitourinary Tract Surgery Training Utilizing a Pig Model and Comparing Stenting Technique

START DATE: Aug 86 ESTIMATED COMPLETION DATE: Open-ended

PRINCIPAL INVESTIGATOR: MAJ Pamela S. Hill

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: -

KEY WORDS: Surgical Training

Study Objective: The training is designed to teach resident physicians the basic knowledge and operative skills required to perform genitourinary surgery while simultaneously evaluating the need for ureteral stenting following the operative procedures.

Technical Approach: This laboratory exercise will concentrate on developing the surgeon's confidence in recognizing genitourinary injuries and repairing ureteric or urinary bladder injuries, as well as increasing surgical acumen in handling the GU tract during standard gynecologic procedures.

Progress: Genitourinary tract surgery utilizing the pig model continues to be a valuable asset in the training of OB/GYN residents. GYN pathology frequently involves or impinges upon the genitourinary tract and prior animal training is advantageous before encountering an actual injury. It also trains the gynecologist for his war time role.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/24 STATUS: Ongoing

TITLE: An Evaluation of Core Temperatures Using the CORTEMP Ingestible Telemetry Monitoring System (ITMS) in Pregnant Patients Undergoing Physical Training

START DATE: Sep 89 ESTIMATED COMPLETION DATE: Feb 90

PRINCIPAL INVESTIGATOR: LTC Kevin C. Kiley

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Larry L. Morgenstern, Chief, Dept of OB-GYN, WBAMC

KEY WORDS: Cortemp, Pregnancy, Exercise

Study Objective: To evaluate core body temperatures in pregnant women during exercise by use of the ingestible CORTEMP system (ITMS).

Technical Approach: Over a six month period women volunteers 18 years of age and older in three groups will be asked to participate in the study.

a. PHASE I: Female soldiers, preferably in the same unit, who are not pregnant will be interviewed and examined after volunteering. They will then be instructed on the use of the CORTEMP. These non-pregnant women soldiers will participate in their unit's designated routine physical training program. Data on their core temperatures will be correlated with their specific PT (i.e. running vs calisthenics) and weather conditions. I anticipate 10-15 soldiers participating.

b. PHASE II: Female soldiers recently diagnosed as pregnant through the Department of OB-GYN, WBAMC will be asked to volunteer for the CORTEMP study if they are cleared to continue unit PT or are transferred into the low impact aerobic class at Ft Bliss. I anticipate 5-10 soldiers participating. Similar instruction, observations and data recording will be performed.

c. PHASE III: Dependent wives cared for by the Department of OB-GYN who are participating in the low impact aerobics program at Ft Bliss will be asked to participate in the study. Women at all gestational ages will be included to document possible differences by gestational age. I anticipate 10-15 women participating in this group.

The primary investigator will supervise all phases or the study to include counselling and observation or PT and low impact aerobics.

Progress: Awaiting arrival of equipment necessary to begin project.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/23 STATUS: Ongoing

TITLE: An Evaluation of the Hollister Female Urinary Incontinence Systems (FUIS) for Women Soldiers in a Field Environment

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Mar 90

PRINCIPAL INVESTIGATOR: LTC Kevin C. Kiley

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Larry L. Morgenstern, Chief, OB-GYN

KEY WORDS: Female urinary device

Study Objective: To evaluate the possibility of extended continuous use of the Female Urinary Incontinence System (FUIS) to assist women soldiers in voiding under field and combat conditions.

Technical Approach: Over a three to six month period, selected volunteer units at Ft. Bliss will be offered inclusion in the study. After counselling and a complete gynecologic examination by the principle investigator, the volunteer soldiers will be instructed on wear and care of the system and then will wear the device under field conditions of up to 14 days. After completion of the field training exercise the volunteers will again undergo an examination and will fill out a questionnaire. These soldiers will be 18 years or older. I expect a total of approximately 25 soldiers to participate.

Exclusion criteria include soldiers who have/are:

1) Active urinary tract disease under treatment.
2) Active gynecologic disease processes (to include "staph" cultures).
3) Anatomic abnormalities (imperforate hymen, double vagina)
4) Pregnancy
5) Active menses

Data to be collected on the soldiers includes:

1) Age, gravidity, parity, race, birth control history
2) Prior obstetric or gynecologic disease
3) Results of a gynecologic exam
4) Pre and post use cultures of urine, and cervix
5) MOS, duty description
6) Level of physical exertion during the FTT.

Progress: This project is awaiting R&D funding.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/13 STATUS: Ongoing

TITLE: Accuracy of Transvaginal Ultrasound in the Diagnosis of Ectopic Pregnancy

START DATE: Jan 88 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: CPT Vincent Lyons

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew W. Robertson; MAJ George G. SanMiguel; CPT Philip, CPT Vincent Lyons; LTC Marcia Kossman; LTC James Brown

KEY WORDS: Ectopic pregnancy, transvaginal ultrasonography

Study Objective: To compare the predictive accuracy of transvaginal sonography to transabdominal sonography in the diagnostic evaluation of patients with suspected ectopic pregnancies.

Technical Approach: One hundred unselected stable patients undergoing diagnostic work-up for a suspected ectopic pregnancy will be recruited to voluntarily participate in the study. Once enlisted in the study, they will receive a transvaginal sonogram utilizing a technique described by Brown, et al. in the antepartum diagnostic center. All transvaginal sonography will be performed by the attending or resident staff using an ultramark four ultrasound machine. A 3.5 MHZ end fire sector transducer covered with an aquasonic gel filled glove will be used. The information obtained will be retained in the ADC and blinded to the physicians who will then perform the standard diagnostic work-up. Once the patient's care is completed, her hospital chart will be reviewed for the information listed on the attached data collection record.

A Fisher extract test with a P of .05 will be used to compare the accuracy of the T/V to the T/A technique for predicting the presence or absence of an ectopic pregnancy.

Progress: To date 30 patients have entered this project. 75-100 more patients will be needed to complete this study.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/19 STATUS: Ongoing

TITLE: The Effect of Ultrasound Training on the Ability of Obstetric Residents to Accurately Predict Fetal Weight

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: CPT Thomas E. Page

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:
CPT Dan Gehlbach, MC; MAJ Andrew Robertson, MC

KEY WORDS: Fetal weight; Ultrasound

Study Objective: To assess the accuracy in predicting fetal weight by the residents during their rotation in the Antepartum Diagnostic Center, by comparing actual birth weights to those predicted by ultrasound within a week of delivery.

Technical Approach: The Antepartum Diagnostic Center records will be reviewed from the past 18 months and those ultrasounds which were performed within one week of delivery will be identified. The patient identification and ultrasound measurements will be entered into a database file, and the percent absolute error in predicted birth weight will be recorded. The data will be stratified according to the resident performing the ultrasound and broken down by week of the rotation. We anticipate approximately 400 deliveries will meet our criteria of delivering within one week of their last ultrasound. The accuracy of the resident's ultrasounds will be compared to those done by the staff perinatologist during the same time period.

Progress: To date, approximately 150 subjects have been enrolled. The study is half completed; the data has not been grouped and no preliminary conclusions have been made.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/65 STATUS: Completed

TITLE: The Antepartum Diagnostic Center (ADA): Its Development and Implementation

START DATE: Jul 87 ESTIMATED COMPLETION DATE: Sep 89

PRINCIPAL INVESTIGATOR: MAJ Andrew W. Robertson

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT J. Vincent Lyons; COL L.L. Morgenstern; Franz Theard, M.D.

KEY WORDS: Antepartum testing/counselling

Study Objective: The specific objectives are to see if all fetal well-being assessment can be performed in one area by a centralized staff and to evaluate various testing schemata specifically to see if one is superior. This concept will be utilized to compare various accepted plans of management to see which is best for the high-risk obstetrical population at this institution.

Technical Approach: Upon entry into the obstetrical population, patients will be screened for risk factors in a routine fashion. Accordingly, they will be programmed to receive routine prenatal care, if considered low risk or complicated obstetrical care if listed as high risk. At any time during pregnancy, any patient who develops high risk factors will be transferred to complicated obstetrics and begin testing.

For the purpose of this study, all high risk patients followed in the Complicated Obstetrics Clinic will be placed in the study. They will be counselled by attending or resident staff in the Department of Obstetrics and Gynecology. Counselling will include indication for placement into Complicated Obstetrics Clinic and that testing is to be performed in the Antepartum Diagnostic Clinic as a one-day admission. After counselling, patients will be referred to the ADC where appropriate testing will be scheduled by the ADC staff. Results will be given directly to patients by ADC staff and any additional testing will be scheduled by ADC staff. All results will be in the patient's chart and a convenience file in the ADC. When indicated, management recommendations will be given by the ADC staff. The ADC staff will consist of a perinatologist, PGY3 or PGY4 OB-GYN resident, a LVN and a 91A. All activities of the ADC will be under the direct supervision of the perinatologist. The potential benefit which may accrue is a more rapid and comprehensive evaluation which may decrease the delay in timely management decisions; therefore, decreasing neonatal morbidity and possibly mortality.

Progress: This study was designed to evaluate the effectiveness of a centralized hospital area devoted to antenatal diagnosis and fetal well-being testing.
Procedures performed in this center included Level I and Level II ultrasounds, non-stress tests, contraction stress tests, tocodynamometry, amniocentesis, genetic counselling, and general pregnancy information. During the study period, improved patient compliance, improved patient flow, improved access to diagnostic procedures was documented. Resident training in counselling, performance of ultrasound examinations, amniocentesis, NSTs and CSTs was greatly enhanced.
Physician and nursing personnel, both in the OB/GYN Clinic and Labor and Delivery unit were allowed to do their primary jobs without interruption. We feel that this unit greatly improved our ability to provide appropriate care to our obstetric patients and provide appropriate training opportunities for a resident staff.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/42 STATUS: Completed

TITLE: An Evaluation of Daily and Intermittent Uterine Contraction Monitoring in Identifying Obstetric Patients with Preterm Labor

START DATE: Jul 88 ESTIMATED COMPLETION DATE: May 89

PRINCIPAL INVESTIGATOR: MAJ Andrew W. Robertson

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Janet Lyons, MC

KEY WORDS: Preterm labor, Contraction monitoring

Study Objective: To evaluate the ability of daily or intermittent uterine contraction monitoring in assisting in the early diagnosis and treatment of patients with preterm labor.

Technical Approach: Over a 6 month period, those obstetric patients between 24 and 36 weeks gestation who have risk factors for preterm birth or who have been diagnosed as having preterm labor will be evaluated for entry into the study. Lists of inclusion and exclusion criteria will be as follows:

Patients will be evaluated initially in the ADC (Antepartum Diagnostic Center) for inclusion in the study. Informed written consent will be obtained before entry into the study.

The study will consist of 2 groups. Thirty patients will then be selected based on their indications for inclusion and followed with daily home monitoring by Healthdyne Perinatal Services. The remainder of the study patients (estimated 120 patients) will be followed in the ADC on a once or twice weekly basis depending on their indication for entry into the study.

All other laboratory and routine obstetric visits will be conducted in the ADC by the resident staff assigned to that area. Any therapeutic decisions will be carried out by one of the principal investigators or the physician on call based on the available data.

Data to be collected on each patient entered into the study include the following: Age, gravidity, parity, race; prior obstetric history; dating criteria - first examination, fetal heart tones heard with doppler and fetoscope, detailed ultrasound examination; indication for entry into the study; physical examination (with special attention to cervical exam); length of time in the study; time from diagnosis of preterm labor to delivery; indication for tocolytic therapy and/or delivery; neonatal statistics to include length of stay, birth weight, and need for specialized care.

Retrospective data will be obtained for a similar period (i.e., 6 months) from FY87 at WBAMC. NOTE: Contraction monitoring was not routinely used during this period of time.

A cohort to the 30 Healthdyne patients will be obtained for the ADC group. Analysis of these 2 groups will be done to compare the effectiveness of the monitoring techniques. As a whole, these 2 groups will be compared to the unmonitored period in FY87 with particular attention placed on perinatal morbidity/mortality and cost-effectiveness of monitoring.

Progress: Sixty-two patients were entered into this study in two assigned groups to determine if increased monitoring of patients who were at risk for preterm delivery was beneficial and/or cost-effective.

The combined services had an improved outcome (neonatal) and saved our institution approximately $162,000 in operating costs in the NICU and antepartum ward compared to a similar period in fiscal year 1987.

This paper is being presented to the Armed Forces District Meeting for the American College of Obstetricians and Gynecologists in November 1989.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 84/76 STATUS: Ongoing

TITLE: Improved Pregnancy Rates After Using Oil-Soluble Contrast Media (OSCM) for Hysterosalpingography (HSG)

START DATE: Dec 84 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Cesar Rosa

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: HSG, Pregnancy Rates, Contrast Media

Study Objective: To determine whether OSCM used for HSG improves pregnancy rates in patients with patent fallopian tubes and no other major cause for infertility.

Technical Approach: Patients from the Gynecology Infertility Clinic will be invited to participate. After a complete initial evaluation which includes history, physical exam, semen analysis, documentation of adequate ovulatory function by BBT and serum progesterone, and postcoital test; patients will be scheduled for HSG to evaluate tubal patency as is routine in the evaluation of these infertility cases. All HSGs will be done using water soluble contrast media (WSCM) in order to establish tubal patency and to evaluate presence or absence of rugal marks. Those individuals with a normal study as evidenced by unilateral or bilateral spillage, without evidence of distal obstruction in either tube, will then be randomized to receive 5 ml of OSCM injected through the HSG cannula or no OSCM at all. For this purpose a table of random numbers will be used assigning each group to odd or even numbers. No effort will be made to blind the study as far as the follow-up will be similar in both groups and the measured parameter will be an objective, all or none end result "pregnancy. Patients with normal studies will be followed expectantly for a minimum of four menstrual cycles during which they will be encouraged to maintain BBT charts and to time intercourse with ovulation. After this period of time, those patients with persistent infertility will be progressed through their infertility evaluation as otherwise indicated. Participation in this study will not change in any way the couple Fs infertility evaluation. The proposed waiting period after a HSG is presently the norm after any normal study; so no unnecessary or extra delay is being introduced into these patient Fs evaluation. The HSG will be performed by residents from the Dept Obstetrics and Gynecology, under the direct supervision of one of the principal investigators, as is the norm for all HSGs performed presently. Generally, whether OSCM or WSCM are used for HSG is a matter of personal choice by the operator. Both contrast media to be used WSCM (Renografin-Squidd Pharmaceuticals, Princeton NJ) and OSCM (Ethiodol-Savage Co, Missouri City, TX) have been in common use for a number of years and are accepted as safe. Patients allergic to iodine, seafood, or x-ray contrast material will be excluded from the study. Statistical Methods: Contingency tables, using chi-square analysis, comparing OSCM vs no OSCM; pregnancy rates in one group vs the other. The subjects to be considered will be healthy females in their reproductive years, attending the Gynecology Infertility Clinic due to involuntary infertility of more than one year duration. This group is heterogenous in terms of military status and age range 18-36. Facilities to be used will be the same fluoroscopy room in the x-ray department which presently is allotted to the Gynecology Department for HSGs one afternoon a week. The maximum number of studies per day will be six, as is the norm presently. We do not anticipate the use of any additional facilities or resources other than the one routinely used for HSGs.

Progress: During this year, only two patients have been added to this study. There has been no adverse reactions noted.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/30 STATUS: Completed

TITLE: Effectiveness of Historical Markers in Determining HBsAG (Hepatitis B Surface Antigen) Positivity in an Obstetrical Population

START DATE: Mar 88 ESTIMATED COMPLETION DATE: Dec 88

PRINCIPAL INVESTIGATOR: MAJ Cesar Rosa

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT C. Butterfield, MC; CPT M. Shockley, MC; MAJ G. San Miguel, MC

KEY WORDS: Hepatitis, pregnancy

Study Objective: To determine if the traditional historical markers associated with HBsAg carrier state are good predictors of HBsAg positivity in an obstetrical population.

Technical Approach:

a. Since the inception of the routine HBsAg screening on all patients and anticipating a retrospective evaluation on our population and its HBsAg positivity rate, the following system was implemented.

At the time of initial evaluation, the physician filled out a data sheet (see appendix A). To facilitate the correlation between historical risk factors and HBsAg results.

b. The variables to be evaluated will be:

- HBsAg: positive or negative

- Historical markers: present or absent

c. This study will be a review and evaluation of an established, routine procedure on all obstetrical patients. No controls or populations outside of the obstetric group will be reviewed. At this point, we are ready to start analysis on the patient group for the first year of this screening test, a population of approximately 2,000 patients.

d. Editorial and statistical support will be required from the Department of Clinical Investigation.

e. This review of the initial 2,000 patients will take approximately 3-4 months.

f. For statistical analysis, logistic regression analysis using a multivariable logistic model is planned.

Progress: A prospective study was performed to determine whether the CDC risk factors for hepatitis B (HB) are reliable predictors of the hepatitis B surface antigen (HBsAg) carrier state in an obstetrical population. At their initial obstetrical visit, 1466 consecutive patients had their serum screened for HBsAg using radioimmunoassay. During the initial interview the physician obtained information regarding the presence of any of the CDC risk factors for HB (ethnicity, or history of: veneral disease, blood transfusion, hepatitis exposure, hepatitis, drug abuse, or occupational exposure). Twelve patients were found to have a positive HBsAg, for a prevalence of 0.82%. Six of these 12 patients had risk factors. Five had ethnic background, and two of those five also had a history of hepatitis. One health care worker (nurse) was also positive for HBsAg. The other six patients had no recognized risk factors. If HBsAg had been evaluated according to the CDC risk factor guidelines, 50% of HBsAg-positive patients would not have been identified.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/47 STATUS: Ongoing

TITLE: Continuous Estrogen/Progesterone Replacement Therapy (Monitor: Dr. Svec)

START DATE: Nov 88 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: LTC Cesar Rosa

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT W.T. McGrail, Jr., MC; CPT Mitchell Silver, MC; CPT Rebecca Cavazos, MC; CPT M.D. Wood, MC; COL Ana Rodriguez, MC;

KEY WORDS: Estrogen, Progesteron, Hormone replacement

Study Objective: Assess the effect of the continuous administration of estrogen/progesterone as replacement therapy on the endometrium, bone, and lipid profile of postmenopausal women.

