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FOREWORD

This has been another successful and challenging year for the Department of Clinical Investigation. In FY 95, we had a 36 % increase in the number of new protocols approved. We also expanded our interaction with the medical, educational, and scientific communities. Locally, we have extensive research and educational relationships with Texas Tech University Medical School, the University of Texas at El Paso, El Paso City/County Health Department, and other local hospitals and institutions. At the national and international levels, members of our department served on the Defense Women's Health Research Program Scientific Peer Review Panel, while others served on the editorial boards of internationally recognized medical journals. In addition, the Chief of the Department had the honor of being selected to chair the ad hoc committee of the American Thoracic Society and American College of Physicians for standardization of clinical exercise testing. She was also selected as a member of the committee for standardization of clinical exercise testing of the European Respiratory Society. The department also conducted numerous medical training activities involving animals, ranging from pediatric advanced life support training and other training programs for WBAMC and Ft. Bliss combat medics, WBAMC nursing staff, and others to state of the art laparoscopic surgery training for surgeons at WBAMC and from throughout the Southwestern United States.

These successes have been achieved despite current and projected budget reductions for the Department of Clinical Investigation, and WBAMC in general. To meet the challenges of a decreasing budget, we have continued to encourage and assist investigators in obtaining extramural research funding and we have implemented measures to make the overall research process more efficient. Within the department, we have expanded cooperation and communication among sections. We are also placing great emphasis on research team building, and on advising and mentoring prospective investigators to insure that their research projects have extremely focused objectives which are attainable within defined budget and time constraints.

Few successes are possible without support from the chain of command. This has been a year of change. We began the year under the command of BG James, who was followed by COL Scully. In July, COL DeWitt assumed command. Each commander provided unwavering support for our department and its mission. Also during this year, our DCCS, COL Cecere, departed WBAMC. COL Cecere was a great advocate of the Department of Clinical Investigation. He insured required command support and provided continuity to our programs, even as Department Chiefs changed. Fortunately, the new DCCS, COL Bowland, is also an outstanding physician who clearly understands the needs and importance of the department. I wish to thank our chain of command for their support.

FY 95 has been a year of challenge and success for the department. Throughout the year, our activities have been aimed at providing the finest possible research and educational support for WBAMC. As the WBAMC Department of Clinical Investigation, we execute a multifaceted program which is guided by our mission statement and which focuses specifically on several key objectives, as listed: 1) Provide clinical research mentorship, 2) Provide research laboratory support and expertise, 3)

Insure legal, regulatory, and ethical compliance of all WBAMC research, 4) Conduct ongoing medical research in which residents may participate, 5) Support RRC requirements by providing research opportunities through facilitation and conduct of clinical research, 6) Support medical training activities, including medical training involving animals, 7) Establish and promote cooperative research and educational relationships between WBAMC and other medical and educational institutions, 8) Promote an atmosphere of inquiry and critical thinking and an appreciation for the dynamic nature of military medicine, 9) Promote dissemination of scientific findings, 10) Provide scientific means for introducing and evaluating new medical products and processes, 11) Foster development and retention of quality teaching faculty, and 12) Assist investigators in obtaining extramural research funding. With continued focus on these objectives, along with a continued commitment toward self-improvement, we look forward to continued success in support of WBAMC in the upcoming year.

IDELLE M. WEISMAN
COL, MC
Chief, Department of Clinical Investigation

UNIT SUMMARY FY 95

MISSION:

Conduct, coordinate, and augment clinical research and education activities in support of WBAMC mission to provide quality professional clinical services, to conduct graduate medical education programs, and to conduct enlisted AMEDD and Army Nurse training programs. As required, conduct educational, analytical, and clinical research activities in support of other WBAMC and Fort Bliss missions.

TECHNICAL APPROACH:

The Department of Clinical Investigation operates under the guidelines of the Clinical Investigation Program (AR 40-38), Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Substances (AR 40-7), Use of Volunteers as Subjects in Research (AR 70-25), Management of Clinical Investigation Protocols and Reports (HSC Reg 40-23), and The Use of Animals in DoD Programs (AR 70-18). Research protocols utilizing laboratory animals also adhere to the guidelines of the National Academy of Sciences-National Research Council, as described in the "Guide for the Care and Use of Laboratory Animals." Departmental animal research facilities are accredited by the American Association for the Accreditation of Laboratory Animal Care.

MANPOWER:

Description	Grade	MOS	Br	Auth	Name	Rank
C, DCI	06	60F	MC	1	Weisman	06
Asst C, DCI	03	71B	MS	1	Pusateri	03
C, Bio Res Svc	04	64C	VC	1	Harris	04
Animal Care NCO	E6	91T		1	Milbradt	E6
Animal Care Sp	E5	91T		1	Charles	E5
Animal Care Sp	E4	91T		1	Stukey	E4
Supv Res Chem	12	1320	GS	1	Bhattacharyya	12
Microbiologist	12	403	GS	1	Veit	12
Chemist	09	1320	GS	1	Enriquez	09
Microbiologist	09	403	GS	1	Smiley	09
Med Technician	07	645	GS	1	Lund	07
Med Technician	07	645	GS	1	Mana	07
Med Technician	07	645	GS	1	McIntyre	07
Health Tech	07	640	GS	1	Revels	07
CI Prot Specialist	05	301	GS	1	Young	05
Sup Clk (Typ)	05	2005	GS	1	Turner	04
Anm Caretaker	04	5048	WG	1	Sigholz	04
Anm Caretaker	01	5048	WG	1	Burton	01

Civilian Personnel with Special Project Funding

Co-Director HP/SCT					Zeballos	
Exercise Physiologist	09	413	GS	1	Taylor	
Exercise Physiologist					Connery	

PERSONNEL TOTAL:

	Required	Authorized	Assigned
Officers	5	3	3
Enlisted	7	3	3
DA Civilian	20	12	12
DA Civilian (Temp)			1[a]
Civilian Contract			2[b]

[a] 1 Temporary civilian with special project funding (Mr. Taylor)
[b] 2 Civilian contracts funded through grants (Dr. Zeballos & Mr. Connery)

Changes in personnel during FY95: MAJ Nauschuetz PCS'd in July 95. CPT Pusateri assumed the position of Asst. Chief, DCI. Ms. Elizabeth Young was selected for the position of Clinical Protocol Specialist in April 95.

GRANTS for FY95

Impact of Smoking on Aerobic and Anaerobic Performance Driving Upper and Lower Body Exercise in Female Soldiers. Defense Women's Health Research Program. Amount received in FY95 $125,000.

Acute Airway Injury and Response: Combined Effect of Smoke Inhalation and Combustion Products on Mucin Gene Expression and Regulated Mucin Production in the Tracheal-bronchial Epithelium. (USAMRMC Combat Casualty Care Research Program). Total Worth $49,000 FY95.

Cooperative Research and Development Agreements (CRDAs) for FY95

CPT Natalie Hoshaw (PI), Dept. of OB/GYN, with Procter & Gamble Company, Cincinnati, OH. "Effect of Psyllium Fiber on Serum Glucose Levels After Abnormal 3-hour 50-gram glucola Screening Test in Pregnant Patients", total worth $5,448.00, amount received $0.00. (Pending an addendum to increase the total worth).

CPT Albert L. Chorens (PI), Dept. of Surgery (PI), with Atrium Medical Corporation, Hudson, NH. "A Prospective Randomized Comparison of Inguinal Herniorrhaphy", total worth, $3000.00, received FY95.

MAJ William F. Nauschuetz (PI), Dept. of Clinical Investigation, with BioVenture, Inc., Murfreesboro, TN. "Amplification of *Mycobacterium tuberculosis* to Predict Antimicrobrial Resistance Using a Novel Single-Step DNA Extraction, Polymerase Chain Reaction and Gene Sequencing" Total Worth $5,400, received in FY95.

MAJ John B. Holcomb (PI), Dept. of Surgery, Arrow International, Reading PA. "Comparison of Arrow Guard to Regular Central Lines with Respect to Infectious Complications", total worth $1000.00, received FY95.

MAJ Bruce E. Pichoff (PI), Dept. of Pediatrics, PPD/Med Immune, Inc., Gaithersbug, MD (Provider) and PPD, Wilmington, NC (Intermediary), " A Phase III Randomized, Double-Blind, Placebo-Controlled Trial of RespiGam™ (RSVIG-IV) Infusions for Bronchopulmonar Dysplasia" Total worth $136,392 all received in FY95.

LTC Thomas S. Gormley, Urology Services, Schering-Plough Corporation, Kennelworth, NJ (Provider) and PPD, Wilmington, NC (Intermediary), "Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin", Total Worth: $17,500. Amount received to date: $0.00 (pending legal review by provider).

EXPENDITURES

	FY93	FY94	FY95
Personnel (Civilian)	520,798	510,723	481,827
Consumable Supplies	258,409	152,517	130,977
Capital Equipment	15,007	9,313	17,125
TDY	8,127	3,966	6,660
Printing and Publications	1,760	1,066	-0-
MEDCASE Equipment	0	64,532	27,296
Military Pay	559,043	491,485	491,485
TOTAL	1,363,144	1,239,602	1,155,370

PROTOCOLS:

Protocols	Ongoing	New	Completed	Terminated
FY 93	110	54	29	30
FY 94	91	44	28	31
FY 95	75	60	26	42

1 Study was withdrawn

PROGRESS FY 95

BIOLOICAL RESEARCH

The William Beaumont Biological Research Service laboratory animal facility has been fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) since 1968. Currently, this facility, totaling 7,134 square feet, occupies three buildings on the William Beaumont Army Medical Center (WBAMC) complex. The main facility, in Building 7776, contains the surgical suites, radiology, treatment rooms, necropsy, the majority of the animal holding areas, and the administrative offices. Building 7774, is utilized as a large equipment storage area, plus a 250 square foot, Class 10,000 bioclean room that became operational in FY93 and has been extensively used to maintain rodent colonies with special requirements. The third unit is a 150 square foot, walk-in refrigerator that provides excellent long term storage of rations required by the research animals.

As was true for the past several years, the Biological Research Service has been extremely active in its support of training, research, and collaborative protocols in FY95. Of the presently 39 active animal protocols, 15 training protocols were supported in FY95 for medical personnel encompassing emergency trauma life support, general surgery, laser surgery, laparoscopic techniques, and vascular microsurgery. Of particular note was the exceptional support provided to the Pediatric Advanced Life Support (PALS) Course, accredited by the American Heart Association and the Advanced Trauma Life Support (ATLS) Course accredited by the American College of Surgeons.

The 24 research protocols supported by the Biological Research Service were not only practical and militarily relevant, but continued to expand areas of research heretofore lacking at WBAMC. Research continued in the disciplines of microsurgery, soft tissue and orthopedic reconstruction materials and techniques, surgical laser applications, laparoscopic and thoracoscopic methodologies, therapeutic efficacy, molecular biology, and immunology. An area of research with exceptional promise is the collaborative development of a unique dry fibrin glue bandage for the control of severe hemorrhage. The WBAMC Department of Clinical Investigation took a leading role along with WRAIR, the Special Forces Medical Training Detachment at Ft. Bragg, and the American Red Cross in performing the first of a planned series of protocols with excellent results. The Biological Research Service, using its established severe combined immunodeficient (*scid*) mouse colony, supported the first phase of a breast cancer protocol dependent upon xenografts and propagation of malignant tumors.

WBAMC and the Biological Research Service have continued collaboration with the Sierra Medical Center in certification of physicians in the application of the surgical laser, as well as expanding training protocols for the combat medical units of Fort Bliss.

The Biological Research Service, currently one of the longest standing fully AAALAC accredited laboratory animal care and use programs in DoD, is looking forward to the triennial re-accreditation site visit and inspection during the summer of 1996. We all feel AAALAC will be appropriately impressed by the quality and productivity of the Biological Research Service.

CHEMISTRY SECTION

The chemistry section of DCI is engaged in research protocols concerning the involvement of mucus in acute and chronic respiratory problems that arise from inhalation of smoke, a lipid-mediated fibrinogen delivery system to stop bleeding from wounds, and the status of vitamins in alcoholics.

The smoke inhalation project is funded by USAMRMC. Recently, we have studied the effect of smoke exposure on mucin gene expression and secretion as well as cell morphology of rabbit tracheal explants and the effect of retinoic and mucin antisense oligonucleotide on this process. When rabbit tracheal epithelium was exposed to smoke from pine wood for a short period of time, the cell morphology indicated inflammation with the presence of numerous mucus secretory granules. After smoke exposure, the explants were cultured in a serum-free and hormone-supplemented medium with and without retinoic acid. The cells, which were cultured in a time-dependent manner in medium with retinoic acid, showed normal features with mucin gene expression still remaining high, whereas the cells indicated sign of starvation and tended to slough off the epithelium when grown in the medium without retinoic acid. The increased mucin gene expression in the cells cultured in medium with retinoic acid as well as mucin hypersecretion was inhibited by a mucin antisense oligomer and the cells showed normal features. We have also developed in our laboratory a lipid-mediated antisense oligomer delivery system which will enhance the capability of the gene to enter the cells effectively. If proved positive and less toxic, the combined therapy of retinoids and mucin antisense oligomers has the potential clinical application for controlling inflammation, normal cell differentiation and proliferation and excessive secretion of mucus in tracheal bronchial epithelium of people, like combat soldiers and the general public, exposed to toxic substances, such as smoke.

In the past year, we, in collaboration with MAJ Holcomb and CPT Craig of the Department of Surgery and MAJ Harris of the Biological Research Service of WBAMC, have developed a lipid-fibrinogen complex (liposome delivery system) with which we are now experimenting to stop bleeding from wounds in animals. We will continue work on this exciting project, which has a real potential for clinical application (especially with wounded soldiers), in the upcoming year.

We are also involved in a protocol with RTF of WBAMC concerning the levels of vitamins and TNF-a in serum of alcoholics. We have measured the levels of Vitamin A and E in serum of patients at the time of admission and later at post-treatment phase by high pressure liquid chromatography. The results showed comparatively lower levels of these vitamins in patients which were admitted for treatment. After treatment in the facility, the levels of these vitamins were elevated and an equilibrium was maintained. The results from this protocol may shed some light on the requirements for vitamins in maintaining a healthy status in people with alcohol problems.

IMMUNOLOGY AND MICROBIOLOGY SECTION

Research interests of the Immunology and Microbiology Section have been focused primarily on three areas of research interest - induction of apoptosis in breast cancer cells, use of PCR in the detection and typing of human papilloma viruses in gynecologic tissues, and studies of the immunocompetence of splenectomized rats following immunization with pneumococcal polysaccharide vaccine and challenge with Streptococcus pneumoniae.

Our studies of human breast cancer cells are directed toward understanding the regulatory influences that autocrine and paracrine-mediated growth factors exert during the growth cycle of breast cancer cells. Breast tumors with high S-phase fractions (more rapidly growing tumors) have high rates of metastasis and poor prognoses even though the largest tumor cell kill attained with chemotherapeutic agents is in tumors with high S-phase fractions. An alternative approach to conventional cancer chemotherapy (which attempts to inhibit DNA synthesis during the S-phase of the cell cycle) is to prevent rapidly cycling cells from proceeding through the growth phases of the cell cycle. Both normal and malignant breast epithelial cells are dependent on paracrine and/or autocrine growth stimulation induced by agents such as estrogen, epidermal growth factor, transforming growth factors, and insulin-like growth factors to induce their movement through the cell cycle (mitogenesis). Without appropriate mitogenic signals, quiescent tumor cells remain in G_0/G_1 until they either become activated to proceed through the cell cycle or are terminated through one of two processes: (1) necrosis or (2) apoptosis (programmed cell death). Apoptosis is not a random event. It appears to be initiated by a signal (i.e. absence of growth factor) which triggers an increase in intra-cellular free Ca^{++} which, in turn, activates a Ca^{++}/Mg^{++}-dependent endonuclease which carries out the orderly degradation of the cell's DNA. Failure of a tumor cell to receive the appropriate cell cycle progression stimuli constitutes a decision point for that cell. Rather than passively awaiting appropriate mitogenic signals in G_0/G_1 indefinitely, quiescent tumor cells recognize the absence of growth factor stimuli and proceed with the initiation of auto-degradation or apoptosis. Growth factor deprivation or the use of agents which induce apoptosis may provide an alternative approach to therapeutic elimination of tumor cells. Treatment modalities which bring about a suppression or modification of growth factor production and/or secretion and/or receptor binding by either stromal cells (paracrine stimulation) or by tumor cells themselves (autocrine stimulation) may be provide an effective alternate approach to breast cancer therapy.

Approximately 16,000 American females are diagnosed with cervical cancer each year. Although routine PAP smears and colposcopy have increased the detection rate and management of pre-cancerous lesions, cervical malignancies have remained a major cause of cancer deaths in women. Recent studies have suggested that human papilloma viruses (HPV) may be involved in the evolution of certain malignancies with 70% of cervical carcinomas having been shown to contain HPV. Our studies are focused on the analyses of cervico-vaginal swabs, amniotic fluids, and colostrum/breast milk from post-partum females for the purpose of determining prevalence of HPV in such samples and identifying the occurrence and rate of transmission to the fetus and/or newborn infant. Polymerase chain reaction (PCR) represents a rapid and highly sensitive method of detecting low copy numbers of HPV DNA in tissue samples.

Splenectomy is commonly performed in patients with hematologic disorders or traumatic injury of the spleen. When compared to normal individuals, splenectomized patients are at significantly greater risk of developing overwhelming infectious diseases, especially those caused

by encapsulated organisms of which pneumococcal pneumonia caused by *Streptococcus pneumoniae* is the most frequently occurring. Although antibiotic therapy has reduced morbidity and mortality, pneumococcal pneumonia is still a concern in patients following splenectomy, especially with the emergence of antibiotic-resistant strains. Prophylactic immunization with a polyvalent pneumococcal polysaccharide vaccine has been recommended for splenectomized patients. However, the benefits of vaccinating asplenic patients remains questionable and controversial. There have been no conclusive studies that demonstrate that prophylactic immunization with the pneumococcal polysaccharide vaccine following splenectomy significantly reduces mortality. Of major importance regarding efficacy is the timing of vaccination following splenectomy. Our studies are focused on determining the optimal time for administering the 23-valent polysaccharide vaccine following splenectomy in a rat model. Blood clearance rates following challenge with virulent bacteria as well as circulating levels of anti-capsular polysaccharide IgG and IgM antibodies are being evaluated as indicators of efficacy.

HUMAN PERFORMANCE LABORATORY

The Human Performance Laboratory at William Beaumont Army Medical Center is a full service cardiopulmonary exercise testing laboratory with multiple research and clinical exercise testing capabilities. As a major regional tertiary referral hospital (300 bed) WBAMC serves a large retired, active duty military and dependent population. The Human Performance Lab is responsible for all asthma exercise protocols as well as cardiopulmonary exercise testing for the medical center and its regional responsibilities.

The Human Performance Laboratory's personnel include an active duty military M.D., an M.D., Ph.D. (civilian), and a GS-9, DAC exercise physiologist. The laboratory is contiguous to a state of the art pulmonary function laboratory which includes: two body plethysmographs, two pulmonary function systems with nitrogen washout for lung volume and D_LCO determinations, bronchial provocation capability, and arterial blood gas machines.

A large clinical and extremely large volunteer population at Fort Bliss make research projects with large n values feasible.

A comprehensive listing of the laboratory's capabilities include: state of the art cardiopulmonary exercise testing which consists of ability to measure metabolic (VO_2, VCO_2, Anaerobic threshold, R), Ventilatory (VE, VT, F), Cardiovascular (ECG, HR, HR/VO_2,V O_2/work rate) and gas exchange (PaO_2, $P(A\text{-}a)O_2$, SaO_2, VD/VT, pH, $P(a\text{-}ET)CO_2$) parameters; simulation of different environmental conditions utilizing FIO_2 manipulation (inspiratory hypoxia simulating, 2300 m, 4000 m, etc.); study of O_2 transport including O_2 dissociation curve (P_{50} capability and separate tonometry set-up); treadmill, cycle ergometry and arm crank modalities; reactive airways dysfunction - diagnostic - exercise induced bronchoconstriction, broncho-provocation, isocapnic hyperventilation, cold air (-10° C) hyperventilation decrease; vocal cord dysfunction - exercise induced, inhalational challenge, bronchoscopy with flow volume loop set-up for documentation; mechanics of breathing including P_{DI} determined (esophageal balloons) and pressure-volume (compliance) curve relationships; sub-maximal exercise D_LCO and measurement of pulmonary capillary blood volume (developing); non-invasive determination of cardiac output using CO_2 rebreathing

technique and acetylene during intrabreath technique; invasive determination of pulmonary gas exchange: SaO_2, PaO_2, $P(A\text{-}a)O_2$, VD/VT, $P(a\text{-}ET)CO_2$; monitoring: weight - sauter scale (accuracy 10 gm), temperature - esophageal, rectal, skin probes (sensor tech system), SpO_2 - HP and pulse oximeters, BP - direct BP monitoring; lactate determination capability; capability of
VO_2,V CO_2, andV E determination under field conditions using dry gas meter and Douglas bag collection; state of the art in house nuclear cardiology and cardiovascular laboratories provide in house research/clinical interaction on issues related to human performance.

The Human Performance Lab has in the past gained national recognition for its work in Sickle Cell Trait. Presently, it is a force in standardization of clinical exercise testing. As such, it serves as a major reference laboratory.

The Human Performance Lab has received extramural funding though the Jackson Foundation for research in COPD as well as a Defense Women's Health Research Program grant for the study of smoking and exercise in female soldiers; additional extramural funding opportunities are presently being considered.

FY95
(October 1994 - October 1995)*
PRESENTATIONS AND PUBLICATIONS FOR WBAMC

DEPARTMENT OF CLINICAL INVESTIGATION

PUBLICATIONS:

Manna B, Ashbaugh P, Bhattacharyya SN: Retinoic Acid-Regulated Cellular Differentiation and Mucin Gene Expression in Isolated Rabbit Tracheal Epithelial Cells in Culture. *Inflammation* 1995; 19:489-502.

Weisman IM, Zeballos RJ. American College of Chest Physicians Pulmonary & Critical Care Update Series, "Cardiopulmonary Exercise Testing". Vol II, Lesson 2, August 1995.

Weisman IM, Zeballos RJ, Cardiopulmonary Exercise Testing. Pulmonary/Respiratory Therapy Secrets, Parson and Haffner, Editors. Hanley and Belfus (Mosby), publishers. 1995 (In Press).*

Connery SM, Zeballos RJ, Taylor MB, Weisman, IM, $\Delta VO2/\Delta WR$ during Cycle and Arm Crank Ergometry. FASEB Journla, 1995 (In Press).*

PRESENTATIONS:

Bhattacharyya SN, Manna B: Retinoic Acid-Regulated Cellular Differentiation and Mucin Gene Expression in Isolated Rabbit Tracheal Epithelial Cells in Culture. Society for Gycobiology Annual Meeting. University of Notre Dame, Notre Dame, Indiana, November 1994.

Weisman IM: The Role of Cardiopulmonary Exercise Testing in the Evaluation of Unexplained Dyspnea, 50th Anniversary of the Massachusetts Thoracic Society, 5 April 1995.

Weisman IM, Co-Chairperson; 1995 ATS Symposium "Cardiopulmonary Exercise Testing: Current Concepts and Its Expanding Role In Clinical Practice". Speak on "Impact of Cardiopulmonary Exercise Testing in the Evaluation of Management in Patients with Respiratory Disease. 21 May 1995.

DENTAC

PRESENTATIONS:

Thompson, Geoffrey: Insertion Appointment. Prosthodontic Short Course, Walter Reed Army Medical Center. September 1995.

ORAL AND MAXILLOFACIAL SURGERY SERVICE

PRESENTATIONS:

Duvernois, MF: Dentistry in Third World Nations. 91C Class, William Beaumont Army Medical Center, El Paso, Texas, August 1995.

Ringgold, CL: Dental Implant Techniques. Fort Bliss Dental Activity, March 1995.

Ringgold, CL: Critical Advances in Oral Surgery. American Association of Oral and Maxillofacial Surgeons Annual Meeting, Toronto, Ontario, Canada, September 1995.

DEPARTMENT OF MEDICINE

PUBLICATIONS:

Chapin BL, Jones RL: Infertility. In: McDermott MT (ed), *Endocrinology Secrets*, 1995; 249-253.
Finger D: Paget's Disease of Bone: In West SG (ed): *Rheumatology Secrets*, 1st ed. Philadelphia, Hanley & Belfus, 1995.

Finger D: Hypouricemic Agents and Colchicine. In West SG (ed): *Rheumatology Secrets*, 1st ed. Philadelphia, Hanley & Belfus, 1995.

Finger D, Plotz P, Heywood G: Myopathy Following Treatment with High Dose Interleukin-2 for Malignancy. *Journal of Rheumatology* 1995; 22(11):2188.

Finger D, Giandoni M: Mees Lines, *Arthritis & Rheumatism*, 1995 (In Press).*

Jarek MJ, Enzenauer RF, Judson P: Pure Red Cell Aplasia in Systemic Lupus Erythematosus - a case report and review of the literature. *Journal of Clinical Rheumatology.* 1995 (In Press).*

Jarek MJ: Storage and Deposition Disorders. In West SG (ed): *Rheumatology Secrets*, 1st ed. Philadelphia, Hanley & Belfus, 1995 (In Press).*

Jarek MJ: Rheumatic Disease and the Pregnant Patient. In West SG (ed): Rheumatolgoy Secrets, 1st ed. Philadelphia, Hanley & Belfus, 1995 (In Press).*

Jarek MJ: Rheumatic Disorders in the Dialysis Patient. In West SG (ed): Rheumatolgoy Secrets, 1st ed. Philadelphia, Hanley & Belfus, 1995 (In Press)*.

Jimenez CE, Moreno AJ, Pacheco EJ, Carpenter AL: SPECT Imaging in a Patient with Monostotic Rib Fibrous *Dysplasia Clin Nucl Med.* 1995 (In Press).*

Keenan LM: Fiberoptic Bronchoscopy and High Resolution CT of the Chest in Patients with Hemoptysis and Nonlocalizing Chest X-ray. *Chest*

Maldonado ME, Hobratsch LV: Fulminant Clostridium Difficle Colitis with Intramural Gas. *Clinical Infectious Diseases* 1995; 30:1163.

Pacheco EJ, Moreno AJ, et al: Diagnosis of Menetrier's Disease with Tc-99m Human Serum Albumin Scintigraphy. *Clin Nucl Med* 1995; 30:114-116.

Pacheco EJ, Moreno AJ, et al: Fortuitous Imaging of a Primary Adenocortical Carcinoma with Technetium-99m HDP. *Clin Nucl Med* 1995; 20:906-908.

Sanchez I, Finger D, Bradshaw D: Orbital Inflammatory Syndrome: a case report and literature review. *Journal of Clinical Rheumatology* 1995; 1:295-8.

Simcic KJ: Famous People with Endocrine Disorders. In: McDermott MT (ed), *Endocrinology Secrets* 1995; 285-86.

Simcic KJ, Bowland W: Cystic Medullary Thyroid Cancer (letter). *Surgery* 1995; 117:356.

Simcic KJ, Moreno AJ: Paget's Disease of Bone. *New Engl J of Med* 1996;3334:161.

Stoll BC, Ashcom TL, Johns JP, Johnson JE, Rubal BJ: Effects of Atenolol on Rest and Exercise Hemodynamics in Patients With Mitral Stenosis. *The American Journal of Cardiology* Mar 1995; 75:482-484.

ABSTRACTS:

Doyle J, Finger D, Dennis G, Eliasson A: Airway Hyperactivity in Rheumatoid Arthritis (Abstract). *Arthritis & Rheumatism* 1995; 15:193-213.

Roane DW, Finger DR, Alloway JA, Erickson AR: The Use of Intramuscular Triamcinolone Acetonide in Pseudogout (Abstract). *Arthritis & Rheumatism* 1995; 38(6):R16.

Medler PC, Sipp WC, Simcic K: Thyroid Carcinoma: A 5-year Review of Near-total Thryoidectomy at WBAMC. (Abstract) *South Med J* 1995; 88:S124.

Jimenez CE, Glushko GM, Pacheco EJ, Moreno AJ: Initial Clinical Management of Patients with Reversible Thallium Cardiac perfusion Defects. (Abstract) *Clin Nucl Med.* 1995 (In Press).*

DEPARTMENT OF MEDICINE

PRESENTATIONS:

Belbel RJ, O'Donnell S: Endovascular Stent Two Year Followup - The William Beaumont AMC Experience. Army 1995 Vascular Conference. February 1995.

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Finger DR: Airway Hyperreactivity in Rheumatoid Arthritis. Poster, ACR Southeast Regional Meeting. Philadelphia, Pennsylvania, April 1995.

Hodges M, Kennan L, Wallingford J, Zacher L. Prospective Comparison of Computed Tomography and Fiberoptic Bronchoscopy in Patients with Unexplained Hemoptysis and Non-Suspicious Chest Roentgenograms. 12th Annual Scientific Meeting of the Army Chapter of the ACP, Reston, VA October 1995.

Jarek, MJ: Classification and Pathogenesis of Vasculitis. Presented at the Columbia Symposium on Vasculitis. Columbia Hospital, El Paso, Texas, August 1995.

Stiles JC: Trauma Associated Histocytosis X. American Academy of Dermatology Scientific Assembly. New Orleans, Louisiana, February 1995.

PHYSICAL MEDICINE AND REHABILITATION SERVICE

PUBLICATION:

Ice DA, Dillingham TR, Belandres PV: Epidural Corticosteroid Injections for Acute Radiculopathy in a 95-year-Old Woman, *S Med J,* Vol 88, No. 2; Feb 1995; 222-224.

PRESENTATIONS:

Sandberg, KJ, "Rehabilitation of the Work Injured Low Back," Neuroscience on the Border - 1995 Annual Symposium, March 1995.

NEPHROLOGY SERVICES

PUBLICATIONS:

Sanders LR: Hypercalcemia. In McDermott, M (Ed): Endocrinology Secrets. Philadelphia, Hanley & Belfus, 1995 pp. 71-80.

Sanders LR: Nephrolithiasis. In McDermott, M (Ed): Endocrinology Secrets. Philadelphia, Hanley & Belfus, 1995 pp. 85-93.

Sanders LR: Disorders of Water Metabolism. In McDermott, M (Ed): Endocrinology Secrets. Philadelphia, Hanley & Belfus, 1995 pp.122-134.

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Hartman WJ: The Emergency Nurse's Role in Disaster Planning. Emergency Nursing Symposium, University of Texas - El Paso. January & July 1995.

DEPARTMENT OF OB/GYN

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DEPARTMENT OF SURGERY

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Sippo, WB, Gore, R: Selective Screening Mammography: Impact on Early Detection. Federal Practitioner, June 1995.

Sippo, WC, Gore, R.: Lower Abdominal Pain Due to Nerve Entrapment. Federal Practitioner, August 1995.

PRESENTATIONS:

Schreiber, MA: Penetrating Neck Trauma on Mount Rainier, Seattle Surgical Society, 1995.

Holcomb, JB: Dry Fibrin Glue Dressing. US Army Medical Research and Material Command, Ft. Detrick, MD, September 1995.

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Orthopaedic Service

PRESENTATIONS

Stevens WR: Indications for Posterior, Anterior Instrumentation for Unstable Thorcolumbar Burst Fractures. Seventh Annual Colorado Orthpaedic Symposium, Englewood, Colorado, June 1995.

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PRESENTATIONS:

Beck, W.G. AMPLIFYING FORCE XXI: Army audiology's distribution of hearing aids in the future. US Army Long Term Strategic Planning Conference, Richardson, Texas, April, 1995.

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**** Thank you to all WBAMC Departments for submitted your presentations to DCI. All publications that are "In Press" in FY95 will not be counted until actually published. These publications will count toward your department next year FY96.***

***** All presentations done after October 95 are considered FY96 and will be printed in next years Annual Report.***

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/17 STATUS: Ongoing

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

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): B Manna, JI Enriquez

MONITOR: NA

START DATE: Mar 86 ESTIMATED COMPLETION DATE: Oct 96

KEY WORDS: Tracheal Mucin, Human

Study Objective: This protocol 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:

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 DNA 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 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: The human mucin antibodies are now being utilized to screen mucin clones, two of which have already been sequenced. So far, sequence analysis did not reveal the usual pattern of mucin gene sequence. Our laboratory, in collaboration with Duke University investigators, is trying to sequence several other clones which may resemble typical sequence profile of mucin. The estimated completion date has changed from Sep 95 to Oct 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 89/16A STATUS: Ongoing

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

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): B Manna, JI Enriquez

MONITOR: NA

START DATE: Jan 89 ESTIMATED COMPLETION DATE: Oct 96

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 establishing their structural identity.

Technical Approach: Growth of epithelial cells from rat and rabbit bronchial tissues: Rats and rabbits will be euthanized and normal appearing tracheal tissues excised aseptically, immersed in cold, sterile L-15 culture medium containing penicillin\streptomycin and transported on ice to the laboratory. Lung tissue is sterilely trimmed away and the bronchus cut into large fragments. Cells are isolated from the human bronchus after an overnight incubation with 0.1% protease solution in minimal essential medium (MEM, Ca++free) done at 4 degrees C. The next day, incubated bronchi are flushed with MEM plus 10% Fetal Calf Serum to remove the digested cells. The cells are washed several times to remove any protease, which is toxic to epithelial cultures. The cell suspension is filtered through a sterile 100U nitrex filter and centrifuged for 10 minutes. Cell pellets are resuspended in cold MEM with 10% FCS and centrifuged again. The cold protease overnight treatment is sufficient to remove most epithelial cells lining the bronchus without much contamination of other cell types from the layer under the basement membrane. After the total cell count is taken, primary cultures are normally initiated by plating 1-2x 10 6 cells per ml per 35mm culture dish. The culture conditions used for the human bronchial epithelial cells consist of M199 media with D-valine substituted for D1-valine, 10% Fetal Calf Serum, L-glutamine, penicillin/streptomycin, gentamicin, insulin, transferrin, epidermal growth factor, hydrocortisone, cholera toxin, bovine hypothalamus extract, and fungizone. Primary epithelial cultures were then placed in an incubator, with conditions of 37 degrees C., 5% CO2, and 95% air, and cells allowed to adhere to the culture dish. After 3-4 days incubation, a confluent primary culture of epithelial cells is routinely observed. The cultures received media change and can be used in various studies.

Secretion of mucin and characterization: The synthesis of mucin will be followed by ^{3}H glucosamine and $^{35}SO4$ incorporation. Once the saturation curve is established, radioactive agents will not be used anymore. At the time of maximum secretion, the culture medium will be collected, lyophilized and chromatographed on Sepharose 2B and ECTEOLA column. The purified mucin will be deglycosylated by chemical procedure and the peptide portion will be partially sequenced by sequenator.

Isolation of mucin mRNA and sequencing by DNA method: The procedure that will follow here is essentially that of Tempt et al. mRNA from tracheal culture will be isolated by guanidine isothiocyanate method followed by oligo(dt)-cellulose chromatography. Construction and screening of the DNA library utilizing human antiapomucin will be done as described.

Control in secretion of mucin: The synthesis of mucin in epithelial culture will be followed by ^{3}H glucosamine and ^{35} SO4 incorporation. The control in synthesis will be studies on transcriptional and translational levels using different inhibitory (acetylcysteine and cyclohexamide) and enhancing (pilocarpine) reagents.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Amendment (Jan 94): Time extended to Oct 96. Additional number of rabbits is required to complete project.

