Department of Clinical Investigation

Annual Research Progress Report

Fiscal Year 2001

Madigan Army Medical Center
Tacoma, Washington

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	30 September 2001	Annual 1 October 2000 - 30 September 2001

4. TITLE AND SUBTITLE
Annual Research Progress Report
Department of Clinical Investigation

5. FUNDING NUMBERS

6. AUTHOR(S)
Barbara Jones Troy Patience
Paul Froude Genie Hough
Mary Porreca

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Department of Clinical Investigation
Madigan Army Medical Center
Bldg. 9040, Reid St, Rm G-15-C2
Tacoma, WA 98431-1100

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

Clinical Investigation Regulatory Office
ATTN: MCCS-GCI
1608 Stanley Road, Suite 2, Bldg. 2268
Fort Sam Houston, TX 78234-5055

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
THE FINDINGS IN THIS REPORT ARE NOT TO BE CONSTRUED AS AN OFFICIAL DEPARTMENT OF THE ARMY POSITION UNLESS SO DESIGNATED BY OTHER AUTHORIZED DOCUMENTS

12a. DISTRIBUTION / AVAILABILITY STATEMENT

APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 2001. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 2001. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during FY 2001.

14. SUBJECT TERMS

Research protocols, investigators, objectives, progress, technical approach

15. NUMBER OF PAGES
545

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL

REPORTS CONTROL SYMBOL RCS MED-300(R1)

ANNUAL PROGRESS REPORT

28 SEPTEMBER 2001

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

Table of Contents

FISCAL YEAR 2001

DEPARTMENT OF CLINICAL INVESTIGATION
MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431

Introduction

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

Acknowledgments

I would like to take this opportunity to thank Barbara Jones, Troy Patience, Paul Froude, Genie Hough, Mary Porreca and Tammie Maple for their effort, in the compilation, preparation, and editing of this publication.

Foreword

2001 was a year of major change in the Madigan Department of Clinical Investigation (DCI). COL Rick Hume (Chief DCI) retired from Active Duty and left a scholarly void that will be difficult to fill. He was replaced by COL Robert Ricks, who is also the Director of Military Unique Research and Training (MURT) at Madigan. Additionally, every other senior leadership position in the Department transitioned during the year, with the exception of the DCI veterinarian, senior protocol management specialist, and Department secretary. We also added a new Administrative Officer position to the DCI staff, and were fortunate to hire Ms. Tammie Maple, MBA (CPT, MSC, USAFR) into that position.

Despite a large turnover in Graduate Medical Education (GME) program leadership, and a marked increase in deployments secondary to the world situation, we again saw an increase in scholarly activity at Madigan. The DCI supported 430 research protocols during the year, of which 141 were new protocols.

The very important GME mission at Madigan continues to receive strong support from the DCI through leadership in curriculum development, medical education, research facilitation, and the unique training opportunities available through our Department infrastructure (e.g. PALS and ATLS courses, combat trauma management training, advanced laparoscopic surgery training, molecular biotechnology techniques courses, etc.). Additionally, the OB/GYN Department, in collaboration with the DCI and University of Washington, initiated an objective surgical skills assessment program to monitor resident progress throughout their training.

DCI leaders continued their outreach program to MAMC Departments, teaching the regulatory requirements for ethical conduct of research, and continuing special emphasis on military unique medical research and training. More than 80 residents, fellows, and faculty participated in this year's "Introduction to Clinical Investigation Short Course," which will be offered twice next year. The DCI also provided pre-review and design support to MAMC medical executives seeking to improve the quality of patient care through a more scientific approach to managed care.

Madigan Research Day 2001 (MRD 2001) was held on 27 April 2001, and once again provided an outstanding forum for showcasing the scope and vigor of multi-service (USA, USAF, USN, USCG) scholarly activity and clinical research conducted at our medical center, and within our region. Sixty-four abstracts were submitted and reviewed by subcommittees, with 29 selected for podium presentations, and 16 presented as posters. The presentations focused on research efforts in the areas of Military Unique Clinical Investigation, Scientific Approach to Managed Care, Medical Education, Experimental Design, and Case Reports. The Day was greatly refined and supported through the generous sponsorship of the COL Patrick S. Madigan, Geneva, and Henry M. Jackson Foundations.