Technical Approach: In this study, we intent to offer continuous estrogen-progesterone replacement to suitable candidates. In so far as this is a relatively new method of estrogen administration, data will be obtained to evaluate the effect of this replacement regimen on bleeding patterns, endometrial stimulation, effect on bone mineral content, and effect on serum lipids.

In this study, no control group will be used. We understand that when given the possibility of not having a monthly bleeding episode, it would be extremely difficult to have the patients agree to submit themselves to randomization (cyclic vs continuous). In addition blinding such a study would be extremely difficult due to the almost certain withdrawal bleeds associated with cyclic therapy. Our goal is to accumulate data on the effects of this type of replacement.

Females presenting to the Gynecology Clinic with symptoms or evidence of estrogen deficiency (hot flashes, genital atrophy, premenopausal syndrome) will be offered inclusion in the study. Criteria for exclusion will be: undiagnosed abnormal uterine bleeding, estrogen dependent malignancies (endometrium or breast), and known pregnancy. Relative contraindications: uterine fibroids, previous thromboembolic disorders. The previous use of estrogens will not be considered a contraindication. Postmenopausal state will be documented with an elevated FSH (over 40 MIU/ML).

a. Conjugated estrogens (Premarin) 0.625mg and medroxyprogesterone acetate 2.5mg daily will be offered as standard replacement.

b. For those patients requiring a higher estrogen dose, conjugated estrogens 1.25mg, and medroxyprogesterone acetate 5mg will be offered. This will be evaluated according to patient's symptoms.

* 0.625mg of CE has been shown to be the minimal effective dose for protection against osteoporosis.

Progress: Only seven patients have been enrolled in this study. Of these, two have discontinued to protocol due to continued vaginal spotting. One subject never returned for follow-up, four continue on the study. Mainly because of the nature of the study, we have not had many participants joining the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/58 STATUS: Ongoing

TITLE: Gonadal Function After Vasectomy

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: LTC Cesar Rosa

DEPARTMENT: OB/GYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Neal Dunn, MC

KEY WORDS: Vasectomy

Study Objective: To evaluate whether there is any clinical or subclinical evidence of testicular function after vasectomy.

Technical Approach: Approximately 30 active duty males (or others) between the ages 25-40, having vasectomies performed by the Urology Service will be considered suitable candidates. There will be no blinding or randomization necessary. All subjects will receive the same tests. Each patient will serve as his own control. The following tests will be performed:

*Prior to vasectomy -

1. Blood for Testosterone, FSH, LH, PRL, Estradiol. Serum to be frozen for future reference.
2. GnRH test: After the above is collected at - 0 min; similar samples will be obtained at 15, 30, 45, 60, 90 and 120 min after injection of 100 mcg of LHRH (Factrel, Ayerst Labs, New York) at 0 minutes.
3. Serum for antisperm antibodies. To document the incidence of antisperm antibodies following vasectomy. There is evidence of an increased incidence of antisperm antibodies in the circulation after vasectomies.
4. A total of 110ml of blood will be obtained per session (at time of vasectomy, then 6 and 12 months afterwards).
5. Testicular ultrasound to objectively measure size of the testicles.
6. Physical examination (as usual prior to surgery) and testicular size determination with orchidometers (particular attention to testicular tenderness or granuloma formation).

*The same tests will be administered at 6 and 12 months after the vasectomy.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/08 STATUS: Ongoing

TITLE: Comparison of Two Endometrial Biopsy Instruments: Novak's Curette vs Pipelle (Monitor: MAJ Andrew Robertson)

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Jul 90

PRINCIPAL INVESTIGATOR: CPT M. Mitchell Silver

DEPARTMENT: OBGYN FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Philip Miles, M.D.; LTC Cesar Rosa, MC

KEY WORDS: Endometrial biopsy instruments

Study Objective: To assess the correlation between the Novak's curette and the Pipelle endometrial biopsy instrument, in terms of amount of tissue and ability to yield a histologic diagnosis. In addition, the relative degree of pain or discomfort associated with endometrial sampling utilizing each instrument will be assessed.

Technical Approach: Patients requiring endometrial sampling due to diverse conditions (postmenopausal bleeding, abnormal uterine bleeding, infertility evaluation, preoperative evaluation) will be invited to participate. No patients (18-60 years of age) will be excluded from the study.

The participants will be randomly divided into 2 groups. One group will have the endometrial biopsy with the Novak's instrument, followed by the procedure with the Pipelle. The second group will have the procedures in the reverse sequence. Whether each procedure has the 1st or 2nd sequence will be determined at random, utilizing a list of random numbers.

Those patients whose biopsies will be performed for evaluation of infertility, will have a single stroke lateral wall sampling, using each instrument on one side of the uterus. The common precautions to avoid inadvertent sampling of an early pregnancy will be observed, i.e., barrier contraceptions during the biopsy cycle, and a sensitive RIA pregnancy test the day prior to the biopsy.

Normally, only one biopsy method would be done. This project would entail a second biopsy procedure done to each patient.

All tissues will be submitted as two separate specimens to the Pathology Department. Patient management decisions will be based on the findings of either or both specimens. At the completion of the study, the histology slides will be coded and reassessed in a blinded, random fashion by one of the investigators (PM). The amount of tissue and its quality will be assessed. A diagnosis will be assigned to each specimen. At completion, the two specimens from the same patient will be compared. To facilitate the review of the slides, at the time of processing the tissues - 2 slides will be prepared from each specimen. One will go to the laboratory files, the other slide will be included in a "study file" for later review.

The two groups receiving the endometrial biopsies will be given a questionnaire immediately following the procedure. This questionnaire will rate the discomfort associated with the procedure and will ask which of the two procedures they would rather have.

Progress: This project is still ongoing and is about 60% completed. To date there has not been any adverse reactions. Due to the nature of the study, there are no preliminary results at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/83 STATUS: Ongoing

TITLE: Analysis of Hospital Bacterial Pathogens - Chromosomal and/or DNA Fingerprinting

START DATE: Oct 87 ESTIMATED COMPLETION DATE: Mar 90

PRINCIPAL INVESTIGATOR: CPT R.R. Gomez

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Michael Lieberman, MS; CPT David Smith, MS

KEY WORDS: Bacterial pathogen fingerprinting

Study Objective: Identification of bacterial strains by subjecting plasmid DNA or chromosomal DNA to restriction endonuclease digestion and then agar gel electrophoresis.

Technical Approach: Plasmid DNA fingerprinting. Methods for plasmid DNA fingerprinting have been described in the literature. A typical method involves isolation of plasmid DNA by lysis and centrifugation. The plasmid DNA is digested with restriction endonuclease. The resultant DNA fragments are analyzed by agarose gel electrophoresis and the pattern obtained from different isolates and compared. Electrophoresis patterns obtained will be compared by visual inspection; thus, statistical analysis is not required.

Progress: Ten different isolates of Pseudomonas aeruginosa with unique sensitivity/resistance patterns are currently under investigation. DNA has been extracted from these isolates and is currently being purified for planned electrophoretic analysis. In addition, a plasmid probe will be inserted once the DNA patterns have been evaluated. Most of this work is being accomplished with the help of Dr. Rick Williams, a medicine resident who has DNA isolation experience.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/72 STATUS: Terminated

TITLE: Susceptibility of Burned and Irradiated Mice to Lethal Infection with Pseudomonas aeruginosa and Protective Effect of Specific Immunotherapy

START DATE: Jul 87 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: MAJ Michael M. Lieberman

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Dennis A. Stewart, MS; MAJ K.O. O'Hair, VC

KEY WORDS: Pseudomonas aeruginosa, immunotherapy

Study Objective: Investigate the effects of infection with Pseudomonas aeruginosa in burned and irradiated mice and to determine if specific immunotherapy (active and/or passive immunization) can protect these traumatized mice (i.e., enhance their survival) subsequent to lethal infection.

Technical Approach: Four groups of 50 mice each are designated as follows: burned only, irradiated only, burned and irradiated, and nontraumatized controls. Pseudomonas aeruginosa strain 1244 is grown and prepared for mouse challenge. Appropriate dilutions of the challenge culture are prepared and administered by the intraperitoneal route or subcutaneously under the burn site subsequent to burning and/or irradiation as described in Protocol 86/48 (MAJ Stewart). Five dilutions of culture will be administered to groups of ten mice each within each group of 50 mice listed above. Mouse survival data will be tallied from each group and the culture dilution yielding 50% lethality calculated. The effect of individual or combined trauma on susceptibility to lethal infection can be determined by comparison of these 50% lethal doses (LD-50) dilutions obtained in each of the four experimental groups. Comparison of the lethality obtained without infection in such traumatized mice to that obtained above in traumatized and infected mice can be done using three additional groups of mice consisting of the individually or combined burned and irradiated, but not infected mice. Effect of active immunization on susceptibility to lethal infection with Pseudomonas aeruginosa in burned and irradiated mice. Ribosomal vaccine from Pseudomonas aeruginosa strain 1244 has previously been prepared and available. Mice are vaccinated and comparison between vaccinated, traumatized, and infected mice and nonvaccinated, traumatized and infected mice for susceptibility to lethal infection.

Progress: No progress on this protocol was made during the past year. One of the associate investigators who had developed the burned and irradiated mouse model was reassigned, and the principal investigator did not have sufficient time to continue this protocol (involving extensive animal work) on his own. Thus, this protocol was terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/90 STATUS: Ongoing

TITLE: Survey of Patients' Serum for Anti-Pseudomonas aeruginosa Ribosomal Antibodies

START DATE: Nov 87 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Michael M. Lieberman

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Pseudomonas aeruginosa ribosomal antibodies

Study Objective: Determine if patients with confirmed Pseudomonas aeruginosa infections have antibodies to ribosomes from these bacteria.

Technical Approach: Patients identified in the clinical microbiology laboratory with Pseudomonas aeruginosa infection will have bacteria isolated and serotyped using a commercially obtained kit. A blood specimen will be drawn from these patients at the time of identification and, if possible, at a later time. Antibodies to ribosomes in the patients' serum will be determined by an enzyme-linked immunosorbent assay that has previously been developed. Test serum ribosomal antibody titers are determined as the reciprocal of the highest serum dilution yielding a specified photometric absorbance. The procedure involves ultrasonic disruption of the bacterial cells and isolation and purification of the ribosomes by ammonium sulphate fractionation, differential ultracentrifugation, and molecular sieve chromatography. ELISA analyses on individual serum dilutions will be performed in triplicate and the mean values and standard deviations calculated. Differences greater than two standard deviations between test serum and control serum values at equivalent dilutions are considered significant.

Progress: No progress has been made on this protocol during the past year. It has proven difficult to obtain patients' blood specimens some time after identification of Pseudomonas aeruginosa isolates from other specimens of these patients. In the few cases where this was done, the isolates were of a different serotype than the serotypes from which ribosomal vaccine preparations are presently on hand. In those cases, new vaccine preparations would have to be made, which requires more time than is presently available to the investigator. However, attempts will continue to be made to obtain appropriate blood specimens for this protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/63 STATUS: Ongoing

TITLE: Analysis of Cellular Immunity Against Pseudomonas Aeruginosa Engendered by Immunization of Mice with Ribosomal Vaccine From P. Aeruginosa

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Michael M. Lieberman

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Dennis A. Stewart, MS; Bruce Veit, Ph.D;

KEY WORDS: Pseudomonas aeruginosa, ribosomal vaccine, cellular immunity

Study Objective: To determine if the cellular immunity (i.e., the adoptive transfer of protection with splenocytes from immune to non-immune mice) engendered by immunization of mice with ribosomal vaccines from P. aeruginosa is mediated by T lymphocytes or B lymphocytes.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: A technique for separation of murine spleen cells into fractions highly enriched for either T-lymphocytes or B-lymphocytes has been developed which is both effective and sufficiently convenient to use to be practical in a typical experiment. The effectiveness of the separation method was determined by both flow cytometric analysis and mitogenesis experiments. However, in vivo protection could not be demonstrated in these latter experiments, most likely due to a decreased virulence of the challenge strain of P. aeruginosa (after numerous in vitro passages), which necessitated challenging the mice with greatly increased numbers of bacteria in order to achieve the same number of lethal doses. (In earlier experiments in which spleen cells were not as well fractionated, the virulence of the challenge strain had been higher and protection of mice with unfractionated immune spleen cells was readily demonstrated.) Thus, the model used will have to be altered somewhat such that fewer challenge organisms can be used. This can be achieved by using mice rendered leukopenic by administration of cyclophosphamide as recipients for the immune spleen cells and the subsequent bacterial challenge.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/76 STATUS: Ongoing

TITLE: In vitro Studies of Bactericidal Activity Associated with Specific Antibody to Pseudomonas aeruginosa Ribosomal Vaccine and Bactericidal Protein(s) Extracted from Live P. aeruginosa

START DATE: Nov 88 ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: LTC Michael M. Lieberman

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Pseudomonas aeruginosa, Bactericidalal protein

Study Objective: (1) To determine the extent of bactericidal activity associated with specific antibodies directed against P. aeruginosa ribosomal vaccines. (2) To characterize the bactericidal "blocking" or inhibiting activities observed in specific antiserum to such vaccines. (3) To further characterize the nature and effects of bactericidal proteins extracted from live P. aeruginosa, and their interaction with bactericidal antibodies.

Technical Approach: In vitro bactericidal and opsonophagocytic assays. Murine antisera to ribosomal vaccines have been prepared previously and are vailable for use. The bactericidal and opsonophagocytic assays have been described in detail. Briefly, the assays involve mixing combinations of bacteria, antiserum (or IgG purified from antiserum by commerically available Protein A affinity chromatography or ion exchange chromatography methods), complement, and phagocytic cells (for opsonophagocytosis). (Phagocytes, i.e., polymorphonuclear leukocytes are prepared at the time of the experiment from a normal human volunteer.) After incubation of the mixtures, aliquots are spread on agar plates to determine the number of viable bacteria (colony forming units) remaining in the reaction mixtures. This number is compared with the initial inoculum in the mixture to determine the relative bactericidal or opsonic capability of the antiserum or IgG being tested.

"Blocking" activity is observed when the addition of more antiserum or purified IgG to a reaction mixture results in less (or no) bactericidal activity than is obtained without the additional antiserum or IgG. Thus, if experiments are performed in which bactericidal or opsonic activity is determined as a function of the concentration of antiserum or purified IgG, in some cases a "prozone" is obtained, i.e., maximal bactericidal activity is found at intermediate concentrations of antiserum or IgG, with significantly less activity at both higher and lower concentrations. Furthermore, it may be shown that IgG purified by one method from an antiserum which exhibits this "prozone" effect also demonstrates the same effect, whereas IgG purified by a different method from the same antiserum no longer exhibits a "prozone" at the same concentrations of IgG.

Interaction of protein extracts of P. aeruginosa with antiserum and purified IgG. Bactericidal and opsonic reaction mixtures will be set up including the proteinaceous, aqueous extracts in addition to antiserum or IgG. In these cases, the extract by itself has no bactericidal activity against the particular strain of P. aeruginosa used, and the antiserum or IgG by itself also demonstrates no such activity. However, when mixed together, bactericidal activity may appear.

Progress: A previous report showed that material with bactericidal activity in in vitro assays can be obtained by aqueous extraction of washed, live cells of some strains of P. aeruginosa. The material was active against some heterologous, but not homologous serotype strains of the same organism. This material, although prepared differently than published methods for extraction of pyocins, has been found to have some pyocin-like properties. The bactericidal activity is destroyed by pronase, analogous to the s-type pyocins. Growth of susceptible strains in iron-deficient minimal medium greatly increases the susceptibility to the bactericidal activity relative to growth in the same medium containing a high concentration of iron, also analogous to s-type pyocins. However, growth of nonsusceptible strains (strains of the homologous serotype as the strain from which the pyocin-like material was obtained) in iron-deficient medium does not render them susceptible to this activity. The addition of serotype-specific monoclonal antibodies (Lam, JS, et.al., Infec. Immun. 55: 1051-1057, 2854-2856, 1987) to the incubation mixtures containing the pyocin-like protein and susceptible bacteria does not inhibit the bactericidal activity, regardless of whether the antibodies are agglutinating (and LPS blotting) or non-agglutinating.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/90 STATUS: Ongoing

TITLE: Cystic Fibrosis: Antibodies to Mucoid and Non-Mucoid Pseudomonas aeruginosa

START DATE: Indefinite ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Michael M. Lieberman

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Robert Wittler, MC; Prof. Marvin Salin, Ph.D.

KEY WORDS: Cystic fibrosis, Pseudomonas aeruginosa

Study Objective: The objectives of this project are to determine the specificity of antibodies against mucoid and non-mucoid Pseudomonas aeruginosa in sera from cystic fibrosis patients and to localize their binding sites on the surface of the bacterium by direct visualization using immuno-gold electron microscopy.

Technical Approach: The bacteriology of sputum specimens from cystic fibrosis patients would be monitored as part of routine clinical procedures. Upon identification of (non-mucoid) P. aeruginosa in the sputum, a serum specimen would be obtained from the patient. Routine bacteriological monitoring would be continued until mucoid organisms are recovered. Subsequent to this conversion to a mucoid phenotype, another serum specimen would be taken. Preliminary ELISA analysis of both sera would be performed using the mucoid and non-mucoid organisms isolated from the patient (autologous strains) as well as a heterologous strain. Specificity of the antibodies will be determined by inhibition studies with purified antigens such as LPS, MEP, and OMP. Localization by immuno-electron microscopy will be performed (at Mississippi State University) using a commercially obtained anti-human IgG conjugated with colloidal gold in an indirect (sandwich) technique.