Progress:
Recently, we have completed a major study concerning the effect of carcinogenic agents on retinoic acid regulated mucin gene expression in rat tracheal explants in culture. Changes in the morphologic characteristics and mucin gene expression were examined in rat tracheal culture in a serum-free and hormone-supplemented medium with and without retinoic acid and two carcinogenic agents. In the presence of retonoic acid, the effect of carcinogenic agents was minimum with prominent mucin gene expression. But in the absence of retinoic acid, the cells were found to indicate metaplastic changes, and the mucin gene expression was clearly affected. Further studies are in progress to identify the retinoid-bound protein patterns in the cells exposed to these agents. The estimated completion date has changed from Sep 95 to Oct 96.

Publication:
Manna B, Ashbaugh P, Kaufman B, and Bhattacharyya SN: Effect of Retinoic Acid on Mucin Gene Expression in Rat Airways in Vitro. Biochemical Journal (London) 1994, 297:309-313.
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DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/08A STATUS: Ongoing

TITLE: Acute Airway Injury and Response: Combined Effect of Smoke and Combustion Products on Mucin Gene Expression and Regulated Mucin Production in the Tracheal-Bronchial Epithelium

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MA Nadjem, P Ashbaugh, F Rodriguez, R Coutinho, M Herawi

MONITOR: NA

START DATE: Sep 93 ESTIMATED COMPLETION DATE: Sep 96

KEY WORDS: Key Words: Airway Injury, Smoke

Study Objective: For several years, we at DCI, WBAMC, have studied the characteristics and synthesis of respiratory mucins. One goal, which has now been accomplished, was to study the structure of the protein portion of these macromolecule and raise an antibody against mucin protein core (22). The other goal, now in progress, is to study the regulation of mucin synthesis as well as control of differentiation and proliferation of tracheal epithelial cells in culture (both organ and isolated cell) and ability of different reagents, such as retinoids, different respiratory drugs and mucin antisense oligodeoxynucleotide to intervene effectively with this process and thereby aid patients with chronic as well as acute respiratory problems due to exposure to different noxious substances. To date, we have found that retinoids are required for normal function of tracheal epithelial cells when grown in a serum-free and hormone-supplemented medium. Without retinoic acid, the cells neither expressed mucin message nor maintained normal cytological appearance. When retinoids were added back to the culture medium, the cells grew normally and the mucin message was expressed again (13). Effects of adding pharmacologic agents, such as atropine, histamine, methacholine, phenylephrine, cimetidine, prednisolone and more recently mucin antisense oligodeoxynucleotide to the culture on the growth, differentiation and mucin mRNA level are currently under study -- the most interesting result to date being a marked reduction in mucin mRNA level by prednisolone. In sum, our laboratory, with aid of consultant Dr. Bernard Kaufman of Duke University Medical Center, Durham, North Carolina, is studying the control of production of respiratory mucins on the cellular as well as molecular level and our specific aims of this project are as follows:

1) Study mucin mRNA expression and mucin secretion in rabbit tracheal cultures exposed to smoke (total smoke, filtered smoke and particulate) generated by burning wood and cotton, singly or in combination, in our inhalation chamber in a time and dose dependent manner. Before exposure, the cell culture will be maintained in a serum-free and hormone-supplemented medium with or without retinoids.

2) Examine the extent of injury to the cells by histologic and ultramicroscopic methodology, i.e., whether converted to squamous or more mucus producing cells.

3) Investigate the effect of addition of retinoids to the retinoid-deficient medium on the nature of the cells as well as the mucin message. The reason for studying separately the effect of filtered gases and particulate is to differentiate between two sources so that we can ascertain the extent of injury contributed by each of them and extent of cure process enhanced by retinoids.

4) Study the effect of pharmacologic agents, such as atropine, cromolyn sodium, steroids and mucin antisense oligodeoxynucleotide on the mucin mRNA level as well as on cell differentiation and proliferation of the tracheal culture exposed to smoke as stated above.

5) Study the effect of retinoids and other agents, as described above, on the injury and mucin synthesis and secretion in trachea of whole rabbits exposed to smoke in our nose-only exposure chamber.

6) Produce an immortal mucin-producing cell line by transfecting the primary tracheal epithelial cells with different nonpathogenic viruses.

7) Examine the effect of long-term exposure of smoke on these cells in terms of their differentiation and expression of mucin message and the effect of retinoids and other agents on this process. Primary tracheal epithelial cells in culture stop producing mucins or sometimes do not survive when maintained in culture medium for more than three to four weeks. The immortalized cell lines will provide us with a system to study long-term effect of smoke-related exposure on mucus production and cell injury at the same time.

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: We have made tremendous progress in cultivating successfully rabbit tracheal epithelial cells in a serum-free and hormone-supplemented medium with retinoic acid. In the presence of retinoic acid, the cells differentiated normally with prominent mucin gene expression. In the absence of retinoic acid, however, the cells did not grow properly and the mucin gene expression was decreased considerably. We have obtained some excellent results regaining control of mucin gene expression in these cells which are published in the journal Inflammation. An antisence mucin oligomer has found to inhibit mucin gene expression in these cells. We are attempting to study the protective effect of retinoic acid on these cells exposed to smoke.

Estimated completion date has changed from Sep 95 to Sep 96.

Publication: Manna B, Ashbaugh P, Bhattacharyya: Retinoic Acid-Regulated Cellular Differentiation and Mucin Gene Expression in Isolated Rabbit Tracheal Epithelium Cells in Culture. Inflammation 1995. 19:489-502.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/21 STATUS: Ongoing

TITLE: Relationship of Alcohol-altered Cytokine Levels and Vitamins in Serum of Patients and Patterns of Induction of Alcohol-Mediated Disease

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JI Enriquez, BC Veit, SK McIntyre, GE Philbin, A Restrepo

MONITOR: NA

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Oct 96

KEY WORDS: Vitamin, Alcoholics

Study Objective: The objective of this study is to analyze TNF and vitamins A, C, E and B_6, in the plasma of patients with alcohol abuse and establish a meaningful relationship between the cytokine and antioxidant levels affected by alcohol consumption. Accurate analyses of these components and statistical interpretation of data may result in new approach in systemetic treatment of these patients.

Technical Approach: The subjects selected for this study will be from groups of patients admitted to the hospital for treatment of alcohol-related problems. Numerical numbers will be assigned to the patients so that their names will not be known to others except to the doctors treating these patients. Only age, duration of alcohol consumption and severity of diseases will be known to those who will analyze the components in plasma.

Blood will be collected by venipuncture at the time of admission to the study and 30 days later. Serum components for clinical evaluation will be analyzed in the clinical laboratory of the hospital. Plasma samples for the determination of cytokine and antioxidants will be collected by venipuncture using Vacutainers or syringe containing Li-heparin or Na_2EDTA, immediately protected from exposure to light and then, without delay, taken to the laboratory at DCI where the formed elements will be removed by centrifugation and the plasma will be aliquoted in small volumes and frozen in dark tubes at -70°C until the time of assay.

Plasma TNF will be measured by kit ELISA (T-Cell Science, Cambridge, MA), as described (6). The assay has a detection limit of 10 pg/ml. High precisions liquid chromatography (HPLC), employing both spectrophotometric and amperometric detection methods, will be utilized for the analysis of the antioxidants and pyridoxal 5'-phosphate (PLP), the active cofactor of vitamin B6. Detection limits for the HPLC methods are well below normal physiological ranges for the antioxidants and PLP.

Progress: Analysis of vitamins and TNF in blood serum and plasma of alcoholic patients are continuing satisfactorily. The estimated completion date has been changed from Mar 96 to Oct 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/31A STATUS: Ongoing

TITLE: Advanced Laparoscopic Training Procedures for Health Care Providers Utilizing the Porcine Model

PRINCIPAL INVESTIGATOR: MAJ Richard A. Harris

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): K McLarty, LH Senter, J Holcomb, J Szigeti

MONITOR: NA

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Surgery, laparoscopic, porcine

Study Objective: Currently available non-animal models for laparoscopic procedures do not create the texture, bleeding, and handling characteristics of living tissues. Laparoscopic approaches and procedures are being developed and perfected for surgical procedures that are currently performed open. The procedures must be evaluated and performed in living tissues prior to use in humans so that the surgeon can accurately determine how specific tissues and the patient will respond to the manipulations performed. The surgeon must be aware of all possible effects this procedure might have on tissue, such as hemorrhage and tissue damage. Synthetic tissues are not adequate for complete evaluation of surgical procedures prior to implementation in humans. This training protocol is designed to train surgeons in various laparoscopic procedures, using state-of-the-art instrumentation, prior to application to human patients.

Technical Approach: Laparoscopic surgery, or "band-aid surgery," is becoming more and more common. Many times an ordinary surgery requiring a 1-2 week stay in a hospital with a painful recovery can be done by "band-aid surgery" within a single day with no time in the hospital. Oftentimes the patient has little if any pain and is allowed to resume work the day after the surgery. The cost of the hospital bill is greatly reduced. Unfortunately, the surgeon who performs the "band-aid surgery" must develop special skills to learn the right way to handle the instruments. The first part of this training is with non-living objects such as cardboard boxes and plastic dummies. The final portion of the training must be on a living body. Fully anesthetized pigs are used as final training in many procedures that the surgeon will next do on human patients. Many times, only one pig is needed since basic skills were learned on non-living objects. In all cases, the pigs are the fewest number needed and maximum use of the pig is guaranteed by many procedures on a single animal.

Progress: Subjects entered at this time are 20 with no reported adverse reactions to date. This protocol represents a "break from the past" in that it provides training in state-of-the-art laparoscopic techniques using ultra-modern equipment with extended training opportunities

to the civilian medical professionals of the Southwest United States. Supported jointly by WBAMC and the Ethicon Endo-Surgical Corporation, this protocol sets the basis for training in emerging technology and techniques. Laproscopic techniques specified in the protocol include 25 abdominal and thoracic procedures plus 8 gynecologic techniques. Additional procedures may be added by amendment to the protocol.

A total of 8 surgeons have been trained in abdominal techniques and 12 surgeons have been trained in gynecologic techniques in FY95. Critiques have shown that this training has been very well received and perceived as extremely valuable. Interest and participation under this protocol is continually increasing.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/46 STATUS: Ongoing

TITLE: Use of High Technology to Determine Risk of Drug-Resistant Tuberculosis in the El Paso Region

PRINCIPAL INVESTIGATOR: MAJ William Nauschuetz

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): N Olisa, MA Escobedo, L Nickey, VV Tryon, M Lund, GA Handal

MONITOR: NA

START DATE: Aug 94 ESTIMATED COMPLETION DATE: Jun 96

KEY WORDS: Drug-Resistant Tuberculosis El Paso, Gene Amplification

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Study Objective: Short Range Goals

Mobilize key medical treatment facilities within the El Paso region to recognize the threat of TB and MDRTB: We have already accomplished this goal. The Dept. of Clinical Investigation, WBAMC has agreements with the El Paso City/County Health District and with the El Paso Managed Health Care Consortium (representing four academic institutions and three medical centers) to address the threat of TB and MDRTB in the El Paso region.

Introduce Polymerase Chain Reaction (PCR) technology for the identification of *M. tuberculosis* and MDRTB: The Dept. of Clinical Investigation, WBAMC is cooperatively working with the El Paso City/County Health District to investigate the sensitivity of PCR compared to routine TB culture and susceptibilities for the detection of *M. tuberculosis* and MDRTB. We also have an agreement with members of the El Paso Managed Health Care Consortium to share clinical specimens to compare PCR with routine TB culture and susceptibilities.

Intermediate Range Goals

Establish the rate of TB and MDRTB for a stable population in Juarez and for Mexican nationals being treated in El Paso medical centers: Clinical specimens submitted to medical facilities in Juarez for the diagnosis of TB are stained for the presence of acid-fast bacilli. Those specimens that are AFB smear positive are transported to the El Paso City/County Health District for culture confirmation and antimicrobial susceptibilities. However, the sensitivity of AFB smears is about 50%, so many citizens in Juarez are not laboratory-diagnosed properly. By choosing a stable population within Juarez and doing a sweep collection, we can determine the incidence of TB and MDRTB by performing routine culture on all specimens, despite smear results, and by running PCR on each specimen

submitted. The PCR should provide a more sensitive method of detecting latent and subclinical TB. We would also use PCR for TB and MDRTB on all Mexican nationals admitted to El Paso medical centers showing respiratory symptoms.

Long Range Goals

The data derived from this study can be used to establish the El Paso region as a high-risk area for TB and MDRTB and as an area that has fulfilled the CDC Task Force Guidelines of implementing high technology for the rapid detection of TB and MDRTB. The data can then be used as a baseline for efficacy studies of newer generation antimycobacterial agents, including those requiring shorter periods of treatment.

Technical Approach: This study is triphasic. In Phase I, primers specific for the amplification of IS6110 will be used for PCR amplification of *M. tuberculosis*. The primers will be evaluated on ATCC strains of mycobacterial species. If the primers amplify a specific sequence, Phase II will then compare the detection of PCR-amplified *M. tuberculosis* DNA with standard mycobacteriologic isolation and identification procedures. In Phase III, we will use a primer set that specifically amplifies a 411 base pair sequence from the RNA Polymerase gene (*rpoB*) of *M. tuberculosis*. Amplification will be done only on pure growth from routine mycobacteriologic media. The 411 base pair fragment that occurs as a result of the amplification will be sent to Dr. Tryon's laboratory at UT-Health Science Center at San Antonio. He will sequence the fragment and determine if mutations indicative of rifampin-resistance are present in the sequence.

Progress: To date, we have identified several problem areas when amplifying *M. tuberculosis* form clinical specimens:

- specimen prep, including cell lysis, can be difficult
- different primer sets greatly alter results

We have decided to amplify using primers specific for IS6110 and for mpt 40. We have made these primers labeled with biotin and TBR, which allows us to assay test results on our QPCR 5000, rather than having to rely on agarose gels.

We are evaluating two simple, clinically applicable methods for release of amplifiable nucleic acid. These methods are (a)boiling and (b) Gene Releaser™. Although Dr. Nauschuetz has PCS'd from WBAMC this study is being continued by Nze Olisa, an associate investigator, DPALS, WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/04 STATUS: Ongoing

TITLE: Growth Dynamics of Breast Cancer Cells: A Study of Growth Regulatory Factors

PRINCIPAL INVESTIGATOR: Bruce Veit, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: NA

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Jan 97

KEY WORDS: Breast Cancer

Study Objective: The aim of this project is to study the biological properties of breast cancer cells as they relate to intra- and extra-cellular growth factor signaling, cell cycle progression, and mutational changes which occur during tumor cell growth as the result of growth factor and chemotherapeutic influence. Information gained from this study should provide a better understanding of the mechanism(s) of breast tumor cell resistance and a rationale for applying appropriate therapeutic methods to the treatment of breast cancer.

Technical Approach: The proposed research program consists of three approaches:

(1) Study of in vitro cultured breast cancer cell lines which express a variety of growth factor receptors, tumor associated antigens and tumor suppressor genes or proto-oncogenes for (a) outgrowth of mutant clones as a function of selective pressure by chemotherapeutic agents, growth factors and cytokines; (b) responsiveness to a variety of growth factors and mitogens; (c) altered expression of cell-surface antigens; and (d) changes in ploidy, S-phase fraction, nuclear antigen expression, and cell cycle variations.

(2) Study of primary isolates of breast tumors (benign and malignant) from patients upon initial diagnosis and at relapse for (a) cellular content of tumor cells, stromal cells, and infiltrating cells (i.e., lymphocytes, monocytes, etc.); use of flow cytometry on single-cell suspensions and immuno-histochemical/immunofluorescence image analysis on tissue sections and (b) tumor cell heterogeneity with respect to tumor-associated antigens, growth factor receptors, DNA content (ploidy, S-phase fraction) and cell-cycle variations.

(3) Study primary isolates of malignant breast tumors (at initial diagnosis and at relapse) in vivo in nu/nu mouse xenografts for (a) growth response and selective pressure of chemotherapeutic agents, growth factors and cytokines; (b) alterations in cellular content of tumor cells, stromal cells and infiltrating cells during growth progression and modification through the use of growth factors, chemotherapeutic agents and cytokines; (c) emergence of chemotherapeutically resistant tumor cells and their characterization with respect to growth

factor responsiveness; and (d) mechanisms of tumor cell death: use of agents (growth factors or inhibitors) which induce cells to enter cycle or inhibit them from entering cycle in combination with chemo-cytotoxic agents to determine whether cell death occurs via apoptosis or as the result of increased susceptibility during cell cycle.

Progress: Primary human breast cancer tissues obtained from biopsies or mastectomies were characterized in terms of their DNA content by flow cytometric and digital image analyses and for expression of growth factor receptors, e.g. estrogen and progesterone receptors. We were able to analyze one breast cancer biopsy which was accompanied by an axillary lymph node which contained metastatic tumor. The primary (breast) tumor was observed to contain two aneuploid stem lines with DNA indices of 1.4 and 1.9 and S-phase fractions of 19.8% and 7.4%, respectively. Metastatic tumor in the axillary lymph node contained only one aneuploid stem line with an S-phase fraction 9.6% and had a DNA index of 1.7 suggesting the possibility of the emergence of a sub-line in the metastatic tumor. We are currently analyzing frozen and paraffin-embedded tissues from this patient to clarify the basis for these differences. Future studies in this area will focus on the use of DNA analysis and breast cancer-associated markers (i.e. ER, PR, c-erb-B, adhesion molecules) to characterize primary and metastatic tumors for possible emergence of aneuploid sub-lines.

Results of flow cytometric analysis of mutant p53 expression in cell cycle compartments of BT-474, DU-4475 and SK-BR3 cells at various times during a 7-day growth period indicated that, regardless of time in culture and cell cycle compartment, almost all BT-474 cells continually expressed mutant p53 gene product suggesting that the constitutive expression of mutant p53 protein is not modulated by normal growth of BT-474 cells. By contrast, DU-4475 and SK-BR3 cells did exhibit variations in the expression of mutant p53 gene product during their growth. DU-4475 cells exhibited low (16%) percentages of p53 protein expression in all three cell cycle compartments at the initiation of culture. After 1 day of culture, percentages of p53 positive cells rose to 80-90% and then decreased to low (18%) levels after 7 days of culture. Again, all three cell cycle compartments exhibited similar increases and decreases. In DU-4475 cells, there appeared to be no preferential expression in specific phases of the cell cycle. SK-BR3, on the other hand, exhibited a 41 % expression of mutant p53 on day 0 which rose to 98.3% by day 1 and remained elevated through day 7. Interestingly, there appeared to be an up-regulation of the expression of this protein in GO/Gl and S phases of the cell cycle by day 1, but its expression in G,/M cells was 96% on day 0 and remained the same throughout the 7-day culture period. Since the p53 tumor suppressor gene product has been reported to be involved in the induction of apoptosis as the result of growth factor deprivation possibly by down-regulating bcl-2 expression, we plan to conduct further experiments that are designed to clarify the differences observed in p53 protein expression in the three cell lines described above and to determine how these differences impact on the induction of apoptosis.

A major goal of our research is to establish a model system for studying the involvement of apoptosis in breast cancer cell death. We used a DNA 3'-OH digoxigenin-nucleotide end extension - FITC-anti~digoxigenin labeling technique for detecting the presence of fragmented DNA in intact cell nuclei as a marker for apoptosis. Since DNA fragmentation occurs within a specific time period during apoptosis, this technique does not detect apoptotic cells that are in pre- or post-DNA fragmentation stages. Therefore, a future goal is to combine this technique with other methods of identifying apoptotic cells during all stages of the process. To assess the ability of the 3'-OH end labeling technique to detect apoptotic cells, three breast cancer cell lines were subjected to a variety of different agents that have been reported to induce apoptosis (hyperthermia, TNF- , camptothecin, and etoposide). Results of these

experiments indicated that the end-labeling method was, indeed, capable of detecting apoptosis in all situations where apoptosis has been detected by other methods.

Adherence is a key growth-requiring characteristic of epithelial-like tumor cell growth in *in vitro* cultures. Adherent BT-474 cells began decreasing in viable cell numbers by 16 to 23 hours after addition of etoposide to the cultures. Interestingly, there was a corresponding increase in numbers of viable, non-adherent cells in these cultures which peaked at about 40 to 45 hours of incubation and then decreased thereafter. Apparently, the presence of etoposide initially caused a detachment of viable cells between 16 to 23 hours of incubation. A different pattern of cell detachment was observed in the growth of MCF-7 cells incubated with etoposide when compared to growth of non-adherent BT-474 cells. Whereas non-adherent viable BT-474 cells incubated with etoposide exhibited a marked increase in numbers from 16 to 40 hours of culture and decreased thereafter, viable non-adherent MCF-7 cells only exhibited a minimal and gradual increase in number throughout the entire culture period. The basis for this difference between these two cell lines in their detachment patterns when incubated in the presence of etoposide is not clear and is currently under investigation.

Percentages of apoptotic BT-474 and MCF-7 cells increased significantly in etoposide-treated cultures during a 70 hours of incubation. When total numbers were quantitated, however, peak numbers of apoptotic cells were observed at approximately 20 to 30 hours of culture with a significant decline thereafter. This dramatic increase in numbers of apoptotic cells was distributed unequally among GdG,, S and G,/M cell cycle compartments with the highest number observed in the S-phase. Whereas numbers of apoptotic S-phase cells decreased after 23 to 30 hours of incubation, the numbers of GO/Gl and G2/M apoptotic cells remained at constant levels throughout the remainder of the culture period. These findings are consistent with the S-phase-associated mode of action of topoisomerase inhibitors which primarily affect cells undergoing DNA synthesis. The method of 3'-OH-end-labeling was used in our studies to identify apoptotic cells which exhibited characteristic DNA fragmentation. Intuitively, it is likely that the length of the DNA fragmentation period would be shorter than was determined in our experiments. As yet to be confirmed, it is possible that the majority, if not all, of 3'-OH end-labeled cells in later stage cultures (50 - 90 hours) were associated with non-apoptotic phenomena. We are pursuing the development of alternative methods of detecting apoptotic cells to further clarify this issue.

We believe that we have established a useful model for continued studies of the involvement of apoptosis in growth regulation of breast cancer cells. With this model, we will study the influences of growth-promoting and growth-inhibiting factors that modulate the growth of breast cancer cells both *in vitro* and *in vivo*. Estimated completion date has changed from Dec 95 to Jan 97.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/05A STATUS: Ongoing

TITLE: Growth Dynamics of Breast Cancer Cells: A Study of Growth Regulatory Factors using the Murine Model

PRINCIPAL INVESTIGATOR: Bruce Veit, PhD

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): K Nauschuetz

MONITOR: NA

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Jan 97

KEY WORDS: Athymic Mice, Nude Mice, Xenograft, Breast Cancer

Study Objective: The aim of this project is to study the biological properties of breast cancer cells as they relate to intra- and extra-cellular growth factor signaling, cell cycle progression, and mutational changes which occur during tumor cell growth as the result of growth factor and chemotherapeutic influence. Information gained from this study should provide a better understanding of the mechanisms of breast tumor cell resistance and a rationale for applying appropriate therapeutic methods to the treatment of breast cancer. Our studies will attempt to answer the following questions: (1) What are the phenotypic and biological characteristics of variant sublines within breast cancers? (2) Do human breast tumors that grow in thymic nude (nu/nu) mice retain their histological grade and variant subline profiles? (3) What are the selective pressures which create heterogeneity in breast cancers? (4) Do breast cancer relapses occur because of physiological (non-genetic) or mutational (genetic) alterations in growth factor signaling pathways? (5) Do normal stromal cells exert growth regulatory influences on tumor cells via growth factor secretion and/or cytokine production? (6) Does growth factor deprivation of growth factor-dependent tumor cells result in the initiation of apoptosis?

Technical Approach: The proposed research program consists of three approaches:

(1) Study of in vitro cultured breast cancer cell lines which express a variety of growth factor receptors, tumor-associated antigens and tumor suppressor genes or proto-oncogenes for (a) outgrowth of mutant clones as a function of selective pressure by chemotherapeutic agents, growth factors and cytokines; (b) responsiveness to a variety of growth factors and mitogens; (c) altered expression of cell-surface antigens; (d) changes in ploidy, S-phase fraction, nuclear antigen expression, and cell cycle variations.

(2) Study of primary isolates of breast tumors (benign and malignant) from patients upon initial diagnosis and at relapse for (a) cellular content of tumor cells, stromal cells, and infiltrating cells (i.e., lymphocytes, monocytes, etc.); use of flow cytometry on single-cell suspensions and immunohistochemical/immunofluorescence image analysis on tissue sections

and (b) tumor cell heterogeneity with respect to tumor-associated antigens, growth factor receptors, DNA content (ploidy, S-phase fraction) and cell-cycle variations.

(3) Study primary isolates of malignant breast tumors (at initial diagnosis and at relapse) in vivo in nu/nu mouse xenografts for (a) growth response and selective pressure of chemotherapeutic agents, growth factors and cytokines; (b) alterations in cellular content of tumor cells, stromal cells and infiltrating cells during growth progression and modification through the use of growth factors, chemotherapeutic agents and cytokines; (c) emergence of chemotherapeutically resistant tumor cells and their characterization with respect to growth factor responsiveness; (d) mechanisms of tumor cell death: use of agents (growth factors or inhibitors) which induce cells to enter cycle or inhibit them from entering cycle in combination with chemo-cytotoxic agents to determine whether cell death occurs via apoptosis or as the result of increased susceptibility during cell cycle.

Progress: Two - 3mm samples of fresh primary human breast tumor biopsy were implanted into the mammary fat pads of nude (athymic) mice. Unfortunately, none of the transplanted tissue samples developed tumors in the xenografted mice. In some cases, tumors did not grow because the implanted specimens were subsequently found to contain either fatty tissue or normal epithelial tissue. In other cases, it is likely that the xenograft failures (later determined to involve estrogen receptor+ tissues) were due to the lack of a suitable estrogen-enriched environment (recipient mice were not routinely treated with estrogen). Recently, it has been reported that estrogen supplementation enhances tumorigenicity somewhat but a much greater level of tumorigenicity was obtained when breast cancer cells were co-inoculated with estrogen and basement membrane matrix (Matrigel). In future attempts to grow xenografted primary breast cancer tissue, we will incorporate these findings into our protocol.

We were successful in growing two established breast cancer cell lines, BT-474 and DU-4475, as tumor xenografts in nude mice. It is likely that our success rate in growing xenografted breast cancer cells from established cells lines will also increase when we combine the cell implants with estrogen and basement membrane matrix.samples for implantation via trocar into the mammary fat pads of nude (athymic) mice as described by Price et al (47). Unfortunately, 0 of 9 implants developed tumors in the xenografted mice. In some cases, tumors did not grow because the implanted specimens were subsequently found to contain either fatty tissue or normal epithelial tissue. In other cases, it is likely that the xenograft failures (later determined to involve ER+ tissues) were due to the lack of a suitable estrogen-enriched environment (recipient mice were not routinely treated with estrogen). A recent report (48) has indicated that estrogen supplementation enhances tumorigenicity somewhat but a much greater level of tumorigenicity was obtained when breast cancer cells were co-inoculated with estrogen and basement membrane matrix (Matrigel). In future attempts to grow xenografted primary breast cancer tissue, we will incorporate these findings into future studies. Because of failures in our early attempts to grow primary human breast cancer xenografts in nude mice and because of the lack of extramural funding (which ended October 1994) to continue this aspect of our studies, we suspended further work in this area and focused our attention primarily on in vitro studies of breast cancer cell lines and the detection of drug-induced apoptosis which will be described later.
Estimated completion date has changed from Dec 95 to Jan 97.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 83/37 STATUS: Completed

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

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: MAJ Lynn Keenan

START DATE: Jul 84 ESTIMATED COMPLETION DATE: Sep 94

KEY WORDS: Sickle Cell Trait, Stress, Hypoxia, Exercise

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

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.
Addendum (Mar 85): Added testing at 7,500 ft

Progress: 100 subjects have been entered into this study with no adverse reactions reported to date. 5 complete peer review papers have been published. 2 additional papers (PFTs and ___ in preparation. Abstracts previously submitted.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 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)

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RJ Zeballos, J Little, TW Martin

MONITOR: MAJ Lynn Keenan

START DATE: Jul 89 ESTIMATED COMPLETION DATE: Jul 97

KEY WORDS: Sickle cell trait, Endurance exercise

Study Objective:

1. To determine if submaximal (50-70% VO2 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: 40 subjects have entered in this study with no adverse reactions reported to date. 4 Abstracts have been published. 4 full length manuscripts are in varying stages of preparation. The final manuscript, however, will be written this year. 4 full abstracts previously submitted. Estimated completion date has changed to Jul 97.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/34 STATUS: Ongoing

TITLE: Comparison of Anaerobic Power Between Female and Male Soldiers

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RJ Zeballos

MONITOR: LTC Larry Tremper

START DATE: Jun 93 ESTIMATED COMPLETION DATE: Oct 96

KEY WORDS: Anaerobic Exercise, AIT Anaerobic

Study Objective:

(1) To measure the anaerobic power for lower and upper body exercise in male and female soldiers, and develop a data base that may be used as a reference to gauge performance levels of anaerobic power.

(2) To determine the impact of intense anaerobic work on cardiopulmonary functions.

Specific Objectives:

To determine if the U.S. soldier is more fit to perform anaerobic exercise using upper or lower body exercise.

To compare the level of anaerobic power of female with male soldiers.

To study the changes in cardiopulmonary physiology during and after intense, all-out anaerobic work.

To apply these results to different military operational field tasks so that specific training standards can be appropriately modified if necessary.

Technical Approach: Prospective study. The same volunteers will be used as their own control. All subjects will undergo the same treatment (AIT) and testing protocols.

Progress: 25 subjects have entered in this study with no reported adverse reactions to date. Estimated completion date has changed from Jun 95 to Oct 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/57 STATUS: Completed

TITLE: Effect of ATROVENT® in Exercise Performance in Patients with Chronic Pulmonary Disease

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RJ Zeballos

MONITOR: LTC Larry Tremper

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Oct 95

KEY WORDS: Chronic Pulmonary Disease (CPD), ATROVENT®

Study Objective:

Ipratropium bromide (ATROVENT®) is an anticholinergic agent with well established bronchodilative properties in patients with chronic obstructive pulmonary disease (COPD) (NEJM 1993;328:1017-22). Ipratropium treatment also reduces the volume of sputum without altering its viscosity (Chest 1991;86:871-6). Recent in vitro evidence also suggests that ipratropium may have anti-inflammatory effect (Rennard, Personal Communication).

Improved airway patency observed after inhalation of ipratropium may also lead to a decrease in static lung volumes, in particular, trapped air volume (TAV) (Brit Med J 1988;297:1506-09). This, in turn, may lead to decrease in work of breathing and a decrease in dyspnea, including exertional dyspnea.

Thus, chronic administration of ipratropium, in patients with COPD may lead to the increase in alveolar ventilation and consequent improvement in oxygen saturation and possible attenuation of the inflammatory process, well documented in lungs of patients with COPD. These physiological improvements may be particularly important during exercise. However, the effect of chronic dosing with ipratropium on exercise tolerance was only rarely studied (Am Rev Respir Dis 1992;145:A758).

Thus, in this study we will examine effect of chronic treatment with ipratropium MDI on exercise tolerance in COPD patients.

Technical Approach: A double-blind, randomized, placebo-controlled, two-arm parallel multi-center study.

Progress: 15 subjects have entered in this study with no reported adverse reactions to date. Abstract of study has been presented. Full length manuscript in preparation. Completion date has changed from Dec 94 to Oct 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/27 STATUS: Ongoing

TITLE: A Randomized, Double-Blind, Double-Dummy, Comparative Clinical Trial of Twelve Week Courses of Salmeterol Xinafoate Versus Ipratropium Bromide Versus Placebo (PRN Ventolin®) in Subjects with Chronic Obstructive Pulmonary Disease

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RJ Zeballos

MONITOR: LTC Wallingford

START DATE: Apr 95 ESTIMATED COMPLETION DATE: May 96

KEY WORDS: Salmeterol, Comparison, COPD

Study Objective:

Salmeterol xinafoate is a selective long-lasting inhaled beta$_2$-adrenoreceptor agonist for the maintenance treatment of reversible airway obstruction and the prevention of bronchospasm. Salmeterol has been shown to maintain lung function in excess of 20% above baseline for at least 12 hours, with peak increases in lung function equivalent to Ventolin®. Chronic dosing studies have shown salmeterol is the optimum dosing regimen for subjects with mild to moderate reversible airway obstruction and is more efficacious than Ventolin®.

Atrovent (ipratropium bromide) is an anticholinergic (parasympathetic) agent that is indicated for maintainance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema.

The goals of the study are:

1. To compare the efficacy of salmeterol treatment with that of ipratropium bromide treatment and placebo (prn Ventolin®) in subjects with COPD as measured by BDI/TDI Dyspnea scale, FEV_1 AUC, exercise test and Borg dyspnea assessment, 12 hour PFTs, daily AM and PM peak flow measurements, self-rating of symptoms, nighttime awakenings due to respiratory symptoms, supplemental Ventolin® use and exacerbation rates.
2. To compare the safety of salmeterol treatment with that of ipratropium bromide treatment and placebo (prn Ventolin®) in subjects with COPD as measured by vital signs, clinical laboratory results, 12-lead ECG, clinical adverse events, medical history, physical exam, chest radiograph and 24-hour Holter recording.

3. To compare the effectiveness of salmeterol xinafoate (42 mcg BID, by inhalation) versus ipratropium bromide (36 mcg QID, by inhalation) versus placebo for reducing subject-perceived sleep quality impairments (as measured by the Pittsburgh Sleep Quality Index (PSQI) scores).

Technical Approach: Multicenter, Stratified, Randomized, Double-blind, Double-dummy study.

Progress: 15 subjects entered in this study with 1 reported adverse reaction removed from study by consent. Asymptomatic ventricular arrythmias noted only on routine holter monitoring. 2 AES for V tach (1 sheet run & 18 beat run). 1 V-asystole reported immediately to FDA through appropriate channels (PPD/Glaxo/FDA) with v-asysterle m/p unrelated to Serevent & 15 beat run of V. tach. Patient admitted to hospital for SAE for PM placement. Asystole was m/p unrelated to Serevent as PM is necessary off drug. Patient is perfectly well. 2 months s/p d/c drug.
Amendment 1: 14 Mar 95; Amendment 2: 10 May 95 Estimated completion date has changed from Jan 96 to May 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/06 STATUS: Ongoing

TITLE: Impact of Smoking on Aerobic and Anaerobic Performance During Upper and Lower Body Exercise in Female Soldiers

PRINCIPAL INVESTIGATOR: COL Idelle M. Weisman

DEPARTMENT: DCI FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RJ Zeballos

MONITOR: MAJ Kevin Kumke

START DATE: Nov 94 ESTIMATED COMPLETION DATE: Apr 96

KEY WORDS: Aerobic, Anaerobic Exercise Performance, Upper Body, Lower Body, Females

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Study Objective: 1- To establish a comprehensive quantitative data base of aerobic (exercise longer than 5 minutes) and anaerobic (short bursts of high intensity exercise) levels of fitness for female Army personnel for lower and upper body exercise.

2 - To determine if female soldiers are more fit to perform aerobic or anaerobic exercise and upper or lower body exercise.

3 - To correlate upper and lower body levels of fitness with Army Physical Fitness Test results.

4 - To determine the chronic and acute effects of smoking on aerobic and anaerobic performance during lower and upper body exercise.

Technical Approach: Prospective controlled study to obtain the data base of exercise performance of female soldiers; parallel design, smokers vs. controls to determine the chronic effect of smoking. The same smokers will also be used as their own control to evaluate the acute effect of smoking.