Madigan Research Day 2002 will be held on 26 April 2002

In addition to the CI Short Course and MRD 2001, the DCI was extended the honor of developing and hosting the 1st Annual Western Region Military Medical Readiness Conference on 28-29 April 2001, in conjunction with MRD 2001. This conference was endorsed by Brigadier General Kenneth L. Farmer, CG Western Regional Medical Command (WRMC/ Army), and Lead Agent - TRICARE Region 11 (OLA), and was sponsored by the Henry M. Jackson Foundation. The objectives of the conference were as follows: 1. Establish Tri-Service dialogue addressing regional medical readiness issues, 2. Showcase and discuss Service-specific medical support successes and challenges, and 3. Collaborate on mutual medical readiness training requirements, resource sharing, and potential joint training and deployment opportunities. The conference attracted military medical leaders from 30 different DoD medical units in the Pacific Northwest, and showcased the DCI's Old Madigan facilities and grounds as an ideal location for multi-echelon field medical training. The second Medical

Readiness Conference is scheduled for 3-4 May 2002, and is being jointly sponsored by the WRMC Readiness and Healthcare Operations Directorate, the OLA - Region 11, and the Jackson Foundation.

In all, 2001 was a very exciting and productive year for clinical research at MAMC, and for the DCI. We remain vigorously committed to quality and compliant clinical investigation, and we deeply appreciate the collegial collaboration opportunities that we enjoy with other military and civilian medical centers, Departments of Clinical Investigation, and with the Clinical Investigation Regulatory Office at Army MEDCOM.

A. Objective:

To provide the facilities and environment to stimulate an interest in clinical and basic investigations within Madigan Army Medical Center and its region.

B. Technical Approach:

All research, investigational and training activities within the Department of Clinical Investigation are conducted under the guidance of AR 40-7, AR 40-38, AR 70-25, AR 70-18, and HSC Reg 40-23. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

C. Staffing:

Name	Rank	MOS	Title
Ricks, Robert E.	COL	60J9B	Chief, DCI
Hume, Roderick F., Jr.*	COL	60J9A	Chief, DCI
Norlund, Lewis L.	MAJ	75C64	Asst Chief, DCI; Chief, Lab Animal Resources Service
Rossignol, Todd**	CPT	71A?	Chief, Research Operations Svc
Carpenter, Steven W.***	SFC	91T4H	NCOIC
Criss, Amy D.	SPC	91T10	Animal Care Specialist
Sanchez, Michael J.	SPC	91T10	Animal Care Specialist
Bullock, Jeff M.	GS11	0644	Chief, Research Admin Svc
Maple, Tammie L.	GS11	0671	Administrative Officer
Patience, Troy H.	GS11	1530	Statistician (Medicine)
Matej, Louis A.	GS11	0644	Medical Technologist
DeHart, Mary J.	GS11	0644	Medical Technologist
Wright, James R.	GS11	0644	Medical Technologist
Spahn-Bridges, Shelley L.	WG05	5048	Animal Caretaker
Jones, Barbara A.	GS09	0301	Research Protocol Specialist
Froude, Paul	GS07	0303	Research Protocol Assistant
Hough, Eugenia R.	GS06	0318	Secretary/Steno

* Retired
** PCA'd
*** PCS'd

Personnel:	Authorized	Required	Assigned
Officers	4	10	2
Civilians	8	13	10
Enlisted	8	9	2

D. Research Funding

Civilian Payroll (includes overtime - $6,727)	$ 579,570*
Incentive Awards	$ 2,300
Operations	$ 103,601
Funds for training protocols (Ranger, ATLS, etc)	$ 7,033
CEEP	$ 0
TDY (CHE)	$ 5,000
TDY for researchers to present	$ 43,159
Reproduction Requests	$ 2,962
Contracts	$ 3,000
OMA Total	**$ 746,625**
Grants Federal (includes grants from all intermediaries)	
Air Force (MFM)	$ 2,000
NIOSH	$ 1,000
Henry M. Jackson Foundation	$ 7,922
The Geneva Foundation (dollars spent at MAMC)	$ 235,157
Behavioral Health (MRMC/TATRC)	$ 332,231
Grants Nonfederal (includes grants from all intermediaries)	
Cooperative Research & Development Agreement (CRDA)	$ 39,342(HMJ)
Henry M. Jackson Foundation	$ 78,591
The Geneva Foundation (includes CRDAs)	$ 227,955
Nonfederal Education Grants	$ 219,656
Grants Total	**$1,143,854**
MEDCASE (DNA Sequencer)	$ 133,043
Military Payroll (est.)	$ 350,601
Other Total	**$ 483,644**
Non OMA Total	**$1,627,498**
FY01 Research Funding Total	**$2,374,123**

* Without benefits

E. Progress

During FY 2001, there were 430 active protocols that received administrative and/or technical support during the year. Of these, 269 are presently ongoing, 1 are in a suspended status, 89 were completed, and 55 were terminated. There were 140 new protocols, of which 13 where Oncology Group protocols and 16 where exempt protocols.