Extraction and purification of antigens, ELISA and immuno-electron microscopy will be performed by standard, published techniques and have all been utilized previously by either the investigator at WBAMC or the investigator at Mississippi State University.

Progress: This is a newly approved study with no results to date. Start date for the project is dependent upon funding from NIH.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/45 STATUS: Ongoing

TITLE: Comparison of Two Techniques of Estrogen Receptor Assay in Breast Cancer

START DATE: Nov 89 ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: CPT Ann R. Price

DEPARTMENT: Path FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Tu Huu Nguyen, MC; CPT Gordon Bell, MC; LTC Steven Arny, MC

KEY WORDS: Estrogen receptor assay, breast cancer

Study Objective: To confirm that the immunohistochemical assay is as reliable as the biochemical assay in determining estrogen receptor content in human breast cancer and to determine whether the immunohistochemical assay would be a more efficient method to perform at William Beaumont Army Medical Center than shipping specimens to another laboratory for biochemical assay.

Technical Approach: Phase I: Phase I will be a retrospective evaluation of the estrogen receptor content of the paraffin embedded tissue blocks of the 50 most recently diagnosed breast cancers at WBAMC. The paraffin imbedded tissue will be pre-processed with the Trypsin and Dnase and the immunohistochemical assay will be performed by a single technician. The slides will then be scored in a qualitative and semiquantitative manner as outlined by Cudahy, et.al., and Pertshuk, et.al. Tumors found to contain more than 10% estimated positive cancer cells will be considered estrogen receptor positive. An ocular grid on the microscope will aid in accurately assessing tumor cellularity. The semiquanitative evaluation will be calculated by estimating the intensity of the nuclear staining as 1+, 2+, or 3+ of 200 cells and then multiplying 1, 2, or 3 by the percentage of cells estimated at each intensity. This figure will then be adjusted by multiplication with the previously estimated cellularity values less than 5 will be "zero-trace", 5-18 will be "low-intermediate", and greater than 18 will be "high". The biochemical assay results are expressed in fentomoles (FMOL) of receptor per microgram of DNA. Tumors with values less than 0.10 FMOL will be considered "negative", 0.10-0.30 FMOL will be "low-intermediate", and greater that 0.30 FMOL will be "positive". The results of the two techniques will be compared to determine concordance. All statistical analyses will be performed by means of the chi-squared test.

Phase II: Phase II will be a prospective, blinded evaluation of the estrogen receptor content of breast carcinomas by two methods - the immunohistochemical technique using the Abbot Kit (ERICA) and the biochemical assay done by PathLab. Each breast biopsy specimen is received in the fresh state in the Pathology Department at WBAMC. Standard operating procedure will be followed and a frozen section will be performed if the specimen is grossly suspect for cancer. Once a diagnosis of cancer is made histologically, additional frozen sections will be cut for immunohistochemical processing for evaluation of estrogen receptors. If the specimen contains sufficient tissue for biochemical assay (at least one cubic centimeter of tumor), a specimen will be sent to PathLab for evaluation as per usual procedure. The remaining specimen will be processed as usual into paraffin embedded blocks for histochemical viewing. Additional sections will again be made for immunohistochemical evaluation also. One histochemical technician will process the special staining as is standard operation in the WBAMC Pathology Department. The slides processed on frozen and paraffin embedded tissue will be read by all pathologists in the department, depending upon the rotational schedule assigned. The evaluators of the slides will be blinded to the results from the PathLab assay. The frozen and paraffin embedded immunohistochemical slides will be evaluated on different days, thus allowing different evaluators to be blinded to the previous result. The results will be reported as previously outlined in phase I. results of the immunohistochemical assays on both fresh frozen and paraffin imbedded tissue will be compared to each other as well as to the results of the biochemical assay to determine concordance. The cost and time involved to obtain a report of the results will also be compared in order to determine the efficiency of the immunohistochemical assay. As stated previously, this study may eventually be expanded through screening of medical records to determine if the immunohistochemical assay is as effective in predicting the response to hormonal therapy as the biochemical assay since this is the ultimate goal of any estrogen receptor assay.

Progress: The project has been delayed due to nonreceipt of equipment and supplies. Project will begin up receipt of above mentioned.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/59 STATUS: Ongoing

TITLE: Yale Children's Inventory-Normative Data

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Jul 90

PRINCIPAL INVESTIGATOR: LTC A.W. Atkinson

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Yale Children's Inventory

Study Objective: To obtain a normative data for Yale Children's Inventory for Routine Use in the Developmental Pediatric Clinic.

Technical Approach: Subjects would be approximately 350 military dependent children between the ages of 5 to 18 years, presenting to School Physicals Clinic whose parent consents to completing the questionnaire. The 2 page, 33 item questionnaire will be given out with volunteer agreements as parents enter the clinic and collected as they exit the clinic. Data will be analyzed by descriptive statistics and by age and sex primarily. If total numbers allow, data will also be analyzed by ethnic grouping. A normative table will be developed for use in assessing the scores obtained on the Yale Children's Inventory for those patients referred to the Developmental Pediatrics Clinic for evaluation of school related problems.

Progress: LTC Atkinson has replaced CPT Nivea Alvarado as principal investigator. 400 subjects have completed quesitonnaires. The data is being collated at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/11 STATUS: Completed

TITLE: Teacher's Perceptions and Interventions in Children with Attention Deficits

START DATE: Oct 88 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: LTC A.W. Atkinson

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: ADD, Teacher's perceptions

Study Objective: Using a questionnaire format, quantify the parent's perception of the child's problems compared with those of the teacher.

Technical Approach: The teacher's questionnaire will be mailed to teachers of children that we are currently treating with stimulant medication for attention deficitgs. A return postcard with the teacher's code will also be enclosed for the teacher to mail separately upon returning the completed questionnaire. This will allow a follow-up mailing to no respondents. The parent's questionnaire will be completed at enrollment, and asked various demographic information, as well as DSM-III and DSM-III-R criteria.

The children will be in grades 1-5, in a classroom with only 1 main teacher (but may also have a resource teacher). Subjects will be enrolled at the time of routine follow-up clinic visits. To enlarge the scope of this study, data will also be obtained from the areas adjacent to Fitzimmons and Madigan Army Medical Centers. The teacher questionnaire has been staffed with the research departments in the El Paso and Ysleta school districts. Descriptive statistics will be used to analyze the data, and this support will be required from the Department of Clinical Investigation. Approximately 50 students will be utilized in the local area, and about 25 each from the Denver and Takoma areas. If greater numbers of students are required, then it may be necessary to extend the study to next year.

Progress: LTC Atkinson has replaced MAJ Charles Morton as principal investigator. 42 patients have been entered into this study, none have withdrawn and no adverse problems have been associated with this project.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/29 STATUS: Ongoing

TITLE: Ceftriaxone for Outpatient Management of Suspected Occult Bacteremia (Monitor: COL Popejoy)

START DATE: Apr 88 ESTIMATED COMPLETION DATE: Sep 90

PRINCIPAL INVESTIGATOR: CPT Valerie A. Bell

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Suzanne Cuda, M.D., Robert Goldbah, M.C.

KEY WORDS: Ceftriaxone, occult bacteremia, pediatrics

Study Objective: To compare the effectiveness of ceftriaxone versus augmentin in the treatment of children with a possible blood infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Total number of patients enrolled is 53. Of these, 5 have had positive Blood cultures. All positives grew strep pneumococcus. This is a multicenter study and is going well.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/91 STATUS: Ongoing

TITLE: Protocol for Determining the Prevalence of Drug Affected Babies in the Military Population

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Mar 89

PRINCIPAL INVESTIGATOR: CPT Valerie A. Bell

DEPARTMENT: Peds FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Howard Oaks, MC; CPT Anna Heisser, MC; CPT Bill McGrail, MC; MAJ Frank Galin, AN; CPT Gordon Bell, MC

KEY WORDS: Drugs, Babies, Military

Study Objective: To determine the prevalence of the use of illicit drugs during pregnancy in a military population.

Technical Approach: This study is to include all pregnant women who present in labor at WBAMC over a 4 month period or 400 patients, and the infants they deliver.

There will be 400 subjects. Two study groups; mothers and infants. A urine drug screen for marijuana, PCP, cocaine and heroin will be done on all subjects. The drug screen is an enzyme immunoassay. This is a test that is not normally done on these type patients. Urine will be collected from all mothers upon admission to labor and delivery, and frozen. All newborn's first void will be collected with a urine bag and frozen. Biweekly both sets of specimens will be sent to toxicology and assigned study identification numbers. The assay will then be performed.

Data will be collected weekly from the toxicology section of the laboratory and analyzed to determine the prevalence of positive drug screens in the mothers and the infants.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 89/15** **STATUS: Completed**

TITLE: A Comparison of Intraosseous Infusion with Standard Methods of Intravenous Infusion in the Porcine Model

START DATE: Feb 89 **ESTIMATED COMPLETION DATE: Jun 89**

PRINCIPAL INVESTIGATOR: CPT John F. Bilello

DEPARTMENT: Ped **FACILITY: William Beaumont Army Medical Center**

ASSOCIATED INVESTIGATORS: John Moore, LTC, MC

KEY WORDS: Intraosseous, Emergency, Therapeutics

Study Objective: To confirm that intraosseous delivery of emergency drugs is as effective as that of the central intravenous route, thus affording an effective alternative when rapid intravenous access is not possible.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Abstract and manuscript pending completion. The study was designed to confirm that intraosseous delivery of emergency drugs is as effective as that of the central intravenous route, thus affording an effective alternative when rapid intravenous access is not possible. there were no physiological differences noted between the intraosseous and the intravenous emergency drug administration groups. There was a significantly higher level of serum lidocaine at one minute post administration in the intravenous infusion group. Although there was a significant difference at this interval, both infusion routes demonstrated therapeutic concentrations by one minute post infusion.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/61 STATUS: Ongoing

TITLE: Neonate Emergency Procedure Training in the Rabbit Model

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Edwin Bollerup

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Emergency procedures, Pediatric training

Study Objective: To train physicians who have not been previously trained in emergency management of neonates, but who will be called upon to perform this function in the Neonatal Intensive Care Unit. the rabbit model will simulate human neonates.

Technical Approach: This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands-on attempts by the interns and residents. The housestaff will then rotate through practical skill stations to perform the assigned tasks. The skill stations and animal lab allow the student to observe and practice to proficiency those life-saving skills necessary in the management and stabilization of the neonatal patient. The animal lab will be held on two separate days with a staff neonatologist and staff veterinarian present on both days.

Progress: This protocol exists to cover for our use of animal models in annual training for new housestaff and refresher experience for residents and medical staff members. This animal model and protocol continues to provide invaluable hands on training for invasive procedures used during housestaff training in pediatrics and neonatology.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/65 STATUS: Ongoing

TITLE: Pediatric Intubation Training Utilizing the Feline Model

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Edwin Bollerup

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Lynn Whittington, MC

KEY WORDS: Intubation, pediatric training

Study Objective: This training is designed to teach physicians and other health care professionals basic knowledge and endotracheal intubation skills required to resuscitate a neonate (newborn) or infant.

Technical Approach: The laboratory exercise described below will concentrate on developing the health professional's confidence in establishing an airway. Each new house officer will be required to intubate 2 cats employing a laryngoscope and endotracheal tube.

Animals will be anesthestized with ketamine HCL (22 mg/kg, given intramuscularly), with atropine (0.04 mg/kg, subcutaneously). Up to 2 additional half-doses (11 mg/kg) of ketamine may be given if needed. Pre-anesthesia with tranquilizer (Acepromazine, 0.2 mg/kg, subcutaneously) may be given to allow easier intubation for first-time trainees. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure. Butorphanol tartrate (0.2 mg/kg SC every 8 hours) will be administered after the procedure to alleviate any possible pain.

At the discretion of the instructor, the stages and planes of anesthesia may be defined and assessed by the students. The animal will be placed in dorsal recumbency. Each trainee will visualize the larynx, noting the similarity of the feline larynx to that of the human infant; palpate the larynx externally; and perform visual intubation using the laryngoscope and endotracheal tube.

Two animals will be intubated by each first-time trainee in each laboratory session. Previously trained individuals will use one animal.

Progress: This protocol exists to cover for our use of animal models in annual training for new housestaff and refresher experience for residents and medical staff members. This animal model and protocol continues to provide invaluable hands on training of intubation technique that must be mastered during pediatric/neonatal residency training.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/58 STATUS: Completed

TITLE: Correlation Between Cord Blood Sepsis Screening, Neonatal Disease States, and Maternal Factors

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: CPT Jay Carlson

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Jeffrey V. Paul, MC; MAJ Edwin J. Bollerup, MC; MAJ Lynn K. Whittington, MC

KEY WORDS: Cord blood, Sepsis screening

Study Objective:

1. To develop normal values for cord blood sepsis screening.
2. to identify any association between cord blood sepsis screening and standard neonatal sepsis screening.
3. To identify any association between cord blood sepsis screening and documented neonatal sepsis.
4. To identify any association between cord blood sepsis screening and non-infectious neonatal disease states.
5. To identify any association between cord blood sepsis screening and maternal factors.
6. To identify any association between maternal factors and documented neonatal sepsis.
7. To identify any association between maternal factors and non-infectious disease states.
8. To determine the efficacy of immature to total polymorphonuclear cell ratio and total WBC count in predicting sepsis.
9. To determine the efficacy of the finding of 5 or greater WBCs on standard gastric aspirate vs. a positive leukocyte esterase on gastric aspirate.
10. To Comp[are the efficacy of the namual differential vs. the atuomated differential.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: 1000 patients were entered in this study. Data is being collated and evaluated at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/83 STATUS: Ongoing

TITLE: Very Early Developmental Intervention - A Comparative Study

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: LTC Pilarita Cortez

DEPARTMENT: Peds FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Shirley Cliff, LPT

KEY WORDS: Developmental intervention

Study Objective: To determine if very earlyh developmental intervention programs for Neonatal Intensive Care Unit (NICU) graduates positively influence the child's developmental outcome at 15 mos. And, to determine if training parents to carry out a home intervention program is an effective, less expensive alternative to direct physical or occupational therapy (PT/OT).

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/69 STATUS: Ongoing

TITLE: Anabolic Steroid Use Among Adolescents

START DATE: Aug 89 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: COL, MC Ret John D. Foley

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Walter K. Imai, LTC, MC

KEY WORDS: Anabolic steroids, Adolescent beliefs

Study Objective: To discover adolescent knowledge of anabolic steroids, their sources of knowledge, their sources of knowledge, their personal beliefs of steroid effects and their own usage or thoughts of potential usage.

Technical Approach: An anonymous survey is proposed to inquire into adolescent beliefs about anabolic steroids, their sources of information, their personal usage and reasons for usage. Perceived need for more factual information about stroids will be asked as well as limited demographic data. A copy of the proposed questionnaire is attached.

Subjects included will be adolescent dependents over age 12 years who come to the WBAMC Adolescent Clinic for preparticipation sports physicals. Sample size will be as large as possible, ideally over 200 adolescents. The survey will begin in August and continued into the fall with completion by December at the latest. Subject participation in the project will terminate with completion of the questionnaire. Adolescents will be asked to complete the survey after their examination by the physician. They will be asked to fold it once and place it in a provided recepticle in each exam room. A "Fact Sheet" about anabolic steroids will be left for each subject to take home and read after completing the survey. This study will entail no risk to the patient and will provide educational benefit.

Progress: Thus far approximately 317 adolescent patients have completed the questionnaire according to protocol. Additional subjects will be included with subsequent sports physicals.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/92 STATUS: Ongoing

TITLE: The Effect of Breastfeeding on the Enteral Absorption of Human IgG in the Neonatal Hartley Guinea Pig

START DATE: Oct 89 ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: CPT Steven W. Jesse

DEPARTMENT: Peds FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Breastfeeding, Enteral Absorption of Human IgG, Human IgG

Study Objectives: To assess the influence of breastfeeding on the enteral absorption of immunoglobulin in the neonatal guinea pig. And to assess whether such enterally absorbed immunoglobulin retains function in the form of opsonic activity against Type III Group B Streptococcus.

Technical Approach: Multiparous, untimed-pregnant Hartley guinea pigs will be obtained from a commercial source. Dams will be allowed to deliver pups vaginally at term. Pups will be randomly assigned to receive all nutrition via either suckling, (Group A), or via a commercially available animal formula, (Group B). Appropriate nutritional additives (vitamin C, etc.) will be added to the formula by the veterinary staff. Pups in each group will be gavaged shortly after birth with a single dose, 3g/kg(3cc/100g) 10% Human IgG obtained through a commercial pharmaceutical company. This unit dose has been demonstrated in past investigations to result in consistent enteral absorption of enough Human IgG to be easily detected by current methods of analysis.

Serum samples will be collected at 1, 2, 3, 7 and 14 days following the administration of the IgG. Sera will be separated and stored at -4 degrees C until analysis.

Positive controls will consist of values from sera obtained from animals from prior investigations who were injected with lg/kg 10% HIgG intraperitoneally. Negative controls will be derived from sera pooled from dams and stillbirths during this current investigation.

Lab analyses:

Serum total Human IgG: Competitive Inhibition Enzyme Immunoassay (25)
IgG Opsonic Activity: Opsonophagocytic Assay (26)

Volume required:

30 uL sera (60 uL blood) per assay
2 assays/sample = 120 uL (0.12 ml)/sample
5 samples/animal over 14 days = 0.6ml total
Estimated blood volume of newborn guinea pig = 7cc. Blood requirements are thus minimal.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/80 STATUS: Completed

TITLE: Rapid Diagnosis of Urinary Tract Infections in Children Using Leukocyte Esterase and Nitrite Tests

START DATE: Nov 88 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: CPT Allen Lieberman

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS:

Study Objective: To determine which tests may be performed easily and rapidly in an office setting that are useful in the diagnosis of UTI.