Progress: 40 subjects have been entered in this study with no adverse reactions reported to date. Subjects are still being accrued. Only preliminary statistical analysis and data are available. Estimated completion has changed from Sep 95 to Apr 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/20A STATUS: Completed

TITLE: Comparison of Osseointegration of Titanium Implants in Cranial and Iliac Autologous Bone Grafts Stabilized with Immediate Titanium Implant Fixtures in Miniature Swine

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: DENTAC FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): COL M.G. Donovan

MONITOR:

START DATE: May 91 ESTIMATED COMPLETION DATE: June 95

KEY WORDS: Titanium Implants, Canial Bone Grafts, Iliac Bone Grafts, Onlay Bone Grafts

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Study Objectives:

1. Examine time interval of osseointegration of titanium implants when placed in immediate bone grafts.
2. Compare the rate of osseointegration, i.e., success rate, of titanium implants in immediate autologous calvarial and iliac bone grafts.
3. Compare the rate of osseointegration, i.e., success rate, between immediate placement of titanium implants in grafted bone to titanium implants in mature bone grafts.
4. Determine the recommended time interval of osseointegration required prior to placement of functional load on implants.

Technical Approach: Six miniature swine will be used for this study. Each animal will serve as its own control by having an implant placed in a non-grafted facial bone site.

Under general anesthesia, each swine will have autologous bone from the outer table of the frontal and parietal bones harvested and a corticancellous bone graft from the iliac crest harvested. Placement of the bone grafts will be to the nasal bones of the swine. The bone grafts will be rigidly fixed utilizing one or more Branemark titanium implant fixtures of 7mm or 10mm lengths.

Four calvarial bone grafts and four iliac bone grafts will be utilized on each animal. The calvarial bone grafts will be on the right side and the iliac bone grafts will be on the left side of the nasal bones.

One swine will be euthanatized at one month, two months, four months, six months, eight months, and twelve months to obtain specimens for histological studies. Twenty-one days prior to scheduled euthanasia and biopsy, the animals will be marked with an I.M. injection of a tetracycline derivative to assess new bone growth in the bone grafts adjacent to the implant fixtures.

Barium sulfate mixed with heparinized formalin will be infused after euthanasia to mark neovascularization in the bone grafts.

Each bone graft site will be physically measured for evidence of bone resorption or growth, and these measurements will be compared with the dimensions of the bone grafts measured at time of initial placement. The titanium implants are of fixed length and will serve as markers for loss or maintenance of the bone graft heights along with the above physical measurements.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: There has been 6 subjects entered in this study with no noted adverse reactions.
Abstract: "Cranial vs. Iliac Autologous Bone Grafts with Immediate Titanium Implant Placement in Miniature Swine": This study was developed to evaluate the feasibility of placing titanium thread type implants immediately into onlay calvarial and iliac bone grafts. the hypothesis was that the titanium implants would provide a foundation which might minimize the greater than 80% resorption seen typically with onlay iliac grafts. Also, the osseointegration of titanium implants placed at the same time as the onlay bone grafts was evaluated and compared with the osseointegration of previously placed implants in ungrafted and mature bone grafts in this same animal mode. Six Pitman-Moore miniature swine were studied at 1, 2, 4, 6, 8, and 12 months with a total of 48 graft sites divided equally between calvarial (membranous) and iliac (endochondral) onlay bone grafts.

The titanium implants did have an influence on the retention of the iliac onlay grafts up until 4 and 6 months compared to previous studies of onlay iliac grafts, but by the end of this twelve month study, the resulting retention of both the calvarial and iliac onlay bone grafts were approximately the same with and without immediate implant placement.

The implant osseointeration success in these onlay bone grafts followed previous clinical trails very closely. The overall success rate for the 24 titanium implants placed immediately with the calvarial onlay grafts was 87.5% compared to the 54.2% success rate of the 24 titanium implants placed immediately with the iliac onlay grafts.

This research of immediate titanium implants in autologous calvarial and iliac onlay bone grafts in miniature swine demonstrated that osseointegration of implants will occur as these onlay grafts heal. When utilizing calvarial onlay grafts the success rate of the implants and the bone retention indicate this as a potentially good reconstructive option.

The presence of titanium implants did not make for a scaffold to help preserve the iliac bone in this study. What would the effects be if these implants were loaded at the 4 and 6 month time frame and resulting bone retention or loss was not addressed in this animal model.

The cortical nature of the calvarial bone and the cortico-cancellous architecture of the iliac bone also proved to be significant in the bone/implant interface and the resulting success of the implants in these different bone grafts. Within the calvarial onlay grafts the bone to implant interface was 67% totally bone and only 38% in the iliac onlay grafts., Nathan Dickerson, DDS, Oral and Maxillofacial Surgery.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 89/37 STATUS: Ongoing

TITLE: Bone-Anchored Craniofacial Prostheses Investigation

PRINCIPAL INVESTIGATOR: COL Michael G. Donovan

DEPARTMENT: DENTAC FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Gary, N Dickerson

MONITOR:

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Implants, 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: The FDA along with Nobelpharma have not closed this study as data is presently being obtained for this multi centered study. Another subject was added retroactively to this study as per Nobelpharma's request to the FDA, and data is being collected for this patient. This institution's clinical investigation service has the correspondence for this action. There have been 5 subjects entered in this study with no noted adverse reactions.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/38A STATUS: Completed FY95

TITLE: Evaluation of Osseointegration of Immediately Placed Titanium Implant Fixtures in Allogeneic Onlay Bone Graft in Miniature Swine

PRINCIPAL INVESTIGATOR: MAJ Trent C. Filler

DEPARTMENT: DENTAC FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): M Donovan, N Dickerson

MONITOR: NA

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Jul 95

KEY WORDS: Titanium Implants

Study Objective: To examine if osseointegration of titanium implants occurs in allogeneic onlay bone graft when placed immediately using the concepts of tissue guided regeneration; to examine time interval of osseointegration of titanium implants when placed immediately into allogeneic onlay bone graft using the concepts of tissue guided regeneration; to compare rate of osseointegration, i.e., success rate between placement of titanium implants in allogeneic grafted bone to titanium implants placed in autogenous bone grafts (study #92/20, Comparison of Osseointegration of Titanium Implants in Cranial and Iliac Autologous Bone Grafts Stabilized with Immediate Titanium Implant Fixtures in Miniature Swine); and to determine the recommended time interval of osseointegration required prior to placement of functional load in implants placed in grafted allogeneic bone.

Technical Approach: Fifteen miniature swine will be used for this study. Up to three animals will serve as a source for the allogeneic calvarial and iliac bone grafts to be grafted to the other twelve animals. The long bones from these three animals will serve as a source for Demineralized Bone Powder. The bone will be harvested and then processed by the Department of Anatomy, Medical College of Georgia and the protocol on Appendix A.

Under general anesthesia each of the twelve swine will have allogeneic bone from the frontal and parietal region and allogeneic bone from the iliac crest grafted to the nasal bones, maxilla and mandibular. The allogeneic bone grafts will be augmented with bone morphogenic protein. The bone grafts will be rigidly fixed utilizing one or more Branemark titanium implant fixtures of 10 mm length and Luhr rigid fixation screws.

Five calvarial bone grafts and five iliac bone grafts will be utilized on each animal. The calvarial bone grafts will be on the right side, and the iliac bone grafts will be on the left side of the nasal bones, lateral maxilla, and mandible ramus.

Two of the calvarial bone grafts and two of the iliac bone grafts will be covered with tissue guided regeneration material from Gore-Tex.

Two swine will be euthanatized at one month, two months, four months, six months, eight months and twelve months to obtain specimens for histological studies.

Barium sulfate mixed with heparinized formalin will be infused after euthanasia to make neovascularization in the bone grafts identifiable radiographically.

Each bone grafts site will be physically measured for evidence of bone resorption or growth, and the measurements will be compared with the dimensions of the bone grafts measured at time of initial placement.

The titanium implants are of fixed length and will serve as markers for loss on maintenance of the bone graft heights as well as the above physical measurements.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: This study has been completed. Dr. Filler, principal investigator submitted an abstract.

ABSTRACT: Autologous onlay bone grafting, using traditional iliac and rib grafts to repair facial bone defects has been less than ideal due to the rapid and significant resorption of the grafts. A previous study at our institution compared iliac and calavarial onlay grafts and found a vast difference in the retained volume of graft material at the six to twelve month time frame. This study compared iliac to calvarial onlay bone grafts with immediate implant placement and attempted to answer three basic questions: a. The feasibility of immediate implant placement in onlay bone grafting. b. Whether or not implant placement helps to maintain graft volume. c. If there is a difference in the implant/bone interface or integration between iliac and calvarial bone grafting. This study evaluated the physical, histologic, and radiographic characteristics of calvarial and corticocancellous iliac onlay bone grafts with immediate implant placement in 6 Pitman-Moore miniature swine at 1, 2, 4, 6, 8, and 12 month intervals. As in the previous study calvarial bone grafts showed a much higher retention of volume at the six to twelve month interval (88% to 12%). There was a significant difference in integration of implants in calvarial bone with 88% as compared to 54% for iliac bone. The presence of implants did not affect the retained graft volume of the mature graft.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/33A STATUS: Ongoing

TITLE: Autologous Pericranium for Temporomandibular Joint Disc Replacement in Sheep

PRINCIPAL INVESTIGATOR: COL John C. Mitchell

DEPARTMENT: DENTAC FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MG Donovan, NC Dickerson

MONITOR: N/A

START DATE: Jun 93 ESTIMATED COMPLETION DATE: Dec 95

KEY WORDS: Temporomandibular Joint, Reconstruction, Discectomy

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Study Objective: (1) Determine the success of autologous pericranium as a temporomandibular joint disc replacement tissue utilizing histological assessments of the morphological changes of the pericranium at timed intervals.

(2) Compare condylar morphological changes in temporomandibular joints repaired with pericranial grafts and joints in which unrepaired discectomies are performed.

Technical Approach: (1) Fifteen domestic sheep will be used for this study. A control for a normal temporomandibular joint disc and condyle have been previously studied histologically.

(2) Under general anesthesia, each of the fifteen sheep will have autologous pericranium harvested via a biocoronal flap. An incision over the zygomatic arch and glenoid fossa will give access to the temporomandibular joint space. The TMJ discs will be excised bilaterally and the pericranium sutured to the anterior and posterior stumps of the TMJ disc attachments with non resorbable sutures unilaterally. The other temporomandibular joint will go unrepaired following its discectomy.

(3) Three sheep will be euthanatized at one month, two months, four months, six months, and ten months to obtain specimens for histological studies.

(4) The pericranium from each joint site will be studied for histological changes and fibrous adhesions.

(5) The condyles of each animal will be studied to assess any changes as a result of the autologous pericranium TMJ disc replacement. These will be evaluated radiographically and by histological sections.

Progress: 10 sheep were used in this study. All necropsies have been performed, all specimens have been sectioned and stained. The histopathologic evaluation, statistical evaluation of results and final draft of research papers remain to be accomplished.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/26A STATUS: Completed FY95

TITLE: Pericranium as a Tissue Barrier in Mandibular Reconstruction in Sheep (*Ovis aries*)

PRINCIPAL INVESTIGATOR: CPT Timothy C. Snyder

DEPARTMENT: DENTAC FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JC Mitchell, MG Donovan, NC Dickerson

MONITOR: NA

START DATE: Oct 94 ESTIMATED COMPLETION DATE: Apr 95

KEY WORDS: Pericranium, Mandibular Reconstruction

Study Objective:

(1) Determine the viability of pericranium used as a free graft over transoral mandibular reconstruction sites.

(2) Compare the incidence of infection, wound breakdown, and retention of autologous corticocancellous iliac bone grafts placed trans orally in mandibular defects closed primarily with and without the use of autologous pericranium.

Technical Approach:

(1) Eight Rambouillet sheep will be used for this study. Each animal will serve as its own control.

(2) Under general anesthesia, each of the eight sheep will have autologous corticocancellous iliac and pericranial bone harvested for grafting. Posterior mandibular bone, teeth, and gingiva will be excised bilaterally. Transoral immediate corticocancellous bone grafts will be placed to reconstruct the osseuos defects of the mandible. Primary closure will be done on one side of the mandible and a two-layered closure, utilizing pericranial grafts, will be done on the remaining side. Sheep will be observed daily following surgery to assess clinical healing and cultures will be obtained if breakdown or evidence of infection develops. Two sheep will be euthanized at each of 2, 4, 6, and 8 weeks and tissue harvested for analysis.

Progress: The surgery start date was October 1994. There have been 10 subjects entered with no adverse reactions noted to date. The estimated completion date has been changed from Jul 95 to Apr 95. *Conclusion::* Under the circumstances of this study, there appears to be no benefit to placing free pericranium over block iliac corticocancellous bone grafts placed transorally. There was no statistical difference in the clinical infection (dehiscence with purulent exudate) rate between the side with the free pericranial graft and the control side. Histologically there was evidence of bacterial colonization of all the grafts; again showing no difference between the control sides and the free pericranial grafted sides.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/24 STATUS: Terminated

TITLE: PCR Detection of Hepatitis C Virus in Serum and Dialysate of Hemodialysis Patients

PRINCIPAL INVESTIGATOR: MAJ Jeffrey Abrams

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): W. F. Nauschuetz

MONITOR: NA

START DATE: Mar 94 ESTIMATED COMPLETION DATE: Jul 94

KEY WORDS: PCR, Hepatitis C, Dialysis

Study Objective: To evaluate hemodialysis patients who are HCV antibody positive, by second generation ELISA testing, for evidence of viremia in serum by PCR and determine if contamination of the dialysate has occurred again with the use of PCR.

Technical Approach: Enroll hemodialysis patients who have been screened by hepatitis serologies and have been found to be HCV antibody positive by a second generation ELISA test. Obtain demographic data (see attached data form) from medical records and patient. Obtain serum and pre- and post-dialysis dialysate samples from these patients and perform PCR to identify HCV RNA. Detection of HCV RNA has been shown to be inhibited by heparinized blood (49). Therefore, serum and dialysate samples are to be collected in EDTA tubes and non-heparinized dialysis treatments will be attempted. Prior to performing PCR on the samples heparinase will be administered to dialysate samples to eliminate interference by heparin. In addition to the PCR the following blood tests will be performed: Biliary panel and Hepatitis B serologies, if not performed previously. For those dialysate samples that are positive by PCR, a repeat study will be performed and a sterilant will be used on the dialysis equipment and PCR repeated on the dialysate to see if sterilant eliminated viral mRNA.

Progress: This protocol has been terminated by the principal investigator, Dr. Abrams due his departure from the service and WBAMC. MAJ Nauschuetz, the associate investigator also PCS'd to TAMC in July 1995. Total number of subjects entered were 2 with no adverse reactions reported.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/32 STATUS: Ongoing

TITLE: A Double-Blind, Randomized, Phase III, Multicenter Study of Suramin and Hydrocortisone versus Hydrocortisone and Placebo in the Treatment of Patients with Metastatic, Hormone-Refractory Prostate Carcinoma (Stage D2) (Protocol 1003-01)

PRINCIPAL INVESTIGATOR: MAJ Jennifer L. Cadiz

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RF Heaven

MONITOR: LTC Elmer Pacheco

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Dec 96

KEY WORDS: Suramin, prostate cancer chemotherapy

Study Objectives: To evaluate (1) the role of Suramin in the treatment of hormone-refractory metastatic prostate cancer to control pain, improve patients' overall functional status, and decrease the size of, or eliminate, sites of disease and/or improve patient survival, (2) the feasibility of administering Suramin in the community hospital setting, and (3) patient tolerance of side effects of treatment.

Technical Approach: This is a randomized, double-blind study of hydrocortisone with either Suramin or placebo. Patients with progression of disease on the placebo arm will be crossed-over to treatment with Suramin.

Progress: There have been no subjects entered in the study. No progress was reported by the principal investigator.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/12 STATUS: Ongoing

TITLE: A Prospective Randomized Comparison of Inguinal Herniorrhaphy : Laparoscopic Extra-Abdominal Pre-Peritoneal vs. Open Tension Free vs. Open Traditional

PRINCIPAL INVESTIGATOR: CPT Albert L. Chorens

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): B Whitlow, SP Hetz, J Holcomb

MONITOR: MAJ Thomas S. Gormley

START DATE: Jan 94 ESTIMATED COMPLETION DATE: Jan 97

KEY WORDS: Ingguinal Hernia, Herniorrhaphy

Study Objectives: The principal objective is to determine which of the three mentioned techniques offers the lowest rate of recurrence, the least morbidity, and the least period of convalescence before a return to the patient's pre morbid baseline.

Technical Approach: Those patients who present to the General Surgery Clinic, who on physical exam by a staff General Surgeon, demonstrate an inguinal hernia (s) will be the target population. From this group, the patient deemed to be a surgical candidate will be advised of the herniorrhaphy protocol.

The surgical candidate with an inguinal hernia(s) will have the risks and benefits of herniorrhaphy explained. Additionally, the goal of the study protocol will be explained , as will each arm (surgical technique) of the protocol be explained. An opportunity for patient's questions regarding the above will be given. At this time, the patient will be given a Volunteer Agreement Affidavit for review and signature, if patient is so inclined to participate.

The patient who agrees to participate in the study protocol, will be scheduled for a return appointment in the General Surgery Clinic. At that time, additional questions by the patient may be answered regarding the herniorrhaphy protocol. Formal enrollment into the protocol will be completed. Actual blind prospective randomizing of patient into protocol treatment arm will be done. Blind randomization is desired, in order to decrease the incidence of patient subjectivity and patient bias regarding herniorrhaphy procedure and potential for decreased participation due to same. The patient will be previously counseled to this condition of protocol participation. The scheduled date of surgery will be finalized.

Blind prospective randomization will be performed by assignment of patient via blind randomization numbers table to a previously determined herniorrhaphy treatment limb (procedure).

The three treatment limbs of the inguinal herniorrhaphy protocol will be as follows:

i) Laparoscopic extra-abdominal pre-peritoneal herniorrhaphy with prolene mesh as described fundamentally by McKernan (11) with modification by Phillips and Carroll (12).

ii) Tension free open herniorrhaphy with prolene mesh as described by Lichtenstein (14).

iii) Traditional open herniorrhaphy as variously described by the standard Bassini, standard McVay, standard Shouldice repairs.

Performance exercise testing via straight leg raises will be determined pre-operatively as an objective independent variable assessing the patient's pre morbid baseline activity level. A post-operative assessment will also be conducted to determine the patient's return to baseline activity as an indicator of *return to normal activity* (9).

Bilateral hernias. Pt assessed with bilateral inguinal hernias on exam by staff General Surgeon will not be excluded. Instead , the patient will have the bilateral hernias repaired via a blind randomized treatment limb of the herniorrhaphy protocol as follows:

i) If randomized to laparoscopic treatment limb- Bilateral repairs will be completed at same operation.

ii) If randomized to either tension free or open traditional repair treatment limb- Patient will have the more subjectively problematic hernia repaired, initially. At that time in post-operative course, the patient is able to return to his pre-morbid activity baseline as assessed by the performance exercising testing as defined above, patient will undergo repair of remaining inguinal hernia by the same treatment limb method.

Recurrent hernias. A recurrent hernia will be defined in the following fashion: presence of an inguinal hernia (as detected by physical exam by a staff General Surgeon), in a patient who was previously assessed as having an inguinal hernia on the ipsilateral side and who has undergone subsequent herniorrhaphy of same. Distinction will be made between *early* and *late recurrence* (15). Early recurrence will further be defined as a hernia that is present within 2 years of ipsilateral herniorrhaphy. Early recurrence will imply technical failure of repair. Late recurrence will further be defined as a hernia that is present 2 years or greater since ipsilateral herniorrhaphy. Late recurrence will not be attributed to technical failure, rather late recurrence will be attributed to an intrinsic disorder of the patient's own physiology (10).

i) Early recurrence of inguinal hernia as assessed by a staff General Surgeon will be re-entered into herniorrhaphy protocol in a blind randomized fashion as above.

ii) Late recurrence of an inguinal hernia as assessed by a staff General Surgeon will be re-entered into herniorrhaphy protocol in a blind randomized fashion as above.

Patients w/ recurrence of inguinal hernia as defined above, unwilling to re-enter herniorrhaphy protocol will be dropped from protocol at that point in time. Further surgical consultation will be offered to these patients, outside the parameters of the herniorrhaphy protocol.

Convalescence leave. All patients in protocol will receive a defined amount of convalescence leave for recovery from his herniorrhaphy procedure. Patients randomized to either the laparoscopic extra-abdominal pre-peritoneal procedure or the open tension free repair, will receive 7 days of convalescence leave from date of operation. The patients in these above treatment arms will have no restrictions of activity post-operatively. Patients undergoing traditional open repair, will receive 7 days of convalescence leave with restrictions of activity to include no lifting greater than 10 lbs., patient may walk at own pace and distance (no running or jogging), no other form of purposeful abdominal straining.

Progress: The principal investigator was deployed to Haiti and was not able to provide a progress to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/05 STATUS: Ongoing

TITLE: The Prevalence and Severity of Band-Keratopathy in Patients with Primary Hyperparathyroidism

PRINCIPAL INVESTIGATOR: CPT Luis M. Irizarry

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): KJ Simcic, DP Mong, WF Davitt

MONITOR: NA

START DATE: Nov 93 ESTIMATED COMPLETION DATE: Jun 94

KEY WORDS: Primary Hyperparathyroidism, Band-Keratopathy

Study Objective: To assess the frequency and severity of BK in patients with PHP. If the frequency of bk is significant in these patients, possible correlations with the duration and or severity of the php will be examined.

Technical Approach: Single center, prospective, single blind case control study.

Progress: There has been 30 subjects entered with no noted adverse reactions. We have now completed eye exams on 22 patients with primary hyperparathyroidism (with an average duration of 8-10 years) and on 8 control patients. We would like to recruit and test a few more control patients before ending the study. The estimated completion date has been changed from June 1994 to March 1995.

Although the study is negative thus far, we feel that our results are still significant. It appears that patients with primary hyperparathyroidism can be permitted to live with their disease untreated for at least 8 -10 years without significant risk of band-keratopathy.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/08 STATUS: Ongoing

TITLE: Comparison of Triamcinolone Acetonide with Indomethacin in Treatment of Pseudogout

PRINCIPAL INVESTIGATOR: CPT Mark Jarek

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): KJ Simcic, DP Mong, WF Davitt

MONITOR: COL Idelle M. Weisman

START DATE: Nov 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Primary Hyperparathyroidism, Band-Keratopathy

Study Objective: To assess the frequency and severity of BK in patients with PHP. If the frequency of bk is significant in these patients, possible correlations with the duration and or severity of the php will be examined.

Technical Approach: Single center, prospective, single blind case control study.

Progress: No progress was reported because Principal Investigator was deployed to Haiti.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/43 STATUS: Completed FY95

TITLE: Initial Clinical Management of Patients with Reversible Thallium Cardiac Perfusion Defects

PRINCIPAL INVESTIGATOR: CPT Carlos E. Jimenez

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): GM Glushko, EJ Pacheco, AJ Moreno

MONITOR: NA

START DATE: Sep 94 ESTIMATED COMPLETION DATE: Sep 95

KEY WORDS: Thallium, Perfusion Defects, Management

Study Objective: To determine how primary care physicians (internists and surgeons) and cardiologists initially utilize positive thallium stress tests revealing reversible defects in the clinical management of patients with angina, congestive heart failure, atypical chest pain syndrome or pre-operative patients. We will also determine if there is any significant correlation between the characteristic of the reversible defect/s (size, location, number of lesions, and the degree of reversibility), as well as other clinical and demographic data, and the initial physician selected cardiac management.

Some questions to be addressed include:

1). Do the majority of patients with reversible cardiac perfusion defects undergo cardiac catheterization?

2). Does the patient's symptomatology or lack of symptoms impact on clinical response?

3). What is the cardiac management of preoperative patients when their thallium stress test is suggestive of ischemia?

4). Does the size, degree of reversibility, location or amount of positive defect(s) impact on the initial clinical response?

5). Are cardiologists faster or more aggressive to pursue a more invasive approach than a general internist when their referred patients have a positive thallium perfusion study?

6). Are patients with a history of ASCAD and a positive thallium perfusion study treated more aggressively than patients with similar thallium results but without a history of coronary artery disease?

Technical Approach: All patients with reversible thallium perfusion defects of the left heart ventricle between September 1994 and April 1995 at William Beaumont Army Medical Center will be entered into the study.

Progress: This study has been completed. Dr. Jimenez submitted an abstract. 109 subjects were entered in this study.

ABSTRACT: One of the best noninvasive tests available for evaluation of myocardial perfusion is scintigraphic imaging with Thallium-201 chloride. This study was undertaken to determine how referring physicians utilize the information obtained from a positive thallium stress test in their initial management of a patient The population observed consisted of 109 referred patients. Four criteria observed were the size of the defect, the degree of reversibility, the location of the defects, and the presenting symptoms. These criteria were compared with three initial modes of management: observation, medication adjustment or cardiac catheterization. Although all four criteria affected the choice of initial management, the most compelling relationships were found when comparing the initial management to: presenting symptoms (p=0.03); the degree of reversibility (p=0.05), and to the specific location of perfusion defects (p=0.05). The size of the defect did not have as pronounced an affect on the choice of initial management (p--O.09). Patients presenting with classic symptoms of angina and positive thallium stress tests were most likely to undergo cardiac catheterization (56%) or medical management (27%) in contrast to asymptomatic patients with positive thallium stress tests who were more often observed (54%) than undergo cardiac catheterization (30%). Of those individuals demonstrating marked areas of reversibility, over twice as many underwent cardiac catheterization (49%) when compared with observation (23%). Finally patients demonstrating perfusion defects in the anterior and septal regions were most likely to undergo cardiac catheterization (69%) when compared to patients with defects in the posterior and inferoposterior regions (29%). This study demonstrates that there are certain criteria that, when elicited, influence a physician's decision regarding initial management of the patient.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/32 STATUS: Ongoing

TITLE: Talc Insufflation vs. Minocycline in a Randomized Double Blind Prospective Trial of Intrapleural Therapy for Recurrent Malignant Pleural Effusions Via Thoracoscopic Guidance

PRINCIPAL INVESTIGATOR: MAJ Lynn M. Keenan

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JL Cadiz, SP Hetz, B Hammacker, P Stanley, GR Ripple

MONITOR: LTC James Wallingford

START DATE: May 94 ESTIMATED COMPLETION DATE: Oct 96

KEY WORDS: Talc, Minocycline, Intrapleural Therapy, Malignant

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Study Objective: To determine the efficacy of minocycline vs. talc insufflation for sclerosis of malignant pleural effusions via thoracoscopic guidance.

Technical Approach: This study follows standard of care for patients with pleural effusion who are scheduled for thoracoscopic pleurodesis. The only deviation involves use of minocycline in the experimental group. We will follow patients from diagnosis through followup.

1) The patient with clinically suspected recurrent free flowing malignant pleural effusion by pleural fluid cytology or pleural biopsy will be identified.

2) The patient will undergo chest X-rays, which should show freely flowing pleural fluid or loculated fluid and confirming the lack of mediastinal shift.

3) If the patient meets eligibility criteria, informed consent will be obtained and the patient will be enrolled into the study.

4) A data sheet (see Appendix I) will be kept recording laboratory data, ECOG performance status, and chest radiograph results as well as demographic information: age, sex, institution, diagnosis, stage of disease, type of chemotherapy received, side effects to the sclerosant including: pain, fever, hypotension, allergic reaction, rash (maculopapular or erythematous), fatigue, anorexia, nausea, vomiting, diarrhea, elevated liver function tests, anemia, neutropenia, and elevated blood urea nitrogen or creatinine.

5) Sclerotherapy procedure:

(a) IV sedation with Versed and Morphine sulfate titrated to drowsiness and slurred speech.

(b) After the patient is placed in the lateral decubitus position and the chest is prepped and draped, a 10 mm thoracoport will be introduced into the pleural cavity under local anesthesia. Any loculated fluid will be aspirated and adhesions gently taken down. Then, the randomly selected sclerosant (talc<3 g vs. minocycline 300 mg) will be sprayed into the pleural cavity coating both the visceral and parietal pleura.

(c) After 20 minutes, a chest tube will be inserted and placed on suction, re-expanding the lung.

(d) Suction will be maintained for at least 24 hours and until pleural drainage is less than 150 ml/day. Then the chest tube will be removed.

(e) From the time the sclerosant is injected the patient will receive 650 mg of Tylenol PO every four hours for a total of 48 hours.

6) Chest radiographs will be obtained at 72 hours to assess for recurrence of the effusion after the sclerosis. If the fluid reaccumulates more than 50% of the original volume after sclerosis, the patient will be considered a treatment failure and considered for either no further treatment or surgery.

7) The following labs will be obtained at 24 and 48 hours for monitoring of side effects: complete blood count, liver function tests, blood urea nitrogen and creatinine.

8) The investigators will monitor for the side effects mentioned on the flow sheet during the first 48 hours after the sclerosis has been completed.

9) Assuming the sclerosis is initially successful, chest radiographs will be obtained at 7 days, 14 days, 30 days, 60 days and 90 days to assess for response. Response rates will be defined in the following manner:

(a) Complete response: No fluid present on chest radiograph.

(b) Partial response: asymptomatic pleural fluid equal to less than 50% of the original width at mid thorax measured on the lateral decubitus film.

(c) Treatment failure: recurrence of the pleural effusion greater than 50% of the original width at mid thorax measured on the lateral decubitus film, a loculated pleural effusion which is 50% of its original volume on PA and lateral roentgenograms or a recurrent symptomatic effusion of any size.

(d) All chest roentgenograms enrolled in the study at WBAMC will be read by the same observer, Dr. Ripple.

Progress: There have been 7 subjects entered with no noted adverse reactions. The estimated completion date has changed from Jun 97 to Oct 96. There has been a change in principal investigator from Dr. Keenan to Dr. Carlson, OB/GYN.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/33 STATUS: Completed FY95

TITLE: Comparison of a High Resolution Computed Tomography Technique and Fiberoptic Bronchoscopy in the Evaluation of Hemoptysis

PRINCIPAL INVESTIGATOR: MAJ Lynn M. Keenan

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JL Wallingford, R Gore, MC Hodges

MONITOR: LTC Gary Ripple

START DATE: May 94 ESTIMATED COMPLETION DATE: May 96

KEY WORDS: Tomography, Bronchoscopy, Hemoptysis, HRCT

Study Objective: We propose a collaborative study to examine the role of combining HRCT with fiberoptic bronchoscopy in the evaluation of hemoptysis. The standard of care presently for hemoptysis of unknown etiology involves a history, physical examination, screening labs, PA and lateral CXR, fiberoptic bronchoscopy if the diagnosis is not readily explainable, and CT of the chest if predicated by the chest roentgenogram.

Technical Approach: Study patients will receive a standardized initial work-up to include history and physical examination, screening labs, and PA and lateral chest roentgenograms. Demographic data to include age, sex, tobacco history, and frequency and amount of hemoptysis will be annotated onto the data sheet. Chest roentgenograms will be designated as normal, abnormal but not localizing, or abnormal and localizing by the criteria outlined on page 8 of the protocol. Fiberoptic bronchoscopy will be performed and a HRCT of the chest will be obtained in the order dictated by the severity of illness of the patient such that their best interests are maintained. The data will be analyzed looking at the clinical characteristics and roentgenographic features associated with certain diagnosis. HRCT-fiberoptic bronchoscopy correlations will focus on their individual and combined efficacy in predicting and/or diagnosing the etiology of hemoptysis. The hope is to identify a population of patients (i.e. nonsmokers) best suited for HRCT screening and therefore obviate the need for fiberoptic bronchoscopy.

Progress: There have been 15 subjects entered with no noted adverse reactions.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/04 STATUS: Ongoing

TITLE: Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhance Cranial MRI in Preoperative Staging

PRINCIPAL INVESTIGATOR: MAJ Lynn M. Keenan

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JL Wallingford, R Gore, JJ Leech, WM Boushka

MONITOR: COL Idelle M. Weisman

START DATE: Nov 94 ESTIMATED COMPLETION DATE: Dec 96

KEY WORDS: Bronchogenic cancer, MRI, brain metastases

Study Objective: We propose a collaborative study to examine the incidence of clinically occult brain metastasis in patients with resectable primary bronchogenic carcinoma.

Bronchogenic carcinoma remains the foremost cause of death from cancer in men in the United States and has risen dramatically for women. Since treatment and survival are greatly influenced by the presence of brain metastases, the detection of such lesions would greatly influence survival. The incidence of metastases from lung carcinoma ranges between 17-40% in autopsy series. The brain is frequently the only site of recurrence in patients who have already undergone thoracotomy for non-small cell carcinoma. Clinically silent lesions can occur and most frequently are seen in patients with adenocarcinoma and small cell carcinoma.

Several groups have documented the utility of cranial CT in the preoperative assessment of bronchogenic carcinoma. Between 5-10% of neurologically intact patients undergoing routine CT of the head were found to harbor intracranial metastatic lesions. Contrast enhance MRI is now the acknowledged gold standard for the evaluation of the CNS for metastasis. The superior contrast resolution, lack of ionizing radiation, and lack of potential complication from iodine contrast media used in CT make enhanced-cranial MRI an ideal screening modality for brain metastases.

Technical Approach: Details are lengthy. Copies of are available in the Department of Clinical Investigation.

Progress: There have been 5 subjects entered in this study, 1 patient withdrew because he refused surgery on a growing nodule. No adverse reactions have been noted to date. An associate investigator has been added to the study: CPT William M. Boushka, M.D., Chief, MR and CT, Dept. of Radiology. Estimated completion date has changed from Nov 96 to Dec 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/19 STATUS: Completed FY95

TITLE: National Survey of the Practice of Withholding and Withdrawal of Life Support

PRINCIPAL INVESTIGATOR: MAJ Lynn M. Keenan

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): SR Hamblin, CA Gerson

MONITOR: NA

START DATE: Jan 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: DNR, Life Support

Study Objective: To participate in learning whether the management of terminally ill patients at University of California at San Francisco is similar to management in other parts of the country and in other types of hospitals.

Technical Approach: This protocol describes a simple longitudinal observational study to document the incidence of withholding and withdrawal of life support in a broad sample of ICUs nationwide.

Progress: 388 subjects were entered in this study.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/18 STATUS: Ongoing

TITLE: A Randomized, Double-Blind, Placebo Controlled, Parallel Group Study to Examine Safety, Efficacy and Pharmacokinetics of a 3-Day Loading Plus Maintenance Infusion Regimen of 619C89 Mesylate Injection in the Treatment of Patients with Symptoms of Acute Stroke

PRINCIPAL INVESTIGATOR: MAJ Albert J. Martins

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Brainman, JM Herrold

MONITOR: MAJ Kevin Kumke

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Summer 96

KEY WORDS: Stroke

Study Objective: To study 619C89 Mesylate injection given as intravenous loading plus maintenance infusions with reference to safety, efficacy and pharmicokinetics in the treatment of patients with acute stroke. Drug treatment period is 3 days with follow-up to 12 weeks.

Technical Approach: This is a multicenter drug study being administered by Facilitators of Applied Clinical Trials.

(a) Medication Used. The proposed Phase II study is a randomized, double blind, multicenter three day maintenance and infusion study of the experimental drug Mesylate (Burroughs-Wellcome Drug 619C89, Research Drug Investigation and Development # 46-615) *only* in selected stroke patients presenting to the hospital within 12 hours of ictus. Mesylate in known to block the uncontrolled neurotoxic effects of the above mentioned excitatory neurotransmitters aspartate and glutamate.

(b) Type of Subjects Represented: Rigorous inclusion criteria will be employed to enter a stroke patient into this Protocol 137-103. [See the F.A.C.T. Trial Subject selection section in the Protocol Dated 19 September 94 (Pages 21-22)]. In short, no patient with significant alteration of consciousness or liver or heart disease will be considered a candidate for the study. N.B. No pre-menopausal or unsterilized women will be offered participation in this study.

(c) Number of Patients to be Involved in the Study: The WBAMC, Department of Medicine presently sees approximately four to five stroke patients per month. If one patient per month meets all the inclusion criteria and is entered into this Multi-Centered study, we can hopefully contribute to alleviating the suffering of an untold number of future stroke victims.