There were 77 publications in nationally recognized journals and 73 presentations at regional or national medical association meetings.

F. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 21 residencies and 5 fellowships, they are: *Residencies*: Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Occupational Therapy, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Pediatric Psychology, Pharmacy, Physician Assistance Program (Emergency Medicine & Orthopaedics), Podiatry, Preventive Medicine (Public Health), Radiology, Transitional Year, and Urology.

Fellowships: Developmental Pediatrics, Faculty Development (Family Practice), Geriatrics, Maternal-Fetal Medicine, and Urogynocology.

68 protocols involving 124 residents
60 protocols involving 22 fellows

Other training programs supported by DCI:
Training protocols: Department of Surgery: 4
Department of Emergency Medicine: 2
Department of Obstetrics/Gynecology: 1
2/75 Ranger Battalion: 1
250th Forward Surgical Team/62nd Medical Brigade: 1
915th Forward Surgical Team/USAR: 1
296th Brigade Support Battalion (Medical Company), 3rd Brigade (IBCT)/ 2nd Infantry Division: 1

G. Committee Members

Clinical Investigation Committee
COL Robert E. Ricks, MC
Chairman

Chief or delegated representative of:

- Department of Anesthesia and Operative Services
- Department of Emergency Medicine
- Department of Family Practice
- Department of Medicine
- Department of Medicine, Cardiology Service
- Department of Nursing
- Department of OB/GYN
- Department of Pathology
- Department of Pediatrics
- Department of Radiology
- Department of Surgery
- Department of Surgery, Orthopedics Service
- Pharmacy Service
- Physical Medicine & Rehabilitation Service
- Preventive Medicine Service
- Department of Clinical Investigation (DCI)
- Clinical Studies Service, DCI
- Medical Statistician, DCI
- Research Administration Service, DCI
- Research Operations Service, DCI
- Research Operations Service, Microbiology Section, DCI

G. Committee Members (cont'd)

Human Use Committee
COL Robert E. Ricks, MC
Chairman

Chief or delegated representative of:
- Department of Alternate Chairperson
- Department of Nursing
- Department of Pediatrics
- Department of Radiology
- Department of Ministry and Pastoral Care
- Department of Clinical Investigation
- Research Administration Service, DCI
- Pharmacy Service
- Social Work Service
- Center Judge Advocate
- Non-institutional Member

Animal Use Committee
LTC Jerome Myers, MC
Chairman

Chief or delegated representative of:
- Department of Clinical Investigation (DCI)
- Department of Pathology
- Department of Medicine
- Department of Surgery
- Northwest Veterinary Service Support Area
- Non-affiliated Member and Alternate Non-affiliated Member
- Attending Veterinarian, DCI
- Animal Care Worker, DCI

H. Awards

Steger Award

This award is given to a resident, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2001:

AlloDerm Tympanoplasty of Chronic Tympanic Membrane Perforations by CPT Timothy J. Downey, MC, Otolaryngology Service, Department of Surgery

COL Patrick S. Madigan Foundation Research Award

This award is given to a fellow, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2001:

Long Term Survival of Individuals with Myelomeningocele by LTC Beth Ellen Davis, MC, Department of Pediatrics.

Kenyon Joyce Award

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2001:

Detection of Micrometastatic Tumor Cells in the Peripheral Blood of Prostate Cancer Patients by Lisa Pierce, D.Sc., Molecular Surgical Research/Urology Service, Department of Surgery.

Madigan Research Day Awards

This award is given during Madigan's Annual Madigan Research Day to recognize the best presentation in the following four categories: Innovation, Change in Practice, Interdesciplinary, and Discovery. This year's winners are:

INNOVATION AWARD
Presented to: LTC Peter Zagursky, DC
Department: Oral & Maxillofacial Surgery
Title: Low Energy Laser (Helium-Neon Diode) Biostimulation and Mucosal Wound Healing
Mentor: COL Wayne Olsen, DC

CHANGE IN PRACTICE AWARD
Presented to: CPT Shawn A. MacLeod, MC
Department: Family Practice
Title: High Dose Corticosteroid Treatment for Hemotympanum in Military Free-Fall Students
Mentor: CPT(P) John P. Barrett, MC

INTERDISCIPLINARY AWARD
Presented to: CPT Andrew C. Peterson, MC
Department: Surgery, Urology Service
Title: The Prevalence of Testicular Microlithiasis in an Asymptomatic Population Of Men Aged 18 to 35
Mentor: LTC Raymond A. Costabile, MC

DISCOVERY AWARD
Presented to: CPT Robert Jean-Luc Organ, MC
Department: Pediatrics, Developmental Pediatrics
Title: Aberrant NF-kB Promoted Cyclin D1 Expression Causes Apoptosis in Mdx Mice
Mentor: Dr. Laura Martin, M.D.