Technical Approach: In my proposed project, all patients will have a urine sample sent for culture, and we will attempt to identify early with the LE and N tests which patients are the most likely to have a positive urine culture, so antibiotic treatment may be started early. The LE test has been shown in several studies to be very sensitive to the presence of pyuria.

Inclusion: Children less than 10 years of age who present with symptoms suggestive of a UTI or those who are being evaluated
for a fever without a source. A urine for culture must be obtained by either clean catch or catheter.

Exclusion: Patients who have been pretreated with antibiotics or on antibiotic prophylaxis. Patients in which the urine was obtained by a bag specimen. I will not exclude a patient with a previous UTI, reflux, or a structural abnormality provided they are not on prophylaxis.

The plan is to obtain 100-200 consecutive urine specimens from the inclusive group, either by clean catch or catheterization (minimum 10cc). The evaluating physician will only perform the standard urine analysis in their initial evaluation of the patient; they will not perform the LE test. Upon completion of their evaluation, a patient data form will be completed, as well as the results of the UA. The patient's social security number will be entered on the data form. The patient will be assigned a number to be given in consecutive order. This number will also be on the patient data form. Approximately 15-30cc's of urine will be collected from the patient, with the patient's assigned number being placed on the specimen container. The specimen will then be evaluated by the principal investigator. The social security number entered on the data form will be used solely to obtain results of the urine. After the results are obtained, the social security number will be discarded. The physician will then decide upon initiation of antibiotics at this time or to wait for the culture results. This is standard procedure at the present time. Factors bearing on his decision include the clinical signs and symptoms of the patient, as well as the UA results and micro results if done. Duration to be approximately 6 months with an expectant rate of 20% positive cultures. Results of the clean catch UA will be recorded and all specimens will be sent to microbiology for culture. Subjects will include mostly outpatients, but inpatients may be included provided they meet the inclusion criteria.

Progress: A total of 100 specimens were included in the study with 19 positive cultures. The sensitivity of the nitrite test was 95% (18/19) and for the LE test was 90% (17/19). The combined sensitivity of the two was 100%. the specificity of the combined tests was 93% (75/81). the positive predictive value of the combined tests was 76% (19/25) and the negative predictive value was 100% (75/75). All 19 of the positive culture results grew E. coli. This is compatible with the finding that greater than 90% of first time UTIs are due to this organism.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/72 STATUS: Completed

TITLE: El Paso Area High School AIDS Survey (Education and Attitudes)

START DATE: Aug 89 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: MAJ Thomas M. Martinko

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Laurance Nickey, M.D.

KEY WORDS: Aids education survey

Study Objective: Test present level of knowledge and some attitudes about AIDS in El Paso high school students.

Technical Approach: The survey was designed to guarantee anonymity. Basic demographic data was obtained, but nothing to identify individual responders. Quesitons were based primarily on the Surgeon General's brochure on AIDS that was sent to every household in the United States in the summer of 1988. The survey tests basic information and attitudes concerning AIDS. The answers are presently being transferred to a spread sheet for collation and analysis. The results will be used by the City county Health Department and school departments to plan further AIDS education. There is also the possibility of publication in a state or national medical journal to allow comparisons with other sections of the country and with different population bases.

Progress: The responses of 4750 high school students in the El Paso School District and several nearby rural school districts have been keyed into a computer and collated. The results are being reviewed and made into graph form. An abstract is being submitted to the Uniformed Services Pediatric Society annual meeting and an article will be submitted for publication.

Example: 80% of all students surveyed believed children with AIDS should be allowed to attend public school. Of those who said they should not, 37% believed someone taking care of an AIDS patient was personally at risk (compared to only 14% of those who felt AIDS patients should attend school).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/88 STATUS: Ongoing

TITLE: Incidence of Corynebacterium Hemolyticum Pharyngitis in an Adolescent Clinic

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Oct 90

PRINCIPAL INVESTIGATOR: MAJ Thomas M. Martinko

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Robert Wittler, MC

KEY WORDS: Corynebacterium Hemolyticum Pharyngitis, Adolescents

Study Objective: The incidence and seasonal variation of corynebacterium hemolyticum pharyngitis will be determined over a one year period in the Adolescent Clinic at WBAMC.

Technical Approach: All patients (13-20 years of age) presenting to the Adolescent Clinic at WBAMC with a complaint of "sore throat" who receive a throat culture will automatically be included in the study., It will be conducted over a one year period. A checklist of associated signs and symptoms will be used to standardize the information charted on each patient. No additional tests are needed. The throat culturette which would be obtained anyway will be sufficient. In the lab, the culturette will be plated out on the usual blood agar plates, but those from the Adolescent will be marked to be held for 72 hours. Group A beta hemolytic strep can be read at 24 hours (or less), but corynebacterium hemolyticum takes 48-72 hours for adequate growth. those plates with growth suspicious for Corynebacterium hemolyticum will be verified using sugar fermentation techniques.

Patients with a positive culture will be contacted and prescribed a ten day course of erythromycin. (The lab will do sensitivity tests periodically on cultures to determine alternate therapies.) The patients will also be requested to return after treatment for a follow-up throat culture to ascertain eradication of infection. Those who have not responded will be tested for co-incident infectious mononucleosis. Household contacts under age 22 will be requested to also have a throat culture (due to the high incidence of positive results in this population shown in Miller's study).

Those patients identified as having corynebacterium hemolyticum will benefit by treatment which should decrease duration of illness, recurrence of infection, and propagation to others in the household. Risks are minimal. No invasive tests are being done. Erythromycin (250mg four times a day for ten days) is among the safest of antibiotics. (Its main side effect is nausea, which can be minimized by taking it with food.)

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/43 STATUS: Ongoing

TITLE: The Treatment of Children with Learning Disorders using Neuro-Linguistic Programming (NLP) Strategies

START DATE: Jan 90 ESTIMATED COMPLETION DATE: Sep 90

PRINCIPAL INVESTIGATOR: M.D. Richard L. Riley

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC A.W. Atkinson, MC; Stephen L. Grouell, Ph.D.

KEY WORDS: Neuro-linguistic programming, Learning disorders

Study Objective: To determine whether Neuro-Linguistic Programming strategies, which can be taught to children and their parents, can help a certain subgroup of learning disordered children, overcome their handicap as compared to the use of more conventional strategies.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this protocol. We plan to begin this project in January 1990.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/60 STATUS: Completed

TITLE: The Effect of Stress and Exercise on Serum DHEAS and Cortisol Levels

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: MAJ Rita Svec

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Suzanne E. Cuda, MC

KEY WORDS: Stress, DHEAS, Cortisol

Study Objective: To follow DHEAS and cortisol levels in a stressed population with and without exercise and to correlate this data with percentage body fat, work hours, level of stress and amount of exercise.

Technical Approach: Stress is an interesting phenomenon; there are different types of stress: physical stress due to exercise, physical and emotional stress due to working long hours with no periods of relaxation, physical stress due to severe illness, emotional stress.

One group of individuals with a high stress job are medical interns. Interns are sleep deprived, eat poorly, and have a high degree of emotional stress due to the novelty of the job and the amount of knowledge yet to be acquired. Most interns lead a sedentary existance, with little exercise and a lot of sitting or standing in one place.

We propose to study the interns as a high stressed group, comparing those interns who exercise regularly, and those who get little physical activity. We intend to compare the following parameters:

DHEAS
AM Cortisol
Activity survey
Stress survey
% Body fat

Measurements at beginning and end of study:
(a) % body fat using Armed Forces tape test
(b) Have participant fill out Jenkins Activity Survey

Measurements every 2 months, beginning the last week in June/first week in July:
(a) DHEAS (Dehydroepiandrosterone Sulfate) using Radioimmunoassay.
(b) 8 AM Cortisol by Radioimmunoassay.
(c) Have paricipants fill out a chart of hours worked/week, exercise pattern, perception of stress.
(d) Have participant fill out a Self-Evaluation Questionnaire.

Progress: Data is being collated and statistical analysis completed. Final results should be out in December 1989.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/89 STATUS: Ongoing

TITLE: Prevalence of Primary Measles Vaccine Failures in a Dependent Military Population and the Effect of MMR Revaccination on Antibody Response

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: MAJ Robert R. Wittler

DEPARTMENT: Ped FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce C. Veit, Ph.D.; COL Lou A. Popejoy, MC; COL Manuel Schydlower, MC; MAJ Robert Martig, MS

KEY WORDS: Measles vaccine, MMR Revaccination, Antibody response

Study Objective: a. Determine the prevalence of primary vaccine failures.
b. Assess risk factors in identifying primary vaccine failures.
c. Determine the antibody response of measles seropositive and measles seronegative subjects to revaccination with MMR.

Technical Approach: All patients 6-20 years of age who wish to receive revaccination with MMR are eligible for the study. These individuals, and if applicable, their guardians will receive a printed explanation of the study. Informed consent concerning the collection of demographic and vaccination data and the risk of venipuncture will be obtained.

A data sheet with the date, subject's name, SSN, phone number, date of birth, date of prior MMR vaccination(s), ethnicity, and gender will be completed. Prior to being revaccinated, a venipuncture will be performed and a 5-7 ml of blood will be collected. The subject will then receive his/her MMR. A second venipuncture will be performed 2-3 weeks following MMR revaccination and 5-7 ml of blood will be collected. Specific measles IgG, IgM, and IgA will be determined by ELISA on each serum specimen. Subjects who are seronegative 2-3 weeks following revaccination will be asked to submit another specimen for antibody determination 6-8 weeks following revaccination.

There will be 500-700 subjects included in this study, and the duration of the study will be 4 months.

Relationships between prevalence of seropositivity, age, age of initial vaccination, interval between vaccinations, and mean DOD will be evaluated using stratified risk ratios, regression analysis and ANOVA.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/79 STATUS: Terminated

TITLE: Admitting Criteria for TCA Overdose, a Prospective Look

START DATE: Oct 88 ESTIMATED COMPLETION DATE: May 89

PRINCIPAL INVESTIGATOR: MAJ Jose E. Aponte

DEPARTMENT: DPCCM FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: TCA, admitting criteria

Study Objective: To determine if the admitting criteria previously validated by several retrospective studies can be utilized in a prospective manner in an emergency room setting.

Technical Approach: As each patient presents with a history of TCA ingestion, they will be logged into a book, maintained in the ED, so as to facilitate retrieving their charts for information or from our computer terminals. Those criteria outlined in the algorithm will be attached to the patient's ED chart. Criteria that are ambiguous (i.e. signs of major toxicity) will be clarified for the house officer treating each patient admitted. During the hospitalization the patient will be monitored daily for signs or symptoms of major toxicity. Significant events during the hospitalization period will be documented on the form (algorithm) attached to the patient's records. Upon discharge, each patient's form will be collected and reviewed. Those patients discharged from the ED will have documented on their ED charts the presence or absence of signs of major toxicity (i.e., QRS width, bowel sounds, etc.). The management of each patient will be the same as any patient thought to have a toxic ingestion. All patients will be lavaged via the orogastric route until bile is noted in the aspirate, at which time they will be given their first dose of charcoal and a cathartic. If prior to lavage the patient demonstrates an altered mental status then the patient will be intubated before initiating the lavage. At that time the patient will also be given thiamine, glucose and Narcan in the standard doses. A lab data base, to include an ABG, CXR, SMA-10, Calcium, PT/PTT, CBC, serum osmolality, serum/urine tox and drug screen, with TCA levels, will be obtained on all patients suspected of a TCA overdose. The method of testing will be by EIA, GLC, HPLC and TLC by the Nichols Institute. This lab data base is routinely obtained on all suspected significant ingestions. So as to allow as large a group as possible, the duration of this study should be about one year or involve 100 patients. Neither sex or age should influence the results of this study. The data will be analyzed for uncomplicated versus complicated hospital stays by the Student T method. The complication frequencies for subgroups versus the hospitalized patient population as a whole will be studied by a comparison of the binomial distribution. The method of Hanley and Lippman-Hand will be used to calculate the 95% confidence interval around the observed rate of complications. Those patients who are negative on their drug/tox screens for TCA's will be used as a control group.

Progress: Principal investigator left the Army. No progress to report.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/71 STATUS: Ongoing

TITLE: Emergency Procedures Laboratory (Carpine Model)

START DATE: Jul 87 ESTIMATED COMPLETION DATE: Open-ended

PRINCIPAL INVESTIGATOR: CPT Michael Peterson

DEPARTMENT: DPCCM FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ C. Eaves, MAJ J. Aponte, MAJ M. Stolpe, CPT M. Peterson

KEY WORDS: Emergency procedures laboratory

Study Objective: To train accredited physicians who are not dealing with emergencies on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate the human emergency patient.

Technical Approach: Cricothyroidotomy, venous cutdown, chest trauma management, and peritoneal lavage procedures will be accomplished in accordance with training manuals for each procedure.

Progress: One group of paramedic personnel has completed the laboratory training (5 April 1989). A total of 12 personnel took part. Training objectives ere met. It is anticipated this training will be repeated on an annual basis.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/14 STATUS: Completed

TITLE: Residential Alcoholism Treatment Patients: MMPI Subtypes and Treatment Outcome

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: MAJ Robert R. Roland

DEPARTMENT: Psych FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Major Robert R. Roland, Health Psychology Fellow

KEY WORDS: Inpatient Alcoholism Treatment Outcome MMPI

Study Objective: The establishment of preliminary prognostic indices for treatment outcomes in RTF patients using psychological test data and demographic information.

Technical Approach: Existing test data and demographic information from the files of previous male inpatients at the RTF will be examined and divided into three equal groups based upon treatment outcome. Those groups will be composed of patients who were successful in 6 weeks, required 8 weeks of treatment, or failed before 6 weeks.

Progress: The analyses of MMPI clinical and validity scales established clear trends toward specific clinical scale elevations within treatment groups. When clinical scales were evaluated beyong the typical Alcoholic "Type" profile, secondary scales produced significant differences between groups (see graphs). Validity scales were important in the discrimination of the three groups. Demographic data consisting of Age and Ethnic Origin did not account for variance between the groups. the marital status (currently married) of successfully treated patients did approach significance (.07) when compared to unmarried or divorced patients who were treament failures.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/35 STATUS: Completed

TITLE: Comparison of AST/ALT Ratio When Done by Different Laboratory

START DATE: May 89 ESTIMATED COMPLETION DATE: Oct 89

PRINCIPAL INVESTIGATOR: LTC Gerald M. Cross

DEPARTMENT: RTF FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: AST, ALT, Alcoholism diagnosis

Study Objective: Determine if AST/ALT ratios are affected by commonly used laboratory technique.

Technical Approach: Thirty consecutive RTF patients diagnosed as alcohol dependent will each have both an AST and ALT analysis done by each method on their admission blood samples. Statistical analysis will then determine if the laboratory method effects the AST/ALT ratio. Student's t-Test will be used for comparison of the means. Otherwise, Chi-Square analysis will be used. AST and ALT values will be recorded on standard laboratory forms, which will be included in the appropriate patient's chart. Since the patient will not be subjected to any additional procedures or drug administration, special consent for additional laboratory analysis is not required.

Addendum: The protocol will be repeated with approximately 30 additional subjects, measuring plasma vitamin B6, in addition to the AST and ALT by two different methods. Pyridoxal 5'-phosphate (PLP), and the active cofactor form of vitamin B6, is the cofactor for the AST and ALT enzymes. We hypothesize that the different results of the two methods for measuring the enzymes are due to differences in the cofactor (PLP) levels of the subjects. One method (ACA) adds cofactor to the assay medium, whicle the other method (SMAC) does not. We have previously found decreased levels in PLP in alcoholic/cigarette smoking subjects.

The additional test (PLP) will require drawing an additional 7cc of blood, at the same time as the blood for the other studies.

Progress: Comparison of different methods used to determine AST and ALT revealed that the method used did not reverse the ratio of the two values.

This is important since the AST/ALT ratio of our alcoholic patients is the reverse of what has been reported in medical literature.

An article has been written and it will be submitted to a medical journal.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/76 STATUS: Ongoing

TITLE: Red Blood Cell Indices (MCV, MCH, MCHC) as Estimators of Alcohol and Smoking Status and Relationship to Nutritional Status

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: LTC Gerald M. Cross

DEPARTMENT: RTF FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Richard C. Keniston, M.D.; G. William Lucker, Ph.D.

KEY WORDS: RBC Indices, Alcohol and Smoking, Nutritional status

Study Objective: Determine relative contribution of alcohol consumption, cigarette smoking, and iron, folate, vitamin B-12, and vitamin B6 to red blood cell indices.

Technical Approach: One-hundred-twenty consecutive RTF patients diagnosed as alcohol dependent will each have blood drawn for SMAC-22 (including iron), CBC, plasma PLP (vitamin B6), folate and vitamin B12 on their admission blood samples (36 cc blood, as opposed to 22 cc previously drawn). Stepwise regression analysis will be used to determine the relative contribution of each parameter to the red blood cell indices and also to determine which red blood cell index best estimates alcohol status, both initial and post-treatment. We will include last drink interval as a variable for defining alcohol status. Alcohol status will be defined two ways (drinks/month and yes/no to heavy drinker status) and cigarette smoking status will be defined three ways (cigarettes/day, by never smoked/ex-smoker/light smoker/heavy smoker status, and yes/no to current cigarette smoking).

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/61 STATUS: Ongoing

TITLE: An Investigation of Substance Abuse and Aggressive Antisocial Behaviors Among Soldiers Indentified as Child and/or Spouse Abusers

START DATE: 25 Aug 89 ESTIMATED COMPLETION DATE: 25 Aug 90

PRINCIPAL INVESTIGATOR: LTC Elwood R. Hamlin

DEPARTMENT: Soc Wk FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: W. Lucker, Ph.D., D.J. Kruzich, Ph.D.

KEY WORDS: Substance Abuse and Family Violence

Study Objective: To determine the extent to which child and/or spouse abuse reflects a probability of involvement in substance abuse as well as other, unrelated, aggressive antisocial behaviors.