Progress: This study has not started it has been FDA postponed.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/54 STATUS: Ongoing

TITLE: Prospective Evaluation of Coccidioidomycosis in Human Immunodeficiency Virus-Infected Individuals Living in an Endemic Area

PRINCIPAL INVESTIGATOR: Lynn McNicol RN

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): N Aronson

MONITOR: NA

START DATE: Aug 1991 ESTIMATED COMPLETION DATE: Aug 2001

KEY WORDS: Coccidioidomycosis, Human Immunodeficiency Virus

Study Objective: To demonstrate whether coccidiomycosis seen in HIV patients is reactivation disease or represents acute infection in an immunocompromised host. To assess the early predictive value for active coccidioidomycosis of the spherulin skin test, coccidioides complement fixation and immunodiffusion antibody studies and coccidioides antigen ELISA in the HIV infected population.

Technical Approach: The is a prospective descriptive study. Subjects will be obtained from individuals participating in the HIV natural history study 86-49 (non-active duty) and HIV infected active duty soldiers who are followed in the WBAMC Infectious Disease Clinic per AR 600-110. Completion date is dependent on number of patients enrolled and severity of their immunologic compromise. Estimated study duration is 5 years.

On entry, a complete geographic history will be obtained to assess travel to Cocci endemic regions (West Texas, Arizona, San Joaquin Valley in California). On entry and every 6 months thereafter, delayed hypersensitivity skin testing will be performed IAW DOD HIV staging. In addition, spherulin 1:100 (Berkeley Biologics) will be included in the battery which is already usual practice in cocci endemic regions. Chest radiograph will be obtained on entry and every 12 months which is current clinical practice during HIV staging. On entry and every 6 months, the following blood tests will be ordered: T cell subset by flow cytometry, quantitative immunoglobulins and STEP, complement fixation Coccidioides antibodies (sent to Dr. Appagianis' laboratory at UC, Davis), Coccidioidal precipitins (sent to FSH, TX), serum for coccidioidal antigen (research test) - will be frozen at -70° F initially. On entry and every 6 months, weight will be recorded. On entry and at every subsequent staging, patient will be clinically evaluated by history and physical examination to assess for presence of active coccidioidomycosis.

Progress: Amended April 1994: Completion date has been extended to 2001. Modifications detailed above are included in the amendment.

70 patients have been enrolled and completed at least two evaluations. Eight additional patients have been enrolled and completed one evaluation. These patients will be counted toward the target enrollment of 100 after completing a second visit. 67 patients are male, 11 patients are female, 14 patients have died since enrollment. No active cocci cases have been diagnosed to date (one enrollee has an antecedent diagnosis) 12 had positive cocci skin tests at 48 hours. 3 had reactive cocci serologies at any time during the protocol (2CF, 1 IgMID).

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/16 STATUS: Terminated FY95

TITLE: Cardiopulmonary Response to Upright Exercise in Patients with Asymptomatic Valvular Aortic Stenosis and Patients with Aortic Valve Prostheses

PRINCIPAL INVESTIGATOR: MAJ Timothy W. Martin

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): R Belbel

MONITOR: COL Idelle Weisman

START DATE: Feb 93 ESTIMATED COMPLETION DATE: Jan 94

KEY WORDS: Upright Exercise, Valvular Aortic Stenosis, Aortic Valve Prostheses

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Study Objective: To determine the effect of valvular aortic stenosis and aortic valve replacement on cardiopulmonary exercise performance and the relationship between ECHO\Doppler measurements and cardiopulmonary performance in patients with valvular aortic stenosis and aortic valve prostheses.

Technical Approach: A total of 75 patients (ages 18-75) will be included in the study (25 with aortic stenosis, 25 with aortic valve prostheses, and 25 controls). Patients will undergo upright cycle exercise, 20 W/min increments, symptom-limited, followed by cool-down exercise with continuous monitoring of O_2 consumption, CO_2 production, tidal volume, anaerobic threshold, respiratory rate, heart rate, power, and blood pressure. Patients will be monitored for 10 minutes following the exercise test.

Progress: No response received from investigator for FY95 annual report. DCI has administratively terminated protocol due to unsuccessful attempts to locate principal investigator who has PCS'd from WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/36 STATUS: Terminated

TITLE: Effect of Heart Disease on the Hemodynamic Response to Supine Upper Extremity Exercise

PRINCIPAL INVESTIGATOR: CPT Timothy W. Martin

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): R Belbel, L Brenner

MONITOR: COL Harry Davis

START DATE: Apr 92 ESTIMATED COMPLETION DATE: Mar 93

KEY WORDS: Exercise, Hemodynamics, Cardiac Catheterization

Study Objective: Characterize and compare the hemodynamic response to supine upper exercise in patients with and without heart disease.

Technical Approach: Patients who require heart catheterization and do not have exclusion criteria will be identified and counseled by cardiology staff. Consenting patients will be brought to the catheterization laboratory in a fasting, mildly sedated state. From the femoral approach, a Swan Ganz catheter will be advanced to the right heart and a pigtail catheter will be advanced to the left heart. Resting pressure and flow measurements and blood samples will be obtained. The patient will then perform five to eight minutes of supine arm cycle exercise, during which rest measurements will be repeated. Based on the results of rest measurements, angiography, and other clinical information, patients will be categorized as normal or as having coronary artery disease, cardiomyopathy, or valvular heart disease. The response to supine upper extremity exercise will be compared among the groups.

Progress: DCI administratively terminated protocol due to unsuccessful attempts at trying to locate principal investigator who PCS'd from WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/33 STATUS: Ongoing

TITLE: The Role of Three Phase Bone Scintigraphy in Women with Pelvic Masses

PRINCIPAL INVESTIGATOR: COL Albert J. Moreno

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Carlson, N Hoshaw, G Maxwell, CE Jimenez, EJ Pacheco

MONITOR: NA

START DATE: May 95 ESTIMATED COMPLETION DATE: May 96

KEY WORDS: Bone Scan, Pelvic Mass

Study Objective: The objective of this study is to perform one bone scan with the anterior pelvis flow and blood pool views in women who are being evaluated in the gynecology clinic for pelvic masses. The bone scan images will be evaluated for the occurrence, size, location, and uptake characteristics of the pelvic mass. The scan would be performed prior to surgical removal of the mass. Other imaging methods, such as ultrasonography, computer tomography, or magnetic resonance imaging will be done to further characterize the pelvic mass if they are needed by the gynecologists.

Technical Approach: The subjects selected for this study will be from patients being evaluated for pelvic masses in the gynecology clinic. A bone scan will be performed on the patients selected for participation in this study. The bone scan will include a flow and immediate blood pool images of the anterior pelvis. The findings on the scan will then be correlated with the gynecologic workup which will include pelvic examination, possible ultrasonographic or computer tomography evaluation, and possible laparotomy/laparoscopy. The bone scan findings will be correlated to the pelvic mass in terms of size of the mass, the type of mass, and the location of the mass. The sensitivity of detection of pelvic masses by the three phase bone scan will be determined.

Progress: To date 15 patients with pelvic masses have been identified and have had bone scans. All appear to have abnormal flow and blood pool images corresponding to the pelvic mass. No comparison of the pelvic pathology and flow/blood pool patterns have been made at this time. No adverse reactions were reported.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 76/33 STATUS: Ongoing

TITLE: Diagnostic Adrenal Scanning with 131I (NP59)

PRINCIPAL INVESTIGATOR: COL Albert J. Moreno

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: NA

START DATE: Mar 76 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Adrenal Scanning, 1-131 NP 59

Study Objective: To determine the usefulness of ^{131}I-NP59 in scanning of the adrenal glands. This agent will be used (1) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma; (2) to image adrenals in patients who require adrenal venography and are allergic to contrast media; (3) to detect unilateral adrenocortical hypofunction - calcification, metastatic carcinoma, post-venography infarction, etc.; (4) to detect functioning adrenal remnant after adrenalectomy for Cushing's syndrome; (5) to aid in assessment of adrenocortical function in patients who have been on adrenocortical steroid therapy.

Technical Approach: Patients with clinical evidence of adrenal disease will be thoroughly evaluated by an endocrinologist. Following intravenous administration of ^{131}I-NP59, adrenal scanning will be performed after 7-10 days. The material will be obtained from the Nuclear Pharmacy, University of Michigan. The WBAMC radiopharmacist will perform sterility and pyrogenicity tests on the radiochemical to ensure that radiopharmaceutical standards are met prior to injection

NOTE: Project was erroneously terminated in Oct 84. Project reactivated in Sep 92 and folder was reconstituted to include required documentation.

Progress: Twelve patients have been studied since this protocol was approved. No adverse effects noted. I-131-NP59 s an adrenal cortical imaging agent produced by the University of Michigan for use as an IND drug. Adrenal cortical imaging is not performed often but when it is, it may reveal hyperplastic adrenal glands or adenomas. Due to the infrequent use of this agent, I-131 NP 59 will probably never come off of investigation status.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/05 STATUS: Terminated FY95

TITLE: Dual Isotope Scintigraphy with ^{201}Thallium/^{99m}TC-Sestamibi in Patients with Palpable and Non-palpable Breast Masses

PRINCIPAL INVESTIGATOR: LTC Elmer J. Pacheco

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): H Feuerberg, S Hetz, W Sippo, R Gomez, C Jimenez, AJ Moreno, MBrodbeck, G Morgan, S Werth

MONITOR: MAJ Alan Carpenter

START DATE: Nov 94 ESTIMATED COMPLETION DATE: Oct 96

KEY WORDS: Tl, MIBI Breast Scintigrams, Non-palpable Breast Masses, Carcinoma

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Study Objective: To determine the sensitivity and specificity of both Tl and MIBI breast scintigrams in patients with palpable and non-palpable breast masses. A cost-analysis ratio will be made between the breast scintigram and mammography for the studied population.

Technical Approach: One hundred and fifty (150) patients with high risk for breast carcinoma (woman with a first degree relative with breast cancer, early menarche, nulliparous women, first pregnancy after the age of 35, moderate alcohol intake) will be entered into the study. Fifty of these (Group 1) will have breast masses palpable by physical examination. Another fifty will have non-palpable breast masses on clinical examination but with a positive mammogram (Group 2). A third group of 50 patients will have no evidence of a palpable breast mass as well as a suspicious mammogram (Group 3). Another 50 patients will be accrued into the study as a control group (Group 4). This last group will consist of women who will undergo routine mammograms and who will not be at high risk for breast carcinoma.
The patients enrolled in the protocol meeting above criteria will then be evaluated as follows:

SUBJECT RANDOMIZATION FLOW CHART

GROUP 1	GROUP 2	GROUP 3	GROUP 4
50 Pts with palpable breast mass	50 Pts of high risk with no breast mass on P.E.	50 Pts of high risk with no breast mass on P.E.	50 Pts with no particular risk for routine Mamm
Mammogram	Positive Mamm	Suspicious Mamm	Mamm
Scintigram	Scintigram	Scintigram	Scintigram
Breast Bx	Breast Bx	Breast Bx	Breast Bx

Mammography: Each patient will have a bilateral mammography in the craniocaudal and mediolateral oblique projections, between 50 and 60 . Low dose film/screen technique using a dedicated mammography unit(GE Senographe 600T, General Electric, Milwaukee, WI). Additional views of any abnormal areas using magnification and cone compression will be

done at the discretion of the radiologist (HF). All mammograms will be read by an experienced radiologist (HF) with complete knowledge of the patient's history and clinical presentation, as well as the results of any available previous mammograms.
Scintigraphic Imaging: Patients will be injected intravenously with 3 mCi of Thallium-201 (Tl) and 25 mCi 0f Tc-99m-sestamibi (same doses used by Waxman et al[3]). A butterfly needle connected to a three-way stopcock with a 10cc saline flush will be used. The MIBI will be injected first, and the IV line will be flushed with 5cc of saline. Five (5) minutes p.i., scout imaging using both, Tc-99m and Tl-201 windows, will be performed. A low-pass filter will be applied to the scout images to reduce noise. Each breast will be imaged in the lateral and 30 posterior oblique image for 2min/image. The Tl-201 will then be injected and the IV line will be flushed with 5cc of saline and removed. Ten minutes post-injection of the Tl-201, lateral and 30 posterior images of each breast, will be taken for 10 minutes, using the same dual radionuclide technique as in scout imaging. The patient will always be imaged in the prone position as described by Diggles et al.[14]

The filtered scout image will be count-normalized for the dual-radionuclide acquisition time and subtracted, pixel by pixel, from the dual radionuclide Tl-201 image to produce the corrected Tl-201 image. The latter will then be multiplied by 0.1 and subtracted from the MIBI images to compensate for Tl-210 crossover, as suggested by Weinstein et al.[15]

The scintimammogram will be performed using a dual-headed Genesys camera from ADAC Laboratories (Milpitas, CA), interfaced with a Pegasys computer system (ADAC). The camera will be equipped with a high-resolution collimator. Images will be acquired in a 128 x 128 matrix (with variation in the matrix allowed for poor count statistics) using a 2x zoom. The Thallium-201 window will be set at 68.9 keV ±10%, while the Technetium-99m window will be set at 140 keV ±7.5%. Scintigrams will be interpreted by the involved Nuclear Medicine Staff (EP, AM).

Breast biopsy: This will be performed in any identifiable abnormality and as deemed necessary by the involved surgical staff (SH, WS). The surgeon involved will ensure that breast parenchyma is obtained during the biopsy. The obtained tissue will be processed accordingly and the pathological interpretation will be performed by the pathologist in the protocol (RG). Tissue will not be stored after the use in this study. The fluids will be disposed of in accordance with WBAMC Infection Control guidelines.

Progress: Protocol depended on funding from a Radio-Pharmaceutical Co. which was not granted since there were other similar funded projects.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/36 STATUS: Terminated FY95

TITLE: Retrospective Review of Occult Anemia on Orthopedic Patients Undergoing Elective Joint Replacement on Chronic Non-Steroidal Anti-Inflammatory Agents and Evaluations of Perioperative Complications

PRINCIPAL INVESTIGATOR: CPT Ines J. Sanchez

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Brazier

MONITOR: NA

START DATE: May 95 ESTIMATED COMPLETION DATE: Jul 95

KEY WORDS: Chronic NSAIDS, Orthopedic Patients, Anemia

Study Objective: Review of the charts of orthopedic patients and recollect laboratory data to support increased prevalence of anemias and complications secondary to chronic NSAIDS therapy. With this information develop a prospective study to see if the early diagnosis of iron deficiency anemia and proper interventions, will result in decreased perioperative blood loss and transfusions.

Technical Approach: Single center, retrospective.

Progress: This study was started by principal investigator but patient records did not contain the necessary information needed to complete the study, therefore study was terminated. Also, associate investigator left WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/49 STATUS: Terminated FY95

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

MONITOR:

START DATE: May 1986 ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

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. Counseling, 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.

Addendum: 12 Feb 90 - This protocol was amended to exclude active duty servicemembers. At the directive of the Secretary of the Army, all active duty HIV+ servicemembers are to be clinically staged periodically.

Progress: This protocol has been terminated by principal investigator due to lack of funding. Collection of data and forwarding to USAHIV data systems is covered under AR 600-100. Funding ended approximately 30 Sep 94.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/05 STATUS: Completed FY95

TITLE: Active Immunization of Early HIV Infected Patients with Recombinant gp 160 HIV protein Phase II Study of Toxicity Immunotherapy, in vivo Immunoregulation and Clinical Efficacy

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): CE Davis (WRAIR), G Martin

MONITOR: COL Preston Cannady

START DATE: Nov 90 ESTIMATED COMPLETION DATE: Nov 95

KEY WORDS: Recombinant gp 160 HIV Protein, Immunotherapy

Study Objective: To conduct a Phase II trial of the recombinant HIV envelope glycoprotein gp160 candidate vaccine, in patients with early HIV infection (Walter Reed Stage I-II). Specific objectives include:

1) To continue to evaluate the immunogenicity and toxicity of this product;
2) To determine the parameters predictive of immunoresponsiveness; and
3) To determine the clinical efficacy of immunization with pg160 in the treatment of early HIV 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.

Addendum: Modifies eligibility criteria. Approved by Tri-Service HUC (26 Feb 91), WBAMC HUC/IRB (23 Apr 91) and WRAMC HUC.

Amendments: (1) Deleted recipe skin testing on Day 180 (typographical error); WBAMC IRB notified 16 Jul 91. (2) Day 210 tetanus immunization shifted to Day 240 and Day 210 visit deleted; WBAMC IRB notified 17 Aug 91. (3) Initiated Phase IIB; presented to IRB 21 Apr 92. (4) Booster vaccinations to be given at 2 month intervals; presented to IRB 21 Jul 92. (5) CHECK PROTOCOL.

Amendments FY95: 20 Apr 94 Updated version of the Invetigator's Brochure submitted. Amendment (#9) to RV21b which allows the use of FDA approved antiretrovirals following Day 210 (changes were made on consent document) and also includes administrative procedures changes relating to the reporting of study events and the shipment samples.

Progress: There were 17 individuals enrolled; plus, there was a transfer from the Walter Reed site as a result of a PCS move, bring the total to 18.

Seven of these individuals are still being followed at WBAMC. Five are still enrolled in the study, but followed elsewhere, as a result of PCS moves, retirements/ETS and one individual died of an AIDS-related complication. Four individuals dropped out secondary to job constraints. One individual disenrolled as a result of prison incarceration. Study was completed in Sep 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/65 STATUS: Ongoing

TITLE: Early Diagnosis of Tuberculosis Using Gene Amplification Techniques (GAT)

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): HM Gelston, TJ Casey

MONITOR: NA

START DATE: Sep 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Polymerase Chain Reaction, Tuberculosis, Gene Amplification

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Study Objective: To compare gene amplification techniques with current culture methods in the diagnosis of tuberculosis.

Technical Approach: This protocol will consist of two phases. Phase I will be the validation phase and Phase II will be the prospective evaluation of clinical respiratory specimens. Sources will be consecutive specimens submitted to the WBAMC Mycobacteriology Lab as well as specimens from TB cases submitted to El Paso County Health Laboratory.

Progress: To date 50 subjects have been entered in study. Protocol has involved collection specimen from TB patients from the El Paso County Health. However, due to lack of technician time PCR reactions have yet to be completed. MAJ Nauschuetz has been deleted from the study due to his PCS in July 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/40A STATUS: Ongoing

TITLE: Comparison of Subcutaneous and Nebulized Trimethoprim-sulfamethoxazole in the Prophylaxis of *Pneumocystis carinii* Pneumonia (PCP) in Rats

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RA Harris, TP Baker

MONITOR: NA

START DATE: Aug 93 ESTIMATED COMPLETION DATE: Nov 97

KEY WORDS: Pneumocystis, Pneumonia, Trimethoprim, Sulfamethoxazole

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Study Objective: To determine if *Pneumocystis* pneumonia can be prophylaxed in rats using nebulized trimethoprim-sulfamethoxazole.

Technical Approach: This will be an animal experiment. Sixty Sprague Dawley rats will be divided into 3 groups of 20 rats. Group I will serve as control and receive nebulized D5W with 1% benzyl alcohol, the vehicle of trimethoporim-sulfamethoxazole. Group 2 will receive nebulized trimethoprim-sulfamethoxazole prophylaxis. Group 3 will receive twice weekly subcutaneous trimethoprim-sulfamethoxazole which has been shown to be 100% effective in preventing PCP in the rat.(25) Each rat will receive the same regimen of oral dexamethasone and tetracycline in the feed on Day 0 as per Hughes.(26) On Day 4 nebulization will be delivered in the same manner to all rats in Groups 1 and 2 using a micronebulizer(Bird Corporation, Palm Springs, Calif). During administration of nebulization the rats will be attached to a plethysmograph to monitor ventilation. Dose administered will be estimated by method as outlined by Girard.(9) Group 3 rats will also receive subcutaneous trimethoprim-sulfamethoxazole on Day 4. Prophylactic drugs will be administered subsequently weekly from Day 4. All rats will be inoculated intra-tracheally with 0.2 ml of a 2×10^6 trophozoite/ml solution on Day 6. Two sentinel rats from each group will be euthanized at weeks 2, 4, 5, 6 and 7 to monitor progress of infection. Plasma, lung and liver will be harvested from the sentinels and stored at -70°C to assay for drug levels. All euthanized sentinel rats and any rats dying during the experiment will be examined for evidence of PCP. PCP infection will be determined by special stains of lung tissue and described as either infected or not infected. Severity of infection will be graded according to the number of *Pneumocystis* cysts as per Girard et al.(25) The experiment will last 8 weeks. All rats will be euthanized at that time and assayed for evidence of *Pneumocystis carinii* infection. Serum liver function tests, BUN, creatinine and complete blood count will be done. Liver and lungs will be examined histologically for any evidence of toxicity. Survival will be expressed by Kaplan-Meier plot.

Progress: This is an animal study. Rat respirators were obtained in Spring 95 - 1 year late due to lack of CEEP money. Anticipate completion of protocol after principal investigator returns from Haiti deployment.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/04 STATUS: Terminated FY95

TITLE: Molecular Epidemiologic Study of Methicillin Resistant *Staphylococcus Aureus* (MRSA) at William Beaumont Army Medical Center (WBAMC) in El Paso, TX

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: NA

START DATE: Dec 93 ESTIMATED COMPLETION DATE: Aug 94

KEY WORDS: MRSA, MECA

Study Objective: (1) To determine and compare MW's of RFLP's (Mec A & Tn 554) in MRSA isolates from different patients throughout WBAMC. Analysis will be used to try to determine if the MRSA arises from a common source or multiple sources.

(2) Epidemiologic chart review from these MRSA positive patients to help determine a common vs. multiple source. Also, we will try and identify a common vector in multiple point sources.

(3) Compare PCR data to antibiograms obtained in the microbiology laboratory.

(4) Compare and contrast data in number two and three.

(5) Hopefully the epidemiologic data derived from this study will improve methods of prevention in order to decrease the spread of MRSA at WBAMC.

Technical Approach: This project will be a single center (at WBAMC) retrospective study analyzing MRSA positive cultures obtained from routine microbiology specimens submitted. *Staphylococcus aureus* chromosomal DNA will be isolated, prepared and digested according to methods outlined by SaFigueiredo and Tomasz (8, 11). PCR probes for Mec A and Tn 554 will be used to identify these RFLP's on an electrophoretic gel to determine their respective MW's in comparison with a standard. Objectives are stated above.

Progress: 27 subjects have been entered in study with no adverse reactions reported to date. Due to the departure of Dr. Steve Miller, the original Principal Investigator, Dr. Sun, the current principal investigator who replaced Dr. Miller has terminated protocol in FY95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/01 STATUS: Completed FY95

TITLE: A Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Investigate the Efficacy and Safety of GG167 Therapy in the Prevention of Progression of Influenza A and B Viral Infections

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): LV Hobratsch, JW Martin, A Larson, ME Duban, C Neil, LB McNicol

MONITOR: MAJ Jay W. Carlson

START DATE: Oct 94 ESTIMATED COMPLETION DATE: May 95

KEY WORDS: Influenza, GG167

Study Objective: The object of this study is to evaluate the safety and efficacy of a GG167, a newly developed compound that inhibits the influenza viral enzyme neuraminidase. Neuraminidase facilitates the release and spread of new virus during influenza infection. GG167 does not inhibit mammalian neuraminidases. Because viral replication takes place in the upper and lower respiratory tract, this drug is being evaluated both intranasally and by the inhaled route. Safety will be evaluated during the study by clinical history, examination and specified laboratory tests. Clinical safety will be assessed by routine laboratories, adverse event monitoring, physical examination and use of concurrent medications. The primary efficacy endpoint will be clinical infection manifested by symptoms of influenza. Influenza will be confirmed by viral cultures or seroconversion. Blood levels of GG167 will also be measured in a subset of patients.

Technical Approach: Double-blind, randomized, placebo-controlled multicenter study.

Progress: Study enrolled one patient fulfilling inclusion criteria. She completed protocol without any adverse events.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/02 STATUS: Completed FY95

TITLE: A Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Investigate the Efficacy and Safety of Inhaled and Intranasal GG167 in the Treatment of Influenza A and B Viral Infections

PRINCIPAL INVESTIGATOR: LTC Wellington Sun

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): LV Hobratsch, JW Martin, A Larson, ME Duban, C Neil, LB McNicol

MONITOR: MAJ Jay W. Carlson

START DATE: Oct 94 ESTIMATED COMPLETION DATE: May 95

KEY WORDS: Influenza, GG167

Study Objective: The object of this study is to evaluate the safety and efficacy of a GG167, a newly developed compound that inhibits the influenza viral enzyme neuraminidase. Neuraminidase facilitates the release and spread of new virus during influenza infection. GG167 does not inhibit mammalian neuraminidases. Because viral replication takes place in the upper and lower respiratory tract, this drug is being evaluated both intranasally and by the inhaled route. Safety will be evaluated during the study by clinical history, examination and specified laboratory tests. Primary endpoint for evaluation of efficacy will be time to alleviation of major influenza symptoms.

Technical Approach: Double-blind, randomized, placebo-controlled multicenter study.

Progress: Study is complete. Two patients with influenza-like illness were enrolled and completed treatment protocol without significant adverse events.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/38 STATUS: Ongoing

TITLE: A Five-Year Observational Study to Evaluate Clinical Response and Recurrence Rate in the Treatment of Basal Cell Carcinoma with Fluorouracil/Epinephrine Injectable Gel

PRINCIPAL INVESTIGATOR: LTC Jeffrey Stiles

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MB Giandoni, MS Lee

MONITOR: MAJ Jennifer Cadiz

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Jun 2000

KEY WORDS: Basal Cell Carcinoma, 5 Flourouracil, Therapeutic Implant

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Study Objective: This is a phase 3 multicenter clinical trial assessing the efficacy of a Fluorouracil/Epinephrine injectable gel for the treatment of uncomplicated basal cell carcinomas. There are three primary objectives with this protocol

OBJECTIVE 1 - To describe the rate of recurrence of basal cell carcinoma 12 months after treatment in those individuals who demonstrated complete response at Month 3 follow up.

OBJECTIVE 2 - To describe the clinical response rate of treatment with 0.5 ml 5-FU/epi injectable gel when administered 3 times weekly for 2 weeks in patients with uncomplicated basal cell carcinoma.

OBJECTIVE 3 - To evaluate the safety of the fluorouracil/epinephrine injectable gel when administered as directed above.

Technical Approach: Open label study. Approximately 400 patients will have one lesion selected for study. Investigators will use a predetermined randomized schedule to select a target lesion in patients with more than one clinically diagnosed and /or biopsy proven eligible lesion. An analysis of the data will be done when the last patient has completed Follow-up Month 12. Subsequent analysis of annual recurrence rates will be performed.

Progress: Seven patients have been entered in this study with no adverse reactions reported to date. Dr. Vogel, principal investigator deployed to Haiti. Dr. Stiles assumed the role of principal investigator. Original principal investigator, Dr. Giandoni left WBAMC due to PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/40 STATUS: Ongoing

TITLE: RV84: Assessment of Risk Factors for HIV-1 Infection Among Active-Duty U.S. Military Personnel with Documented Recent HIV-Antibody Seroconversion - Phase II

PRINCIPAL INVESTIGATOR: Patricia A. Frank, RN

DEPARTMENT: Med/Peds FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Sep 94 ESTIMATED COMPLETION DATE: Jul 97

KEY WORDS: HIV-POC, Army, Navy, Airforce, Seroconverter,

Study Objective: To evaluate biological and behavioral determinants of HIV-1 Seroconversion by comparing medical, demographics, and behavioral histories of active duty personnel recently infected and/or diagnosed, with HIV-1 histories of individuals who have not seroconverted over a similar period of time.

Technical Approach: The study will be conducted by military and civilian personnel (principal investigator, associate investigators and HIV-POC's) in the Army, Navy and Air Force. The sites where we plan to conduct the study have already agreed to participate in Phase II.

Enrolling subjects: A roster of seroconverter cases and matched controls will be provided to each HIV-POC. The roster will contain the name, rank, and unit assignment. Two male controls for each male case and three female controls for each female case should be recruited form the list of eligibles provided. It is the HIV-POC's responsibility to contact potential respondents and to invite these individuals to participate in the study. Recruitment will be conducted in accordance with the information provided on the consent agreement affidavit (enclosure #2). The importance of this study, along with the absolute safeguards to anonymity and confidentiality, should be stressed.

Upon enrollment, a study ID number will be assigned to each participant. This number will be entered into the computerized questionnaire and on the log of study participants (enclosure #5) with the corresponding case/control status of all participating individuals. HIV-POC will also be provided with the interval dates (i.e., last negative - first positive) for each seroconverter case. Interval dates for controls will be the same as their matched case. These dates should be entered into the computerized questionnaire of each participant. Subjects' names or other identifiers must not appear on the log or the questionnaire. The log will be kept by the HIV-POC and will be mailed to WRAIR after interviews at the facility have been completed, so that case or control status can be determined for each completed questionnaire.

In addition to the log of study participants, another log (enclosure #6) of eligible cases and controls who decline to participate will be maintained by the HIV-POC. This log will allow for comparison of demographic information between case/control participants and nonparticipants to determine if those who volunteer for the study are different from those who do not, thus indicating the existence of potential study bias.

The HIV-POC must obtain signed consent before cases or controls are interviewed. Consent forms are to kept locally until the end of the study in 1997 and then will be turned over to the principal investigator.

The location and time schedule for interviewing must be flexible and designed for the ease and convenience of study participants. Individuals may wish to complete the computerized interview during duty hours (~0730-1630) or before/after duty hours.

Interviews: In order to minimize response bias, maximize confidentially, and standardize
interview procedures, interviews will be conducted using a computer program modeled after the audio computer assisted self-interview system (ACASI) developed by Research Triangle Institute (RTI).(8) With this technology, the computer plays a recorded version of question and answer choices to the respondent over headphones. The participants responds through the keyboard. The computer records the response and, based upon the answer, plays the next appropriate question. A laptop PC, programmed with the questionnaire in ACASI-type format, will be provided to each participating post. (A hard copy of the questionnaire for men and for women is presented at enclosure #7). Prior to beginning each interview, the HIV-POC will explain to the participant the nature of the study and the reason for the interview. Although the participant will have received this information previously from the HIV-POC and will have signed a consent form, the HIV-POC will again describe the study and stress that anonymity will be maintained at all times. The computerized interview will commence only after the HIV-POC is satisfied that the participant understands the procedures and has no questions.

The laptop computers will be stationed in a quiet and private room. Individuals directly associated with recruiting and assigning code numbers to study subjects will never have access to information obtained during the interviews of cases or controls. To ensure total confidentiality of the interview, the responses entered into the computer will be encrypted. This process will make it impossible for anyone to examine the contents of the interview. The decryption key needed to translate the interview record into a usable format will be kept by the investigators at WRAIR.

Progress: Study has just started, therefore, no progress has been reported.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/36 STATUS: Ongoing

TITLE: Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT)

PRINCIPAL INVESTIGATOR: CPT Andrew Quint

DEPARTMENT: Med/Peds FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): L Marcus

MONITOR: COL Albert Moreno

START DATE: Aug 1994 ESTIMATED COMPLETION DATE: Aug 2001

KEY WORDS: Hypertensive, Lipid Lowering

Study Objective: This study is a practice-based randomized, clinical trial of antihypertensive pharmacological treatment and, in a specific subset, cholesterol-lowering, in 40,000 high-risk hypertensive trial, including at least 55% African-Americans. The purpose of the antihypertensive trial component is to determine whether the combined incidence of fatal coronary heart disease (CHD) and non-fatal myocardial infarction differs between diuretologic treatments -- a calcium antagonist (amlodipine), an ACE inhibitor (lisinopril), and an alpha adrenergic blocker (dixazosin). Because of the morbidity and mortality from cardiovascular diseases, and all-causes mortality, the antihypertensive trial component will not include a placebo or no-treatment control group. The purpose of the cholesterol-lowering trial is to determine whether treatment of hypercholesterolemic men and women aged 60 years and older with the 3-hydroxymethlglutaryl coenzyme A (HMG CoA) reductase inhibitor pravastatin will reduce all-cause mortality as compared to control group receiving "usual care".

Secondary objectives of both trial components are to compare the effects of their respective treatment regimens on cardiovascular mortality, major morbidity, health costs, and health-related quality of life. Additional secondary objectives of the antihypertensive trial are to compare the effects of alternative treatments on all-cause mortality and on major hypertension-related morbidity such as incidence and regression of left ventricular hypertrophy and progressive renal dysfunction. Additional secondary objectives of the lipid-lowering trial are to assess the long-term safety of HMG CoA reductase inhibitors in men and women aged 60 years and above (particularly with regard to mortality from non-cardiovascular causes), the effect of lipid-lowering on cancer incidence and mortality, and the effect of lipid-lowering on the combined incidence of fatal CHD and non-fatal myocardial infarction, especially in key subgroups (over age 65, women, African Americans, type II diabetics). Also, because this component of the trial will not be blinded, the incidence of myocardial infarction based on centrally coded changes in biennial study ECG will be looked at as an end point. The mean duration of the trial is expected to be 6.0 years, ranging from 5.0 years (for the last patient entered) to 7.5 years (for the first patient entered)

To maximize statistical power for the primary hypothesis of the antihypertensive trial, i.e., the comparison of each alternative drug regimen to diuretic, 1.7 times as many patients will be assigned to its diuretic arm as to each of its other three arms (Table 1). It is anticipated that half of ALLHAT participants will be randomized to both trial components and that half will be randomized only to the antihypertensive trial component.

Technical Approach: ALLHAT will employ an organizational structure that differs markedly from the usual NHLBI-supported clinical trial. The trial will be performed by a large number (250-300) of practicing physician-investigators who will be compensated on a per capita basis for each patient seen according to a fixed payment schedule. Approximately 20% of study patients are expected to be recruited by the Department of Veterans Affairs (VA) hypertensive clinics.

Progress: Due to administrative delay, no patients have yet been entered into study. We are awaiting final approval from ALLHAT, to be followed by arrival of study medications/supplies.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/39 STATUS: Terminated FY95

TITLE: Identifying Process Variations Via Risk-Adjusted Outcome

PRINCIPAL INVESTIGATOR: MAJ Kathryn J. Dolter

DEPARTMENT: Medical Surgical CNS FACILITY: William Beaumont AMC

ASSOCIATE INVESTIGATOR(S): S Pardi

MONITOR: NA

START DATE: June 95 ESTIMATED COMPLETION DATE: Oct 94

KEY WORDS: Risk-Adjusted

Study Objective: A descriptive study designed to answer the following questions:

1) What are the differences between DOD medical center actual and predicted CABG mortality rates?
2) What is the hemodynamic knowledge and hemodynamic measurement and treatment practice of nurses and physicians caring for patients in DOD medical centers?
3) What is the relationship between hemodynamic knowledge and hemodynamic measurement and treatment practice of nurses and physicians caring for CABG patients in DOD medical centers?
4) Are there differences between nurse hemodynamic knowledge and hemodynamic measurement and treatment processes at DOD medical center with higher than expected mortality rates and DOD medical centers with lower than expected mortality rates?
5) What are the other unit and provider characteristics and processes of DOD medical centers with higher than expected CABG mortality rates and DOD medical centers with lower than expected CABG mortality rates?

Technical Approach: The purpose of this study is to assess the validity of using risk-adjusted mortality as a screening mechanism to identify variations in practice impacting on quality of care. It will utilize Department of Defense (DOD) risk-adjusted mortality to identify medical centers having the potential for post-operative CABG patient care process variations, and then assess these medical centers' processes, specifically focusing on post-operative hemodynamic practices of nurses and physicians caring for these patients.