BG GEORGE J. BROWN MENTOR'S CUBE
Presented to: COL Dennis Allison, AN
Department: Anesthesia and Operative Services

NANCY J. WHITTEN OUTSTANDING IRB MEMBER AWARD
Presented to: LTC Lanie Olmsted, JA
Department: Center Judge Advocate

BG MACK C. HILL FACILITATOR'S AWARD
Presented to: Troy H. Patience, BS
Department: Clinical Investigation

I. Publications

Department of Anesthesia & Operative Services

Miller JP, Lambert AS, Shapiro WA, Russell IA, Schiller NB, Cahalan MK. The adequacy of basic intraoperative transesophageal echocardiography performed by experienced anesthesiologists. Anesthesia & Analgesia 92(5): p. 1103-10, 2001.

Admin. Residents, Deputy Commander for Administration

Lenza R. Clinical Outcomes and Resource Utilization of Well Managed Diabetics in the Military Medical Care System. THESIS (p. 36 pages), 2001.

Hospital Dental Clinic

Fowler EB, Breault LG, Cuenin MF. Periodontal Disease and Its Association with Systemic Disease. Military Medicine 166(1): p. 85-89, 2001.

Department of Emergency Medicine

Bellis YM, Linnau KF, Mann FA. A complex atlantoaxial fracture with craniocervical instability: A case with bilateral type 1 dens fractures. American Journal of Roentgenology 176(4): p. 978, 2001.

Benson PJ, Klein EJ. New-onset absence status epilepsy presenting as altered mental status in a pediatric patient. Annals of Emergency Medicine 37(4): p. 402-5, 2001.

Della-Giustina DA, Kilcline BA. Acute Low Back Pain: A Comprehensive Review. Comp Ther. 26(3): p. 153-159, 2000.

Vinson DR, Drotts DL. Diphenhydramine for the Prevention of Akathisia Induced by Prochlorperazine: A Randomized, Controlled Trial. Annals of Emergency Medicine 37(2): p. 125-131, 2001.

Vinson DR, Migala AF, Quesenberry CP. Slow Infusion for the Prevention of Akathisia Induced by Prochlorperazine: A Randomized Controlled Trial. The Journal of Emergency Medicine 20(2): p. 113-119, 2001.

Department of Family Practice

Pappas CG. The Ranger Medic. Military Medicine 166(5): p. 394-400, 2001.

Department of Medicine

Reed HL, Reedy KR, Palinkas LA, Do NV, Finney NS, Case HS, Lemar HJ, Wright J. Impairment in cognitive and exercise performance during prolonged antarctic residence: effect of thyroxine supplementation in the polar triiodothyronine syndrome. Journal of Clinical Endocrinology & Metabolism 86(1): p. 110-6, 2001.

Internal Medicine Service, Department of Medicine

Randall DC, Strong JS, Gibbons RB. A Longitudinal Subspecialty Experience for Internal Medicine Residents. Military Medicine 166(1): p. 40-43, 2001.

Pulmonary Disease & Critical Care Service, Department of Medicine

Lee JS, Caras WE. Pulmonary Varix. Clinical Pulmonary Medicine 2001.

Roth BJ, Hammers LM, Dillard TA. Methacholine Challenge Testing in Reserve Officer Training Corps Cadets. Chest 119: p. 701-707, 2001.

Department of Ministry and Pastoral Care

Bassett CA. Critical Incident Stress in the Emergency Department and ICU's: The Chaplain's Role and Response. THESIS 2001.

Robison RH. The Effectiveness of a Hospital Chaplain as a Pastor to Patients Claiming No Religious Preference (NRP) Status. THESIS 2001.

McCarthy MS. Use of Indirect Calorimetry to Optimize Nutrition Support. AACN Clinical Issues 11(4): p. 619-630, 2000.