Technical Approach:

a. Subjects: Records of 100 soldiers residing in Army housing who have been identified and referred to Social Work Service, WBAMC for child or spouse abuse.

b. Controls: 100 age, race, rank and sex matched-controls who have NOT been identified as spouse or child abusers.

c. Design of Experiment: Records of 50 soldiers identified for spouse abuse and 50 soldiers identified for child abuse will be obtained from WBAMC SWS. The following information will, if available, be extracted from their records: age, race, rank, offense, number of domestic violence offenses, number of children, number of marriages, number of years in current marriage, number of months living in Ft. Bliss housing, any prior treatments for substance abuse, and any referrals to other agencies (e.g. RTF, MHCS, CCC.). Names and SSN's of these soldiers will be compared with client lists as the DWI Program and Ft. Bliss CCC to determine whether they have sought or been referred for services at those agencies. Then their Ft. Bliss Military Police records will be examined and all arrests and convictions recorded for data processing. Finally, a matched control group of soldiers NOT apprehended for domestic violence will be obtained through the Ft. Bliss PAC. Their names and SSN's will be compared with DWI and CCC client lists and their MP records will be screened for any arrests. Statistics to be utilized are non-parametric frequency counts, including chi-squared, and log-linear analysis.

d. Forms: No special forms will be used.

e. Patient notification: This is a non-intrusive screening of existing records. No patient contact is required. To guarantee confidentiality once complete subject information has been compiled, each subject will be assigned a study case number (from 1 to 100) and all other identifying information will be destroyed. Original data will only be reviewed by one individual - the research associate who will gather the data. Computer data files will have no information that can be used to personally identify any individual.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 78/03 STATUS: Ongoing

TITLE: National Intraocular Lens Implantation Study

START DATE: Oct 1977 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC George Amegin

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Surgery/Ophthalmology

Study Objective: To participate in the study of clinical results of implantations of intraocular lens organized by the intraocular Lens Manufacturer's Association in response to directives of the Ophthalmic Classification Panel, FDA.

Technical Approach: An intraocular lens is a prosthetic replacement for the eye's crystalline lens. It is placed in the eye at the time of cataract surgery, where it is fixated by a variety of means, with the intention that it remain permanently and correct the large refractive error remaining after conventional cataract surgery.

Progress: Protocol is ongoing with a total of five core lens implanted in 1988-89 with no complications or unusual occurrences noted.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/02 STATUS: Jun 1988

TITLE: Surgical Stapling Procedures Laboratory (In Dogs)

START DATE: Indefinite ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: LTC Warren F. Bowland

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ongoing

KEY WORDS: Stapling

Study Objective: To train accredited attending physicians and residents in the use of automatic suturing devices including their applications and limitations in a laboratory environment before they are called upon to use these instruments in human surgery.

Technical Approach:

I. Gastrointestinal Applications Procedures

   a. Splenectomy

   b. Hemigastrectomy w/Billroth II Reconstruction or Hemigastrectomy w/Billroth I Reconstruction

   c. Small Bowell Resection w/Functional End-to-End Anastomosis

II. Other Abdominal Applications

   a. Nephrectomy

   b. Large/Small bowel Resection w/End- to-End Anastomosis by Triangulation

III. Closure

   a. Fascial Closure Techniques

   b. Skin Closure Techniques

Progress: The General Surgery Services utilizes the "stapling" laboratory to train "junior" general surgery house staff in the use of surgtical stapling instruments.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/59 STATUS: Ongoing

TITLE: Animal Model (Ovine) Laboratory, Advanced Trauma Life Support Course (ATLS)

START DATE: Jun 1988 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren F. Bowland

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Steve Carey, MC

KEY WORDS: Trauma

Study Objective: To train accredited physicians who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate human trauma.

Technical Approach: Animal Procedures -

1. Cricothyroidotomy
2. Venous Cutdown
3. Chest Trauma Management
    a. Needle decompression
    b. Tube thoracostomy
    c. Pericardiocentesis
4. Peritoneal Lavage

Training manuals will be used for each training procedure.

Progress: The Department of Surgery provides four ATLS courses per year (two providers and two instructors). The NASA Shuttle Flight Surgeon training is performed on an annual basis. ATLS is an integral part of this training.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/12 STATUS: Ongoing

TITLE: Combat Trauma Surgery Using a Portable contact Nd-(YAG) Laser

START DATE: Feb 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John McPhail, MC; CPT Michael J. Snyder, MC; MAJ Steven Carey, MC

KEY WORDS: Surgery, Laser training

Study Objective: The main purpose of this laboratory will be to train physicians who are involved in the care of trauma victims, in the use of the Neodymium (Nd):YAG laser in surgery, and to familiarize them with the laser's applications in trauma management.

Technical Approach: Prior to the actual experiments, each participant in the protocol will be instructed in the safety precautions and the proper use of the (Nd)-YAG laser. Two animals will be used to demonstrate proper technique to the surgeons participating. After proper instruction, two surgeons and one to two assistants will perform the procedures on each animal, allowing each surgeon to be the primary surgeon on two operations. The actual operations will proceed as follows: Each animal will undergo one survival and one non-survival abdominal surgical procedure. After the animal is adequately anesthetized (see alleviation of pain and distress below), IV lines and EKG monitors will be placed.

A midline abdominal incision will be made and a brief exploration of the abdomen will be performed. A segment of the liver will then be injured with a combination of blunt and sharp trauma so as to cause injury deep into the parenchyma of the tissue. At this point, the (Nd)-YAG laser will be used to obtain hemostasis via a combination of resection and coagulation techniques. After appropriate repair of the liver, similar injuries to the pancreas, spleen, kidney, and intestines will be produced. Each injury will be repaired using the (Nd)-YAG Laser. No more than 50% of the liver parenchyma, or the parenchyma of the other abdominal organs will be injured during the operation. After appropriate hemostasis is obtained, the abdomen will be closed with a standard 3 layer closure, and the animal will be allowed to recover from general anesthesia. The animals will be managed as described below in the post operative care plan.

Each animal will be allowed to recover 1-2 weeks from the initial surgery prior to the second operation. At this surgery the abdomen will be entered in similar fashion and explored. The healing of the liver, pancreas, spleen, kidney, and intestinal repair sites will be assessed by the operating team for the following items: 1 Hemostasis, 2 tissue necrosis, 3 and evidence of any injury to surrounding organs and tissue. After evaluation of the intrabdominal healing, a similar procedure will be performed on other segments of the above named organs, as described above, and the repair will be made using the (Nd)-YAG laser. At the conclusion of the surgery the animal will then be euthanatized according to the protocol listed below. At no time during the operation or the recovery time will the animal be allowed to suffer, and if appropriate alleviation of pain can not be achieved, the animal will be euthanatized.

Progress: This project has gone well with 8 animals used to date. We have found the laser extremely useful in resection of the liver and spleen, especially to obtain hemostasis of solid organs in the abdomen. It is also effective to cut and coagulate in muscle, as it does not cause contraction of the muscles as is seen with electrocautery. We have used both contact tips and the free laser beam, and have found each to be effective for different applications. We still have further work to do in defining other applications in abdominal surgery for the laser. We are going to do further work on the pancreas, kidney and intestines to help further define the role of lasers in trauma surgery. Also, there are new quartz fibers that are available that have polished tips and may obviate the need for the more expensive sapphire tips. To date I feel that the project has been successful and we are progressing towards the goals of the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/31 STATUS: Onging

TITLE: Combat Trauma surgery Using a Portable contact Nd-(YAG) Laser in the Porcine and Ovine Models

START DATE: Apr 89 ESTIMATED COMPLETION DATE: Sep 90

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail, III, MC

KEY WORDS: Surgery, Laser visceral

Study Objective: Compare the use of the Nd-(YAG) to conventional surgical techniques, with respect to blood loss and operative time. Actually test this laser in a field environment using an animal model in a F.A.S.T. unit with a wartime casualty scenario. Determine if advanced surgical techniques using a new portable contact Nd-(YAG) laser can be realistically and effectively used in a field surgical unit.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This project entails the comparison of trauma surgery with laser vs. conventional techniques. We have operated on 3 pigs and 1 sheep to date. Both models are adequate for trauma models with the pig having a more similar anatomy to humans and the sheep having more hemorrhage than the pig due to the differences in the coagulation pattern. The laser surgery provides a quicker means of hemostasis in the face of a bleeding liver or spleen, with hematocrits and weights showing less blood loss. The crucial element in this study is to generate sufficient numbers of surgeries to adequately compare the two techniques and see if, indeed, the blood loss is less and surgery time diminished.

Now that we have a laser in our possession at the animal research lab we are able to perform the surgery weekly or twice a week, and should have the bulk of procedures done by the end of November. Our field portion of this project has been scheduled for the second weekend in December. At this time we will have the support of the Medical Company of the 3rd ACR at Ft. Bliss.

The engineer that designed the portable laser that we are using, came to WBAMC recently and discussed the feasibility of a more field ready laser. He mentioned some modifications which can be made to the present system, as well as the ability to dramatically reduce the size and weight of the laser. The technology presently exists. If a definite need for a laser in the field setting could be established, the future laser that could be built would be much smaller and lighter. This project is currently well underway and we should have most of the results by the end of December or early in January.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/32 STATUS: Ongoing

TITLE: Intestinal Surgery Evaluation with the Neodymium (Nd): YAG Laser in the Rabbit

START DATE: Pending ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail, III, MC

KEY WORDS: Surgery, Bowel, Laser, Anastomosis

Study Objective: Demonstrate the ability to weld an end to end intestinal anastomosis utilizing a ND:YAG laser and an absorbable stint.

Technical Approach: Four rabbits will be used initially to evaluate the procedure and determine if it is a feasible project. The small bowel will be transected in four rabbits. The bowel of two rabbits will be anastomosed with the laser technology described above and the other two by conventional suturing techniques. Two rabbits will be assigned to each group to allow evaluation of the surgical sites on days 4 and 10 post surgical. If there is a trend demonstrated that the laser anastomosis site is equal to or stronger than the sutured site, then a full study will be considered.

Progress: This project got off to a slow start due to the lack of a laser. However, now that a laser has been purchased, the investigator plans to start with this project in November. Dr. Sauer will be visiting at that time and they plan to perform intestinal ansatomosis on several rabbits using the exoscope fiberoptic device and absorbable intestinal stints. This technique is still experimental and the work that is underway should determine its usefulness and application in surgery.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/07 STATUS: Ongoing

TITLE: The Use of Intraoperative Ultrasound During Cholecystectomy

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Dennis P. Eastman

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: John McPhail, Colonel, MC

KEY WORDS: Intraoperative ultrasound

Study Objective: Comparison of intra-operative ultrasound vs. cholangiogram in the evaluation of common bile duct abnormalities during cholecystectomy. The study will be an attempt to show that ultrasound is as effective as and can replace intraoperative cholangiogram (IOC) during cholecystectomy. It will also afford the General Surgery residents and staff the opportunity to gain facility in the use of intraoperative ultrasound.

Technical Approach:

a. Experimental design - 2 phase study

(1) Group 1 - Ultrasound vs. IOC

(a) During cholecystectomy prior to IOC, an intraoperative ultrasound of the CBC will be performed and interpreted by the investigator. Results of the ultrasound will then be compared to the IOC. Variables measured wll be: size of the CBC, and presence of CBD stones. Estimated time for completion of the ultrasound is 10 minutes. By videotaping the ultrasound in each case a permanent record of the exam will be made and can be compared to the IOC by an independent observer, this data can be compared to the data obtained by the investigator and determine if investigator bias exists.

(b) The number of cholecystectomies in each group (normal/abnormal) will be at least 10.

(c) If no significant difference is noted between modalities in phase I, then phase II will be undertaken.

(2) Group 2 - Ultrasound vs IOC taking into account operator variability.

This phase will be conducted the same as phase I, except the ultrasound will be performed by the surgeon. The objective of this phase is to determine the effect of interoperator variability on ultrasound results and to determine if ultrasound has a wide applicability during cholecystectomy.

Progress: The study has been slowed due to the fact that the ultrasound equipment on hand was manufactured for another purpose, i.e., neurosurgery. It became apparent after the first few subjects that the probe head was to large to be totally satisfactory. Therefore, patients have been added to the study slowly while awaiting acquisition of a more applicable probe.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/70 STATUS: Oct 89

TITLE: Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model

START DATE: Mar 90 ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: MAJ Frederick T. Garner

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ongoing

KEY WORDS: Tracheal reconstruction, Tracheal prosthesis

Study Objective: To identify a tracheal prosthesis material and surgical technique which may be suitable for reconstruction of the human trachea.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Protocol will not start until March 1990.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/28 STATUS: Ongoing

TITLE: Anastomosis of Flap Veins to Bone: An Alternative for Microvascular Free Flaps in Tibial Wound Coverage (Pig Model)

START DATE: Mar 1989 ESTIMATED COMPLETION DATE: Apr 1989

PRINCIPAL INVESTIGATOR: CPT S.D. Jones

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Icochea, MC

KEY WORDS: Surgery Anastomosis, Tibial Wound Coverage

Study Objective: To determine the efficacy of anastomoses of free flap veins to bone via pre-drilled channels into the Haversian canals.

Technical Approach: The pig will be prepped and placed in dorsal recumbent position. An incision will be made over the medial aspects of the lower extremity bilaterally. The tibias will be exposed and holes drilled into the bone in two sites per tibia. The resting pressure of the Haversian canals will be measured. The holes will be approximately 2mm in diameter to correspond with the veins found in the flaps. Free myocutaneous flaps will then be taken from the calf of each lower extremity. These flaps will be designed with one artery and two veins per flap. The anastomoses of the veins will be to periosteum immediately adjacent to the predrilled holes.

Progress: No progress to report. The principal investigator is attempting to find another plastic surgeon to be an associate investigator, as Dr. Icochea has PCS'ed.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/93 STATUS: Ongoing

TITLE: TPA as Treatment for Experimental ARDS in the Porcine Model

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Joseph J. Kaplan

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Henry E. Butler, LTC, MC; Robert M. Hardaway, BG, MC (Ret); Charles H. Williams, Ph.D.; Michael J. Sborov, LTC, MC

KEY WORDS: TPA, ARDS

Study Objective: (1) To confirm the beneficial effect of tissue plasminogen activator (TPA) on experimental ARDS in a porcine model, as recently demonstrated by Hardaway and Williams. (2) To determine whether the beneficial effect ofTPA is present when the drug is given after the onset of hypoxia, as would be the case with patients. (3) To determine the most beneficial time and method of TPA treatment. (4) To determine if correlation between phospholipid levels and the degree of severity of ARDS exists.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 85/56 STATUS: Ongoing

TITLE: Porocoat Synatomic Knee Device (Depuy IND #G830152) (Monitor: COL Scully)

START DATE: Dec 85 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: CPT Steven Kulik

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Synatomic Knee Device

Study Objective: To demonstrate the safety and efficacy of the Porocoat Synatomic Knee System.

Technical Approach: Investigators will follow the manufacturer's protocol, which has been approved by the FDA. This protocol is extensive and is available in the Department of Clinical Investigation.

Progress: No new subjects have been entered in this study during the past three years. However, periodic follow-up studies are being conducted on all subjects. The study will be completed when all followup assessments have been completed on all 26 subjects previously enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/28 STATUS: Ongoing

TITLE: The Flexor Carpi Ulnaris: Anatomy

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: M.D. Umesh Raturi

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Thomas J. Scully, MC, CPT Cameron S. Perkins, MC, MAJ Kevin C. O'Hair, COL William Burkhalter, MC (Retired)

KEY WORDS: Flexor carpi ulnaris

Study Objective: The feasibility of using this forearm muscle as a transposition flap to replace tissue loss due to blast injuries, high velocity wounds and side swipe injuries of the elbow is to be confirmed. The shattered elbow is now routinely aggressively fixed with orthopedic hardware to maximize early motion and rehabilitation. Coverage of this area remains a problem and usually needs microvascular free flap transfers.

Technical Approach: The study would be done on fresh cadaver (eg: autopsies with consent). The subject should not have had anatomical injuries to the forearm to be included. A total of ten muscles would be needed. Commercially available radioopaque latex (microfil), would be injected into the brachial artery above the elbow. The muscle would then be removed from the forearm, weighted and measured (length,with markers placed). The specimen will be fixed in a receptacle and cooled overnight for latex consolidation. Twenty four hours later, the soft tissues would be progressively digested with an mild acid (clorox or household bleach) and the arterial supply documented. Photographs and X-Rays will be taken. The nerve supply, though not essential would also be documented when the muscle is elevated.

Progress: Two autopsies with consents were available so far for this study. Eight more dissections are needed.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/64 STATUS: Ongoing

TITLE: Microvascular Anastomosis of the Rat Femoral Vessels

START DATE: Nov 88 ESTIMATED COMPLETION DATE: 1990

PRINCIPAL INVESTIGATOR: MAJ Franklin D. Richards

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Microvascular Anastomosis

Study Objective: To gain proficiency in microvascular technique so that the technical proficiency gained can be applied to clinical conditions.

Technical Approach: Two survival femoral vessel anastomosis procedures and a third non-survival abdominal vessel surgical procedure will be conducted on each of 40 rats during the training year. At least one staff surgeon will supervise the resident training until they have become proficient. The first procedure (right femoral vessel anastomosis) will be conducted on day 0; the second (left femoral vessel anastomosis) on day 14; and the third (aortic artery anastomosis) will be conducted on day 28 for each respective rat. By the third training day, one of each of these procedures will be done every training period using 3 different rats. The rats will always be euthanatized immediately following completion of the abdominal procedure.

Progress: MAJ Franklin D. Richards has replaced LTC Rosendo Icochea as principal investigator on this project.