The study will utilize a combination case control and exploratory descriptive design to assess input, process and outcome variables of the coronary artery bypass graft surgery (CABGS) patient care process. It will consist of two phases. Phase I will utilize a DOD database to risk-adjust DOD medical center CABGS mortality to identify medical centers having potential positive and negative CABGS patient care process variations. Twelve DOD medical centers perform this procedure. Phase II-A will involve in-depth review of patient care processes, specifically focusing on nurse and physician hemodynamic and organizational practices at 6 DOD medical centers: 2 with higher-than -expected CABGS mortality (the cases) and 2 with lower-than-expected and 2 with "median" CABGS mortality (the controls). A combination of observation of provider hemodynamic assessment and intervention practices and assessment of provider hemodynamic knowledge and organizational process via

questionnaires will be utilized for the in-depth process reviews. Phase II-B will involve hemodynamic and organizational practice questionnaire administration to CABGS patient care personnel at the remaining 6 DOD medical centers which perform CABGS. Phase II-C will involve description of the CABGS care processes of DOD CABGS intensive care units through chart audit of all CABGS patients from the first 6 months of 1994 at the 6 DOD medical centers undergoing site visits. There are no safety concerns related to use of these methods. Descriptive statistics, logistic regression and correlation will be utilized to analyze the data.

Progress: DCI has administratively terminated this protocol because the principal investigator has PCS'd from WBAMC and could not be contacted.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/45 STATUS: Ongoing

TITLE: Decay and Reacquisition of Field Medic Knowledge and Skills

PRINCIPAL INVESTIGATOR: Co-Investigators MAJ (P) Voepel, Leo F. COL (Ret) Beeman, Thomas A.

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RA Wisher

MONITOR: N/A

START DATE: Jul 95 ESTIMATED COMPLETION DATE: Apr 96

KEY WORDS: Field Medic Knowledge

Study Objective: To gauge the proficiency of IRR soldiers completing a rapid train-up of field medic tasks through a comparison with active duty soldiers participating in medical proficiency training.

Technical Approach: A 72-item knowledge test will be given before and after the military proficiency training. Half of the students will complete one form of the test, the other half of the students will complete a different form of the test before the training. The opposite version of the test will be given to the students after the training. A hands-on test of 20 field medic tasks will be conducted before and after the military proficiency training. These tasks are: temperature, pulse, respiration, blood pressure, oropharyngeal airway, nasopharyngeal airway, supplemental oxygen administration, bag-valve-mask apneic patient with pulse, impalement injury, abdominal wound, chest wound, tourniquet, shock, splint-joint, splint-long bone, splint-traction, intravenous infusion, primary survey, mast survey, and secondary survey. Performance will be recorded as a Go or No Go on each task. Data averaged across n=60 field medics will be used as a comparative baseline for gauging the proficiency of IRR soldiers before and after a rapid train-up program of instruction designed for a mobilization.

Progress: There have been some problems in the past. No subjects have been interviewed or tested. MPT classes, from where participants are recruited have been canceled since this research proposal was formulated. Cancellation is due to Fort Bliss not participating in MPT. At this time the end date may need to be extended passed April 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/53 STATUS: Completed FY95

TITLE: Blood Conservation through Nursing Education

PRINCIPAL INVESTIGATOR: Vickie A. Bradley RN

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): None

MONITOR: N/A

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Oct 95

KEY WORDS: Blood Conservation, Nosocomial Anemia, Nursing Education

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Study Objectives:

(1) Determine WBAMC's ICNS's nurses':

(a) usual blood draw volume for a battery of commonly ordered chemistry assays,
(b) knowledge of minimal blood volume required for this battery of assays,
(c) past experiences with blood drawing in relation to sample volume, and
(d) anticipated difficulties with blood drawing in relation to sample volume.

(2) Educate WBAMC's ICNS's nurses regarding the etiology and risks of nosocomial anemia and the appropriate blood draw volume for a battery of assays.

(3) Establish a profile of nurses with various blood drawing behaviors and categorize their past experiences and anticipated difficulties to determine whether overdrawing is, for example, due to: habit, lack of education, miscommunication between nursing and clinical laboratory, or some other problem.

(4) Utilize the above information as a basis for further study.

Medical Approach: Experimental pretest-post test survey utilizing a questionnaire and a written educational intervention.

Progress: 50 subjects have been entered in data collection study.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/66 STATUS: Terminated FY95

TITLE: Workload Management for Nurses in the Trauma Resuscitation Unit

PRINCIPAL INVESTIGATOR: CPT Virginia S. Hathaway

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MAJ Susanne Clark

MONITOR: NA

START DATE: Jan 93 ESTIMATED COMPLETION DATE: Oct 94

KEY WORDS: Workload Management, Trauma Resuscitation

Study Objective: To develop an accurate tool to measure nursing workload in the Trauma Resuscitation Unit; to develop an accurate tool to measure trauma patient acuity in terms of nursing care hours; and to develop an accurate tool that can predict nurse staffing needs.

Technical Approach: This is a descriptive, exploratory study of all incoming trauma patients, "code 3" designated for the Trauma Unit beginning 1 October 1992 through 1 October 1993. We will use a specially designed Trauma Resuscitation Acuity Worksheet to calculate nursing care hours for each "code 3" trauma.

Progress: No subjects were entered. This study has been administratively terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/03 STATUS: Terminated

TITLE: Evaluation of the Effects of the Addition of Morphine Sulfate to a Standard Bier Block Solution in Peripheral Arm Surgery

PRINCIPAL INVESTIGATOR: LTC Charles B. Hauser

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MAJ Susanne Clark

MONITOR: NA

START DATE: Jan 93 ESTIMATED COMPLETION DATE: Oct 94

KEY WORDS: Morphine, Bier Block Solution, Postoperative Pain

Study Objective: The objectives of this study are (1) to determine whether addition of morphine sulfate to a Bier block solution for peripheral arm surgery provides greater postoperative pain relief (as measured by a verbal descriptor scale) than does standard Bier block solution, and (2) to determine whether there is a difference in duration of postoperative pain relief between morphine sulfate Bier block solution and standard Bier block solution. Documentation in the literature has not been found describing the effects or the appropriate dosing of MS04 in Bier blocks. This study will add empirical data for use in clinical practice and promote further research involving the addition of morphine sulfate to Bier block solution for postoperative pain relief.

Technical Approach: This is a descriptive, exploratory study of all incoming trauma patients, "code 3" designated for the Trauma Unit beginning 1 October 1992 through 1 October 1993. We will use a specially designed Trauma Resuscitation Acuity Worksheet to calculate nursing care hours for each "code 3" trauma.

Progress: No subjects were entered this year. The principal investigator has changed form

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/11 STATUS: Ongoing

TITLE: A Review of HIV-Infected Women Evaluated at a Southwestern Military Medical Center

PRINCIPAL INVESTIGATOR: RN Lynn B. McNicol

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): LTC Wellington Sun

MONITOR: NA

START DATE: Jan 94 ESTIMATED COMPLETION DATE: Jan 97

KEY WORDS: HIV, Women

Study Objective: (1) Describe characteristics of HIV-infected women evaluated at William Beaumont Army Medical Center. Characteristics of particular interest include duty status, marital status, race/ethnicity, source of referral for HIV testing, number of children, serostatus of spouse (if known), initial and most recent Walter Reed Stage and person months/years of followup within DoD.

(2) Assess the quantity and quality of data available for further study from existing files and the US Army HIV Data System.

Technical Approach: This is a descriptive retrospective case review study.

Progress: 30 files of HIV infected women seen at WBAMC since the program began have been identified thus far. Formal data collection will be done in the next 2 to 3 months. The quantity and qualify of information has not yet been assessed. The estimated completion date has changed from Jan 96 to Jan 97.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/46 STATUS: Completed FY95

TITLE: The Effect of Perceived Social Support on the Competency Level of US Army Perioperative Nursing Students

PRINCIPAL INVESTIGATOR: MAJ Louann Peraulta

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): Co-Investigaor for Madigan AMC: MAJ JE Newman

MONITOR: N/A

START DATE: Aug 95 ESTIMATED COMPLETION DATE: Dec 95

KEY WORDS: Social Support

Study Objective: The purpose of this study is to determine if a relationship exists between the US Army perioperative students' perceived social support received during their 16 week course of instruction and their competency level upon completion of the course. If a relationship is determined to exist between perceived social support and the competency levels in perioperative students, the resident perioperative nursing staff may need to be targeted to receive instruction and education on preceptorship and social support behaviors. In a profession that experiences frequent staffing shortages and position justification, it is necessary to support the education process that develops new specialists.
Research Question: What is the effect of perceived social support on the competency level of US Army perioperative nursing students?

Technical Approach: A correlation survey design will be used to study the job performance of the perioperative students and social support received by the perioperative students during the 16 week course of perioperative instruction. The variables are competency level and perceived social support.

Questionnaires will be sent to each of the three US Army Perioperative Course sites by the Principle Investigator (PI). The course instructors will distribute the questionnaires to each of the perioperative students who have agreed to take part in this research study. No control has been placed on where subjects will complete the data collection forms; a classroom, in the privacy of a home, or other place.

Progress: 11 subjects were entered from William Beaumont AMC in this collaborative study with Madigan AMC.

ABSTRACT: The purpose of this study was to determine if a relationship existed between the US Army perioperative nursing students' perceived social support during their 16 week course of instruction and their competency level rating received upon completion of the course. The Interpersonal Relationship Inventory (IPRI) (Tilden, 1989) was used to evaluate the student subjects' perceived social support. Three perioperative course instructors recorded the students' competency level ratings based on a 10 point scale with 1 representing the lowest level and 100 representing the highest level. The students' competency level ratings were annotated on the Competency Level Numeric Rating Form (Newman, 1995). Sources of support were identified by subjects, with parents and friends cited most frequently by subjects as support persons. Although a positive relationship was found between

perceived social support and competency and an inverse relationship was found between conflicted support and competency, neither relationship was statistically significant. One implication was that resident perioperative nursing staff may need to be targeted to receive instruction and education on preceptorship and social support behaviors.

Estimated completion changed from Mar 96 to Dec 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/09 STATUS: Terminated

TITLE: Assessment of Recalled Medical Reservists' Needs

PRINCIPAL INVESTIGATOR: MAJ Christine M. Piper

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: NA

START DATE: Dec 90 ESTIMATED COMPLETION DATE: Mar 94

KEY WORDS: Stress, Depression

Study Objective: To determine the degree of adjustment difficulty that reservists are experiencing and to assess the needs for additional support measures and programs.

Technical Approach: This study will utilize an anonymous voluntary questionnaire. This is a pilot study to survey medical and medical support reservists who were called to active duty to support Operation Desert Shield while assigned or attached to WBAMC.

Progress: No response received from investigator for FY 95 principal investigator PCS'd from WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/37 STATUS: Terminated

TITLE: Use of Awareness of Stressors to Manage Burnout in Department of Nursing Midlevel Managers

PRINCIPAL INVESTIGATOR: MAJ Christine M. Piper

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: May 92 ESTIMATED COMPLETION DATE: Mar 94

KEY WORDS: Burnout, Stress in Nursing

Study Objective: To identify current levels of burnout in midlevel nursing managers and work-related stressors and increase awareness of stressors in order to address staff burnout more effectively.

Technical Approach: This study will survey midlevel managers in Department of Nursing. Three instruments will be completed prior to an educational offering on burnout and stress management. Subjects will be asked to complete the same three instruments at 1 month, 6 months, and 2 year post workshop to identify any measured changes.

Progress: No response received from investigator for FY 94 annual report.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/54 STATUS: Ongoing

TITLE: Comparison Of Four Analgesic Agents For Venipuncture Pain

PRINCIPAL INVESTIGATOR: LTC Martha J. Skipper

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): TA Newcomer, CM Hackman, P Patterson, AA Hussa, KA Fedele, RL Gledhill, GL Vegh

MONITOR: NA

START DATE: Oct 95 ESTIMATED COMPLETION DATE: Jun 96

KEY WORDS: Venipuncture, Pain, Analgesic

Study Objective: This study is designed to compare the following four analgesics: 2.5% lidocaine-2.5% prilocaine topical cream, dichlorotetrafluoroethane topical spray, 0.5% lidocaine subcu., and saline with 0.9% benzyl alcohol subcu. The specific objectives of this study are : (1) to determine if a difference exists in the analgesic efficacy of the four analgesics, (2) to determine if there is a cost difference among these four analgesic groups, and (3) to determine if there is a convenience difference in the four groups. No studies were found in the literature comparing the four study analgesic agents in the above three areas simultaneously. This study will add empirical data for use by both medical clinicians as well as health care administrators.

Technical Approach: This study will be a completely randomized design. Subjects will be randomly assigned to treatment groups using a table of random numbers (Polit and Hungler, 1991). Subjects will be assigned to treatments in the order in which they volunteer for the study. A sample of convenience will be utilized of patients who present for surgery over the time frame of the study. The subjects will be informed that they will receive an analgesic before the insertion of their 16 gauge IV catheter. They will not be made aware of any reported differences between the four types of analgesics, and to the extent possible, they will be unaware of the agent which they are receiving.

Progress: 50 subjects have been entered in the study with no adverse reactions reported to date. Estimated completion date has changed from Sep 96 to Jun 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 88/65A STATUS: Ongoing

TITLE: Pediatric Intubation Training Utilizing the Ferret Model

PRINCIPAL INVESTIGATOR: LTC Anne Varner

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): L Tremper

MONITOR: NA

START DATE: Jul 88 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Pediatric Advanced Life Support, pediatric Intubation ferret

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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 ferrets employing a laryngoscope and endotracheal tube.

Animals will be anesthetized 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 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.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Amendment Jun 93: Feline model changed to ferret model.

Progress: 140 Nursing students have been enrolled in this study. Ferrets are used to train nursing and medical staff on pediatric intubation.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/24 STATUS: Ongoing

TITLE: The Effect of Relaxation Therapy on Patients with Asthma

PRINCIPAL INVESTIGATOR: Helen Villegas RN

DEPARTMENT: Nursing FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Jan 87 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Asthma Relaxation Therapy

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 improve asthma symptoms and decrease medication intake and the need for emergency medical care.

PROGRESS: Abstract: In 1988, the Asthma Task Force on Mortality reported that the number of deaths from asthma has been increasing since 1978 after 10 years of decreasing. They recommended asthma education and the development of self-care management programs with self-observation and peak flow meter readings. In 1989, the American College of Allergy and Immunology Conference identified education, relaxation, and medication as the most important interventions in the treatment of asthma.

The role of stress in asthma is not well understood. Three- to fifty four-month studies have shown that the reduction of stress significantly improves the small airways and the peak expiratory flow rate (PEFR).

The Orem Self-Care Model was used as a conceptual framework for this 6 week pilot study in which the effects of teaching Jacobson's -Progressive Relaxation to ten adult asthma patients were measured. It was hypothesized that stress reduction would overcome a major health care deficit and result in the highest level of wellness possible for the asthma patient.

The first three weeks each subject recorded PER, medication intake, assessment of mood, and asthma symptoms after baseline pulmonary function test (PFT) values were documented. PFTs and a 30-minute training session in Jacobson's Progressive Relaxation comprised the second clinic visit. The next three weeks the patients continued to record their PER, medication intake, assessment of mood, and asthma symptoms. In addition, they listened to a 14-minute relaxation tape each morning and evening. PFT was repeated on their third visit.

Wilcoxson Matching-Pair Signed Rank Test and Kendall's Tau C Test of objective data did indicate a significant improvement in the small airways. Patients also verbalized their perception of increased productive energy during the second half of the study. Changes in other clinical parameters were not significant after three weeks.

Reduction of stress should be a goal for all patients. In other chronic conditions it is important. In asthma it may be life saving. Teaching asthma . patients relaxation techniques may be one of our most valuable nursing interventions.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/23 STATUS: Terminated

TITLE: Effect of Psyllium Fiber Wafers on Serum Glucose Levels after One Hour 50 Gm Glucose Screening Test in Pregnant Patients

PRINCIPAL INVESTIGATOR: CPT J. Scott Bembry

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

ASSOCIATE INVESTIGATOR(S): Dr. Butterfield

MONITOR:

START DATE: Mar 94 ESTIMATED COMPLETION DATE: Jan 95

KEY WORDS: Fiber Wafers, Serum Glucose Levels

Study Objective: To determine if dietary fiber supplementation (using commercially available flavored psyllium wafers) influences glucose tolerance in pregnant patients.

Technical Approach: Two groups of obstetric patients will be enrolled. One group will consist of 10 patients of ideal body weight (IBW) and the other will consist of 10 obese patients (>150% IBW). All patients will undergo the standard diabetes screening at 24 - 28 weeks EGA, consisting of a 50 gm glucola challenge with serum glucose determination 1 hour later. These patients will then supplement their preexisting diets by consuming Metamucil wafers (2 wafers QID) for 72 hours. The patients will then repeat the 50 gm glucose challenge test. Each patient will serve as her own control.

Progress: There were 2 subjects entered in this study with no noted adverse reactions. We are considering changing protocol to just having patients consume fiber wafers at the time of their second 1 hour DMS. This would test the hypothesis and improve patient desire to participate. Dr. Hoshaw started a similar protocol and is currently ongoing WBAMC #95/10.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/67 STATUS: Ongoing

TITLE: GOG #90, Evaluation of Cisplatin, Etoposide and Bleomycin (BEP) Induction followed by Vincristine, Dactinomycin and Cyclophoshamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): C Hawley-Bowland

MONITOR: LTC Elmer Pacheco

START DATE: Nov 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Ovarian Germ Cell Cancer

Study Objective: To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophoshamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors. To evaluate the effect of BEP chemotherapy in patients with recurrent or progressive disease during or after previous non-cisplatin containing chemotherapy. To further investigate the relevant prognostic factors. To evaluate the acute and chronic toxicity of such chemotherapy, particularly in gonadal and reproductive function. To evaluate the effect of chemotherapy on menstrual status and reproductive function in patients in whom the uterus and one tube and ovary are preserved.

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: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/68 STATUS: Ongoing

TITLE: GOG #93, Evaluation of intraperitoneal chromic phosphate suspension therapy following negative second-look laparotomy for Epithelial Ovarian Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): C Hawley-Bowland

MONITOR: LTC Elmer Pacheco

START DATE: Oct 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Ovarian Epithelial Cancer

Study Objective: To evaluate the efficacy of P32 therapy in patients with no residual ovarian cancer and to evaluate the morbidity from intraperitoneal P32 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: No patients have been enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/30 STATUS: Ongoing

TITLE: GOG #122, Whole Abdominal Radiotherapy versus Circadian-Timed Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): C Hawley-Bowland

MONITOR: MAJ Robert Sheffler

START DATE: Apr 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Endometrial Carcinoma (Advanced)

Study Objective: To compare treatment outcomes (survival and progression free interval) and failure patterns in patients with stages III and IV endometrial carcinoma (< 2cm residual disease) treated with whole abdominal irradiation versus circadian-timed combination doxorubicin-cisplatin chemotherapy. To determine and compare the incidence and type of acute and late adverse events observed with the two treatment regimens.

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: No patients have been enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/34 STATUS: Ongoing

TITLE: GOG #109, A Randomized Comparison of 5-Fu Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy versus Radiation Therapy Alone in Selected Patients with Stages IA2, IB and IIA Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): C Hawley-Bowland

MONITOR: LTC Elmer Pacheco

START DATE: Apr 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Cervical Carcinoma

Study Objective: To determine whether the combination of 5-fluorouracil (%-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement or positive surgical margins following radical hysterectomy and lymph node dissection for stages IA2, IB, and IIA carcinoma of the cervix. To determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

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: No patients enrolled to date. Estimated completion date has changed from Apr 97 to Indefinite.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/51 STATUS: Ongoing

TITLE: GOG #114, Phase III Randomized Study of IV Cisplatin and Cyclophosphamide vs IV Cisplatin and Taxol vs High Dose IV Carboplatin followed by IV Taxol and Intraperitoneal Cisplatin in Patients with Optimal Stage III Epithelial Ovarian Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): NA

MONITOR: MAJ Robert Sheffler

START DATE: Sep 92 ESTIMATED COMPLETION DATE: Aug 97

KEY WORDS: Epithelial Ovarian Carcinoma

Study Objective: To compare recurrence-free interval, complete pathologic response, and survival between the standard regimen of intravenous cisplatin/cyclophosphamide and the two experimental regimens: (1) Intravenous cisplatin/taxol and (2) intraperitoneal carboplatin followed by intravenous taxol and intraperitoneal cisplatin in patients with optimal (<1 cm residual) Stage III epithelial ovarian carcinoma. To compare the toxicities and complications of the three treatment regimens. To correlate serial serum CA-125 levels with negative second look and recurrence-free interval.

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 FY95 there was one patient enrolled with no adverse reactions reported to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/52 STATUS: Ongoing

TITLE: GOG #135, Evaluation of Drug Sensitivity and Resistance with the ATP-Cell Viability Assay (ATP-CVA)

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): NA

MONITOR:

START DATE: Aug 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: ATP-CVA, ATP, Cell Viability

Study Objective: a. To evaluate the correlation between the ATP-cell assay and patient response to chemotherapy in untreated primary epithelial ovarian carcinoma; to correlate laboratory results with the achievement of pathologic CR at time of second look surgery; to correlate laboratory results with progression-free survival; and to correlate single agent and combined agents in vitro studies with clinical outcome. Single drugs as well as drug combinations will be tested in vitro.

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 has been enrolled in study with no adverse reactions reported to date. Estimated completion date has changed from Aug 97 to Indefinite.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/63 STATUS: Ongoing

TITLE: GOG #134/NCCTG #92-61-51, A Phase III Trial of Taxol at Three Dose Levels and C-CSF at Two Dose Levels in Platinum-Resistant Ovarian Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Robert Sheffler

START DATE: Sep 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Ovarian Carcinoma

Study Objective: To determine if the dose of Taxol affects response rate, progression free interval or survival in patients with platinum-resistant ovarian cancer; to compare the toxicities of the three regimens; to compare the efficacy and toxicity of two dose levels of G-CSF (5 micrograms/kg/day versus 10 micrograms/kg/day) in patients who receive the highest Taxol dose (250 mg/m^2); and to determine the relationship between peak Taxol plasma concentration and toxicity/response.

Technical Approach: 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: No patients have been erolled to date. Estimated completion date has changed from Sep 97 to Indefinite.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/14 STATUS: Ongoing

TITLE: GOG #136, Acquisition of Human Ovarian and Other Tissue Specimens and Serum to be Used in Studying Causes, Diagnosis, Prevention and Treatment of Ovarian Cancer

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR:

START DATE: Jan 93 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Ovarian Carcinoma, Tumor Bank

Study Objective: To accomplish the collection of human ovarian tissue specimens and serum within GOG participating institutions; to provide a repository for long term storage of ovarian tumor, tissue, and serum. This material will be used in studies to better understand the molecular biology of ovarian tumors; and to make available. through the Cooperative Human Tissue Network (CHTN), tumor tissue and serum for proposed projects conducted by GOG Investigators (internal bank) and by researchers nationally (external bank).

Technical Approach: 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: 19 patients have been enrolled with no adverse reactions.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/21 STATUS: Ongoing

TITLE: GOG #140, An Assessment of Age and Other Factors Influencing Protocol versus Alternative Treatments for Patients with Epithelial Ovarian Cancer Referred to Gynecologic Oncology Group Institutions

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR:

START DATE: Apr 93 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Epithelial Ovarian Cancer

Study Objective: To assess the frequency at which patients with epithelial ovarian cancer are enrolled in prospective clinical studies at institutions participating in gynecologic oncology group protocols; to assess whether patient age affects enrollment in prospective gynecologic oncology group protocols; and to assess what demographic or clinicopathologic factors affect patient enrollment in prospective gynecologic oncology group protocols.

Technical Approach: 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: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/42 STATUS: Ongoing

TITLE: GOG # 9207, Laparoscopic retroperitoneal lymph node sampling followed by immediate laparotomy in women with cancers of the cervix

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: LTC Thomas Gormley

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Laparoscopic, Cancer of Cervix

Study Objective: To determine the adequacy of laparoscopic sampling of pelvic and aortic lymph nodes followed by immediate laparotomy in women with cancers of the cervix.

To obtain information of adverse effects and difficulties associated with laparoscopic sampling of pelvic and aortic lymph nodes.

Technical Approach: 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: No patients have been enrolled to date. The estimated completion date of this study has changed from Oct 98 to Indefinite.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/48 STATUS: Ongoing

TITLE: GOG # 144, Molecular genetic analysis of ovarian cancer families

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR:

START DATE: Sep 93 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Genetic Analysis, Ovarian Cancer Families

Study Objective:

1.) To determine the frequency of chromosomal rearrangements in women with familial ovarian cancer.

2.) To identify genetic markers linked to familial ovarian cancer.

3.) To identify deletions or rearrangements that signal the site of the mutation.

Technical Approach: 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: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/09 STATUS: Completed FY95

TITLE: Chemoprophylaxis with Oral Cirpfloxacin in Ovarian Cancer Patients Receiving Taxol

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): GL Maxwell, J Webb

MONITOR: LTC Carla Hawley-Bowland

START DATE: Dec 94 ESTIMATED COMPLETION DATE: Oct 95

KEY WORDS: Ovarian Cancer, Chemoprophylaxis, Oral Cirpfloxacin, Taxol

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Study Objective: To review the clinical outcomes and cost of administration of a prophylactic antibiotic compared to observation for the prevention of neutropenic morbidity associated with Taxol regimens in ovarian cancer patients.

Technical Approach: The efficacy of the oral ciprofloxacin to prevent fever and bacterial infection in patients with ovarian cancer being treated with Taxol will be evaluated in a prospective randomized phase II trial under an FDA INDA (#44-4350). Eligible patients will be evaluated for a maximum of six Taxol cycles. During episodes of grade four toxicity, Arm I will receive cirprofloxacin while Arm II will be observed. Patients randomized to receive ciprofloxacin will be given a 10 day supply at the time of their Taxol infusion. The ciprofloxacin will be taken orally at a dosage of 500 mg twice a day once the ANC is less than $500/mm^3$ and continued until the ANC is greater than $100/mm^3$. They will be instructed to start the ciprofloxacin by the investigator who monitors their counts. Written neutropenia precautions will be given to both arms (all patients) at the time of their Taxol infusion and reviewed during episodes of grade 4 toxicity. Laboratory values will be obtained twice a week with results being called to the patient by the investigator or his designee. Patients will have a physical examination by a physician prior to each Taxol cycle and the laboratory tests. The primary outcome measured would be the onset of febrile morbidity at which time the patients would be removed from this study and managed according to current standards of care.

Febrile morbidity is defined by a documented temperature greater than or equal to 100.4F on two separate occasions four hours apart or a single episode greater than or equal to 100.8F. Febrile morbidity for those on ciprofloxacin is any significant fever more than 12 hours after the first dose of oral antibiotic. Clinical examinations, chest roentgenograms, and cultures for aerobic and fungal cultures will also be routinely performed. Episodes of febrile morbidity will be called to the investigators.

Progress: 5 patients were enrolled in this study with no adverse reactions reported to date. The estimated completion date has changed from Indefinite to Oct 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/34 STATUS: Ongoing

TITLE: Protocol GOG #151, A Phase II Trial of Intraperitoneal Paclitaxel (Taxol) as Salvage Therapy in Patients with Small Volume Residual Ovarian Cancer Following Initial Systemic Chemotherapy

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Julius Szigeti

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Ovarian Cancer

Study Objective: To determine the surgically defined objective response rate of intraperitoneal Paclitaxel (Taxol) when administered on a weekly schedule to patients with small volume residual ovarian cancer following initial systemic chemotherapy.

To further evaluate the safety of intraperitoneal Paclitaxel administered on a weekly schedule as a salvage treatment program to patients with ovarian cancer.

Technical Approach: All subjects must have a reassessment laparotomy per GOG surgical manual for disease measurement prior to therapy on this study. At completion of treatment, subjects may initially undergo laparotomy to verify response, but a laparotomy must be performed if no disease is detected at laparoscopy.

The drug or drugs will be administered intraperitoneally through an implantable peritoneal dialysis catheter i.e., Tenckhoff catheter, which may be connected to an indwelling port, such as a Port-A-Cath. The catheter will be placed at the time of second-look laparotomy or at a subsequent operation. Surgical placement of catheters should be performed according to GOG guidelines. These catheters are inserted into the peritoneal cavity, tunneled through the subcutaneous tissue, and either exteriorized through a stab incision (Tenckhoff catheter), or the implantable port, i.e., Port-A-Cath, is placed in the subcutaneous tissue of the anterior, inferior thorax.

Progress: No patients have been enrolled in this study to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/35 STATUS: Ongoing

TITLE: Protocol GOG #154, Human Immunodeficiency Virus Testing In Patients with Invasive Cervical Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: NA

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: HIV, Cervical Carcinoma

Study Objective: To determine the frequency of HIV serostatus among patients 50 or under who present with invasive cervical cancer and who consent to HIV testing.

To correlate HIV serostatus with various clinical, pathologic, epidemiologic and demographic factors.

To obtain preliminary data comparing the clinical course, response to therapy and toxicity of therapeutic regimens for HIV-positive women to those for HIV-negative women with similar disease status.

Technical Approach: HIV Testing - Part A

Patients will be tested for HIV. Either one or both of the ELISA or Western Blot tests will be administered. Confirmation of HIV serostatus - results of HIV testing (4 copies) must be submitted along with HIV test result form.

For HIV negative result: Negative ELISA test (or appropriate substitute test must be FDA approved).

For HIV positive result: Positive ELISA plus positive Western Blot (or appropriate substitute must be FDA approved).

Pathology: Confirmation of diagnosis of invasive cervical cancer.

Progress: No patients have been enrolled in this study to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/47 STATUS: Ongoing

TITLE: GOG #150, A Phase III Randomized Study of Accelerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) Versus Combination Ifosfamide-Mesna with Cisplatin in Optimally Debulked Stage I, II, III, or IV Carcinosarcoma (CS) of the Uterus

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Julius Szigeti

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Survival, Progression-free Interval, Carcinosarcoma, Uterus

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Study Objective: To compare treatment outcomes (survival and progression-free interval) and failure patterns in patients it stages I-IV carcinosarcoma (CS) of the uterus ($\leq$ 1 cm residual diseases) without extra-abdominal distant disease treated with AHWAR versus cisplatin and ifosfamide/mesna.

To determine and compare the incidence and type of acute and late adverse events observed with the two treatment regimens.

Technical Approach: 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: No patients have been enrolled in this study to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/50A STATUS: Ongoing

TITLE: The Evaluation of the Intrinsic Tensile Strength of Rectus Fascia Incised with a Scalpel versus the Electrosurgical Instrument

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Richard A. Harris

START DATE: Sep 95 ESTIMATED COMPLETION DATE:

KEY WORDS: Rectus Abdominis Fascia, Scalpel, Electrosurical Instrument

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The electrosurgical instrument is used daily in operating suites throughout the world. The surgeon's use of this instrument is frequently based on their exposure during their training and not based on objective data. Consequently, the electrosurgical instrument has frequently been used to incise the rectus abdominis fascia while performing a laparotomy without any understanding of the healing implications of doing so. In general, there is a paucity of data concerning the healing ability of tissues after conducting an electrical current. The only comparison data of wound healing to date is the observance of macrophages and neutrophils in the histologic specimen of wounds created by a scalpel verses the electrosurgical instrument. The infiltration of these inflammatory cells appeared to be directly related to the power setting of the instrument and the speed at which it traveled.

Study Objective: To evaluate the intrinsic tensile strength of rectus fascia incised with a scalpel versus the electrosurgical instrument.

Technical Approach: A total of 10 goats will be used in this randomized, blinded study. Each goat will receive a 35 cm vertical fascial incision with either a scalpel (n=5) or an electrosurgiical instrument using a coagulation current at 40 watts of power (n=5). All fascial closures will be performed in a continuous running fashion using 0-vicryl suture in 1cm x 1cm bites.

Approximately 30 days after the procedure, euthanasia of each animal will be performed and each abdominal wall will be excised en-bloc. Specimens will be placed in liquid nitrogen and then stored at
-70 degrees C until analyzed. The fascia from each animal will be cut into 30 1 cm strips for analysis on the tensiometer. The tensile strength of the 150 specimens from each group will be compared in the final analysis.

Progress: This study has not been started.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/51 STATUS: Ongoing

TITLE: GOG #157, Randomized Phase III Trial of Carboplatin (AUC 7.5) and Paclitaxel 175 MG/M^2 Q 21 Days X 3 Courses Versus the same Regimen X 6 Courses, in Patients with Selected Stage IC and II (A, B, C) and Selected Stage IA and IB Ovarian Cancer

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Julius Szigeti

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Tumor, Pelvic Extension, Malignant Ascites, Peritoneal Washings

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Study Objective: In definitively staged patients who have tumor involving one or both ovaries with pelvic extension (completely resected) and/or malignant ascites and/or positive peritoneal washings (Stages I-C, II-A, II-B, II-C with no macroscopic residual disease), and in those Stage I-A and I-B patients with poorly differentiated tumors.

To compare the progression-free interval and overall survival of the two treatment regimens.

To define the relative toxicities of the two treatment approaches.

Technical Approach: 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 No patients have been enrolled in this study to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/52 STATUS: Ongoing

TITLE: GOG # 152, A Phase III Randomized Study of Cisplatin (NSC#119875) and Taxol (Paclitaxel) (NSC #12973) with Interval Secondary Cytoreduction vs. Cisplatin and Paclitaxel in Patients with Suboptimal Stage III, & Selected Stage IV Epithelial Ovarian Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Jay W. Carlson

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

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Julius Szigeti

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Epithelial Ovarian Carcinoma

Study Objective: To determine if secondary cytoreductive surgery contributes favorably to progression-free interval and survival in patients with suboptimally debulked stage III & selected stage IV epithelial ovarian cancer.

To determine the morbidity of secondary cytoreductive surgery in patients with suboptimally debulked stage III & selected stage IV epithelial ovarian cancer.

To prospectively assess the quality of life of suboptimally debulked stage III & selected stage IV epithelial ovarian cancer patients and to determine if secondary cytoredutive surgery affects their quality of life.

Technical Approach: 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: No patients have been entered in this study to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/22 STATUS: Ongoing

TITLE: Modified Cytobrush Technique Versus Endocervical Curettage In The Evaluation Of Cervical Dysplasia

PRINCIPAL INVESTIGATOR: CPT Kristine A. Eule

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

ASSOCIATE INVESTIGATOR(S): J Szigeti, R Gomez

MONITOR: N/A

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Nov 96

KEY WORDS: Modified Cytobrush, Endocervical Currettage

Study Objective: To show that a sleeved cytobrush technique is a better method of endocervical evaluation than the currently practiced ECC.

Technical Approach: Prospective data collection. All patients referred to the dysplasia clinic who meet inclusion criteria will receive the usual evaluation including colposcopy, repeat PAP, ECC, and cervical biopsies as indicated. Instead of the standard cytobrush a sleeved cytobrush will be used to do the PAP. The glass slide for the PAP will be divided in two by etching with a diamond pencil, and the cytobrush endocervical specimen will be rolled out on one half and the ectocervical spatula specimen placed on the other half. The slide will be processed in the usual manner for cytology. The pathology report will comment on which parts of the slide any abnormality / pathology is found. The ECC will be processed and read as usual. Patients with dyplasia or findings worrisome for cancer on either ECC or endocervical cytobrush cytology will then undergo CKC - this is the actual study group. The CKC findings shall be considered the "gold standard" for assessing endocervical pathology. Each study case will have all pathology reviewed by Dr. Richard Gomez, Department of Pathology co-investigator. The sensitivity, specificity, and positive and negative predictive values will then be determined for ECC versus sleeved cytobrush cytology to determine if a statistically significant ($p<0.05$) difference exists. Statistical analysis will be performed under the guidance of Lyle Broemeling, our statistical consultant.