Department of Nursing

Bianchi AM, Clary KA, Loan LA. Improving Soldier Access to Urinary Incontinence Therapy. Psi Chapter-At-Large News 36(2): 2001.

Bice-Stephens WM. Career path. Stages of employment: Where do you fit in? Nursing 2001 31(5): p. 68-69, 2001.

Bice-Stephens WM. Designing a learning needs survey: Ten steps to success. Journal of Continuing Education in Nursing 31(4): 2001.

Blackburn S, Depaul D, Loan LA, Marbut K, Taquino LT, Thomas, Wilson SK. Neonatal Thermal Care, Part I: Survey of Probe Practices. Neonatal Network 20(3): p. 15-18, 2001.

Blackburn S, Depaul D, Loan LA, Marbut K, Taquino LT, Thomas, Wilson SK. Neonatal Thermal Care, Part II: Microbial Growth Under Temperature Probe Covers. Neonatal Network 20(3): p. 19-23, 2001.

Blackburn S, DePaul D, Loan LA, Marbut K, Taquino LT, Thomas, Wilson SK. Neonatal Thermal Care, Part III: The Effect of Infant Position & Temperature Probe Placement. Neonatal Network 20(3): 2001.

Jennings BM, Loan LA. Misconception among nurses about evidence-based practice. Journal of Nursing Scholarship 33(2): p. 121-127, 2001.

Jennings BM, Loan LA, DePaul D, Brosch LR, Hildreth PS. Lessons Learned While Collecting ANA Indicator Data. Journal of Nursing Administration 31(3): p. 121-129, 2001.

McCarthy MS, Morales M, Fabling J. Improving ALI/ARDS Patient Outcomes with Metabolic Support. Psi Chapter-At-Large News 36(2): p. 2, 2001.

Rivero CC, Mittelstaedt EA, Bice-Stephens WM. A model for self-directed learning in a military facility. Military Medicine 166(8): p. 711-3, 2001.

Whitney JD, Heiner S, Mygrant BI, Wood C. Tissue and Healing Effects of Short Duration Postoperative Oxygen Therapy. Biological Research for Nursing 2(3): p. 206-215, 2001.

Nursing Research Service, Department of Nursing

McCarthy MS, Brosch LR. Improving Outcomes in Patient with ARDS. AJN 5: p. 28-32, 2000.

Department of Obstetrics/Gynecology

Apodaca CC, Hume RF, Evans WJ, Martin LS, Evans MI, Calhoun BC. Parental decision-making differences between patients in two healthcare systems for choroid plexus cysts. Australian & New Zealand Journal of Obstetrics & Gynaecology 40(4): p. 427-9, 2000.

Apodaca CC, Hume RF, Evans WJ, Martin LS, Evans MI, Calhoun BC. Parental decision-making differences between patients in two healthcare systems for choroid plexus cysts. Fetal Diagnosis & Therapy 15(6): p. 338-41, 2000.

Apodaca CC, Moore KH, Rossignol TM, Pierce BT, Matej LA, Hume RF, Calhoun BC. Localization of Messenger Ribonucleic Acid for Adrenomedullin and Adrenomedullin Receptor in the Human Placenta in Normal Pregnancies and Pregnancies Complicated by Oligohydramnios. American Journal of Obstetrics and Gynecology 183(5): p. 1213-9, 2000.

Bergemann JL, Hibbert ML, Harkins GJ, Narvaez JC, Asato AJ. Case Reports: Omental Herniation through a 3-mm Umbilical Trocar Site: Unmasking a Hidden Umbilical Hernia. Journal of Laparoendoscopic & Advanced Surgical Techniques 11(3): p. 171-173, 2001.

Brandsma C, Calhoun BC, Vannatta JE. Uncomplicated pregnancy: clinical pathway genesis based on the nursing process. Military Medicine 165 165(11): p. 839-43, 2000.

Calhoun BC, Hume RF. Integrated Obstetric Curriculum for Obstetrics and Gynecology Residency, Radiology Residency and Maternal-Fetal Medicine Fellowship Program at an Accredited American Institute of Ultrasound in Medicine Diagnostic Ultrasound Center. Ultrasound Obstetrics Gynecology 16: p. 68-71, 2000.

Farley JH, Heaton J, O'Boyle JD. Adenocarcinoma of Unkown Primary Site Presenting as an Isolated Retroperitoneal Mass and Trousseau's Syndrome. Military Medicine 166(9): p. 831-2, 2001.