Approximately 1 microvascular anastomosis and a rat femoral vessel is being performed a week. To date our anastomotic patency rate has been excellent. this protocol also gives the plastic surgery resident a mechanism for learning microsurgical techniques.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 84/55 STATUS: Terminated

TITLE: Radiolabeled Triazines for Evaluation of Soft Tissue Damage in Rabbits

START DATE: 1984 ESTIMATED COMPLETION DATE: 1989

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Soft tissue damage

Study Objective: To synthesize and test a series of radiolabeled triazine compounds as nuclear imaging agents for soft tissue damage in rabbits.

Technical Approach: Phase I: Synthesize a stable complex of Indium with a chlorotriazine dye.

Phase II: Inject rabbits with radio-indium-labeled chlorotriazine dye after producing controlled soft tissue and bone lesions. Scan for radiotracer distribution within four hours.

Progress: All efforts to synthesize a chemically stable, radi[illegible]beled triazine have been unsuccessful. This project has been terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/42 STATUS: Ongoing

TITLE: Torsion as a Factor in Patency of Microvascular Anastomosis in a Rat Model

START DATE: Oct 88 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Jose Monsivais

KEY WORDS: Microvascular anastomosis

Study Objective: To determine the effect of torsion on the patency rates of microsurgical venous grafts.

Technical Approach: The rat will be prepped with surgical scrub, sterile drapes applied and placed in a dorsal recumbent position. An incision will be made over the medial aspects of the lower extremities bilaterally. The femoral artery will be exposed from the femoral canal to the bifurcation of the profundus, as well as exposing numerous branches.

The femoral artery of the rat will be transected and a vein graft of equal diameter will be sutured into place. A series of five grafts using 20o, 40o, 60o, and 90o of torsion will be performed. The contralateral leg will be used as a control, grafting a vein with 0o torsion into the transected femoral artery.

The animals are to be kept alive and allowed to heal for approximately two weeks, at which time they will be explored, and the patency of the vascular grafts determined by direct visualization.

AMENDMENT #1: One hundred rats will be randomly selected and divided equally into 5 groups of 20 animals. The groups will be delineated as follows: 0° torsion (control); 90° torsion; 180° torsion; 270° torsion; and 360° torsion. The procedures will be completed in blocks completing one procedure from each group before repeating the same surgical prep. This will reduce differences between groups which could result due to improvements in surgical techniques during the progress of the research or differences in animal health or physiological status during the study. This method will also allow the investigator to statistically evaluate the data throughout the study to determine when adequate numbers of animals have been utilized, thus, possibly reducing the total number of animals required for the study.

AMENDMENT #2: Having determined that free flap survival is at its greatest risk at 90° and above, but does not progressively decrease after 90°, the question arises addressing the affects of free flap rotation within the implied safety margin below 90°. To confirm that there is also no significant affect on the patency of the vascular pedicle within the safety margin, 20 animals from the original experiment will be divided into 2 groups of 10 animals per group. The free flaps and pedicles will be based on the left femoral artery and vein. In one group, the free flaps will be rotated at 30°. The ramaining group of 10 animals will have the free flaps rotated at 60°. Additional animals will not be required for this investigation. All other procedures will be in compliance with the original protocol.

Progress: The initial principal investigator, LTC Monsivais, has ETS's from the Army. COL Scully has assumed the role of principal investigator. The protocol was modified in May 1989 to include additional animals with varying degrees of graft torsion.

One hundred-twenty rats have been entered in the protocol. All grafts have been performed. All grafts will be harvested in November 1989 and submitted for microscopic histopathologic analysis. This will be followed by data analysis and manuscript preparation.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 86/51 STATUS: Terminated

TITLE: Changes in Bone Micromorphology and Fatigue Fracture Resistance Resulting from Repeated Physical Stress, Phase II. (Monitor: LTC Bowland)

START DATE: Jul 86 ESTIMATED COMPLETION DATE: Sep 89

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL R. Turnbull, MC; MAJ A. Moreno, MC

KEY WORDS: Stress fracture

Study Objective: To determine the changes in fatigue fracture resistance of human living bone resulting from repeated physical stresses and to correlate these changes with changes in bone micromorphology.

Technical Approach: Small (approximately 1 cm square) biopsies of cortical bone will be taken from the proximal medial tibial metaphysis of basic trainees undergoing surgical procedures on their lower limbs for other acute conditions such as arthrotomy of the knee for treatment of a torn meniscus. The specimen will be cut and ground with a Buehler isomet and a lap machine to produce rectangular beams 2mm xs 2mm by 18 mm. The fatigue life of the prepared specimens will be determined using a Beaumont cyclic stress apparatus. The specimens will be cyclically stressed by four point bending loads producing a deformation of 500 microns at 10 cycles per second. The fatigue life of the specimens (number of cycles to failure) will be recorded. The fracture specimens will then be examined by scanning electron microscopy and routine light microscopy. Findings of these studies will be correlated with the number of days of completed training.

Basic trainees at Fort Bliss will be asked to participate in the study. Each trainee will complete a training activities questionnaire which will provide data on the number of days of training completed, pre-entry physical fitness activities, and routine medical historical information. Each trainee will then undergo technetium bone scan. Bone biopsies will then be obtained from the proximal, posteromedial tibial crest (a common site for stress fractures) of each trainee. The biopsies will be examined by scanning electron microscopy and by conventional histology. The fatigue life of each biopsy specimen will be determined.

Progress: Since the start of this project only one subject has met the criteria for entry into the study. In consideration of the planned termination of basic training at Fort Bliss, it is unlikely that additional subjects will be entered. Therefore, it is recommended that the project be terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/80 STATUS: Ongoing

TITLE: The Role of the Flexor Carpi Radialis and its Retinaculum in the Stability of the Wrist

START DATE: Undetermined ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Joan Sullivan, MC

KEY WORDS: Wrist, stability

Study Objective: We hypothesize that the flexor carpi radialis and its retinaculum is the strongest stabilizer of the wrist on the radial side and as such should be included in the surgical repair of wrist injuries.

Technical Approach: Thirty fresh frozen adult cadaver wrists will be rapid loaded to ailure utilizing Instron biomechanical testing equipment. Each wrist will be prepared by stripping the soft tissue from the radius and ulna to within 4cm of the wrist. The intraosseous membrane and the flexor carpi radialis will be preserved. The radius and ulna will then be cemented into a steel pipe to preclude forearm rotation. The forearm-assembly will be mounted vertically in the Instron with a force place across the palmar aspect of the metacarpal head at an angle of leading to create wrist extension with ulnar deviation (equivalent to forces observed in actual clinical injuries). Proximalportion of the FCR will be fixed in one gorup by attaching it to the acrylic base and the tension should be 1.2 kilogram. Radiographs will be obtained of the wrists prior to and following loading. Photographs and dissection of the wrists will document the type and extent of injury. Three groups of 10 wrists each will be loaded to test the author's hypothesis:

Group I - Whole undissected cadaver wrists.

Group II - Wrists with the FCR and its retinaculum divided.

Group III - Wrists with radial side wrist ligaments divided (radial collateral ligament, radio-capitate ligament, radio-triquetral ligament), but with the FCP intact.

The force required to disrupt each wrist will be measured by the Instron. Then each disrupted wrist will be radiographed, photographed and a limited dissection performed to document extent and type of injury.

The second portion of the cadaver wrist study will retest surgically repaired wrists. Wrists from Groups I, II, and III will be equally divided (five from each group) and balanced for extent of injury, then repaired surgically. Repair Group A will be corrected in the "Standard" manner, i.e., without requiring the FCR and its retinaculum. Repair Group B will be surgically corrected to include the FCR and its retinaculum. Force loading will then be repeated in each repair group in the same manner as above.

Progress: This study requires a materials testing system to determine ligament strength. Instron Corporation has designed and fabricated the system. Although the instrument has been delivered, it has not yet been installed. The study will not be initiated until the instrument is installed and tested.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 87/93 STATUS: Ongoing

TITLE: Prevention of Stress Fractures Through Modification of Basic Combat Training Physical Training Activities Based on Biodynamics

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Roy W. Tate, MAJ Bruce H. Jones, MC, Janice E. Morales, RN/BioMedical Engineer

KEY WORDS: Stress fracture, Bone

Study Objective: To compare the incidence and distribution, over the course of basic training, of the occurrence of stress fractures, stress reactions, and other musculoskeletal injuries, among Army Basic Combat Trainees participating in one of four variations in physical training. The variations to be studied are (1) progressive training, (2) cycle training with avoidance of running and jumping during the second week, (3) cyclic training with avoidance of running and jumping during the third week and (4) reduced total running mileage.

Specifically, the purpose of this study is to determine whether avoidance of running and marching in the second or third week of training will reduce the incidence of stress fractures, stress reactions of bone and musculoskeletal injuries in general, when compared to progressive training. If there is a decrease in injury is specific to the response to cyclic training or rather due to the decreased running miles.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: 1454 subjects from 6 training companies at Fort Bliss have been entered into the study. Demographic data and anthropomorphic measurements have been collected on all volunteers. Injury reports and APFT scores are being collected as per protocol. Bone scans are being performed as per protocol. Data collection is now complete for 3 companies. Data collection for the remaining companies will be completed by December 1989.

Computer data entry has been initiated. Analysis of the study will begin in December 1989.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/17 STATUS: Ongoing

TITLE: Free Vascularized Parathyroid Gland Transfer in Dogs

START DATE: 1988 ESTIMATED COMPLETION DATE: Jul 90

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Paul R. Cordts, MC; MAJ Albert J. Moreno, MC

KEY WORDS: Parathyroid, transplant

Study Objective: To determine if a total parathyroidectomy with vascularized autotransfer can be performed with consistently greater success than avascular autotransfer techniques.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Twelve dogs have undergone parathyroid transplantation. Data collection has been completed on 10 dogs. The remaining 2 dogs will have completed the study in December 1989. Data analysis and manuscript preparation will begin immediately thereafter.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/24 STATUS: Completed

TITLE: Influence of Vessel Size Discrepancy on Patency in Microvascular Reanastomosis using the Rat Model

START DATE: Oct 88 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Microvascular anastomosis

Study Objective: To determine patency, after healing,in vessels grated end-to-end with discrepancies in lumen diameter.

Technical Approach: The rat will be prepped with surgical scrub, sterile drapes applied and placed in a dorsal recumbent position. An incision will be made over the medial aspects of the lower extremities bilaterally. The femoral artery will be exposed, from the femoral canal to the bifurcation of the profundus, as well as exposing numerous branches.

The femoral artery in the adult rat is approximately 1mm in diameter. The femoral artery will be measured, the results recorded, then a branch of the femoral artery of 0.25mm, 0.5mm, or 0.75mm will be isolated. The femoral artery, if 1mm in diameter, will be transected distal to a branch of suitable size, then grafted to the transected branch using 10-0 nylon suture. A series of 5 grafts will be performed with each size vessel (0.25mm, 0.50mm, and 0.75mm) as well as a series of 5, using grafts of similar size. On the contralateral leg, the femoral artery will be transected and reapproximated for use as a 1mm to 1mm control. The animals are to be kept alive and allowed to heal for approximately 2 weeks, at which time they will be reopened and explored, and the patiency of the vascular grafts determined by direct visualization.

Progress:

Group I. Graft to artery ratio 1:1. Patency rate 90% (18/20).
Group II. Ratio 0.75 : 1. Patency rate = 80% (16/20).
Group III. Ratio 0.5 : 1. Patency rate = 60% (12/20).
Group IV. Ratio 0.25 : 1. Patency rate = 20% (4/20).
Group V. Ratio 2 : 1. Patency rate = 60% (12/20).

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/44 STATUS: Ongoing

TITLE: Determination of Bone Manganese Levels in Patients with Chondromalacia Patella. (Monitor: COL Maldonado)

START DATE: May 88 ESTIMATED COMPLETION DATE: May 90

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John Cook, MC; MAJ John Uhorchak

KEY WORDS: Chondromalacia, Manganese

Study Objective:

1. Identify and characterize by symptoms and physical findings the patient group with patellofemoral pain syndrome.
2. When performing diagnostic arthroscopy of patients with knee impairments, observe and record the character of the patellofemoral articular cartilage including objective measurement of cartilage softness.
3. Obtain 1 gram bone biopsy specimens from the distal femoral metaphysis at the time of arthroscopy and determine manganese content of bone mineral.
4. Perform multivariate analysis of data to observe possible correlations of bone manganese levels with severity of signs and symptoms of chondromalacia, cartilage appearance and measure cartilage softness.

Technical Approach: The study will be conducted at WBAMC and UTEP. Clinical evaluation will take place at WBAMC. The patients presenting to the Orthopaedic Clinic with knee disorders requiring arthroscopy or arthrotomy will be counseled and asked to volunteer for this study. If their informed consent is obtained they will be asked to provide information to complete the clinical questionnaire. The results of a comprehensive physical examination of the knees will also be recorded. At arthroscopy or arthrotomy the character of the articular cartilage will be noted and graded for severity of chondromalacia by the criteria of Hugston, et al. The indentation hardness of the cartilage will then be measured by a modification of the Brinell hardness measurement technique. This will be done with a locally fabricated instrument which can be autoclave sterilized. A biopsy specimen consisting of 1 gram of bone will be obtained from the distal femoral metaphysis using standard bone biopsy techniques. A portion of the specimen will be submitted for routine histology and the remainder will be analyzed for manganese content. The portion for manganese assay will be asked at 900 degrees centigrade, the ash weighed, dissolved in EDTA decalcifying solution, and analyzed with a Beckman plasma spectrophotometer at UTEP. All biopsy specimens sent to UTEP will be identified by code number only.

Progress: The initial phase of this study was directed towards the design, fabrication and testing of an instrument to measure cartilage hardness in patients undergoing surgical procedures on the knees. We are satisfied that the instrument will perform adequately.

A modified arthroscope has been produced which can perform this function. The instrument has a linear response from 0.1 to 2.4 mm of cartilage induction with a 2.0 mm round probe.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/25 STATUS: Ongoing

TITLE: Vascular Changes Associated with Stress Reaction of Bone in the Rat

START DATE: May 89 ESTIMATED COMPLETION DATE: May 90

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John M. Uhorchak, MC

KEY WORDS: Stress reaction, bone

Study Objective: To determine the sequence and character of vascular changes which occur in living bone after it has been subjected to repeated physical stress.

Technical Approach: We will study the character and chronological sequence of vascular changes which occur in rat legs subjected to mechanical stress in the absence of confounding electrical shocks.

a. Thirty anesthetized rats will have their left leg cyclicly mechanically stressed using the techniques of Scully et.al. The tibias will be cyclicly strained to 0.5 mm by repeated application of a 3 point bending load. 10,000 cycles of strain will be applied to the left tibia of each rat at a rate of 10 Hz. The animals will then be recovered from anesthesia and maintained in standard laboratory cages with unrestricted activity, on a standard laboratory diet. Groups of 2 animals will be selected at random on days 0, 1, 2, 3, 4, 5, 6, 7, 10, 12, 15, 18, 24 and 30 days after the initial strain loading.

b. On the date selected the animals will be anesthetized with Nembutal at a dose of 25mg/kg intravenously. The rats will then be heparinized and injected with Xylocaine to prevent vascular thrombosis and to ensure maximum vasodilation. The animals will then be given a lethal dose of Nembutal. After euthanasia the abdomens will be opened through a midline abdominal incision. The aorta and inferior vena cava will be transected and cannulated. Using techniques prescribed in the Microfil product literature the aorta and both lower extremities will be perfused with Microfil at a pressure of 150 mm of mercury. Perfusion will continue until the flow of the Microfil is returned via the inferior vena cava. At that point the animals will be refrigerated to allow overnight curing of the Microfil. As each animal has had only one leg stressed, the contralateral leg will serve as a control. Radiographs will be taken of both lower extremities to delineate the microvascular structure. Microfil is a radio-opaque material. After the radiographs are obtained, tissue clearing will be performed by the following technique: on the first day both tibias will be immersed in a 25% ethanol solution. On the second day 50% ethanol, on the third 75% ethanol, on the fourth day 95% ethanol and on the fifth day a new solution of absolute alcohol. On the sixth day the specimen will be immersed for 24 hours in methylsalicylate. If the tissue is not clear it will be returned to a 95 % ethanol solution and the fine cleaning procedure steps will be repeated. Photographs will then be taken of the vascular tree which will have been filled with colored Microfil. The tibias will then be imbedded and sectioned for standard histologic sectioning.

Progress: Techniques for the injection of the vascular structures in rat legs were developed in 6 rats.

The left legs of 9 rats were then subjected to cyclic stress (10,000 cycles). These rats are being harvested as per protocol and their vascular trees are being injected with microfil. The soft tissues are then being clarified as per protocol.

The study is progressing quite satisfactorily and should be completed by May 1990.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/82 STATUS: Ongoing

TITLE: Ultrasound Screening for AAA in Asymptomatic Males Over Age 55

START DATE: Jan 90 ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: CPT James B. Smith

DEPARTMENT: Surg FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail III, MC; CPT Donna Corvette, MC; MAJ Cass Conaway, MC; LTC James C. Griffith, MC

KEY WORDS: AAA, Ultrasound Screening

Study Objective: To ascertain the incidence of AAA (Abdominal Aortic Aneurysm) in asymptomatic males over age 55 admitted to WBAMC for other reasons.

Technical Approach: All males age 55 and older admitted to Internal Medicine or Department of Surgery wards at WBAMC will be included in the study (approximately 180 per month) and will receive an abdominal aortic ultrasound examination. Patients with prior abdominal aortic surgery for aneurysm or occlusive disease will be excluded. All participants will be provided with a written explanation of the protocol. Patients with known AAA previously proven by ultrasound or CT Scan need not be submitted to repeat examination, if last previous study was within the past 6 months. Patients will be notified of the results of the ultrasound examination. Patients with positive findings for AAA will be referred to Vascular Surgery Service for Appropriate follow-up. A negative finding will result in completion of participation in the study. The study will run for six months.

Success/failure criteria: Aneurysm will be defined as enlargement of the anteroposterior or transverse aortic diameter more than 1.5 times the diameter of the proximal aorta, or greater than 4 centimeters in diameter.