Progress: 20 subjects have been entered in the study with no adverse reactions noted to date. The estimated completion date has changed from Sep 96 to Nov 96. Out of the large number of patients seen in the Dysplasia Clinic, only a very few ultimately undergo a LEEP or a cone biopsy (~ 1/100 patients). Originally, we had anticipated a larger number of such patients. Currently, we can not even make preliminary conclusions on our limited data. Nevertheless, we anticipate that we will be able to obtain sufficient numbers within a reasonable time period.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/63A STATUS: Terminated FY95

TITLE: Certification Trng: Advanced Laser Laparoscopic GYN Procedures in the Porcine Model

PRINCIPAL INVESTIGATOR: LTC Carla Hawley-Bowland

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

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Sep 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Surgical Training: Advenced Laser Laparoscopic Gyn Procedures.

Study Objective: To provide training and certification of OB-GYN Surgery Staff in laser and non-laser laparoscopic and vaginal surgical procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The ability to suture during laparoscopy greatly expands the indications for laparoscopic surgery and increases the confidence of the surgeon performing more difficult procedures. There will be two live animal surgical stations and one station where some procedures will be taught with inanimate tissue such as bovine tongue and uterus. After the skin is prepped, an insufflation needle will be inserted near the umbilicus and the abdomen will be filled and maintained with 15mm Hg pressure of CO_2. The insufflation needle will then be removed and replaced with a trocar/cannula for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. Training will involve extracorporeal and intracorporeal suturing techniques of various urogenital tissue through the laparoscopic cannulas. The argon-beam and ND:YAG laser will be used to train in techniques of tissue coagulation and excision. Abdominal lymph nodes will also be excised laparoscopically. Training will be conducted on endometrial ablation and tumor excision procedures with lasers and electrosurgery (roller-ball and large loop wire electrodes) via a hysteroscope. If difficulty is encountered with introduction of the scope through the vagina, the uterus will be exposed by laparotomy via a mid anterior suprapubic abdominal incision. Additional training for endometrial ablation and tumor removal will also be conducted with bovine uterus and bovine tongue, respectively.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No subjects have been entered. This protocol was established when Sierra Medical Center provided an advanced laser laparoscopic GYN procedures course. There were no courses offered this year and I know of none planned. Principal investigator recommends termination of this study.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/07 STATUS: Completed FY95

TITLE: "Lady J" and "Freshette Complete System"; A Field Trial for the Active Duty Woman

PRINCIPAL INVESTIGATOR: LTC Carla Hawley-Bowland

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

ASSOCIATE INVESTIGATOR(S): B Jennings, D Myers

MONITOR:

START DATE: Feb 95 ESTIMATED COMPLETION DATE: Jul 95

KEY WORDS: Keywords: Freshette, Lady J, Urinary Device

Study Objective: 1) To determine the incidence of urinary tract infections in women assigned to field duty.

2) To evaluate the effect of the "Lady J" and "Freshette Complete System" urinary diversion on dehydration, urinary tract infections, and quality of life in the field.

Technical Approach: 1) Fifty Army active duty service women will be issued "Lady J" urinary diversions devices. These soldiers will be instructed in their use and care. An initial urinalysis will be collected on each servicewomen. The servicewoman will than use the device in the field for three months. Urinalyses will be collected during and after field use.

2) After three months' use of the "Lady J" system the same fifty servicewomen will be issued the "Freshette Complete System". This device will be used for three additional months with the same evaluation performed (i.e., urinalysis during and after use).

Progress: This study was completed in FY95. 53 subjects were entered in the study; 10 withdrew. ABSTRACT: Women assigned to field duty have traditionally had problems with urination. The lack of privacy predisposes to bladder distention and increased risk of urinary tract infections. The "Lady J" (LJ) and "Freshette Complete System" (FCS) were designed for the female backpacker to allow urination through the fly opening in their trousers. During a field training exercise (FTX), 37 women participated in evaluation of either the LJ or the FCS. Half-way through the FTX, the devices were exchanged. A UA and C&S were obtained prior to entrance in the study, when the devices were exchanged and at the completion of the FTX. Questionnaires were completed after the use of each device. Controls (n-16) were evaluated with similar urine studies obtained at the beginning and end of the FTX. Two of the controls needed to be rehydrated with IV fluids and one control had a culture-proven urinary tract infection, while none of the field testees had such problems. Based on the questionnaire results, both the LJ and FCS significantly increased the quality of life of female soldiers in the field. The FCS was preferred four to one over the LJ. Many favorable comments were received, especially concerning the FCS. This was only a pilot study and should be expanded, including the field testing of a disposable device, currently under development.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/25 STATUS: Ongoing

TITLE: Influence of Parental Progesterone Administration on the Prevalence and Severity of Mastodynia
in Active Duty Servicewomen: A Multi-institutional Cross-sectional Study

PRINCIPAL INVESTIGATOR: LTC Carla Hawley-Bowland

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

ASSOCIATE INVESTIGATOR(S): B Jennings, D Myers

MONITOR:

START DATE: Sep 94 ESTIMATED COMPLETION DATE: Apr 96

KEY WORDS: Mastodynia, Progesterone, Depo Provera, Survey

Study Objective: A study questionnaire will be distributed to approximately 6% of active duty servicewomen in the United States between the ages of 18 and 44 in a multi-institutional cross-sectional study comparing women receiving parenteral progesterone (medroxyprogesterone acetate or levonorgestrel) with a control group. The specific aims of this study are to:

1) Assess the efficacy of progesterone in the prevention and treatment of mastodynia.
2) Determine the prevalence and quantitate the severity of mastodynia among Army servicewomen.
3) Quantitate the impact of mastodynia on productivity and military readiness.
4) Assess whether health care providers are meeting the expectations of women with mastodynia.

As outlined in the preceding and subsequent sections, mastodynia is a common, often debilitating condition with few proven therapies. This study will determine the prevalence and quantitate the severity of this condition among active duty servicewomen. Data will also be gathered which either support or deny a role for progesterones in the prevention and/or treatment of mastodynia. If the results are positive, women suffering from mastodynia could reasonably be counseled to consider long-acting parenteral progesterones for contraception.

Progress: 24 subjects were enrolled at WBAMC and there were 10 returned questionnaires.

Abstract: Breast pain (mastodynia) afflicts more than 30% of women attending surgical breast clinics. The pain can be quite severe and may impair job performance and interpersonal relationships. The use of progesterones in the treatment of mastodynia remains controversial, but is commonly practiced in some settings. The literature supporting the approach is inconclusive because the studies typically involve only small numbers of patients and are generally uncontrolled. In addition, questions of medication compliance are never addressed. This study employs a validated survey instrument and a cross sectional design to assess the prevalence and severity of mastodynia in a large cohort of women receiving long acting parenteral progesterones and in an even larger group of age-matched controls. At the time of this writing, 11 gynecology and family practice clinics have obtained human use approval and are actively enrolling patients. Thus far, 1,3000 patients have been enrolled, and 533 have

returned completed questionnaires. Questionnaires have also been mailed to 3,449 randomly selected age-matched controls. Detailed analysis of the data generated by this study will provide an accurate measure of the prevalence of mastodynia among active duty service women, assess attitudes about medical care for mastodynia and either support or refute a role for progesterones in the prevention and treatment of this common condition.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/10 STATUS: Ongoing

TITLE: Effect on Psyllium Fiber on Serum Glucose Levels after Abnormal 3 hour 100 gram Oral Glucola Tolerance Test in Pregnant Patients

PRINCIPAL INVESTIGATOR: CPT Natalie J. Hoshaw

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

ASSOCIATE INVESTIGATOR(S): JW Carlson

MONITOR: MAJ Julius Szigeti

START DATE: Dec 94 ESTIMATED COMPLETION DATE: Nov 96

KEY WORDS: Glucola Test, Pregnant Patients

Study Objective: To determine if dietary fiber supplementation (with commercially available flavored psyllium wafers) influences serum glucose levels in pregnant patients with a previously documented abnormal 1 hour 50 gram glucola test.

Technical Approach: Two groups of obstetric patients will be enrolled. All patients will undergo the standard diabetes screening at 24-28 weeks EGA, consisting of a 50 gram glucola challenge with serum glucose determination 1 hour later. Patients with abnormal values will be offered participation in the study. Each group will consist of 50 randomly assigned patients. One group will supplement their pre-existing diets with Metamucil wafers (2 wafers QID) for 72 hours. All patients will repeat the 50 gram glucola challenge 4 days after the initial screening test. Each patient will serve as her own control.

Amendment #1: Submitted 27 Mar 95. Current FDA approval of Metamucil dosing TID, the protocol will change to dietary fiber supplementation TID with meals. (Previously: QID, with meals and HS).
Protocol will also change to use of the sugar-free powder product which contains only 2 cal/dose. (Previously: fiber wafers containing 100 cal/dose).

Amendment #2: Submitted 10 Oct 95. Change from 1 hour to 3 hours and 50 grams of Glucola to 100 grams. This protocol was made into a multi-center military study.

Progress: This protocol has been amended such that we will be investigating the "Effect of Psyllium Fiber on Serum Glucose Levels After Abnormal 3 Hour 100 Gram Oral Glucose Tolerance Test in Pregnant Patients". Due to the low number of gestational diabetic patients in our facility, we have elected to open the study as a multi-center military study. Due to the long process of Cooperative Research & Development Agreement (CRDA) approval, this has only recently been finalized (Oct 95). Funding has not yet been received, but should be arriving soon. At the time of protocol amendment to the 3 hour GTT (from the 1 hour DMS) we had 12 patients enrolled. Consent forms are available and these patients will be compensated $25.00 upon receipt of funds from Proctor & Gamble. The estimated completion date has changed from Nov 95 to Nov 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/44 STATUS: Ongoing

TITLE: The Role of Three Phase Bone Scintigraphy in Women with Lower Back, Pelvic or Hip Pain

PRINCIPAL INVESTIGATOR: CPT Natalie J. Hoshaw

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

ASSOCIATE INVESTIGATOR(S): CE Jimenez, EJ Pacheco, AJ Moreno, JW Carlson

MONITOR: MAJ Alan L. Carpenter

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Sep 96

KEY WORDS: Pelvic Pain, Bone Scintigraphy

Study Objective: The objective of this study is to perform a bone scan over the anterior pelvis with blood flow and blood pool views in women being evaluated in the gynecology clinic for lower back, pelvic or hip pain. The bone scan images will be reviewed for the occurrence, size, location, and uptake characteristics of the pelvic pathology. Other imaging methods, such as ultrasonography, computer tomography (CT), or magnetic resonance imaging (MRI) will be done to further characterize the pelvic pathology.

Technical Approach: The subjects selected for this study will be from patients being evaluated in the gynecology clinic for lower back, pelvic or hip pain. A bone scan will be performed on the patients selected for participation in this study. The bone scan will include blood flow and immediate blood pool images of the anterior pelvis. The findings on the scan will then be correlated with the gynecologic workup, to include pelvic examination, possible ultrasonography, CT or MRI, and possible laparoscopy/laparotomy. The bone scan findings will be correlated to the pelvic pathology in terms of size, type, and location. The incidence of soft-tissue pelvic pathology in women undergoing evaluation for lower back, pelvic or hip pain will be determined.

Progress: 15 patients have been entered in the study with no adverse reactions reported to date.

Although we see many cases of chronic pelvic pain, not all patients will be surgical candidates (particularly for gross pathologic specimen such as hysterectomy). One hundred participants may take a significant time to enroll. Also, since the "uterine blush" noted on bone scan is of unknown significance, (i.e. may be a perfectly normal uterine finding related to the phase of woman's menstrual cycle) it would be optimal to have a control group. The control group could consist of women undergoing hysterectomy for such indications as pelvic prolapse or menorrhagia. It would also be helpful to blind the physician reading the studies for a second interpretation to evaluate intra- (and/or inter) observer variability.

Due to complexities of bone scintigraphy, the Department of Nuclear Medicine has assumed the responsibility of patient consent. I was told consents would be placed in each patient's convenience file within the Department. I do not currently have ordinals within my possession, but will obtain them.

After discussion with co-investigators, I anticipate submitting an amendment to reflect:
(1) Two arms of 15-20 patients (study & control)
(2) Blinded interpretation of bone scans
(3) Amended consent to involve control patients

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/47 STATUS: Terminated FY95

TITLE: The Clinical Management of Patients with Mild Dysplasia of the Uterine Cervix

PRINCIPAL INVESTIGATOR: CPT George L. Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, C Hawley-Bowland, HC Crawford

MONITOR:

START DATE: May 91 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Dysplasia (mild)

Study Objective: To determine the incidence of HPV infection in young women with histologically proven mild dysplasia (CIN I) of the uterine cervix.

Technical Approach: Patients with dysplastic cervical cells detected by cytology will undergo standard colposcopic examination, colposcopically-directed biopsies of suspicious cervical lesions found during colposcopy, and endocervical curettage. Patients with the following clinical and pathologic characteristics will be considered for study entry: (a) histologically proven mild dysplasia (CIN I) of the ectocervix; (b) adequate colposcopic examination; (c) absence of dysplastic epithelium in the endocervical canal as proven by endocervical currettage. These patients will be thoroughly counseled about study entry. Samples from patients who elect to participate will undergo in-situ DNA hybridization to detect specific subtypes of HPV within cervical cells using the Vira-Type kit. Patients with even last digit SSN will receive standard therapy using cryotherapy or laser vaporization of the transformation zone of the cervix (Group A). Patients with odd last digit SSN will be assigned to the observation group (Group B). All study participants will be monitored every 3 months in the Gynecology Clinic using cervical cytology (PAP Smear), colposcopic examination, and colposcopically directed biopsies of suspicious lesions. All women will be followed for a minimum of 2 years. The sexual consorts of study group patients will be referred to the Male Dysplasia Clinic.

Progress: Over 30% of the patients enrolled on this protocol were lost to follow-up. Enrollment stopped on Oct 94.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/31 STATUS: Terminated FY95

TITLE: Loop Electrosurgical Excision Procedure Treatment for Dysplasia of the Uterine Cervix

PRINCIPAL INVESTIGATOR: CPT George L. Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, P Miles

MONITOR:

START DATE: May 93 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Loop, Dysplasia, Cervix

Study Objective:

(1) To compare methods of preparation of the cervix prior to Loop Electrosurgical Excision Procedure (LEEP) in treatment of cervical dysplasia. Specifically, to determine if colposcopic visualization of the dysplastic lesion or the absence of staining by iodine containing solutions on dysplastic lesions is a more efficacious method of defining the full extent of the lesion prior to excision.

(2) To determine the success rate of treatment of cervical dysplasia with LEEP, based on cytologic analysis of surgical specimens.

Technical Approach:

(1) Patients with dysplastic cervical cells detected by cytology from Pap smears will undergo standard colposcopic evaluation, colposcopically directed biopsies of suspicious cervical lesions, and endocervical curettage.

(3) Patients with the following clinical and pathologic characteristics will be considered for study entry: a) histologically proven dysplasia of the ectocervix, b) adequate colposcopic examination, c) proven absence of dysplastic epithelium in the endocervical canal by endocervical curettage.

(4) Patients with these characteristics will be thoroughly counseled about study entry.

(5) The patients enrolled in the study will be treated with LEEP using standard protocols. A paracervical anesthetic block will be performed with 10cc 1% xylocaine with 1:100,000 epinephrine. Loop electrosurgical excision will be performed with bipolar cutting/coagulation wire loops using a Valley Lab Electrosurgical generator unit and large wire loops when possible (for better specimen analysis). Patients will be randomized by pseudo number generation to colposcopy followed by LEEP or application of Lugol solution to the cervix followed by LEEP of the non-staining areas. Comparison will be made to LEEP specimens collected using Lugol's solution for demarcation of the cervical abnormal epithelium, on the principle that normal squamous epithelium contains enough glycogen to stain and dysplastic tissue does not. Neither of these preparation techniques, however, are foolproof and both false positive and negative areas may be highlighted. We seek to determine whether colposcopy/LEEP is more efficacious than Lugol/LEEP, the surgical margins will be evaluated by standard histopathologic techniques. Treatment success will be analyzed 3 months after therapy when colposcopy and cervical cytology is performed.

Progress: Patients were enrolled but were frequently lost to follow-up. Dr. Maxwell, principal investigator has left WBAMC due to PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/39A STATUS: Completed FY95

TITLE: The Hemodynamic Response of Meconium Infusion in a Pregnant Sheep Model: Attempted Simulation of the Amniotic Fluid Embolism Syndrome

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, PC Brittain, RA Harris, P Bayliss, M Kestner, J Galloway, P Miles

MONITOR: COL Stephanie Sherman

START DATE: Sep 93 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Sheep, Amniotic Fluid, Embolism Syndrome

Study Objective: The purpose of this blinded prospective randomized controlled trial will be to study the effects of intravenous injection of meconium and amniotic fluid on hemodynamic function and subsequent cardiopulmonary pathology in the sheep model.

Technical Approach: A total of 16 pregnant sheep over 130 days gestation (corresponding to a near term human pregnancy) with a confirmed singleton fetus will be used to investigate the effects of intravenous infusion of meconium emboli. The pregnant sheep will undergo placement of a Swan-Ganz jugular catheter and carotid arterial catheter to evaluate the hemodynamic changes associated with infusion of the amniotic fluid specimens. Baseline hemodynamic measurements will be obtained one hour after placement of the Swan-Ganz and carotid catheters with the animal unanesthetized restrained in a standard sheep stanchion with head gate. Two samples of amniotic fluid will be used for injection: light meconium stained and thick meconium stained amniotic fluid. The animals will be divided into two groups according to the type of meconium stained amniotic fluid that will be infused (light or thick stained fluid): two animals will receive intravenous saline (control), two will receive unstained amniotic fluid, six will receive light meconium stained amniotic fluid, and six will receive thick meconium stained amniotic fluid. In the 12 animals that will receive meconium stained amniotic fluid, 2 will be infused with whole light meconium stained fluid, 2 will receive whole thick meconium stained fluid, 2 will receive the supernant from light meconium stained fluid, 2 will receive the supernant from thick meconium stained fluid, 2 will receive the precipitate from light meconium stained fluid, and 2 will receive the precipitate from thick meconium stained fluid. The investigator administering the solutions will be blinded to the identity of the infused substances. Following infusion into the venous system, hemodynamic parameters will be measured for the first hour after infusion. Doppler echocardiography will be used to determine cardiac ejection fractions at the time of infusion and at one hour post-infusion. After euthanasia has been performed, histologic sections from each animal's lung will be submitted to the pathology department for analysis and confirmation of amniotic fluid embolism. Data obtained before and after infusion of the various substances will be compared statistically.

Amended #1, May 1994: Original protocol is being finished with inclusion of the remaining animals. An additional 16 animals will be utilized to investigate the effects of hypoxia on meconium embolism. COL Sherman has been designated as veterinary medical monitor.

Progress: This study was completed in Jun 95. Dr. Maxwell PCS'd but submitted an Abstract. Estimated completion date changed from Oct 94 to Jun 95.

ABSTRACT: The objective of this study was two-fold: 1) To study the effects of meconium and autologous amniotic fluid injection; and 2) To determine if hemodynamic responses of emboli could be augmented by preceding fetal and/or maternal hypoxia. Twenty one nonanesthetized pregnant sheep received 30cc intravenous emboli. Thirteen unstressed animals were randomly assigned to receive one of four injections: 30% meconium, normal saline, 10% meconium or amniotic fluid. Eight additional animals underwent either uterine artery ligation or hypoxia under general anesthesia prior to injection of 30% meconium. Hemodynamic responses were observed incrementally for 1 hour after intravenous injections. The injection of 30% meconium resulted in a transient systemic and pulmonary vasopressor response which was associated with a brief fall in cardiac output ($p<0.05$). The hemodynamic responses of amniotic fluid and 10% meconium were similar to controls. Preceding uterine artery ligation augmented the systemic and pulmonary systolic pressure responses without an effect on cardiac output ($p<0.05$). The intravenous circulation of concentrated meconium leads to the compromise of cardiac function. Maternal surgical stress or fetal hypoxia may amplify this response.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/51 STATUS: Terminated FY95

TITLE: A Prospective Randomized Comparison of Tocolysis and Expectant Management After Mature Fetal Lung Studies

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): P Bayliss

MONITOR: MAJ Jay Carlson

START DATE: Sep 93 ESTIMATED COMPLETION DATE: June 95

KEY WORDS: Tocolysis Mature Fetal Lung

Study Objective: The purpose of this study is to determine the role of tocolytic therapy in preterm labor patients once fetal lung maturity has been established.

Technical Approach: This is a prospective and randomized study. All preterm labor patients with biochemical evidence of lung maturity will be randomized into a tocolytic or expectant management group. Maternal and neonatal outcomes will be compared.

Progress: This protocol was terminated because of ACOG standards and new staff did not endorse protocol. It did not enroll patients for several months. Also Dr. Maxwell, principal investigator has left WBAMC due to PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/25 STATUS: Ongoing

TITLE: Perinatal Transmission Rates of Human Papilloma Virus in Various Maternal Fluids

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): M Zacharean, JW Carlson, AP Soisson, WF Nauschuetz, F Harlass

MONITOR:

START DATE: Apr 94 ESTIMATED COMPLETION DATE: June 95

KEY WORDS: HPV, Prenatal Transplacental Transmission

Study Objective: The purpose of this prospective blinded trial is two-fold:
1) To determine the incidence & respective viral DNA type of HPV in cervical & peripheral blood specimens of pregnant patients.

2) To determine the perinatal transmission rate of HPV by perinatal analysis of transabdominally collected amniotic fluid as well as maternal/fetal blood and breast milk taken immediately postpartum.

Technical Approach: A total of 100 patients will be entered in this prospective study. It is a collaborative study between WBAMC and Texas Tech. Each patient will have cervical swab & amniotic fluid samples analyzed for HPV type using PCR amplification techniques. Maternal and cord blood samples and breast milk samples will be analyzed on those patients identified as HPV positive; similar techniques will be used in determining the presence and type of HPV. Questionnaires will also be filled out on each participant in order to provide demographic data for statistical comparison (i.e., age, gravidy, paridy, smoking history, race, sexual history, past medical problems, history of abnormal PAP smears, indication for amniocentesis, gestational age).

Amendment #1 (Apr 94): Changed title from "Determination of Prenatal Transplacental Transmission Rates of HPV in an Infected Pregnant Population" to present title. Added breast milk as sample to be obtained. Added M Zacharean as an associate investigator.

Amendment #2 (May 94): Funding implications modified.

Progress: 80 patients have been entered to date with no adverse reactions. There has been a change in principal investigator from Dr. Maxwell to Dr. Natalie J. Hoshaw, Dept. OB/GYN.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/30 STATUS: Ongoing

TITLE: Detection of Human Papillomavirus in Ovarian and Uterine Cancers Using Q-PCR

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, J Carlson, WF Nauschuetz, P Miles, KM Brady

MONITOR:

START DATE: Apr 94 ESTIMATED COMPLETION DATE: Sep 96

KEY WORDS: HPV, PCR

Study Objective: The purpose of this study will be to demonstrate the presence of HPV in gynecological neoplasms other than cervical cancer (i.e., ovarian and endometrial carcinomas; uterine sarcomas) using quantitative PCR techniques.

Technical Approach: A total of 50 ovarian (Stage III and IV) and 50 endometrial (all stages) carcinomas in addition to approximately 10 uterine sarcoma cancer specimens will be identified in a collaborative effort by investigators from WBAMC and SMC. Ten benign tissue specimens (5 ovarian and 5 uterine) will be collected from each institution, providing a total of 20 ovarian controls and 20 uterine controls. Ribbons of tissue will be prepared by the pathology associate investigators Brady and Miles in conjunction with histopathology technicians at both SMC and WBAMC. The paraffin embedded tissues will be transported in glass containers to the Department of Clinical Investigations at WBAMC and stored at -70 degrees Celsius until analysis. DNA will later be extracted and analyzed for the presence of HPV using Q-PCR. The analysis will specifically determine the presence of HPV viral types 6, 11, 16, 18, 31 and 33 in each of the specimens.

Progress: Although Dr. Maxwell has PCS'd from WBAMC, analysis is being conducted by the Immunology Section, DCI. Estimated completion date has changed form Sep 94 to Sep 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/31 STATUS: Terminated FY95

TITLE: Messenger Ribonucleic Acid (RNA) Expression of E6/E7 Oncogenes in Cervical Carcinoma

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, J Carlson, WF Nauschuetz, P Miles, KM Brady

MONITOR:

START DATE: May 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: RNA, E6/E7

Study Objective: The purpose of this retrospective study is to demonstrate the presence of increased E6/E7 expression in cervical tumors from past cervical cancer patients.

Technical Approach: A total of 50 cervical cancer specimens will be identified in a collaborative effort by investigators from both WBAMC and SMC. Ribbons of tissue will be prepared by the pathology associate investigators Brady and Miles in conjunction with histopathology technicians at both WBAMC and SMC. The paraffin embedded tissues will be transported in glass containers to the Department of Clinical Investigations at WBAMC and stored until analysis. Messenger RNA will later be extracted and complimentary DNA produced from corresponding E6/E7 sequences in the tissue sample. This complimentary DNA will then be quantitatively detected following PCR amplification. Positive and negative controls will be provided by cell lines SiHa and K562, respectively.

Progress: This protocol has been terminated due to technical difficulties and because Dr. Maxwell PCS'd June 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/34A STATUS: Terminated FY95

TITLE: The Use of Oxidized Regenerated Cellulose (Interseed) in Preventing Adhesions Associated with the Use of Marlex and GORE-TEX Meshes (*Oryctolagus cuniculus* model)

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

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

ASSOCIATE INVESTIGATOR(S): AP Soisson, RA Harris, M Wood, J Carlson

MONITOR:

START DATE: Aug 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Interseed, Marlex, GORE-TEX

Study Objective: The purpose of this prospective randomized study will be to determine whether the use of Interseed reduces intra-abdominal adhesions which normally accompany the use of Marlex and GORE-TEX when used as an abdominal wall prosthesis.

Technical Approach: A total of 50 rabbits will be used in the study. Each animal will be randomly assigned to one of two postoperative interval groups: 4 days or 4 weeks. Animals will then undergo surgery to create a full-thickness abdominal wall defect approximately 3 cm square. The defect will then be randomly repaired using one of five methods: 1) closure involving rotation of a 3x3 cm vascularized pedicle of external oblique muscle and fascia; 2) closure with a 3x3 cm piece of Marlex only; 3) closure with a 3x3 cm piece of Interseed bound to the back of a similar sized piece of Marlex; 4) closure with a 3x3 cm piece of GORE-TEX only; 5) closure with a 3x3 cm piece of Interseed bound to the back of a similar sized piece of GORE-TEX. All randomization will be performed using a pseudorandom number generating program. Upon completion of the assigned postoperative period, each animal will undergo euthanasia as described in animal procedures. The abdominal wall will then be dissected from each animal and the adhesive involvement quantified. When adhesions are present, calculation of area differential (equals pretreatment area minus posttreatment area) and percent improvement (equals area differential minus [area differential/pretreatment area] x100) will be performed to determine whether the use of Interseed reduces the extent of adhesion formation. Finally, a previously described subjective scale will be used to rate the overall tenacity of resultant adhesions (none=0; adhesions fell apart=1; adhesions lysed with traction=2; adhesions required sharp dissection for lysis=3).

Progress: This study was never started. Dr. Maxwell, principal investigator PCS'd and there was no interest among remaining residents to take over protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/29 STATUS: Ongoing

TITLE: Platelet Count Changes in Term, Low Risk Deliveries

PRINCIPAL INVESTIGATOR: CPT Roger J. Rembecki

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

ASSOCIATE INVESTIGATOR(S): P Bayliss

MONITOR:

START DATE: Aug 94 ESTIMATED COMPLETION DATE: Feb 95

KEY WORDS: Platelet Count, Low Risk Deliveries

Study Objective: Determine platelet count changes in term, low risk deliveries.

Technical Approach: We will review the platelet counts measured at parturition and post partum (less than or equal to 48 hours). Data will be analyzed to discover significant changes chronologically and significant differences between vaginal and cesarean deliveries.

Progress: No progress was reported.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/48 STATUS: Completed FY95

TITLE: Routine Thyroid Function Tests in Infertility Patients

PRINCIPAL INVESTIGATOR: CPT Pamel A. Schmagel

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

ASSOCIATE INVESTIGATOR(S): D Meyers, JC Webb, M Wood, JW Carlson

MONITOR: N/A

START DATE: Apr 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: TSH, Infertility Clinic, Ovulatory Function, Mid-Luteal Progesterone

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Study Objective: To further evaluate the necessity of routine thyroid function testing in the infertile female; especially those with normal ovulatory function.

Technical Approach: A retrospective review of patients who presented to WBAMC infertility clinic was performed. Demographics including the patient's age, gravity, parity, and menstrual history was also recorded. Charts were screened for the level of thyroid stimulating hormone (TSH). Patients with a TSH greater than 5.5 uIU/ml were considered hypothyroid. The charts of hypothyroid patients were then reviewed for menstrual history and function. Patients who were hypothyroid had their ovulatory function determined by mid-luteal progesterone, as measured on day 20-22 of the cycle. Patients were considered to have been ovulatory if their mid-luteal progesterone was greater than 6.5 ng/dl. If patients had mid-luteal progesterone less than 6.5 ng/dl on day 20-22 of cycle, amenorrhea or irregular cycles they were considered to be anovulatory.

Progress: The number of patient who's charts were reviewed were 1,635. This was a retrospective data collection study. This study was completed in FY95.

ABSTRACT: Recent literature suggests that thyroid function testing, in the absence of ovulatory dysfunction, is not necessary in the routine evaluation of infertility patients. Our objective was to evaluate the use of routine thyroid function testing in an outpatient infertility clinic population. A retrospective chart review was performed in 1,635 infertility patients who were evaluated at WBAMC between 1988 and 1995. Charts were screened for Thyroid Stimulating Hormone (TSH) values. Patients with an abnormal TSH had ovulatory function determined by the serum mid-luteal progesterone, irregular menses, or amenorrhea. By TSH values, 18 patients were found to be hypothyroid. Fifty percent (n=9) of these patients had a mid-luteal progesterone consistent with normal ovulatory cycles. Screening of thyroid function tests may be necessary in all infertility patients rather than only those with ovulatory dysfunction as previously reported.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/08A STATUS: Ongoing

TITLE: OB/GYN Bowel Training Utilizing the Pig Model

PRINCIPAL INVESTIGATOR: MAJ Julius Szigeti

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

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Jul 86 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Surgical Training in Residency - GI

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: The laboratory exercise described will concentrate on developing the surgeon's confidence in recognizing bowel injuries, resecting and anastomosing small bowel, and large bowel exteriorization. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of small bowel resection and re-anastomosis. The surgical site is then closed and the animal awakens from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of resecting the colon and creating a colostomy. Afterward, the surgical site will be closed and euthanasia administered while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Ongoing surgical training for residents using the pig model.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/33A STATUS: Ongoing

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

PRINCIPAL INVESTIGATOR: MAJ Julius Szigeti

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

ASSOCIATE INVESTIGATOR(S): M Wood

MONITOR:

START DATE: Mar 86 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Tubal Re-anastomosis, Surgical Training in Residency - Rabbit

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Study Objective: This training is designed to teach resident physicians the basic knowledge and operative skills required to perform microscopic tubal surgery.

Technical Approach: The laboratory exercise described 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. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of unilateral uterine cornua resection and re-anastomosis. The surgical site is then closed and the animal awakens from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted. The first microsurgical anastomosis site will be re-explored for patency and the training procedure will be repeated on the contralateral cornua. After completion of the procedure euthanasia will be administered as described below.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Ongoing resident training lab for microsurgical tubal re-anastomosis technique using the rabbit model.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 86/64A STATUS: Ongoing

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

PRINCIPAL INVESTIGATOR: MAJ Julius Szigeti

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

ASSOCIATE INVESTIGATOR(S): NA

MONITOR: NA

START DATE: Aug 86 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Surgery Training, Genitourinary Tract

Study Objective: This 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: The laboratory exercise described will concentrate on developing the surgeons confidence in recognizing GU injuries, resecting and anastomosing ureters, and reimplanting ureters into the urinary bladder. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery will consists of unilateral ureter resection and re-anastomosis. Upon completion of this procedure, the laparotomy incision will be closed and the animal awakens from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of transecting the contralateral ureter at the point of entry into the urinary bladder and reimplanting the ureter through the bladder wall. Afterward, the laparotomy incision will be closed and euthanasia administer while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Ongoing surgical training lab for residents using the pig model.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/23 STATUS: Completed FY95

TITLE: Determine if the seasonal variation in preterm birth exists in an arid environment in a military population.

PRINCIPAL INVESTIGATOR: CPT Nathan Tillotson

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

ASSOCIATE INVESTIGATOR(S): C Butterfield, S Borquaye, JS Bembry

MONITOR: NA

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Preterm, Seasonal

Study Objective: Determine if the inflammatory pap smear correlates with preterm delivery and if treating patients with inflammatory pap smears during pregnancy decreases the preterm delivery rate.

Technical Approach: Retrospective.

Progress: There has been a change in principal investigator from Dr. Tillotson to Dr. Bembry who PCS'd in the spring of 1995.

ABSTRACT: "Is there Seasonal Variation of Preterm Deliveries?"
Preterm deliveries (PTD's) are a leading cause of neonatal morbidity and mortality. Inspite of many different regimes of tocolytic therapy, improved patient education, and improved diagnosis provided by ultrasound. PTD's have remained over 9% of all live births over the past 40 years. This retrospective review is an attempt to determine if there are any environmental factors contributing to PTD's. The ration of total PTD's and non-iatrogenic PTD's to total deliveries for each month was plotted against time, average monthly temperature, total monthly precipitation, and the month of delivery. There was not trend noted by time, monthly temperature, or monthly precipitation. The plot of months of delivery did show an increase in preterm deliveries in April and November raising the question of a possible viral etiology, however this increase was not statistically significant.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/24 STATUS: Ongoing

TITLE: The Role Of The Inflammatory Pap Smear In Preterm Delivery

PRINCIPAL INVESTIGATOR: CPT Nathan Tillotson

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

ASSOCIATE INVESTIGATOR(S): C Butterfield, S Borquaye, JS Bembry

MONITOR:

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Nov 95

KEY WORDS: Pregnancy, Pap Smear, Inflammatory, Preterm

Study Objective: Determine if the inflammatory pap smear correlates with preterm delivery and if treating patients with inflammatory pap smears during pregnancy decreases the preterm delivery rate.

Study Design: Retrospective.

Progress: Number of subjects entered is 2300. The retrospective review entitled "The Role Of The Inflammatory Pap Smear In Preterm Delivery" is near completion. The preterm delivery rate for patients with dysplastic Pap smears was 10.67% (6/64), for those with inflammation and an underlying infection 5% (5/101) and for patients with simple inflammation 9.1% (8/73) having reviewed approximately 2,300 deliveries so far. These values will be compared to the baseline preterm delivery rate to determine their significance. The statistical analysis is still to be completed.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/28 STATUS: Completed FY95

TITLE: Efficacy of Routine Prolactin Screening in Infertile Women

PRINCIPAL INVESTIGATOR: CPT Joel Webb

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

ASSOCIATE INVESTIGATOR(S): MD Wood, K Eule

MONITOR: NA

START DATE: Feb 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Infertile Women, Serum Prolactin Level, Galactorrhea, Anovulation, Amenorrhea, Luteal Phase Defect

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Study Objective: To review the effectiveness of screening all infertile women with a random serum prolactin level, versus screening only a selected subgroup of infertile women with galactorrhea, anovulation, amenorrhea, or documented luteal phase defect.

Technical Approach: Data will be collected in a retrospective fashion from the existing infertility convenience files in the clinic. The files of patients that are documented with elevated prolactin levels will have the following data documented:

- Age, gravity, & parity
- Prolactin level (with repeat levels, broken down into ranges 20-99 & >100)
- Subsequent diagnostic workup (CT, MRI, visual fields, etc.)
- Associated Infertility Diagnosis
  - Anovulation
  - Luteal Phase Defect
  - Combination (w/ tubal factor, cervical factor, etc.)
  - Unexplained
- Presence or absence of galactorrhea
  - Contributing factors
    - Recent delivery or pregnancy
    - Breast feeding
    - Medications
    - CNS tumor or head trauma
    - Renal insufficiency
    - Chest wall lesions
    - Acromegaly
- Menstrual history

If the data is significant, a cost analysis will compare the use of routine screening versus screening only the indicated population.