Fugate SR, Apodaca CC, Hibbert ML. Gender Reassignment Surgery and the Gynecological Patient (Honorable Mention). Primary Care Update OB/GYNs 8(1): p. 22-24, 2001.

Hawley-Bowland C, Hume RF, Cahill W, Willig S, Winter KA, Ventura VL, Calhoun BC. Obstetrical Pre-Packs: Improving Quality, Efficiency, and Cost. Journal of the Army Medical Department 4: p. 26-28, 2001.

Hibbert ML, Salminen ER, Dainty LA, Davis GD. Credentialing Residents for Intraoperative Cystoscopy. Obstetrics & Gynecology 96(6): p. 1014-1017, 2000.

Hoeldtke NJ, Calhoun BC. Perinatal Hospice. American Journal of Obstetrics and Gynecology 185(3): p. 525-529, 2001.

Hoeldtke NJ, Wagner RK, Calhoun BC, Hume RF. Vasodilatory Response of Fetoplacental Vasculature to Adrenomedullin After Constriction with the Thromboxane Sympathomimetic U46619. American Journal of Obstetrics and Gynecology 183(6): p. 1573-1578, 2000.

Nielsen PE, Thomson BA, Jackson RB, Kosman K, Kiley KC. Standard obstetric record charting system: evaluation of a new electronic medical record. Obstetrics & Gynecology 96(6): p. 1003-8, 2000.

Parker JD, Hibbert ML, Dainty LD, Larsen FW, Dance VD. Instruments & Methods: Micro-Hydrovaginoscopy in Examining Children. Obstetrics & Gynecology 96(5): p. 772-4, 2000.

Pierce BT, Dance VD, Wagner RK, Apodaca CC, Nielsen PE, Calhoun BC. Perinatal Outcome Following Fetal Single Umbilical Artery Diagnosis. The Journal of Maternal-Fetal Medicine 10(1): p. 59-63, 2001.

Pierce BT, Hancock EG, Kovac CM, Napolitano PG, Hume RF, Calhoun BC. Influence of Gestational Age and Maternal Height on Fetal Femur Length Calculations. Obstetrics & Gynecology 97(5): p. 742-746, 2001.

Pierce BT, Napolitano PG, Pierce LM, Apodaca CC, Hume RF, Calhoun BC. The Effects of Hypoxia and Hyperoxia on Fetal-Placental Vascular Tone and Inflammatory Cytokine Production. American Journal of Obstetrics and Gynecology 185(5): p. 1068-1072, 2001.

Pierce BT, Pierce LM, Wagner RK, Apodaca CC, Hume RF, Nielsen PE, Calhoun BC. Hypoperfusion Causes Increased Production of Interleukin 6 and Tumor Necrosis Factor a in the Isolated, Dually Perfused Placental Cotyledon. American Journal of Obstetrics and Gynecology 183(4): p. 863-867, 2000.

Wagner RK, Hinson RM, Apodaca CC, Hoeldtke NJ, Buchanan T, Hume RF, Calhoun BC. Effects of Lipopolysaccharide on Interleukin-6 Production in Perfused Human Placental Cotyledons. The Journal of Maternal-Fetal Medicine 9(6): p. 351-355, 2000.

Department of Pathology

Chapeaux AL, Groo SC, Ainbinder DJ. Pathologic quiz case: a healthy 31-year-old-man with sinusitis. Pathology & Laboratory Medicine 125(9): p. 1253-4, 2001.

Vos JA, Coad JE, Brissette MD, Myers JB. Phenotypic Variations in the Mucosal Lymphoid Tissue of Celiac Disease. The FASEB Journal, A Multidisciplinary Resource for the Life Sciences 15(4): p. A594 (Abstract 475.6), 2001.

Wheeler DT. Pathology and the internet. Adv Anat Pathol 8(2): p. 111, 2001.

Department of Pediatrics

Carter ER, Pulos E, Delaney J, Matheson EJ, Moffitt DR. Allergy history does not predict skin test reactivity in asthmatic children. Journal of Asthma 37(8): p. 685-90, 2000.

Mahnke CB. The growth and development of a specialty: the history of pediatrics. Clinical Pediatrics 39(12): p. 705-14, 2000.

Miller RI, Stephan MJ, Hume RF, Walker WO, Kelly P, Calhoun BC, Hoeldtke NJ, Hayden JE. Extreme elevation of maternal serum alpha-fetoprotein associated with mosaic trisomy 8 in a liveborn. Fetal Diagnosis & Therapy 16(2): p. 120-2, 2001.