Data Collection: Patients will be interviewed by a physician for pertinent history of smoking, HTN, CAD, ASPVD, hyperlipidemia, or family hisotry of AAA (maternal versus paternal).

Ultrasound examination will be performed by the Department of Radiology using their standard real-time ultrasound equipment: Diasonics model DRF 400, and read by a staff radiologist.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/52 STATUS: Ongoing

TITLE: Combat Trauma Life Support Procedure in the Sheep Model

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CW2 G.A. Bendeck

DEPARTMENT: FBT FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CW2 Mark Adelman, PA-C

KEY WORDS: Life support, combat trauma

Study Objective: To train Physicians Assistants and Line Medics who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function in a combat environment. The sheep model will simulate human trauma.

Technical Approach:

ANIMAL PROCEDURES:

1. Cricothyroidoctomy
2. Venous Cutdown
3. Entubation
4. Chest Trauma Management
    a. Needle decompression
    b. Tube thoracostomy

ATLS training manuals will be used for each training procedure.

Progress: A total of 48 field medics received training in emergency trauma life support techniques utilizing the sheep model. The training proved invaluable in that the medics gained a great deal of confidence and skill by directly participating in these laboratories.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/38 STATUS: Ongoing

TITLE: Oxygen Desaturation in Patients Using Nalbuphine or Midazolam for Sedation Under Spinal Anesthesia

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Feb 90

PRINCIPAL INVESTIGATOR: CPT Kimberly A. Beres

DEPARTMENT: Nursing FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Steven P. Kelsch, MAJ, AN; Joel J. Schretenthaler, CPT, AN

KEY WORDS: Osygen desaturation, Nalbuphine, Midazolam

Study Objective: To determine if sedation, using nalbuphine or midazolam, is associated with oxygen desaturation under spinal anesthesia.

Technical Approach: Fifty ASA I patients undergoing lower limb surgery under spinal anesthesia (to a dermatomal level of T-4 or below) who have given informed consent will be studies. This is a small sample and it will provide an answer to the question posed in this study, although it is too small to allow for generalized assumptions.

Each study patient will randomly be assigned to one of two study groups using the last digit of their sponsor's social security number. The odd numbers will be assigned to the nalbuphine group and the even numbers to the midazolam group.

All patients will be premedicated with diazepam, 0.15 mg/kg up to 10 mg. by mouth, one hour before induction of anesthesia. Upon arrival in the operating room, an intravenous cannula will be placed in the nondominant hand. Baseline values for heart rate, blood pressure, respiration, temperature, oxygen saturation, and time of premedication will be recorded. After the lumbar puncture, vital signs, oxygen saturation, and upper level of the spinal block (analgesia to pinprick) will be recorded at 5 minutes after the block and every 5 minutes up to 45 minutes or until the end of the case, which ever comes first. Sedation will begin 10 minutes after the xylocaine has been injected into the subarachnoid space. The dose will be recorded on the data collection sheet. Maximum dosages are as follows: nalbuphine, up to 0.4 mg/kg; midazolam, up to 0.1 mg/kg, with the optimal level of sedation determined by the investigators as a score of 2. This level of sedation will also be recorded. If the oxygen saturation falls below 5% of baseline for any given patient, the study will be terminated and oxygen, 3 liters via nasal cannula, will be administered and normal intraoperative monitoring will continue.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/70 STATUS: Transferred

TITLE: Efficacy of Immunotherapy for Systemic Allergic Reaction to Imported Fire Ant Stings

START DATE: ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: LTC Antonio L. Bunker-Soler

DEPARTMENT: Med FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Systemic allergic reaction, Fire ant stings, Immunotherapy

Study Objective:

a. To ascertain the relative efficacy of immunotherapy with whole body extracts and venom compared to placebo in the treatment of systemic hypersensitivity to stings of the imported fire ant.

b. To ascertain the natural history of imported fire ant hypersensitivity.

c. To identify possible subgroups who may undergo spontaneous desensitization and not require immunotherapy.

Technical Approach: Study groups will include (1) a whole body aqueous extract treatment group and (2) a placebo treatment group, and (3) Venom treatment group. Group sizes will range from 8 to 10 patients in the whole body extract treatment group and 16 to 20 patients in the placebo group. The placebo group is expected to follow a clinical course representative of the natural history of the disease without the interference of therapy. This design will allow the elimination of any subgroup with spontaneous desensitization.

Progress: This protocol was approved by the William Beaumont Army Medical Center IRB, with the stipulation that it could not be initiated until receipt of written approval by the Wilford Hall IRB. This office has never been notified of Wilford Hall IRB's decision.

The principal investigator has PCS'd, and a new principal investigator (from Dwight David Eisenhower Army Medical Center) was appointed. This protocol no longer fall under the purview of the William Beaumont Army Medical Center IRB and is, therefore transferred to Dwight David.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/77 STATUS: Ongoing

TITLE: Use of Venous pH in the Initial Evaluation of Pediatric Patients with Diabetic Ketoacidosis

START DATE: Oct 88 ESTIMATED COMPLETION DATE: Oct 90

PRINCIPAL INVESTIGATOR: CPT Charles W. Callahan

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Daniel J. Dire, MC

KEY WORDS: Venous pH, diabetic ketoacidosis

Study Objective: To determine the utility of venous pH to define the degree of acidosis in the initial evaluation of the pediatric patient with diabetic ketoacidosis.

Technical Approach: We will compare an arterial and venous pH sample in all patients who present in diabetic ketoacidosis to the emergency room at Darn Army Community Hospital over an 18 month period, or until a sufficient population size is reached (N=100). Patients will be eligible for this study if they are between the ages of 1 and 18 years old, and have clinical and laboratory evidence consistent with ketoacidosis or who are known diabetics who have presented with similar symptoms of ketoacidosis in the past. A single (1.5cc) sample of arterial blood will be obtained from the radial artery of the patient by an emergency room staff member or by the investigators, as is the standard for defining acidosis in this setting. A single (1.5cc) sample of venous blood will also be obtained simultaneously with the other venous samples taken from the IV once intravenous access has been established. These two values will be compared and the results analyzed statistically. consent for the additional laboratory study will be obtained, although no additional sampling procedures will be necessary.

Demographic and laboratory data will be recorded on a database form initiated in the emergency room and subsequently entered into a computer for statistical analysis in collaboration with the department of Clinical Investigation at William Beaumont Army Medical Center.

Progress: Slower progress than anticipated in collection patients. However, in few cases so far, have noted a trend. Anticipate completion of study with additional 1-15 patients. May need additional time beyond June 1990 to gather sufficient number of patients.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/18 STATUS: Ongoing

TITLE: A Prospective Evaluation of Subcutaneous Epinephrine Combined with Nebulized Albuterol in the Initial Treatment of Acute Asthma in the Emergency Department

START DATE: Apr 89 ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: MAJ Richard E. Collister

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Daniel J. Dire, MC

KEY WORDS: Asthma, Epinephrine, Albuterol

Study Objective: Firstly, to determine whether subcutaneous epinephrine adds significantly to bronchodilation obtained with a nebulized beta-agonist alone in the setting of an acute asthmatic exacerbation. Secondly, to determine any additional side affects of simultaneously administered subcutaneous epinephrine and nebulized albuterol.

Technical Approach: Patients aged 18 to 65 who present to the Emergency Department with a history of asthma and clinical evidence of an acute exacerbation (dyspnea, diffuse wheezing, and a significantly reduced FEV_1) or those presenting with new-onset asthma will be considered for enrollment in this double-blinded study. Those with a history of albuterol allergy, cardiovascular disease, chronic steroid dependence, emphysema, chronic bronchitis, or cigarette smoking will be excluded. Pregnant women willl also be ineligible. After a brief history is obtained and supportive (such as nasal oxygen) instituted, initial spirometry will be performed. The best FEV_1 of three attempts will be recorded as the pre-treatment baseline. Those with an initial FEV_1 in the 25% to 75% range of predicted values will be randomized (with their informed consent) into one of two treatment groups by alternating every other patient.

The first group (GROUP I) will receive an initial treatment consisting of 0.01 mg/kg of subcutaneous 1:1000 epinephrine (maximum of 0.3 mg or 0.3 cc). The second group (GROUP 2) will receive 0.3 cc of sterile normale saline subcutaneously. Simultaneous with the injection, both groups will receive an aerosolized updaft of albuterol 2.5 mg in 2.5 cc of normal saline. Both treatment groups will receive additional doses of aerosolized albuterol at 20 minutes and 40 minutes after the initial doses, if clinically indicated. All patients will be placed on a cardiac monitor and have their vital signs taken every 15 minutes. Post-treatment spirometry will be performed 30 minutes and 60 minutes after the initial treatment.

Once post-treatment spirometry has been completed, the physician in attendance may use any and all therapeutic modalities he/she deems necessary, to include theophylline loading and intravenous corticosteroids. Since all study participants receive prompt bronchodilator therapy and since the study's design excludes those with severely impaired pulmonary function, the risk of participation should be minimal. The treating physician will be blinded to the treatment group. Only the ER nurse who gives the subcutaneous injection will know whether the patient received epinephrine or placebo. If a patient's clinical condition deteriorates, the physician will remove him/her from the study, the ER nurse will inform the physician what treatment group the patient was entered into (i.e., did the patient receive epinephrine or placebo), and maximum therapy will be initiated.

Data will be entered into a computer data base and statistical analysis will be based upon the following null hypothesis: the mean FEV_1 percent-improved observed in Group 1 is not significantly better than that observed in Group 2. The two-tailed t-test will be utilized to accept or reject the null hypothesis.

Progress: Twenty-six subjects have been entered into this protocol. There have been no adverse effects, and no one has required hospital admission.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/47 STATUS: Ongoing

TITLE: CSCC Program Evaluation

START DATE: Nov 89 ESTIMATED COMPLETION DATE: Mar 90

PRINCIPAL INVESTIGATOR: CPT Lang Coleman

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: CSCC

Study Objective: This project is designed to determine the relative therapeutic effectiveness of the CSCC program.

Technical Approach: All subjects will be active duty soldiers treated at Ft. Hood's CMHS. Participation is strictly voluntary. There will be 50 subjects from the CSCC program and 50 matched control subjects from other modalities of outpatient treatment. All subjects will be selected from cases dispositioned at the CMHS. The controls will be matched within five days of their initial CMHS sign in, and will be matched to the CSCC subjects for demographic as well as selected clinical criteria, e.g., type of problem, severity.

This project uses a quasi-experimental approach with a pre-test/post-test design. The project design also includes follow up evaluations at one and three month intervals. Data collection involves the use of three standardized psychometric instruments, (labeled the basic battery) and four instruments of local design addressing the subject's military performance. Of the locally designed instruments, two are intended for use as phone questionnaires, and are to be answered by the subject's first line supervisor regarding performance of the subject within his unit.

Once a subject agrees to participate in the study, he will be given a pre-test consisting of the basic battery and the subject's self evaluation questionnaire. A research assistant will ensure completion of the first line supervisor's pre-evaluation. The post-test will be given after three weeks. It will consist of the basic battery and subject post-evaluation. At both the one month and three month followup evaluations, the subject will retake the basic battery and the post self-evaluation. A research assistant will complete post evaluations from first line supervisors at both of the followups. The data collected will be analyzed using a completely randomized block design.

Any of the following will result in premature termination of a subject as a part of the study: failure to complete CSCC, subject refusal to continue participation in the project, ETS or PCS. Otherwise, subject's participation will be terminated after the completion of the three month followup evaluation.

Progress: Funding for research assistants which will commence on or about 1 Nov 89 enables us to begin the project. Computer programs and evaluation materials are in place.

DETAIL SUMMARY SHEET

DATE: 1 October 89 **PROTOCOL #: 89/74** **STATUS: Ongoing**

TITLE: Effectiveness of Splinting for Carpal Tunnel Syndrome During Pregnancy

START DATE: Nov 89 **ESTIMATED COMPLETION DATE: Nov 90**

PRINCIPAL INVESTIGATOR: CPT Robbie Courts

DEPARTMENT: Darnall **FACILITY: Darnall Army Community Hospital**

ASSOCIATED INVESTIGATORS: CPT Madelyn Otts, AMSC (LOTR)

KEY WORDS: Carpal tunnel syndrome, pregnancy, splinting

Study Objective: **To determine if volar wrist splints are effective in decreasing subjective and objective symptoms of carpal tunnel syndrome during pregnancy.**

Technical Application: **Use of survey form to assess subjective and objective symptoms of CTS during pregnancy, to be measured over a period of time: (1) initial referral, (2) one week after splinting, (3) additional follow-up if no improvement of symptoms after one week of splinting, (4) four weeks postpartum to see if symptoms are absent without splinting (indicating full recovery), (5) additional follow-up or referral to orthopedics PRN if symptoms persist postpartum.**

Treatment includes patient education on carpal tunnel syndrome and importance of wrist positioning during sleep and activities, fabrication of thermoplastic volar wrist splint(s), measurements of grip and pinch strength, sensation (sharp/dull and two-point), range of motion (if not within normal limits), and documentation of subjective symptoms. Nerve conduction studies will not be ordered due to expense, uncomfortableness of the test, and expected short duraiton of the CTS symptoms during pregnancy.

The subjects included in the study will consist of all pregnant women referred to OT with symptoms consistent with CTS.

OT staff will collect data on a survey form using patient interview and standard methods of testing for grip, pinch, sensation, Tinnel's and Phalen's.

Progress: **This is a newly approved study with no results to date.**

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/02 STATUS: Ongoing

TITLE: A Comparison of the Stimson and Hennepin Techniques in the Reduction of Anterior Shoulder Dislocation (Monitor: MAJ R. Wilkerson)

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Apr 89

PRINCIPAL INVESTIGATOR: CPT Robert G. Creath

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Daniel J. Dire, CPT, MC

KEY WORDS: Shoulder dislocation

Study Objective: To determine if three are significant differences between the Hennepin and Stimson techniques of shoulder reduction in regards to the time required for reduction, subjective patient appraisal of discomfort during reduction, and post-reduction complications.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Progress to date has been slower than anticipated. The study is going well and without complications. All patients have been managed well. anticipate asking for extension to obtain 50 total patients for adequate statistical analysis.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/16 STATUS: Ongoing

TITLE: A Prospective Analysis of Demerol, Phenergan, and Thorazine Administration to Pediatric Emergency Department Patients (Monitor: CPT Bernard Smyle)

START DATE: May 89 ESTIMATED COMPLETION DATE: Dec 89

PRINCIPAL INVESTIGATOR: CPT Daniel J. Dire

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Howell E. Davis, MC

KEY WORDS: Demerol, Phenergan, Thorazine

Study Objective: This study is being undertaken to prospectively identify specific measures of efficacy and determine the incidence of minor side effects for the use of Demerol, Phenergan, and Thorazine (DPT) in combination for a preselected group of pediatric emergency room (ER) patients. The study will demonstrate the benefits of using DPT in preselected patients in terms of patients time in the ER as well as how DPT can prevent some of the emotional trauma that frequently besets children and parents during ER care (i.e. suturing lacerations). We hope to demonstrate the enhanced means by which the health care provider can perform their work on the child while obtaining excellent results.

Technical Approach: Pediatric ER patients will be preselected upon their arrival to the ER based on a set criteria for entry into the study. By preselecting the patients according to a set criteria we can standardize our results and comment accurately on appropriate dosage, efficacy, side effects, and monitoring procedures pertaining to the study population. In order to complete the study a minimum of 200 participants will be selected pertaining to age, presenting complaint, history of chronic illness, initial vital signs, indications, and initial mental status with further assessment pertaining to dosage of DPT required, interval exams pertaining to vital signs and mental status, and complications both serious and minor. The dosage utilized for the DPT injections will be 2 mg/kg for Demerol with a maximum dose of 50 mg; 1 mg/kg of Phenergan with a maximum dose of 25 mg; and 1 mg/kg of Thorazine with a maximum dose of 25 mg, all to be given intramuscular.

Progress: Thirteen patients have been enrolled in this study to date. No complications and no withdrawals to report.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/87 STATUS: Ongoing

TITLE: A Prospective Evaluation of Topical Antibiotics in Preventing Infections in Uncomplicated Soft Tisue Laceration

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Jan 90

PRINCIPAL INVESTIGATOR: CPT Daniel J. Dire

DEPARTMENT: Darnall FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: David A. Dwer, CPT, MC; Marco Copola, CPT, MC; Jerry Karr, CPT, MC; John J. Lorette, Jr., CPT, MC

KEY WORDS: Infections, Topical Antibiotics

Study Objective: To show whether there is a statistically significant difference in the infection rates among uncomplicated repaired lacerations that are dressed with topical Bacitracin, NeosporinR, SilvadeneR, or placebo.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: This is a newly approved study with no results to date.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/56 STATUS: Terminated

TITLE: Single Dose Ceftriaxone for Uncomplicated UTI in Women (Monitor: MAJ Karl Kreder)

START DATE: Aug 88 ESTIMATED COMPLETION DATE:

PRINCIPAL INVESTIGATOR: CPT Douglas B. Ferguson

DEPARTMENT: Darn FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Ceftriaxone IV

Study Objective: This study intends to document the efficacy, and decreased side-effects, with 250mg and 500mg of Ceftriaxone versus a 5-day course of Trimethoprim-Sulfamethoxazole in the treatment of uncomplicated urinary tract infections in women.

Technical Approach: Specific methods and techniques: Patients with uncomplicated urinary tract infections will be asked to enter into the randomized controlled study. Both urinalysis and urine cultures and sensitivities will be obtained from all of them. They will be randomized into 3 treatment groups. the 3 treatment groups include: single intramuscular dose of 500mg Ceftriaxone, single intramuscular dose of 250mg Ceftriaxone, and 5-day course of oral trimethoprim-sulfamethoxazole 2 times per day. The method of treatment, and an informed consent, will be enclosed in an unmarked envolope. The envelopes will be arranged in random order by the hospital pharmacy.