Progress: 1105 patient records were reviewed. Estimated completion date has been changed from May 95 to Jun 95. Abstract submitted by Dr. Webb.

ABSTRACT: Elevated prolactin levels have been implicated to play a role in infertility ranging from anovulation and amenorrhea to luteal phase defect. To determine the effectiveness of routine prolactin screening in evaluating the infertile woman, records were reviewed from 1105 infertility evaluations over a 5 year period. Of the 31 women with documented hyperprolactinemia (greater than 20 ng/mL on two separate random evaluations), 22 women had one or more of the following findings: galactorrhea, irregular menses, or ovulatory dysfunction documented by basal body temperature charts or mid-luteal progesterone levels. By screening only the subset of women with galactorrhea, irregular menses, or ovulatory dysfunction, 29% of infertility patients with elevated serum prolactin levels would not have been detected.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/28 STATUS: Ongoing

TITLE: Evaluation of Phenobarbital in the Prevention of Intraventricular Hemorrhage in the Very Low Birth Weight Infant (<1500gms or 32 Weeks)

PRINCIPAL INVESTIGATOR: CPT Gary C. Wharton

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

ASSOCIATE INVESTIGATOR(S): FE Harlass

MONITOR:

START DATE: Oct 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Intraventricular Hemorrhage, Phenobarbital

Study Objective: To retrospectively compare WBAMC records where the current standard of care includes phenobarbital administration to any mother suspected or imminently delivering an infant 1500gms or less, to those of R. E. Thomason General Hospital (RETGH), where the current standard of care does not include this administration. Through this comparison, an attempt will be made to demonstrate that such administration is beneficial in reducing the incidence and severity of intraventricular hemorrhage in this population as previously suggested.

Technical Approach: This will be a retrospective case controlled analysis of maternal and infant records. WBAMC's data will be with the data from RETGH.

Progress: Protocol delayed due to lack of research time for computation of data. Still interested in project hope to complete in very near future. All data collected but not analyzed. Estimated completion date has changed from Jan 95 to indefinite.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/38 STATUS: Ongoing

TITLE: Sterilization Regret in a Military Population

PRINCIPAL INVESTIGATOR: MAJ Michael Wood

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

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Jul 94 ESTIMATED COMPLETION DATE: Sep 94

KEY WORDS: Sterilization

Study Objective: Among women in a military population who seek reversal of tubal ligation, to determine what factors they identified as responsible for their desire to overturn a permanent procedure.

Technical Approach: Questionnaire

Progress: Study has just begun. There is no data to report as yet.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/30 STATUS: Completed FY95

TITLE: Envision 2000 - A Forecast of the Issues and Associated Competencies required by Federal Nurse Executives into the 21st Century

PRINCIPAL INVESTIGATOR: CPT Ronald A. Duperroir

DEPARTMENT: Office of the CofS FACILITY: William Beaumont Army Medical Ctr

ASSOCIATE INVESTIGATOR(S): None

MONITOR: NA

START DATE: Oct 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Delphi Method

Study Objective: Envision 2000 is a graduate management project that seeks to identify major future nurse executive issues beyond the year 2000. The project will further expound on anticipated skill, knowledge, and ability requirements that professionals in the field expect will be needed to successfully operate in a complex and fluid environment.

Technical Approach: The technique being employed is known as the Delphi Method. The Delphi was initially developed by the Rand Corporation and is a means of eliciting and gaining expert group judgments. Panelists are not required to travel; nor is advanced reading required. It has three hallmark features: 1) all responses are anonymous and expert opinions are obtained by questionnaire; 2) interaction among panelists is accomplished at each round by synthesizing all responses, informing each panelist of the group's current position and redistributing the questionnaire results for further consideration; and 3) the group generally achieves a consensus after a few rounds.

Progress: This study was completed in FY95. CPT Duperrior left WBAMC due to PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/39 STATUS: Ongoing

TITLE: Evaluation of PCR for Use in Diagnosis of Microbiologic Infections

PRINCIPAL INVESTIGATOR: CPT Steve D. Mahlen

DEPARTMENT: Pathology FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): M Lund

MONITOR: NA

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Sep 95

KEY WORDS: TB, HCV, HPV, DNA Synthesizer

Study Objective: To evaluate gene amplification for the ID of TB, multi-drug resistant TB, HCV, and/or HPV.

Technical Approach: Primers for specific infectious agents will be manufactured in DCI using the DNA Synthesizer. Microbiology, DPALS and DCI will standardize those primers using positive controls for known positives. After standardization, procedures will be recorded.

Progress: No progress was reported Principal investigator was deployed to Haiti.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/15 STATUS: Completed

TITLE: Comparing the Laurin and Merchant Radiographs with Computerized Tomography in Assessment of the Patellofemoral joint

PRINCIPAL INVESTIGATOR: CPT Bryan C. King

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JS Jackson, RL Gore

MONITOR: NA

START DATE: Jan 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Laurin, Merchant Radiographs, Computerized Tomography

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Study Objective: Comparison of Laurin and Merchant radiographs with Computerized Tomography to determine which test is the most sensitive in predicting patellofemoral pathology.

Technical Approach: Single centered, prospective

Progress: This study was completed FY95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/26A STATUS: Ongoing

TITLE: The Use of Pneumatic Tourniquet in Extremity Surgery Following End-to-End Arterial Anastamoses in the Caprine Model.

PRINCIPAL INVESTIGATOR: LCDR Harold T. Pye

DEPARTMENT: Orthopedics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): SD O'Donnel, RA Harris

MONITOR: NA

START DATE: Apr 95 ESTIMATED COMPLETION DATE: Sep 95

KEY WORDS: Pneumatic Tourniquet, Blood Pressure, Caprine Model

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Study Objective: The objective of this study is to evaluate the effect of the use of a pneumatic tourniquet on a vascular repair when the tourniquet is used proximal to that repair during the immediate postoperative time period (one to fourteen days).

Technical Approach: The use of a tourniquet after repair of blood vessels has not been properly studied. Unfortunately, many times when repair of a blood vessel in an arm or leg is needed, other problems are also present that need surgery. The usual technique to repair these problems requires the use of a tourniquet to keep bleeding from obstructing the view of the surgeon. Healing of the blood vessel tissues after repair is a process that gives the repair strength over time. Since placing a tourniquet on an arm or leg will pool blood in the blood vessels, pressure can build up over a short period of time and break the repair of the blood vessel. This protocol is an attempt to determine in the goat model the shortest period of time after repair of a blood vessel that will allow the use of a tourniquet without damage to the repaired blood vessel. By determining the shortest period of time required, a patient can have other problems repaired in a timely manner that may well increase function, or even use, of the arm or leg in the future.

Progress: This study was postponed by principal investigator but will continue at a later date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/55A STATUS: Ongoing

TITLE: The Use of Demineralized Bone Matrix and Titanium Cage in Interbody Fusion of the Spine Using the Goat (*Capra hircus*) Model.

PRINCIPAL INVESTIGATOR: MAJ William R. Stevens

DEPARTMENT: Orthopedics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): L Hoban-Stevens, R Copeland, G Gill, J Cartwright

MONITOR: MAJ Richard A. Harris

START DATE: Oct 95 ESTIMATED COMPLETION DATE: Jun 96

KEY WORDS: Spinal Fusion, Animal Models

Study Objective: To determine the effectiveness of a new demineralized bone matrix (DBM) and titanium mesh cage (TMC) construct in achieving anterior interbody fusion of the spine in a goat model.

Technical Approach: For some injuries of the spinal column, a common surgical procedure is to attempt to fuse the bones of the affected area to provide a stable section of the spinal column to relieve the patient's pain, other symptoms, and worsening of the condition. In the past, surgeons have used many techniques to produce this fusion. Of the current techniques, packing of the affected section of the spinal column with bone taken from the hip or enclosing the area in a special rigid metal cage is popular. Both of these techniques have a number of problems. One of the biggest problems is not achieving the fusion of the area.

This study will combine the use of a special rigid metal cage with a new form of specially processed bone material on a created spinal column defect that requires fusion. The bone material should offer many important advantages over bone donated from the patient's hip. The most probable advantage should be greatly increased healing of the defect and production of an excellent fusion. Twenty goats will be used to test the new bone material in the both the neck and chest areas of the spinal column. If fast fusion results occur as expected, this study would be an important step in getting the new bone material into human trials.

Progress: At this time, the first animal in the protocol has been completed. This animal was used for harvest of long bones, and refinement of surgical procedure. No significant obstacle to the planned procedure was encountered. In fact, the anterior lumbar fusion was far easier than anticipated. Blood loss for the procedure was under 10cc. Long bones were forwarded to Osteotech Corporation for processing.

Refinement of the protocol is requested, and formal request will follow within one week. Briefly, the investigators wish to delete the cervical portion of the study in order to minimize animal morbidity and potential interference with the lumbar study. A separate cervical study may be undertaken at a later date. Also, the investigators wish to place a third cage in the lumbar spine filled with gelfoam as a negative control. The procedure done on animal number one makes clear that this will be possible.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/01 STATUS: Ongoing

TITLE: Retrospective Analysis of the Association between Attention Deficit Disorder and Central Auditory Processing Problems

PRINCIPAL INVESTIGATOR: COL Alva W. Atkinson

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): R Dennis, MC Knott, D Penow

MONITOR: NA

START DATE: Jan 92 ESTIMATED COMPLETION DATE: May 96

KEY WORDS: ADD, CAPP

Study Objective: Two hypotheses will be addressed: (1) Central auditory processing problems (CAPP) occur in high frequency (>20%) among patients diagnosed with Attention Deficit Disorder (ADD) and (2) the incidence of CAPP in ADD will be represented equally among the subtypes of ADD (ADD with hyperactivity and ADD without hyperactivity).

Technical Approach: The medical records of patients assessed by Developmental Pediatrics Clinic for ADD and by Audiology and Speech/Language Clinics during 1989-1990 will be reviewed. Data will be collected for age, grade, diagnoses, auditory and language evaluation results. Specifically, data from the audiologic assessment data from the SCAN (central auditory processing battery) will be collected. From the language evaluation, the overall receptive and expressive language assessments (normal, mild moderate, or severe) and the TOKEN test results will be noted. Data will be studies for frequencies and association using descriptive and simple comparative statistics. The investigators consider this a pilot study which will potentially be the basis of a prospective, more tightly controlled large study.

Progress: There has been 100 subjects entered in the study. Slow progress but ongoing at this time. The estimated completion date has been changed from Jan 94 to May 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/27 STATUS: Completed FY95

TITLE: Male Adolescent Attitudes about Condom Use and Barriers to Effective Use

PRINCIPAL INVESTIGATOR: LTC Denise C. Cabeza

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JD Foley

MONITOR: NA

START DATE: Feb 94 ESTIMATED COMPLETION DATE: Aug 95

KEY WORDS: Male, Adolescent, Attitudes, Condom

Study Objective: 1. To identify the obstacles encountered in obtaining condoms.
2. To understand the reasons why teens do not use condoms.
3. To identify factors which result in condom failure or improper use.

Technical Approach: All adolescent males between the ages of 15 to 21 years who seek health care at the Adolescent Clinic WBAMC, will be provided with a self-administered questionnaire. Teens who are not sexually active will complete demographic data only. Teens, who acknowledge past sexual activity on the questionnaire, will continue on and complete the remainder of the questionnaire. Responses will be made by circling the best answer from five choices arranged on a "Likert" scale format for each question. The respondent will remain anonymous. Completed questionnaires will be placed by the patient in a defined, secure receptacle. Participation in the study will be completely voluntary. At the end of 6 months this data will be collected, analyzed and submitted as an article format to the Dept. of Clinical Investigation.

Progress: 420 subjects have been entered in this study with no noted adverse reactions.

Abstract: To investigate possible barriers to effective condom use by sexually active adolescent males. An anonymous self administered 37 item questionnaire was distributed to 420 males ages 15 through 21 who sought health care at an adolescent clinic. The instrument consisted of 6 questions of a demographic nature and 31 items which inquired about issues on beliefs we hypothesized might be a barrier to effective condom use. The responses to these items were in a Likert scale format with low number selections likely to be barriers and higher number
selections unlikely to be barriers to effective condom use. 260 of the 420 survey respondents were sexually active (61.9%). Neither stated religion nor ethnicity had any correlation with the choice to be sexually active or condom use. Age of the respondent did, with 36.4% of 15 yr. olds acknowledging sexual activity with step wise increments with each advancing year of age. 100% of the 21 yr. olds had been sexually active. 59% of the sexually active sample had used a condom with first intercourse and 43% of respondents claimed to always use condoms. There was no association found between those who failed to use condoms and responses to hypothesized barriers including condom cost, condom availability, embarrassment with condom purchasing, embarrassment with partner, or education level obtained. In fact among those in school, there was negative association of educational level and condom use. Higher use rates were found among those in lower grade levels. (P=.0001 via chi-square) The lowest mean use level, not attending school. There was some association of strong fear of AIDS with

condom use (P -.0893) but not with fear of other STD's (P=0.1434). There was an association of condom use with first intercourse and continued condom use (P = .0000). 29% reported condom breakage but no relationship was found between breakage and how adolescent carried condoms or where they stored them. Continued effective condom use by adolescents may be enhanced if condoms are used with first intercourse. Efforts to emphasize this appear to be important.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/45 STATUS: Ongoing

TITLE: Up-Front Intensive 6-MP/Methotrexate VS Up-front Alternating Chemotherapy for Acute Lymphoblastic Leukemia in Childhood. POG: 9006

PRINCIPAL INVESTIGATOR: MAJ Kelly Faucette

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Swaney

MONITOR: MAJ Robert Sheffler

START DATE: Jul 93 ESTIMATED COMPLETION DATE: Feb 96

KEY WORDS: Methotrexate Leukemia

Study Objective: Our objective is to continue this patient on the randomized trial on which he was started at WRAMC. The objective of this study is to compare, in a randomized trial of children with Acute Lymphoblastic Leukemia (ALL) who are at a higher risk for relapse, the efficacy and toxicity of A: 12 early intensive courses of IV methotrexate (MTX) plus IV 6-mercaptopurine (6-MP) vs. B: 12 early intensive courses of alternating intensive chemotherapy combinations (6-MP/MTX), VM-26/Ara-C, vincristine/ prednisone/ PEG-L-asparaginase/ daunomycin/ Ara-C.

In addition the study is designed to determine if RBC methotrexate/folate levels can be correlated with sites of relapse and event-free survival.

Technical Approach: In summary the protocol is designed to test a potentially more successful method of achieving remission, and maintaining a complete remission until a cure is achieved in a large number of high risk pediatric patients with ALL. Multiagent chemotherapy will be given using standard drugs, but changing the effective oral 6-MP to an IV form to achieve better and more standard drug levels, and drug kinetics, to potentially increase cell kill and effectiveness of therapy. In addition alternating Daunomycin and VM-26, which share some mechanism of cell kill may increase ultimate cell kill and thus survival per the Goldie-Coldman hypothesis.

Progress: We continue with one patient in remission in the WBAMC arm of this protocol. The patient remains stable with no significant side effects. Should another child be diagnosed with leukemia and fit the criteria for the study, we would anticipate enrolling him/her as well. The estimated completion date has changed from Indefinite to Feb 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 89/91 STATUS: Terminated FY95

TITLE: Protocol for Determining the Prevalence of Drug Affected Babies in the Military Population

PRINCIPAL INVESTIGATOR: MAJ S Gwynne Geddie

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): None

MONITOR:

START DATE: Oct 89 ESTIMATED COMPLETION DATE: Dec 95

KEY WORDS: Meconium, Neonate, Drugs, Cocaine, Marijuana, Newborn, Drug Affected

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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.

Amendment #1 (Sep 90): Added new associate investigators and amended para 7d and 7g.

Amendment #2 (Nov 91): Changed PI to CPT Knight; deleted associate investigators Gordon & Valerie Bell, Howard Oaks & Ingrid Chamales; added LTC Rosa, MAJ Jesse and Dr. Handel as associate investigators. Amendment extended study completion date to Oct 92 and added R.E. Thomason General Hospital (RETGH).

Amendment #3 (Sep 92): Added CPTs Murphy and Maxwell as associates; added another paragraph to status; changed Plan to read: Due to the recently initiated "early discharge" policy for selected newborns at WBAMC, difficulties in obtaining sufficient uncontaminated urine specimens (non-invasively) have arisen and make this source for analysis of illicit drugs impractical. Collection of meconium specimens from newborns at WBAMC is much easier than obtaining uncontaminated urine specimens (non-invasively). WBAMC DCI currently has the technical ability to analyze meconium specimens for illicit drugs and their metabolites; changed 7.d to incorporate previously approved changes (Amendments #1 & #2); amended Duration of Study read: Through October 1992 or until 400 paired maternal urine/neonatal meconium specimens have been obtained; added references (4) and (5).

Progress: This protocol was terminated by principal investigator because they were unable to get GCMS analysis to work.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/43 STATUS: Completed FY95

TITLE: A Phase III Randomized, Double-Blind, Placebo-Controlled Trial of Monthly RespiGam (RSVIG-IV) Infusions for Reduction of the Rate of RSV Hospitalization in Premature Infants with Bronchopulmonary Dysplasia

PRINCIPAL INVESTIGATOR: MAJ Bruce E. Pichoff

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): M Rettke, S Lindow, S Remich, C Moreno, A Varner

MONITOR: MAJ William Raszka

START DATE: Sep 94 ESTIMATED COMPLETION DATE: June 95

KEY WORDS: RespiGam, Infants Bronchopulmonary Dysplasia

Study Objective: The primary objective of this study is to determine the safety and efficacy of monthly RespiGam prophylaxis in reducing the rate of RSV hospitalization in premature infants and infants with BPD. Secondary objectives include determining the effect of monthly RespiGam prophylaxis among study participants on the following hospital parameters: (1) total days of RSV-related hospital stay, (2) supplemental oxygen requirement and oxygen saturation, (3) WHO LRI score, (4) frequency of ICU care and total days of ICU stay, and (5) frequency and total days of mechanical ventilation.

Technical Approach: See basic protocol (pages 14-37). There will be no deviations by WBAMC from the basic plan.

Progress: This protocol enrolled a total of 15 patients, the last of which was seen on 15 Jun 95. Final monitoring visit was conducted on 24 Jul 95. Dr. Pichoff PCS'd July 95 from WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/25 STATUS: Terminated

TITLE: Prevalence of Hypogammaglobulinemia in Children with Recurrent/Persistent Otitis Media

PRINCIPAL INVESTIGATOR: MAJ William Raszka

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Apr 92 ESTIMATED COMPLETION DATE: Jul 94

KEY WORDS: Hypogammaglobulinemia, IgG Deficiency

Study Objective: To determine the prevalence and extent of IgG deficiency in otitis prone children.

Technical Approach: Patients meeting the criteria below will have the study explained to them, and after informed consent is obtained, blood will be drawn for 1) complete blood count with differential, 2) quantitative immunoglobulin A, E, G, M, and 3) immunoglobulin G subclasses. If patient has an acute infection with fever at the time of clinic visit, the tests will be drawn at the next visit that the patient is seen and the acute infection is resolved.

Children 1 to 10 years of age presenting to pediatric clinic with history of 3 episodes of acute otitis media in the preceding 6 months, or duration of serious effusions greater than or equal to 3 months after an episode of acute otitis media, will comprise the study population.

All patients will be followed by the principal investigator and the lab results explained. Treatment options/considerations based on clinical and laboratory evaluations will be discussed and most appropriate and acceptable therapy will be implemented.

Progress: Dr. Raska left WBAMC due to ETS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/21 STATUS: Ongoing

TITLE: Immunoregulation and Pathogenesis of Symptomatic, Primary HIV-1 Infection

PRINCIPAL INVESTIGATOR: MAJ Timothy Endy

DEPARTMENT: Medicine FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): ML Robb

MONITOR:

START DATE: Jan 94 ESTIMATED COMPLETION DATE: Jan 97

KEY WORDS: Immunoregulation, Pathogenesis, HIV-1

Study Objective: The objective of this study will be to determine and follow the genotypic expression of the HIV from the earliest moments of infection and the very specific patient immune response to the evolving genotypic expression. We also hope to characterize viral burden and correlate viral burden with genotypic expression, specific immune responses, and clinical disease. This will be important as it is not known which factors (viral specific or host specific) that lead to the expression of HIV virus during the acute retroviral syndrome and the ability of the host's immune response to at least initially control the viral infection. A better understanding of this mechanism may lead to effective immunotherapeutic approaches to this disease.

The role of the WBAMC PI will be in identifying patients with acute retroviral syndrome and following the patients clinically. WBAMC (the PI) will be responsible for blood drawing and shipment of clinical specimens.

Technical Approach: The study will be prospective, natural history. Details are lengthy and are specified in the original protocol. Copies are on file at DCI.

NOTE: This is a Tri-Service protocol which originated at Walter Reed Army Medical Center and was approved at the Human Subject Research Review Board meeting in May 93.

Progress: A single patient from WBAMC has been enrolled. There were no complications to her blood draws. Her virus is an unusual strain of the typical North American Clade. In October 95 MAJ Endy took over this protocol. MAJ Raska ETS'd in Sep 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/35 STATUS: Ongoing

TITLE: Knowledge of Immunization Practices Among Pediatric Health Care Providers in Medical Centers

PRINCIPAL INVESTIGATOR: MAJ William Raszka

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR: NA

START DATE: July 94 ESTIMATED COMPLETION DATE: Feb 95

KEY WORDS: Immunization, Health Care Providers

Study Objective:
1) To determine the body of knowledge regarding current pediatric immunization practices that pediatric housestaff have at each level of training.
2) To determine the body of knowledge regarding current pediatric immunization practices that pediatric staff have by type of specialty.
3) To determine if housestaff from military programs are any different from civilian programs.

Technical Approach: Survey using a validated survey form. The survey was validated by administering it to pediatric infectious disease specialists and general pediatricians not participating in the study.

Progress: There have been 200 subjects entered in this study. Eight centers completed the survey. Data has been entered and has not been analyzed. The estimated completion date has been changed from Jan 95 to Feb 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/17 STATUS: Completed

TITLE: Auralgan®, a Topical Analgesic, versus Placebo in the Symptomatic Treatment of Otalgia Associated with Acute Otitis Media

PRINCIPAL INVESTIGATOR: CPT Scott Sheets

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MAJ William R. Raszk, Jr.

MONITOR:

START DATE: Feb 95 ESTIMATED COMPLETION DATE: Sep 95

KEY WORDS:

Study Objective: The objective of the study will be to determine if Auralgan´, applied to the external auditory canal, provides symptomatic relief of the otalgia associated with acute otitis media.

Technical Approach: Study design: prospective, randomized, double blinded, placebo controlled study

Progress: Dr. Raska left WBAMC due to ETS.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/55 STATUS: Ongoing

TITLE: Parents Opinions about Disorders of Vigilance in their Children with Attention Deficit Disorder

PRINCIPAL INVESTIGATOR: LTC Robert Sayers

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): AW Atkinson

MONITOR:

START DATE: Aug 91 ESTIMATED COMPLETION DATE: Jan 94

KEY WORDS: Primary Disorder of Vigilance (PDV), Attention Deficit Hyperactivity Disorder

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Study Objective: Through the use of a parent questionnaire, determine the incidence of symptoms of Primary Disorder of Vigilance (PDV) in a population previously diagnosed with Attention Deficit Disorder (ADD) or being evaluated for ADD. Furthermore, this project will seek to differentiate this symptom cluster (PDV) as either a unique diagnosis or a subtype of ADD.

Technical Approach: The Developmental Pediatric Clinic at WBAMC follows approximately 180 patients with the diagnosis of ADD. Patients who are taking medication for ADD are seen in clinic at least every three months and parents come in for a brief interview on progress and refill every month. During one of these routine follow-ups, the parent will be asked to complete a questionnaire which addresses the major criteria for PDV for both the child and his/her parents. These criteria are taken directly from the article "Primary disorder of vigilance: A novel restlessness, and sleepiness" by Weinberg describing this "new" disorder.

Progress: .Number of subjects entered in the study is 120. At this time data collection has been completed but data analysis is still ongoing.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/41 STATUS: Completed FY95

TITLE: Hepatitis B Virus Immunization Rates Among Adolescents

PRINCIPAL INVESTIGATOR: CPT Steven E. Spencer

DEPARTMENT: Pediatrics FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): W Raszka

MONITOR:

START DATE: Aug 94 ESTIMATED COMPLETION DATE: Mar 95

KEY WORDS: Hepatitis B, Immunization, Adolescents

Study Objectives: To determine the HBV immunization rate among adolescents seen at WBAMC with both high and low risk behaviors for acquiring HBV infection.

Technical Approach: Medical records of adolescent patients seen at the WBAMC adolescent clinic will be reviewed. Information recorded will include evidence of sexual activity (as noted in chart), immunization record, last name, family member prefix, and last four digits of sponsor's social security number. This is to ensure that there is no duplication of chart reviews. All identifiers will be purged after data collection and analysis.

Progress: 185 subjects were entered in this study.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/07 STATUS: Terminated

TITLE: Clinical Comparability of Two Once-Daily Forms of Diltiazem: Effect of Substitution on Blood-Pressure Control & Resource Utilization

PRINCIPAL INVESTIGATOR: MAJ John D. Grabenstein

DEPARTMENT: Pharmacy FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): P Stanley, RP Potyk

MONITOR:

START DATE: Jun 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Diltiazem, Interchangeability, Formulary Substitution, Hypertension, Blood Pressure

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Study Objective: To assess the comparability of clinical effects of *Cardizem*^{R} *CD* (Marion Merrill Dow Inc., Prescription Products Division, Kansas City, MO 64114) and *Dilacor XR*^{TM} (Rhône-Poulenc Rorer Pharmaceuticals Inc., Collegeville, PA 19426) in the treatment of hypertension. The Food & Drug Administration has already found evidence of the safety and efficacy of these two dosage forms for this indication.

Technical Approach: Retrospective analysis of patient records (medical records and/or convenience charts) to determine blood pressures during the course of routine medical practice, at medical treatment facilities that have already switched from *Cardizem*^{R} *CD* to *Dilacor XR*^{TM} at the direction of the MTF's Pharmacy & Therapeutics (P&T) Committee.

Progress: We have been unsuccessful in obtaining sufficient patient records that document the patients' blood pressures. Only one site with sufficient data was identified: Irwin Army Hospital, Fort Riley Kansas. Since this hospital is outside of William Beaumont Army Medical Center's regional purview, the study at WBAMC is terminated. The study will continue at Fort Riley.
Conclusions: No conclusions will be drawn until the data from Irwin Army Hospital, Fort Riley, Kansas, can be analyzed.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/38 STATUS: Terminated FY95

TITLE: T-lymphocyte (CD4) counts in patients with diagnosed tuberculosis or other mycobacterial disease who are not infected with the Human Immunodeficiency Virus.

PRINCIPAL INVESTIGATOR: COL Arthur Morton

DEPARTMENT: Preventive Medicine FACILITY: William Beaumont AMC

ASSOCIATE INVESTIGATOR(S): R Lundy, MA Escobedo, P Frank

MONITOR:

START DATE: Nov 94 ESTIMATED COMPLETION DATE: Nov 95

KEY WORDS: T-Lymphocyte Counts, Tuberculosis Mycobacterial

Study Objective: (1) Determine if T-lymphocyte (CD4) cell counts are depressed in patients with mycobacterial disease.

(2) Determine if T-lymphocyte (CD4) cell counts predict treatment success in patients with mycobacterial disease.

Technical Approach:

(1) Criteria for initial enrollment of subjects:

(a) Anti-tuberculosis drug naive

(b) Mycobacterial disease suspected because of a "positive" acid-fast smear of a clinical specimen

(c) Anti-Human Immunodeficiency Virus drug naive.

(d) Patients who present at the El Paso Health and Environmental District or at WBAMC for care.

(2) The initial evaluation will include the following:

(a) A specially designed questionnaire which requests information about: Name, social security number (or another number used for tracking purposes), age, sex, ethnic origin, country of birth, months of residence outside of the U.S., months of residence in the U.S.; history of cough, fever, sweats, weight loss, hemoptysis: prior tuberculosis treatment: IPT, BCG, multiple drug therapy; and AIDS risk factors: multiple sex partners, sex with men, IVDU, frequent blood transfusions, tissue transplants; and other immunosuppressing factors: end-stage renal disease (dialysis), diabetes mellitus (uncontrolled, insulin dependent, or non-insulin dependent), low body weight (less than 80% of ideal), previous partial or complete gastrectomy, regular alcohol use, regular steroid use, cancer, leukemia, cancer chemotherapy, cancer radiation therapy, or regular cyclosporin use.

(b) A serum HIV antibody test.

(c) Sputum or other clinical specimens for culture and sensitivity at days 0,1,2, 30, 90, and 180.

(d) A single Posterior-Anterior x-ray study of the chest will be done at day 0 and will be interpreted by the principal investigator. Each study will be classified into one or more of the following categories:

[(1)] No evidence of past or present tuberculosis.

[(2)] Evidence of healed primary tuberculosis (Ghon lesions or calcified hilar lymph nodes).

[(3)] Infiltrates associated with hilar adenopathy suggestive of an active infectious process consistent with a diagnosis of non-cavitary pulmonary tuberculosis, mycobacterioses, or Pneumocystis Caranii pneumonia.

[(4)] Cavitation consistent with a diagnosis of active pulmonary tuberculosis.

[(5)] Pleural thickening with or without pleural effusion consistent with a diagnosis of pleural tuberculosis.

[(6)] Multiple lesions consistent with a diagnosis of miliary tuberculosis.

[(7)] Other significant abnormalities of the lung which may or may not be associated with tuberculosis.

[(8)] No evidence of chronic obstructive lung disease (COLD).

[(9)] Generalized pulmonary congestion consistent with a history of smoking or other chronic inflammatory lung diseases.

[(10)] Increased lung volume consistent with a diagnosis of early COLD.

[(11)] Increased lung volume with decreased markings consistent with a diagnosis of moderately advanced COLD.

[(12)] Severely increased lung volume, decreased markings, and bleb formation suggestive of advanced COLD.

(e) Each film will also be interpreted by a radiologist for evidence of other pulmonary abnormalities such as lung cancer, enlarged heart, degenerative changes in the thoracic spine, etc.

(f) A tuberculin skin test by the Mantoux method using 5 tuberculin units (0.1 ml.) of Purified Protein Derivative (PPD).

(g) A physical examination which will include measurement of height and weight, examination for and evaluation of a scar suggestive of BCG vaccination and for lymphadenopathy.

(h) A complete blood count.

(i) A Westergren Erythrocyte Sedimentation Rate.

(j) A serum ALT (SGOT) test.

(3) A T-lymphocyte (CD4) cell count below 400 cells per cubic millimeter will be considered to be evidence of a significantly depressed count. These patients will be referred to physicians of their choice for further evaluation.

(4) This study design parallels the routine evaluation done by physicians when evaluating patients for evidence of disease caused by the various members of the family Mycobacterium. Additional studies not normally included in the routine evaluation will include the demographic and historical information questionnaire, a T-lymphocyte (CD4) cell count and a HIV test. All patients will be re-evaluated at 30, 90, and 180 days. At the time of the subsequent evaluations, the T-lymphocyte (CD4) cell count, HIV test, and sputum or other clinical specimens will be obtained for direct microscopic examination for acid fast bacilli and culture will be repeated.

(5) Since there is a long lead time required to obtain mycobacterial culture results and since there is a 6 week to 6 month "window" period between the time of HIV infection and a "positive" HIV serum antibody test, all patients suspected of having a disease caused by a member of the Mycobacterium family will be eligible for initial enrollment. Subjects who are subsequently found to be infected with HIV or who do not receive a final clinical diagnosis of mycobacterial disease will be excluded later.

Progress: This protocol was never started and was administratively terminated by DCI due the principal investigator's retirement from the Army in April 1995. Response was submitted by COL Oronoz, C, Preventive Medicine Service.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/50 STATUS: Terminated

TITLE: The Application of Civilian Pre-Authorization Standards to Inpatient Admissions in a Military Treatment Facility

PRINCIPAL INVESTIGATOR: CPT Ronald Szyjkowski

DEPARTMENT: Region FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): LA Popejoy, JJ James

MONITOR:

START DATE: Jul 93 ESTIMATED COMPLETION DATE: Jan 94

KEY WORDS: Pre-Authorization Standards, Inpatients Admissions

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Study Objective: To disprove the hypothesis that civilian healthcare industry pre-authorization program can be effectively applied in a military treatment facility to reduce inpatient expense.

Technical Approach:
Phase I: A study of a small sampling of previously admitted patients. Outpatient chart information on randomly selected cases will be evaluated by experienced civilian peer review nurses using Interqual screening criteria. Subsequently, civilian practicing specialists will review copies of the entire inpatients chart of the same admission episodes.

Phase II: The same peer review evaluation and subsequent physician review of the inpatient chart on concurrent, contemporary admissions. The sample size is estimated at approximately 25 admissions from each of the major inpatient departments.

Phase III: Peer review nurse evaluation for pre-authorization approval of 100% of admissions during a 3-4 month period of time and selective physician review of inpatient charts of these same admissions. A coincident training and education module for providers will be instituted.

Progress: Could not locate principal investigator, has departed WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/61A STATUS: Ongoing

TITLE: Comparison of Current Antiadhesive Treatments in the Rat Tensiometer Model

PRINCIPAL INVESTIGATOR: MAJ Chester C. Buckenmaier

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Richard A. Harris

START DATE: Oct 95 ESTIMATED COMPLETION DATE: Feb 96

KEY WORDS: Antiadhesive, rat

Study Objective To compare and contrast the various current methods of adhesion prevention following laparotomy utilizing the objective rat tensiometer model for evaluating adhesion formation.

Technical Approach: Abdominal adhesions following laparotomy develop in two-thirds of patients and are the most common cause of acute and recurrent small bowel obstruction (Thompson et al 1989). Peritoneal adhesion formation represents a significant problem for the surgeon, not only because of the morbidity associated with adhesive disease but also the heightened difficulty inherent with subsequent abdominal operations in patients with extensive adhesion formation. Historically, a number of antiadhesive agents have been proposed and tested with a spectrum of success. Unfortunately these antiadhesives have been tested on a number of different animal models making comparison of the various agents difficult. Additionally, most of the models have utilized subjective scoring criteria when
evaluating adhesion formation which is inherently biased. In the proposed study the most successful antiadhesive agents, as defined in the current literature, will be compared utilizing an objective rat tensiometer model for adhesion formation as described by Harris *et al* 1995.

Progress: This study has not started it is pending financial support.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/03 STATUS: Terminated

TITLE: Clinical Results of the Biomet Total Knee Arthroplasty Utilizing the Lone Star Extraarticular Alignment Jig

PRINCIPAL INVESTIGATOR: CPT Jefferson J. Cartwright

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): T Scully, MG Anderson

MONITOR:

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Arthoplasty, Lone Star Jig

Study Objective: To determine if an extraarticular alignment jig allows for more accurate cuts in TKA as evidenced by improvement in radiographic findings and clinical outcome.

Technical Approach: Retrospectively review all TKA patients over the last 2-3 years (approximately 50 patients) who had Biomet implants utilizing the Lone Star Knee jig. Radiographs as well as clinical follow up utilizing the knee society rating score will be performed.