Physical Medicine & Rehabilitation Service

Lauder TD, Campbell CS. Abnormal Eating Behaviors in Female Reserve Officer Training Corps Cadets. Military Medicine 166(3): p. 264-268, 2001.

Preventive Medicine Service

Nusbaum MR, Gamble G. The Prevalence and Importance of Sexual Concerns Among Female Military Beneficiaries. Military Medicine 166(3): p. 208-210, 2001.

Young SYN, Gunzenhauser JD, Malone KE, McTiernan A. Body Mass Index and Asthma in the Military Population of the Northwestern United States. Archives of Intern Medicine 161(13): p. 1605-1611, 2001.

Department of Psychiatry

Hough DW. Low-Dose Olanzapine for Self-Mutilation Behavior in Patients With Borderline Personality Disorder (Letters to the Editor). The Journal of Clinical Psychiatry 62(4): p. 296-297, 2001.

Department of Radiology

Benson AJ, Reinschmidt J, Billingsley JL, Timmons JH, Parish GH. Biliary-colonic fistula diagnosed via hepatobiliary scintigraphy. Clinical Nuclear Medicine 26(2): p. 150-1, 2001.

Keadle DM, Bauman JM, Billingsley JL. Nonvisualization of the liver on a Tc-99m sestamibi parathyroid scan. Clinical Nuclear Medicine 25(11): p. 921-2, 2000.

Keadle DM, Light DE, Bauman JM. Mesenteric Varices Mimicking Right Lower Quadrant Inflammation on Hepato-Biliary Imaging. Clinical Nuclear Medicine 26: p. 584-9, 2001.

Light DE. Adrenal Hemorrhage. www.Emedicine.comp. 11 pages, 2001.

Monson M, Keadle DM, Bauman JM, Cowan C. Abnormal upper body soft tissue uptake on skeletal scintigraphy: A sign of superior vena cava obstruction. Clinical Nuclear Medicine 26(5): p. 456-7, 2001.

Reinschmidt JP, Murray SP, Casha LM, Gagliano RA, Tracy DP, Collins GJ. Localization of pulmonary nodules using suture-ligated microcoils. Computer Assisted Tomography 25(2): p. 314-8, 2001.

General Surgery Service, Department of Surgery

Place RJ. Isolated colon cancer metastasis to the spleen. American Surgeon 67(5): p. 454-7, 2001.

Place RJ. Blue rubber bleb nevus syndrome: a case report with long-term follow-up. Military Medicine 166(8): p. 728-30, 2001.

Place RJ. Idiopathic colonic varices as a cause of lower gastrointestinal bleeding. Southern Medical Journal 93(11): p. 1112-4, 2000.

Sanborn CK, O'Connor A, Sawin RS, Moore K, Dehart MJ, Azarow KS. Comparison of telomerase levels before and after differentiation of two cell lines of human neuroblastoma. Journal of Surgical Research 93(2): p. 206-10, 2000.

Sebesta JA, Brown TA, Williard WC, Dehart MJ, Aldous WK, Kavolius J, Azarow KS. Does telomerase activity add to the value of fine needle aspirations in evaluating thyroid nodules? American Journal of Surgery 181(5): p. 420-2, 2001.

Ophthalmology Service, Department of Surgery

Brady SM, McMann MA, Mazzoli RA, Bushley DM, Ainbinder DJ, Carroll RB. The Diagnosis and Management of Orbital Blowout Fractures: Update 2001. American Journal of Emergency Medicine 19(2): p. 147-154, 2001.

Mazzoli RA, Raymond WR, Ainbinder DJ, Hansen EA, Parmley VC, Skidmore EC. Reply to B. Fayet et al.'s Letter "Suggested Precautions When Using a Monocanalicular Stent". Ophthalmic Plastic and Reconstructive Surgery 17(1): p. 77-78, 2001.

Nelson ML, Brady S, Mader TH, White LJ, Parmley VC, Winkle RK. Refractive changes caused by hypoxia after laser in situ keratomileusis surgery. Ophthalmology 108(3): p. 542-4, 2001.

Otto CS, Nixon KL, Mazzoli RA, Raymond WR, Ainbinder DJ, Hansen EA, Krolicki TJ. Chorioretinitis sclopetaria from BB ex memoria. Ophthalmic Surgery & Lasers 32(2): p. 152-5, 2001.

Orthopedics Service, Department of Surgery

Arrington ED, Hoschild DP, Steinagle TJ, Mongan PD, Martis LS. Monitoring of somatosensory and motor evoked potentials during open reduction and internal fixation of pelvis and acetabular fractures. Orthopedics 23(10): p. 1081-3, 2000.