All patients who are treated will be instructed to return to the emergency Department for re-examination 3-5 days, and 4-6 weeks after treatment. At each visit, urine culture and sensitivity will be obtained. Also, the investigator will fill out a questionnaire in the first visit about drug intolerance, and in both visits about recurrent urinary tract symptoms.

Progress: The protocol has been terminated due to the inability to enroll enough patients into the protocol in a timely manner.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/17 STATUS: Ongoing

TITLE: The Incidence of Abnormal Electrocardiograms in Emergency Department Patients with Head Trauma

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Jul 90

PRINCIPAL INVESTIGATOR: CPT David E. Hogan

DEPARTMENT: ER FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Daniel J. Dire, MC

KEY WORDS: Electrocardiograms, Head trauma

Study Objective: To show whether there is a significant incidence of electrocardiographic (EKG) abnormalities especially dysrhythmias in Emergency Department (ED) patients with head trauma.

Technical Approach: All patients who present to the ED for initial treatment of any head injury (e.g. blunt trauma such as from falls, assaults, or vehicular accidents, and penetrating trauma such as gunshot wounds or open skull fractures) will be evaluated for participation in this study. Informed consent will be obtained from all patients except those with an altered mental status.

Patients will be excluded from this study if they have any of the following:

1. History of chest pain, cardiac disease, prior abnormal electrocardiograms, or a history of prior dysrhythmias.
2. History of seizure disorders or patients who are actively seizing.
3. Patients on any of the following type of drugs: anticholinergics, antihistamine, antidysrhythmics, antileptics, beta blockers, calcium channal blockers, decongestants, theophylline, sympathomimetics (including cocaine and amphetamines.
4. Age less than 16 years old.
5. Major blunt or penetrating chest trauma with signs or symptoms of myocardial injury, pulmonary contusions, or hypoxia.
6. Patients in circulatory shock.

All patients will have cardiac monitoring initiated upon their presentation for treatment to the ED and continued for a minimum of one hour. A 12 lead EKG will be performed during the course of their treatment.

A healthy, nontraumatized, age/sex matched control will be solicited from the ED waiting room who must not have any of the exclusion criteria listed above. Also, they must not be a patient waiting to be seen. Informed consent will be obtained from these subjects, a 12 lead EKG will be taken, and cardiac monitoring will be initiated for 1 hour.

Epidemiological and clinical data will be collected at the time of initial presentation.

All EKG's will be read by a staff internist who will be blinded to its source. The EKG interpretations will be recorded. Data will be entered into a computer database and analysed in collaboration with the Department of Clinical Investigation, WBAMC.

Progress: Continuing to follow protocol for patient and data collection. At this point no clear trends can be identified.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/28 STATUS: Completed

TITLE: Marital Dynamic Survey

START DATE: Aug 88 ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: CPT David Hurlbert

DEPARTMENT: Psych FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Spouse abuse, family violence, marital adjustment

Study Objective: To study many facets of the interrelationship of married couples in order to better understand the complexities of wife abuse and some of the dynamics associated with it.

Technical Approach: The research design includes a questionnaire to be administered to both spouses involved in one of two types of marital therapy groups: the DCCP (Domestic Conflict Containment Program) and the Social Work Couples Group. The Social Work Couples Group includes people who seek therapy for the purpose of marital enrichment, to improve communication, to help them to attain greater levels of intimacy. These couples were screened to eliminate those with problems of family violence or drug or alcohol abuse. It may be assumed that these are relatively happily married people who are seeking to enrich an already stable relationship. The second group consists of people who were referred because of reports of family violence, which usually means wife abuse. They are required to participate in the group. Among the variables to be studied are: length of marriage, how long couples knew each other before marriage, attitudes toward traditional gender roles, household division of labor, power distribution within the family, autonomy of spouses, liking and loving, marital satisfaction, and levels of marital conflict. Participating couples in each group will be matched by racial or ethnic background, age, and military rank in order to provide as much control as possible over possibly relevant variables. The questionnaire is self-administered, with utmost precaution taken to protect confidentiality, even between spouses. It should take between 30 to 45 minutes to administer. Couples in each group will be asked to complete a questionnaire at the beginning and end of the eight-week session, in order for within-group and between-group comparisons to be made. The use of the two groups provides a perfect opportunity for comparison because if there are significant differences on any of the measures between the groups, then these measures might be inferred to be predictors of potential wife abuse. If scores on any of these measures change after therapy, particularly for the couples in the DCCP group, then some conclusions might be drawn about the effects of therapy, particularly if spouses become more egalitarian with regard to power or less rigid with regard to gender roles. A precursory review of the relevant literature suggests some preliminary hypotheses:

(1) Wife abuse is associated with subscription to traditional gender roles.
(2) Wife abuse is associated with a rigid household division of labor.
(3) Wife abuse is associated with an unequal power distribution within the family.
(4) Wife abuse is associated with significantly less autonomy for the wife than for the husband.
(5) Wife abuse is associated with lack of outside employment for the wife.
(6) Wife abuse is associated with higher liking and loving scores for the wife than for the husband.

Progress: Study was completed. Sixty subjects were entered into this study; no adverse reactions or withdrawals noted.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/57 STATUS: Ongoing

TITLE: Animal Model (Caprine) Laboratory, Advanced Trauma Life Support Course (ATLS)

START DATE: Jul 1988 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL John W. Kolmer

DEPARTMENT: HQ FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: MAJ Michael W. Yehle

KEY WORDS: Trauma

Study Objective: This protocol will mandate the following - proper procurement of animals, humane care of animals prior to and during surgical procedures, appropriate anesthetics and monitoring of anesthesia level during the procedures, detailed description of surgical procedures involved, and humane euthanasia with proper disposal of euthanized animals.

Technical Approach: The Advanced Trauma Life Support (ATLS) training program is designed for physicians who are primarily responsible for managing the critically injured patient; The American College of Surgeons (ACS) Committee on Trauma defines the standards that the ATLS course must adhere to. Initial assessment and management of specific types of injuries are presented to the students through lecture and slide presentations. Students then rotate through practical skill stations associated with the lecture content previously presented. The skill stations and animal lab allow the student to observe and practice to proficiency those life-saving skills necessary in the initial management and stabilization of the trauma patient. The animal lab is a one hour affair with one instructor and four students assigned to each animal.

Procedures:

a. Preparation of animals
b. Intravenous administration of fluids
c. Tracheal intubation
d. Venous cutdown
e. Peritoneal lavage
f. Needle Thoracocentesis
g. Chest tube insertion
h. Pericardiocentesis
i. Cricothyroidotomy

Progress: Twenty-four students and six instructors participated in the Animal Model (Caprine) Laboratory, Advanced Trauma Life Support course (ATLS). All procedures were successfully completed and all students completed the laboratory. There were six animals (goats) used during the laboratory.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/05 STATUS: Completed

TITLE: Treatment of Hypercalcemia Arrest in the Swine Model: Efficacy of Verapamil, Magnesium Sulfate and Sodium Bicarbonate

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Mar 89

PRINCIPAL INVESTIGATOR: CPT Brent A. Smith

DEPARTMENT: ER FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Gregor P. Moore, CPT James A. Morgan, CPT James E. Ellis

KEY WORDS: Magnesium, Sodium Bicarbonate, Verapamil, Resuscitation, Arrest

Study Objective: To study the efficacy of 3 different treatment modalities for hypercalcemic cardiac arrest in the intact pig.

Technical Approach: Five animals in each of 4 groups will be studied. Each animal will be given anesthesia by the veterinary staff. Femoral arterial and venous catheters will be placed via cutdown utilizing 1% lidocaine as a local anesthetic in a sterile manner. these catheters will be used for continuous blood pressure monitoring and venous access for the treatment modalities respectively.

Continuous lead II ECG monitoring utilizing externally placed leads will be done. Following an equilibration period a 10% solution of CaC1 100mg/kg will be given IV push; cardiac arrest is expected and will be confirmed by ECG and arterial pressure monitoring. Repeat doses of CaC1 will be given as needed to achieve cardiac arrest should the first dose fail. Following arrest 1 of 4 intervention drugs will be given IV push.

Group 1: 0.9% NaC1 20cc (Control Group)
Group 2: Magnesium sulfate 50% solution at a dose to provide approximately 1 equivalent of Mg ion per equivalent Ca ion.
Group 3: Verapamil HC1 2.5mg/kg body weight. A repeat dose will be given in 3 minutes if no response is obtained.
Group 4: Sodium bicarbonarte 1meq/kg body weight. A repeat dose will be given in 3 minutes if no response is obtained.

Arterial blood gas samples will be drawn at the onset of cardiac arrest and after the intervention drug for group 4. A technician or one of the authors will record the response of mean arterial blood pressure, heart rate and cardiac rhythm for each group.

Survival manifested by an organized cardiac rhythm and measurable blood pressure will be determined at 5 minutes and 15 minutes after intervention.

ADDENDUM: Experimental Design: The design is the same, except that there will be 6 animals per group and 1 additional animal will be used to determine calcium chloride dosage required to achieve cardiac arrest.

Progress: The study protocol was completed in March 1989 at WBAMC. Data has been analyzed, the literature reviewed and a first draft of a manuscript towards submission of a paper for publication in the Emergency Medicine literature has been completed.

Hypercalcemia is a common medical disorder which may cause cardiotoxicity. Current treatment of life-threatening hypercalcemia is either too slow, unavailable, or risky. A swine model of acute hypercalcemic cardiac arrest was utilized to test the efficacy of three readily available, rapidly acting agents with calcium antagonist properties. Hypercalcemic arrest was induced with the rapid infusion of CaC12 (300mg/kg) and swine were randomly assigned to receive one of four interventions through a central venous catheter: 0.9% NaCl (Control), verapamil HCl, Magnesium Sulfate, or Sodium Bicarbonate. continuous ECG and arterial blood pressure monitoring was performed. Cardiac arrest manifested as ventricular fibrillation within 4 to 12 seconds of CaCl2 injection. A total of 14 animals were studied and none of the interventions were effective in reversing the arrest rhythm. We conclude that at the doses used, these agents were not efficacious in reversing acute hypercalcemic arrest, but further study may be warranted.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/44 STATUS: Terminated

TITLE: CooperVision CILCO Intraocular Lenses (IOLs)

START DATE: May 89 ESTIMATED COMPLETION DATE: Nov 89

PRINCIPAL INVESTIGATOR: M.D. Peter J. Speicher

DEPARTMENT: Surg FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Cataract

Study Objective: To determine, through clinical study, the safety and efficacy of CooperVision CILCO IOL implants following cataract extractions.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: One patient was given an anteria chamber lens, when a posterior chamber lens could not be placed. The patient is doing well at the present time.

The study was terminated by CooperVision CILCO.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 88/66 STATUS: Ongoing

TITLE: Treatment of Hypercholesterolemia with Psyllium Hydophilic Mucilloid (Metamucil)

START DATE: May 1988 ESTIMATED COMPLETION DATE: Oct 1990

PRINCIPAL INVESTIGATOR: CPT Richard E. Whitlow

DEPARTMENT: ER FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Julia A. Morgan, D.O.; Richard D. Harwood, R.N.P.; Rebecca J. Oskey, R.N.P.; Elizabeth Kist, R.D.; Ann Andersen, R.D.

KEY WORDS: Hypercholesterolemia, Psyllium Hydophilic Mucilloid (Metamucil)

Study Objective: To define the optimal safe dosing of psyllium huydophilic mucilloid to lower total and LDL cholesterol and define the long-term efficacy and safety of psyllium hydophilic mucilloid. this study will be conducted in a randomized prospective, controlled manner.

Technical Approach: Patients will be enrolled from a variety of sources: random cholesterol screening tests, over-40 physical examinations, commanders' physical examination, commanders' total fitness course, and patients referred to Nutrition Clinic for dietary therapy. The patients will initially undergo a battery of screening tests as well as a history and physical exam to determine secondary causes of hypercholesterolemia (untreated hypothyroidism, obstructive liver disease, nephrotic syndrome). The study medication is psyllium hydophilic mucilloid (blond Plantago psyllium, Metamucil) in varying doses and intervals. Only patients with serum cholesterols between 200 and 260 mg/dl with two coronary heart disease risk factors will be studied since therapy is recommended for this group by the NCEP and the magnitude of expected response is reasonable to assume a lowering of serum cholesterol by Metamucil to a normal range. Throughout the study laboratory evaluations will be obtained to assess known aberrations induced by increased dietary fiber.

Progress: This study will enroll the last patients on October 3, 1989, bringing the total patients enrolled to about 115. This is far short of the 300 desired. This study has been plagued with many problems, which I am finding out to be common at MEDDAC's.

1. The entry criteria to the study were far too rigid, thus excluding many potential patients. This is the primary reason our numbers are so low.

2. There has been a severe lack in support personnel to maintain the clinical records of participants. This has been remedied by assigning one of our nurse practitioners this task. By doing this, we have captured an inordinate amount of workload otherwise not account for.

3. Followup of patients is very difficult because of the demands of our primary mission, however, this has been accomplished.

Study failure or dropouts: 16 patients were disenrolled because of poor response to treatment. 2 patients were disenrolled because of PCS move out of the area.

Results: In general terms, because the data has not been compiled statistically, if patients stay on a low fat diet, the treatment groups of Metamucil, 1 tsp t.i.d. and 2 tsp b.i.d. have shown a 10-20% lowering of total cholesterol and concommittant lowering of LDL cholesterol of that amount also. We have had no adverse reactions to the therapy except minor changes in stool consistency and frequency, bloating, and eructation.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/36 STATUS: Terminated

TITLE: Patient Preferences in Health Care Provider's Dress, Attire, and Office Appearance in Relation to Perceived Competence

START DATE: Mar 89 ESTIMATED COMPLETION DATE: Jun 89

PRINCIPAL INVESTIGATOR: CPT Richard E. Whitlow

DEPARTMENT: Med FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Rebecca J. Oskey, AN; CPT David Hogan, MC

KEY WORDS: Patient preferences, Perceived competence

Study Objective:

1. Determine the impact of physician attire on patients' impressions of medical competence.

2. Determine patients' attitudes concerning how they are addressed and how they address their physician.

3. Determine the impact of the physicians' work area on patients' perception of competence of the health care provider.

4. Determine the influence of various factors singularly affecting patient's perceptions of care in the Emergency Department.

Technical Approach: This study will be conducted in a prospective manner utilizing a standardized patient questionnaire distributed to all patients entering the Medicine Department and Emergency Department. The survey may also be distributed in other areas of the hospital to determine patient preferences in specific areas, i.e., Pediatrics, Surgery, OB-GYN, Nursing Care Units, and Troop Medical Clinics to determine if the regimented dress standards and office settings affect patient perceptions in those environments also.

Progress: This protocol has been terminated for a number of reasons:

1. This protocol was designed as a survey monitor of patients' preferences administered in the Emergency Room and Department of Medicine. As such, it required the participation of ancillary workers in these areas to distribute and retrieve the survey. This function, as we found out after beginning the study, is not part of their job description and they have not complied with our requests to do it.

2. It was found to be impractical to have individual physicians and health care providers distribute the surveys from their offices.

DETAIL SUMMARY SHEET

DATE: 1 October 89 PROTOCOL #: 89/42 STATUS: Ongoing

TITLE: The Utility of Thermographic Evaluation in the Diagnosis of Lower Extremity Injuries During Army Initial Entry Training

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: LTC Bruce H. Jones

DEPARTMENT: USAREM FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Murray Hamlet, DVM; COL (Ret) Margarete Di Benedetto

KEY WORDS: Thermogram (graphic), Scintigraphic

Study Objective:

1. To document the sensitivity and specificity of thermography to detect the presence or absence of injuries in general compared to clinical standards and more specifically to:

(a) To document the specificity and sensitivity of thermography in the diagnosis of stress fractures verses bone scans and x-rays as the diagnostic standard. Also, to calculate the positive and negative predictive value of thermography in the diagnosis of stress fractures based on the prevalence of stress observed in this and other epidemiologic studies.

(b) To document the sensitivity and specificity of thermography to detect injuries other than stress fractures verses the level of certainty of clinical diagnosis, i.e., the presence or absence of observable signs and the number of positive signs such as swelling, erythema, ecchymosis, point tenderness, decreased range of motion, etc. for a particular diagnosis. Also, to document the sensitivity and specificity of thermography verses the degree of severity of injury measured in days of limited duty or hospitalization. Also, positive and negative predictive value will be assessed once the prevalence of specific injuries in the cohort are established. (As an aside, the potential for paradoxically decreased sensitivity of thermography when such soft clinical standards are used is recognized, however, the use of two or more operationally defined clinical standards, i.e., level of clinical certainty and degree of severity of the diagnosis should help to recognize a paradox when it arises.

2. To qualitatively and quantitatively describe the thermographic patterns for specific injuries if they are perceived to exist.

3. To determine whether the thermographic patterns "normalize" as injuries heal in a way that would assist in making decisions regarding return of soldiers to duty.

4. To determine whether individuals with flat feet or high arches are likely to suffer more injuries to the lower extremities than those with "normal" feet. Also, to determine whether the thermograms of individuals with flat feet or those with high arches are more likely to be positive (indicating "chronic stress") than individuals with "normal" feet at baseline (prior to onset of basic training) and episodically during basic training.

5. To determine the effect of training volume (running and marching mileage) on the incidence of injuries and on the qualitative and quantitative patterns of lower extremity thermograms.

6. To determine whether the thermographic patterns observed are more likely to be positive for sub-populations grouped on the basis of age, race, body composition, past activity, and physical fitness.

7. To determine the incidence of commonly occurring training-related injuries and the amount of morbidity (days of limited duty, etc.) associated with each. With these data estimates of the impact of early diagnosis and appropriate return to duty through use of thermography will be made.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Basic trainees that have positive bone scans and "hot" thermograms require weekly followups with thermograms to determine when the thermogram changes. One thousand subjects will have been entered into the study when data collection is completed @ 23 Nov 89.

AUTHOR INDEX

KEYWORD INDEX

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