Progress: Follow up available on study subjects is inadequate to obtain meaningful data. Only 8 of over 60 subjects had all necessary pre-op and post-up x-rays and clinical data. 8 of 60 is not adequate. Therefore, study has been terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/14A STATUS: Completed FY95

TITLE: Repair of Common Bile Duct Injury Using Fibrin Glue in the Anesthetized Porcine Model *(Sus scrofa)*

PRINCIPAL INVESTIGATOR: CPT Robert Craig

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): None

MONITOR: MAJ Richard A. Harris

START DATE: Mar 95 ESTIMATED COMPLETION DATE: Jan 95

KEY WORDS: Fibrin Glue

Study Objective: To evaluate the efficacy of repairing injuries to the common bile duct through the laparoscope using fibrin glue.

Technical Approach: This study is being conducted to assess if the common bile duct can be repaired through the laparoscope using fibrin glue. The study will be carried out using thirteen pigs, three for refinement of technique and ten in the study group. Each anesthetized pig will undergo laparoscopic cholecystectomy. A choledochotomy will be made under direct vision to simulate inadvertent injury to the common bile duct, as might take place when obtaining an intra-operative cholangiogram. The duct will then be repaired by placing a wire through the cystic duct and into the common bile duct, past the site of the injury. Next a balloon-tipped catheter will be advanced over the wire and into position in the bile duct so as to stent open the lumen of the duct during the repair. Next the hole in the duct will be re-approximated using a single absorbable suture. The area of injury will then be sealed using fibrin glue. The balloon-tipped catheter will then be withdrawn and the cystic duct closed. The animals will then be allowed to recover from the anesthetic. One animal will then be euthanized at the end of one week, two weeks, and then at two week intervals. The repair will be studied using retrograde Cholangiography to look at duct patency, and to detect any stricture present. The animal will also be evaluated for evidence of bile leak and pre-operative and post-operative blood specimens will be taken for evaluation of liver function. The specimens will also be sent for histopathologic examination, to evaluate the presence of fibrin glue at different times in the healing process and to evaluate for healing of common duct. The results of the repairs will be compared against the known control of open repair of the common bile duct with t-tube drainage.

Progress: All animal procedures have been completed. Data are currently being analyzed.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/58A STATUS: Ongoing

TITLE: *In vivo* Biodistribution of Radiolabeled Fibrinogen-Coated Lecithin/Cholesterol Vesicles in the Anesthetized Rat Model

PRINCIPAL INVESTIGATOR: CPT Robert Craig

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Holcomb, S Bhattacharyya, P Alsbugh

MONITOR: MAJ Richard A. Harris

START DATE: Oct 95 ESTIMATED COMPLETION DATE: Nov 95

KEY WORDS: Non-fribrinogen-coated Liposomes, Blood Clotting

Study Objective: To determine whether Fibrinogen-coated liposomes will have the same in vivo biodistribution as that of non-fibrinogen-coated liposomes.

Technical Approach: This study will attempt to determine how a new chemical compound, designed to lessen the loss of blood after a major injury, is distributed throughout the body. The new experimental compound consists of a fatty carrier portion linked to the blood clotting portion. A total of thirty rats will be divided into three groups of 10 rats each. Under anesthesia, one group will have the new compound with a low level and short-lived radioactive substance attached to it injected into the blood stream. Another group will be injected with only a radioactive labeled fatty carrier portion of the compound. The last group of ten rats will be injected with only the radioactive substance without the experimental compound. The images obtained by the radioactive scanning will be compared to determine the distribution of the experimental compound in the body. Tissue specimens from the euthanized rats will be examined for gross as well as for microscopic abnormalities.

Progress: This protocol has not been started.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/37 STATUS: Ongoing

TITLE: Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin

PRINCIPAL INVESTIGATOR: LTC Thomas S. Gormley

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): L Maldonado

MONITOR: MAJ Michael D. Bagg

START DATE: Jun 95 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: D_2, CAP

Study Objective: The objective of this study is to compare the clinical effectiveness of a new dosing regimen 500 mg (QD) for administering flutamide to the currently indicated dosing regimen of 250mg q 8 hours according to:

Percent of patients normalizing PSA

Quality of life differences between the two Regimens.

Technical Approach: This is a Phase IV, multicenter trial in which 400 available patients with *de novo* Stage M metastatic prostate cancer will be randomized to one of two treatment groups.

Group 1: flutamide, 250 mg Q8H + LHRH/orchidectomy

Group 2: flutamide, 500 mg QD + LHRH/Orchidectomy

Progress: Two patients have been enrolled in study. The estimated completion has been changed from Dec 95 to indefinite. This study is awaiting final approval on a collaborative research agreement .

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/40A STATUS: Completed FY95

TITLE: Ballistic Testing of Fibrin Adhesive Dressing in the Caprine Model

PRINCIPAL INVESTIGATOR: MAJ John B. Holcomb

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): RA Harris, SP Hetz, J Gillman, RA Adams

MONITOR: CPT Andrew Wilkinson

START DATE: Aug 95 ESTIMATED COMPLETION DATE: June 96

KEY WORDS: Fibrin glue, Extremity, GSW

Study Objective: To evaluate the ability of the fibrin dressing to stem hemorrhage in a ballistic animal model.

Technical Approach: Hemorrhage kills 20-38% of soldiers dying on the battlefield (1). Hemorrhage kills up to 47% of soldiers after they reach a hospital (2). The U. S. Military has used the same techniques, gauze pressure dressing and tourniquets, to control bleeding since at least WW II. The high death rate from preventable hemorrhage points us in the direction for combat casualty research opportunities (3). A new fibrin dressing that essentially places fibrin glue on the hemorrhaging area is currently available. It has been tested in a surgically induced femoral artery wound and found to significantly reduce bleeding and maintain mean arterial pressure (4). This dressing needs to be tested in an animal model under ballistic injury conditions. This testing must be done to determine it's usefulness in a war type injury. The lives saved if this and other experiments are successful would be tremendous.

The caprine model will be used with a standard high velocity wound to the hind leg, after induction of general anesthesia with non-invasive blood pressure monitoring. A standard Army field dressing will be applied immediately to one-half of the animals while being transferred to the caprine OR for monitoring of blood pressure and blood loss. The other one-half will have a fibrin dressing applied in the same fashion. After one hour the dressing will be removed and animals euthanized. The results will be compared.

Progress: 18 subjects were entered in this study. Dr. Holcomb, principal investigator submitted an abstract:

ABSTRACT: Hemorrhage control is vital to survival, both on the battlefield and in civilian practice. Up to 10% of deaths in Vietnam were from uncontrolled extremity hemorrhage, yet field hemorrhage control methods have not significantly changed for 2000 years (gauze packing and ligatures). To address this issue, a new dry fibrin glue dressing has been developed.

At an approved animal facility, ballistic injury was created and hemorrhage control studied in a randomized fashion in 18 anesthetized goats (average weight- 60 kg). Pairs of Army field and dry fibrin glue dressings were applied on entrance and exit wounds within 5 seconds of wounding. Animals were monitored for blood loss and mean blood pressure for one hour post-injury. Necropsy was performed and injuries documented.

Injuries were uniform between the two groups, including transacted femoral arteries and veins, shattered femurs and large exit wounds. Mean blood loss was 139 cc in the dry

fibrin dressing group and 375 cc in the regular gauze dressing group (p=.02). Mean arterial pressure was maintained at 90 mm Hg in the dry fibrin dressing group and decreased to 76 mm Hg in the regular gauze dressing (p=.03).

Dry fibrin glue has all the-benefits of regular liquid fibrin glue, with many other advantages. It is a powder, storable at room temperature, and no mixing is required. Efficacy of fibrin glue is dependent on fibrinogen content. Most liquid preparations do not exceed 30mg/ml. The dry powder preparation has 1800 mg of fibrinogen on each dressing. Use of this dressing markedly decreased blood loss and preserved blood pressure in a ballistic injury model. The concept of decreasing blood loss and preserving blood pressure by using only a new type of dressing is appealing in its simplicity. The implications of decreased hemorrhagic morbidities, i.e. transfusion, sepsis and multi-organ failure, should be significant.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/22 STATUS: Terminated

TITLE: Iontophoresis: Efficacy of Use in the Treatment of Plantar Fascitis

PRINCIPAL INVESTIGATOR: 1LT Penny P. Griffith

DEPARTMENT: Physical Therapy FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Mar 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Iontophoresis, Plantar Fasciitis

Study Objective: To compare the effects of iontophoresis delivering the dexamethasone corticosteroid to the effects of iontophoresis delivering distilled water when treating plantar fascitis.

Technical Approach: A randomly assigned double blind study. Patients referred to the physical therapy clinic with the diagnosis of plantar fasciitis will be asked to take part in this study. Subjects participating will undergo standard physical therapy evaluation of range of motion, palpation, ambulatory status, foot biomechanical analysis, and a thorough subjective evaluation. Baseline data will be stored. Each subject will be randomly assigned to one of two treatment groups:

Group 1 (treatment): This group will receive iontophoresis with dexamethasone every other day for 4 sessions.

Group 2 (sham/placebo): This group will receive iontophoresis with distilled water every other day for 4 sessions.

An analysis of variance will be used to detect significant differences between the two groups for each of the tested variables. Significance will be set at 5% level ($p<0.05$).

Progress: Principal Investigator terminated the study because it was never started.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 90/42A STATUS: Ongoing

TITLE: Fiberoptic Endoscope Cholecystectomy in the Porcine Model

PRINCIPAL INVESTIGATOR: LTC Stephen P. Hetz

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Oct 90 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Resident education, laparoscopic, Fiberoptic Endoscope Cholecystectomy

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Study Objective: To determine feasibility of conducting cholecystectomies at WBAMC with endoscopic equipment rather than a laparoscope. The experience gained by the professional staff will enable them to develop proficiently to perform such operations in human patients and to determine if additional equipment will be required for the conduct of this procedure.

Technical Approach: No surgical procedures will be conducted without the administration of general anesthesia. Anesthesia will be administered and monitored by Dr. Harris and animal care specialists in the Biological Research Service. The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. After the skin is prepped, an insufflation needle will be inserted and the abdomen will be filled with CO_2. A trocar will be placed near the umbilicus for introduction of the fiberoptic video endoscope to enable monitoring of the procedure on a video screen. Two to three additional trocars will be placed for introduction of alligator forceps. The cystic duct and artery will be bluntly dissected free, double ligated or clipped, and transected. The gall bladder will be dissected free from the liver bed by sharp, blunt, and electrosurgical techniques. The laser may be used to control hemorrhage and to cut adventitial tissue. Once free from hepatic parenchyma, the gall bladder will be approximated to the body wall and drained with suction. After the bladder is decompressed, it will be pulled through one of the central trocar puncture sites.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No progress was reported by principal investigator.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/13A STATUS: Ongoing

TITLE: Resident Training in Laparoscopic and Open Stapling Techniques

PRINCIPAL INVESTIGATOR: LTC Stephen P. Hetz

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): W Bowland

MONITOR:

START DATE: Mar 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Laparoscopic Training

Study Objective: The objectives are to teach the surgical staff and residents proper thoracic and abdominal laparoscopic procedures utilizing stapling instruments and suturing techniques and proper open stapling techniques utilizing the multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers.

Technical Approach: Both video laparoscope and open surgical training techniques will be conducted in the porcine model. The experimental design is such that one or both of the techniques will be conducted on each animal. When both laparoscopic and open techniques are utilized, the laparoscopic techniques will precede the open procedures. The determination of the techniques to be conducted will be done at the time of the training session and will be dependent upon the knowledge and expertise of the residents and staff being trained. After anesthesia induction, the following procedures will be conducted:

(1) Video laparoscopic - Abdominal: cholecystectomy, gastrectomy, small bowel resection, nephrectomy, hysterectomy, splenectomy and partial hepatectomy. Thoracic: esophagectomy, pulmonary resections and vagotomies will be performed utilizing the various stapling instruments and liga clips.

(2) Laparotomy (Open) - Abdominal: A midline incision from the xiphoid process to the pubis will be made. Then a multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers will be utilized to complete end-to-end, side-to-side colon and small intestinal anastomosis. Additionally, anastomosis will be completed between portions of the small intestine; from the small intestine to stomach and colon; and between the colon and rectum. Transection of the stomach, colon and small intestine will also be performed. Pulmonary: Transection of pulmonary tissue, bronchi, pulmonary arteries and veins will be performed utilizing the various instruments through an intercostal incision.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No progress was reported by principal investigator.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 91/15A STATUS: Completed

TITLE: Certification Training: Advanced General Surgery Laser Laparoscopic Procedures in the Porcine Model

PRINCIPAL INVESTIGATOR: LTC Stephen P. Hetz

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): W Bowland

MONITOR:

START DATE: Jun 91 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Laser Laparoscopy Training

Study Objective: To provide training and certification of General Surgery Surgeons in laser laparoscopic cholecystectomy, hernia repair, and appendectomy. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. After the skin is prepped, an insufflation needle will be inserted and the abdomen will be filled and maintained with 15 mm Hg pressure of CO_2. A trocar/cannula will be placed near the umbilicus for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. The cystic duct and artery will be bluntly dissected free, double ligated or clipped, and transected. The gallbladder will be dissected free from the liver bed by sharp, blunt, electrosurgical and laser techniques. Once free from hepatic parenchyma, the gallbladder will be approximated to the body wall, decompressed and pulled through one of the central trocar puncture sites.

Other advanced laparoscopic procedures will include hernia repair and appendectomy. Laparoscopic cannulas will be repositioned as necessary for subsequent procedures to enable visualization and tissue manipulation. Hernia repair- A defect will be created in the internal inguinal ring by sharp and blunt technique. Subsequently, the created hernia will be repaired by laparoscopic suture and stapling techniques. Appendectomy - The distal cecum will be isolated and mobilized. The distal segment will then be resected and closed by laparoscopic suture and stapling techniques. The appendix will be approximated to the body wall with large graspers and removed through a central puncture site.

Training is scheduled for six (6) WBAMC surgeons and ten (10) Sierra surgeons.

Amendment (AUC Approved Apr 91) increased the number of training sessions, animal requirements and resource requirements to accomodate training of 32 physicians.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal

Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: This study was completed in FY95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/29 STATUS: Ongoing

TITLE: A Comparison of Antiseptic Impregnated Central Venous Catheters and Standard Central Venous Catheters in Catheter Related Bloodstream Infection

PRINCIPAL INVESTIGATOR: MAJ Darwin D. Karr-Peterson

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): B Burlingame, SP Hetz, J Holcomb

MONITOR: MAJ Martin A. Schrieber

START DATE: Sep 95 ESTIMATED COMPLETION DATE: Sep 97

KEY WORDS: AICVS's CRBSI's, Intensive Care Unit

Study Objective:The purpose of this study is to determine whether or not the use of AICVC's will result in fewer CRBSI's by comparing the infection rate between standard CVC's and AICVC's being used in the same intensive care unit during the same time period.

Technical Approach: This study will be confined to WBAMC surgical intensive care patients, will be prospective, and randomized. Treatments will be randomly assigned in blocks of two with patients assigned to blocks, in the order that they volunteer for the study.

Progress: This study has not yet begun.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/13 STATUS: Ongoing

TITLE: A Prospective Randomized Clinical Controlled Trial of Laparoscopic Vs. Open Appendectomy

PRINCIPAL INVESTIGATOR: CPT Thomas McCrorey

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): S Hetz

MONITOR: MAJ Jay W. Carlson

START DATE: Dec 94 ESTIMATED COMPLETION DATE: Jun 96

KEY WORDS: Surgery, Accute Appendicitis, Laparoscopic Techniques

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Study Objective: Compare the postoperative courses; time to discharge, time until return to full activity; operative time, and wound infection and complication rate.

Technical Approach: All patients presenting to the surgery service with a diagnosis of acute appendicitis will be offered randomization to either the open or laparoscopic arm of the trial. Laparoscopy will be pursued in all in whom it is technically possible. The only exclusion will be made for women in the third trimester of pregnancy, under the assumption that the laparoscopic technique is more risky than the open. Conversion to open appendectomy will not be done for other reasons, including for the ruptured or gangrenous appendix.

Progress: There have been 30 subjects entered in the study with no noted adverse reactions to date. The estimated completion date has changed from Dec 95 to Jun 96.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/59 STATUS: Ongoing

TITLE: A Randomized, Double-Blind, Multicenter Trial Assessing the Efficacy of Intravenous Cp-116,517 Followed by Oral Cp-99,219 Compared to Intravenous Imipenem/Cilastin Followed by Oral Amoxicillin/Clavulanic Acid for the Treatment of Complicated Intra-Abdominal Infections

PRINCIPAL INVESTIGATOR: MAJ Martin A. Schrieber

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): S Hetz

MONITOR: MAJ Timothy Endy

START DATE: Nov 95 ESTIMATED COMPLETION DATE: May 96

KEY WORDS: Intra-abdominal Infections, Cp-116, 517, Oral Cp-99,219

Study Objective: To evaluate the safety and efficacy of intravenous CP-116,517 followed by oral CP-99,219 in the treatment of complicated intra-abdominal sepsis. This regimen will be compared to intravenous imipenem/cilastin followed by oral amoxicillin/clavulanic acid in a parallel group of patients. WBAMC'S role in this study will include patient recruitment, patient treatment, data collection and submission of data to PFIZER and the National Medical Research Corporation.

Technical Approach: This is a prospective, randomized double-blind study comparing intravenous CP-116,517 and oral CP-99,219 to intravenous imipenem/cilastin followed by oral amoxicillin/clavulanic acid in patients with evidence of a systemic inflammatory response and proven intra-abdominal infection. The maximum length of total treatment will be 14 days. The efficacy of the two regimens will be evaluated based on clinical response and bacteriological response. All patients will be monitored for adverse effects of the two regimens.

Progress: No progress reported to date. The protocol start date is Nov 95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 95/60 STATUS: Withdrawn FY95

TITLE: A Randomized, Double-Blind, Multicenter Trial Assessing the Safety and Efficacy of a Single Intravenous Dose Of Cp-116,517 Compared with Cefotetan for the Prophylaxis of Infection Following Elective Colo-Rectal Surgery

PRINCIPAL INVESTIGATOR: MAJ Martin A. Schrieber

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): S Hetz

MONITOR: MAJ Timothy Endy

START DATE: Nov 95 ESTIMATED COMPLETION DATE: May 96

KEY WORDS:

Study Objective:The purpose of this study is to compare the safety and efficacy of CP-116,517 with cefotetan in prophylaxis for elective colo-rectal surgery. WBAMC'S role in this study will include patient recruitment, patient treatment, data collection and submission of data to the PFIZER Corporation and the National Medical Research Corporation.

Technical Approach: This study is a prospective, randomized, double-blind trial comparing CP-116,517 with cefotetan in prophylaxis for elective colo-rectal surgery. After obtaining informed consent, patients undergoing elective colo-rectal surgery will be randomized to receive a single pre-operative dose of one of the two drugs. Patients will then be assessed for signs of infection during their hospital stay and at follow-up. Assessment will include physical examination and laboratory testing looking for signs of infection or adverse affects of the treatment.

Progress: This protocol was not started because the multi-center trial enrollment was completed before WBAMC's final approval of the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/56 STATUS: Ongoing

TITLE: The Use of Marcaine in the Prevention of Post Operative Pain in the Laparoscopic Cholecystectomy Patient

PRINCIPAL INVESTIGATOR: CPT James Sippo

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): SP Hetz, JH Chiles

MONITOR:

START DATE: Oct 93 ESTIMATED COMPLETION DATE: Oct 94

KEY WORDS: Marcaine Pain Laparoscopic Cholecystectomy

Study Objective: To determine the effectiveness of Marcaine in minimizing post-opeative pain in the laparoscopic cholecystectomy patient.

Technical Approach: The study will be a single center, double-blind study which will be prospective in nature.

Progress: Ninety subjects were entered in the study. Fifteen subjects withdrew secondary to conversion to open technique or loss to follow-up. There were no noted adverse reactions. Project is currently ongoing to collect results from 70 patients and is currently under investigation to see if enough data has been collected to form a conclusion to the study.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 93/24 STATUS: Completed

TITLE: Pediatric Thyroidectomy: Complications and Strategy

PRINCIPAL INVESTIGATOR: LTC Troy M. Reyna

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Jan 93 ESTIMATED COMPLETION DATE: Jan 94

KEY WORDS: Thyroidectomy

Study Objective: To determine by retrospective analysis of charts of children undergoing thyroid surgery; what mistakes or acts of omission contributed to the reported complications. Through this study the authors would hope to arrive at a recommended technique for surgical management of thyroid disease in children that optimally treats malignant and benign processes with minimal morbidity.

Technical Approach: A retrospective analysis of all cases of surgically-treated thyroid disease in CONUS will be conducted. The cases will cover the twelve year period 1980-1992. Evaluation will be detailed demographic data, including pathology, type of operation, results, and complications. Analysis will include study of operative reports with regard to documentation and visualization of all parathyroid glands and appropriate-sided recurrent laryngeal nerves and other pertinent anatomical structures.

Progress: Principal investigator is no longer at WBAMC. Protocol has been completed.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 89/25A STATUS: Ongoing

TITLE: Vascular Changes Associated with Stress Reaction of Bone in the Rat

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): JM Uhorchak

MONITOR: NA

START DATE: May 89 ESTIMATED COMPLETION DATE: Jun 96

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 . 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.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: All goals of this research project have been successfully completed except for histologic study of sections of the legs (tibias) of rats subjected to cyclic loading stress. The specimens have been maintained in the preserved state. However, all efforts produce thin sections of undecalcified, cleared, rat legs suitable for histologic staining have been only partially successful. Therefore, the specimens have not been processed. Since decalcification results in some loss of histologic detail, we have been reluctant to use this process prior to histologic staining. However, we have reluctantly decided to accept the slight loss of histologic detail resulting from decalcification and will submit the specimens for routine histologic study after decalcification. This will permit completion of the study. The estimated completion date has changed from 1 June 1995 to 30 June 1996. No adverse reactions reported to date.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/20 STATUS: Terminated FY95

TITLE: Patient functional outcome, range of motion, and single leg stance differences between two total knee replacement rehabilitation protocols

PRINCIPAL INVESTIGATOR: LTC Noreen M. Rossi

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S):

MONITOR:

START DATE: Feb 94 ESTIMATED COMPLETION DATE: Jun 95

KEY WORDS: Total Knee Replacement Rehabilitation

Study Objective: Determine the more effective post-operative rehabilitation of total knee replacement patients.

Technical Approach: All subjects will have pre-operative testing which will include functional assessment score based on results of the Knee Society Clinical Rating System (6, 7) and modified Noyes Knee Questionnaire (11), knee range of motion, timed single leg stance, and gross manual muscle testing of both knees. Subjects will be randomly divided into two groups matched for age, gender, weight, surgeon, prosthesis, preoperative diagnosis and intactness of ACL/PCL ligament. Group 1 will receive post-operative physical therapy according to our present protocol which includes standard strengthening and range of motion exercises, CPM use, ambulation, gait and transfer training; Group 2 will receive ambulation, gait and transfer training only. Interim assessments will be performed at one, three and six month intervals post-operation.

This will be a blind study - neither the researchers evaluating the subjects nor the surgeons performing the operations will know the treatment group to which the patient was assigned.

Mean, standard deviation, and standard error of the mean will be used to describe each of the variables. One way analysis of variance with repeated measures will be used to detect significant differences for each of the tested variables induced by the two protocols employed. Significance will be chosen at the 5% level ($p<0.05$).

Progress: No response received from principal investigator in FY95. DCI has administratively terminated protocol due to unsuccessful attempts to locate principal investigator who is no longer at WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 89/70A STATUS: Completed FY95

TITLE: Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model

PRINCIPAL INVESTIGATOR: CPT Charles Whitlow

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): MF Rhodes, M Kestner

MONITOR: NA

START DATE: Nov 90 ESTIMATED COMPLETION DATE: Jun 94

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: This study will be conducted in two phases. Phase I will be to determine the maximum graft length allowing successful tracheal reconstruction. Phase II will be designed to determine the minimum interval for subcutaneous implantation required to have successful tracheal reconstruction.

In both Phase I and II the grafts will be implanted in two stages. The first stage will consist of implantation of the Gore-Tex prosthesis in the subcutaneous tissue with a silastic stent to keep the lumen patient and induce fibrous capsule formation. The animals will then be recovered from anesthesia and monitored for a prescribed period of time. The second stage will consist of harvesting the graft, after an appropriate amount of time is allowed for ingrowth of fibrous tissue, and replacing a segment of trachea with the graft. The animals will then be recovered and observed over a period of three weeks time while receiving prophylactic antibiotics.

Initially, two animals will be used to develop the technique and verify suitability of the rabbit as a model. The graft length for these animals will be 1 cm for each rabbit. The graft will remain in the subcutaneous pouch for three weeks prior to the tracheal reconstruction. Three weeks following the tracheal reconstruction, the rabbits will be evaluated to verify patency, infection rates, and degree of re-epithelization in the following manner: The animals will be anesthetized with spontaneous ventilation occurring. Utilizing telescopic bronchoscopy the lumen will be inspected for stenosis. The animal will be euthanatized and the graft cultured and histologically examined for infection and tissue morphology, respectively.

If the outcome of the pilot is successful and the model appears to be appropriate, then the study will proceed as follows:

Phase I: Rabbits will be divided into four groups of six rabbits each:

Group I - 3 cm. prothesis length
Group II - 4 cm. prothesis length
Group III- 5 cm. prothesis length
Group IV - 6 cm. prothesis length

The grafts in these animals will be evaluated at intervals of 4 days, 1 week, 3 weeks, 6 weeks, 9 weeks, and 12 weeks. The evaluation will consist of direct laryngoscopy and bronchoscopy with video recording of the procedure and computer analysis of the dynamic change in lumen size with inspiration and expiration.

Criteria for a failed graft will be 30% obstruction of the resting lumen size or a dynamic decrease to 30% of the lumen diameter with respiratory movement. Brush biopsies of the lumenal surface will be taken for bacterial culture and for microscopic evaluation of lumen epithelium.

All surgical and bronchoscopy procedures will be conducted only after animals are appropriately anesthetized as stated below. If unable to prevent animal pain or suffering following procedures, the respective rabbits will be euthanatized according to methods stated below. Any animals that die or are euthanatized prior to the termination of the experiment will be necropsied to determine the cause of death, if applicable, and to evaluate the graft sites grossly and microscopically.

With the exception of 8 long term animals, all remaining animals will be euthanatized 12 weeks following the tracheal reconstruction. The grafts will then be excised and examined grossly and microscopically. Two of the remaining animals from each group will be observed for a total of 6 months to determine if any long term complications occur.

Phase II: After determination of the maximum graft length allowing successful reconstruction, the interval between subcutaneous implantation and transfer of the graft for tracheal reconstruction will be evaluated. On this basis the minimal allowable time between subcutaneous transplantation of the Gore-Tex graft and the tracheal reconstruction can be determined. This will be the final phase of the study as planned. Four groups of six animals each will be required. The graft will be implanted as described in Phase I.

Grafts will be harvested as follows:

Group I - one week
Group II - two weeks
Group III- three weeks
Group IV - four weeks

Following harvesting of the PTFE graft and tracheal reconstruction, each group of animals will undergo evaluation as described in Phase I.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Thirteen rabbits were used in FY93. Improvements in surgical technique have greatly enhanced the success rate for these implants. Problems with stenosis and infection, both of a chronic nature, remain as complications. Principal investigator CPT Canfield has departed WBAMC and is now deployed in Somalia. CPT Charles Whitlow has assumed duties as principal investigator. MAJ Mark Kestner has been added as an associate investigator. This study was completed in FY95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/18A STATUS: Completed FY95.

TITLE: Thoracoscopic Introduction of Microfibrillar Collagen for Inducing Pleural Symphysis in the Porcine Model (*Sus scrofa*)

PRINCIPAL INVESTIGATOR: CPT Charles Whitlow

DEPARTMENT: Surgery FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): S Hetz, R Craig

MONITOR: NA

START DATE: Feb 94 ESTIMATED COMPLETION DATE: Jan 95

KEY WORDS: Thoracoscopic Pleudesis (Chemical, Talc), Symphysis

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Study Objective: To use thoracoscopic techniques for the introduction of microfibrillar collagen in the pleural cavities of pigs to induce pleural symphysis.

Technical Approach: Eighteen adult pigs will be divided into three groups. After undergoing general endotracheal anesthesia (as later described in Part VII, paragraph 9), a 10mm incision will be placed in the lateral chest at the sixth intercostal space. A 10mm thoracoscope will then be introduced and exploration of the pleural cavity performed. A 5mm thoracoport will be placed to facilitate exploration. In six animals (Group A) no further procedure will be performed. A chest tube will be inserted in the thoracoport and residual air removed. The incisions will be closed with absorbable suture and dressed. The animal will be awakened, extubated and returned to the holding area and kept without restrictions. Postoperative analgesia will be under the direct supervision of the staff veterinarian. In six animals (Group B), after exploration is performed mechanical pleurodesis will be performed by abrading the parietal pleura using a gauze sponge introduced through the thoracoport. A third group of six animals (Group C) will undergo thoracoscopic exploration followed by instillation of microfibrillar collagen through the thoracoscope. The removal of residual air, wound closure and postoperative care will be the same in Groups B and C as was described for Group A. At weekly intervals for six weeks one animal from each group will be euthanized. The animals will be necropsied by the investigators. An estimate of gross pleural symphysis will be made and described as a percentage of total pleural surface. Using a tensiometer the lung will be separated from the chest wall at multiple points to judge the degree of pleural symphysis. Finally, microscopic sections of the parietal and visceral pleura will be examined to assess the degree of inflammation and fibrosis. Examiners for all three methods of assessing degree of symphysis will be blinded with regards to the group from which each animal came.

Progress: To date 15 pigs have been pleurodesed and euthanized. Microscopic and gross examination has been performed on those animals. Three more animals will be pleurodesed on 5 Oct 94 and euthanized within the ensuing 6 weeks. Tensiometry will be performed on all specimens following completion of pleurodesis on all 18 animals. The estimated completion date has changed from Aug 94 to Jan 95. This study was completed in FY95.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 92/11A STATUS: Ongoing

TITLE: Emergency Life Support Training for Combat Medics in the Small Ruminant (Ovine or Caprine) Animal Model

PRINCIPAL INVESTIGATOR: 2LT Hector Vega

DEPARTMENT: ADA FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): J Walls

MONITOR: NA

START DATE: Jan 92 ESTIMATED COMPLETION DATE: Indefinite

KEY WORDS: Emergency Life Support

Study Objective: This training will enhance the combat medical aidman's (Medic's) capabilities of administering emergency lifesaving procedures to patients with emergency medical conditions which require establishment of airways, venous access, and chest trauma management.

Technical Approach: The emergency life support training program is designed for medics who are responsible for providing first to third echelon care to the critically injured patient (echelon 1- self & buddy aid; echelon 2- combat lifesaver; echelon 3- medical specialist). Procedures taught will be according to the American College of Surgeons (ACS) Committee's Advanced Trauma Life Support Course. Initial assessment and management of specific types of injuries are presented to the student through lecture and slide presentations and a written examination. Students who successfully complete lecture and examination requirements, then rotate through animal laboratories associated with the lecture content previously presented. The animal laboratory allows 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 laboratory is approximately 2-3 hours per cycle. Each animal station will consist of one instructor and no more than four to five students.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: A total of 18 combat medics and physician's assistants completed the ATLS training program under this protocol in FY94. After action reports and critiques indicated that this training was very well received and judged as extremely valuable in familiarizing emergency medical personnel in actual hands-on life saving techniques.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 88/52A STATUS: Ongoing

PRINCIPAL INVESTIGATOR: (Interim) MAJ Richard A. Harris

DEPARTMENT: 3ACR FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): NA

TITLE: Combat Trauma Life Support Procedure in the Sheep Model

MONITOR: NA

START DATE: Oct 88 ESTIMATED COMPLETION DATE: Indefinite

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 include:

1. Cricothyroidotomy
2. Venous Cutdown
3. Intubation
4. Chest Trauma Management
    a. Needle decompression
    b. Tube thoracostomy

ATLS training manuals will be used for each training procedure.

Progress: This protocol has provided extremely valuable training for medical personnel of a deployable, combat-ready unit. Each trainee has benefited from hands-on techniques essential to saving lives on the battle field. Maximum use of each animal model was assumed during the procedure. Critiques following the procedures by the trainees and associate instructors have been very positive.

A total of 64 combat medics and physician's assistants completed the ATLS training program under this protocol in FY95. No adverse reactions were reported to date. Training under this protocol is expected to decrease with the relocation of the 3d ACR to Fort Carson, CO in FY96. The interim Principal investigator is MAJ Harris, Chief, Biological Research Service.

DETAIL SUMMARY SHEET

DATE: 1 October 1995 PROTOCOL #: 94/44A STATUS: Ongoing

TITLE: Gene Amplification as a Tool for the Rapid and Direct Diagnosis of *Mycobacterium bovis* and *Mycobacterium tuberculosis* in Dairy Cattle

PRINCIPAL INVESTIGATOR: John B. Westover, DVM

DEPARTMENT: USDA FACILITY: William Beaumont Army Medical Center

ASSOCIATE INVESTIGATOR(S): WF Nauschuetz, S Mahlen, SD Pillai

MONITOR: NA

START DATE: Oct 94 ESTIMATED COMPLETION DATE: Dec 94

KEY WORDS: Mycobacterium Tuberculosis, Mycobacterium Tuberculosis

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Study Objective: The purpose of this study will be to demonstrate the presence of *M. bovis* and *M. tuberculosis* in nasal swabs and milk samples from dairy cattle, as well as sputum samples from humans. A rapid diagnostic test for mammalian *Mycobacterium* species utilizing quantitative PCR techniques is to be evaluated as the primary objective for this project.

The study proposes to introduce the Polymerase Chain Reaction (PCR) technology for the identification of *M. tuberculosis* and *M. bovis*. Veterinary Services, APHIS, USDA will participate in a joint investigation with the Department of Clinical Investigation, WBAMC and the El Paso City/County Health District to investigate the sensitivity of PCR compared to routine TB culture and susceptibilities for the detection of *M. tuberculosis* and *M. bovis*. The principal investigators are working towards an agreement with management from TB quarantined dairies in Texas and dairies at risk for the infection in Chihuahua, Mexico to acquire clinical specimens for PCR and TB culture evaluation.

The data derived from this study can be used to evaluate and establish the El Paso-Juarez region as a high-risk area for bovine and human forms of tuberculosis, and provide some insight on the dynamics of *M. tuberculosis* and *M. bovis* in human and livestock populations. The implementation of the PCR amplification techniques for the rapid detection of TB is to be evaluated for field application in an endemic region.

Technical Approach: EXPERIMENTAL DESIGN: Amplification of the IS6110 sequence in *M. bovis* and *M. tuberculosis* will be optimized with primers IS1 (5'- CCTCGCAG CGTAGGCGTCGG-3') and IS2 (5'-CTCGTCCAGCGCCGCTTCGG-3'). These primers will be used to amplify DNA from an ATCC strain of *M. tuberculosis* (Eisenach, 1991). Amplifications will be run on the Perkin-Elmer 9600. The amplification cycle will be 95°C, 65°C and 72°C. Length, and number, of cycles will be determined during optimization.

The presence of amplified mycobacterial DNA will be detected by electrochemiluminescence using the automated Perkin-Elmer QPCR 5000. Amplified DNA will be hybridized to the specific detection probe (5'-CTGCCCAGGTCGACACAT-3').

DESCRIPTION OF PROCEDURES, TECHNIQUES, OR TESTS: Specimen material, in the form of nasal swabs and milk samples, will be collected from cattle maintained at local commercial dairies. Microbial determination for *M. bovis* and *M. tuberculosis* will consist of

standard PCR amplification procedures conducted within the Department of Clinical Investigation, with histopathologic and bacterial culture techniques performed within the Department of Pathology. No surgical procedures or invasive techniques are to be utilized as a result of this protocol.

Progress: This study has just started therefore no progress has been reported.