Bal GK, Duo RS, Chapman JR, Henley MB, Benirschke SK, Claudi BF. The anterior T-frame external fixator for high-energy proximal tibial fractures. Clinical Orthopaedics & Related Research 380: p. 234-40, 2000.

Urology Service, Department of Surgery

Lance RS, Fridrichs PA, Kane C, Powell CR, Pulos E, Moul JW, McLeod DG, Cornum RL. A comparison of radical retropubic with perineal prostatectomy for localized prostate cancer within the Uniformed Services Urology Research Group. Bju International 87(1): p. 61-5, 2001.

Peterson AC, Joyner BD, Allen RC. Plastibell Template Circumcision: A New Technique. Urology 58(4): p. 603-604, 2001.

Sprenger CC, Peterson AC, Lance RS, Ware JL, Drivdahl RH, Plymate SR. Regulation of proliferation of prostate epithelial cells by 1,25-dihydroxyvitamin D3 is accompanied by an increase in insulin-like growth factor binding protein-3. Journal of Endocrinology 170(3): p. 609-18, 2001.

J. Presentations

Madigan Center Judge Advocate

Olmsted FE, Hume RF, Martin LS, Geib RP, Hartley MW, Jones BA, Azarow KS, Myers JB. A Regional Military Health Care System Response to Expanding Genetic Research: Ethical, Legal, and Social Implications. Presented at Current Issues in Federal Sectors Healthcare Law, USUHS Meeting, Bethesda, MD, USA, January 2001.

Department of Clinical Investigation

Apodaca CC, Pierce BT, DeHart MJ, Napolitano PG, Calhoun BC. Comparison of Adrenomedullin and Adrenomedullin Receptor mRNA Expression in Placentas from Normal and Complicated Pregnancies. Presented at Society for Maternal Fetal Medicine Meeting, Reno, NV, USA, February 2001.

Hume RF, Martin LS, Hancock EG, Wood R, Everett M, Patience TH, Calhoun BC. Maternal Serum Analyte Screening Protocols: Cost Consequence Study of Alternative Programs. Presented at Annual Clinical Genetics Meeting, Miami, FL, USA, March 2001.

Opitz K, Ricks RE. Train the Trainers Program: Introduction of Formal Curriculum and Exercise Program for Instructors I Corps/MAMC PSWP. Presented at Health Issues of Military & Veteran Women Research Symposium at the Women in Military Service for America Memorial Meeting, Arlington, VA, USA, September 2001.

Department of Emergency Medicine

Gruppo L. The Incidence of Ocular Injuries in Military Free Fall Parachutists. Presented at Special Operations Medical Association Meeting, Tampa, FL, USA, December 2000.

Department of Family Practice

Krueger MV. Barriers to Breast-feeding Experienced by Active Duty Women. Presented at The First Interagency Research Symposium on Health Issues of Military and Veteran Women Meeting, Arlington, VA, USA, September 2001.

Hume RF, Azarow KA, Olmsted FE, Myers J, Calhoun BC, McCune DE, Freund C, Martin LS. A Regional Military Healthcare System Response to Expanding Genetic Research: Ethical, Legal and Social Implications. Presented at A Decade of ELSI Research Meeting, Bethesda, MD, USA, January 2001.

Internal Medicine Service, Department of Medicine

Do NV, Case S, Finney N, Fletke M, LeMar HJ, Merriam G, Mino L, Palinkas L. Elevations in Serum Thyroglobulin During Prolonged Antarctic Residence: Effect of Thyroxine Supplement in the Polar T3 Syndrome. Presented at The Endocrine Society Meeting, Denver, CO, USA, June 2001.

Duncan MB, Hirota WK, Tsuchida AM. Cost Analysis of Prescreening for Hepatitis A Before Immunization in Patients with Chronic Liver Disease & Prescreening in ROTC Cadets -- 2 posters. Presented at American College of Gastroenterology Meeting, New York, NY, USA, October 2000.

McKinley BT, Mulhall B. Pilot Study to Evaluate Perceived versus Actual Medication Regimens in Internal Medicine Patients. Presented at National Chapter of ACP-ASIM Meeting, Atlanta, GA, USA, March 2001.

Morales M, McCarthy MA. Improving ALI/ARDS Patient Outcomes with Metabolic Support. Presented at AMSUS Meeting, USA, November 2000.

Anesthesia Students, Department of Nursing

Smith BM, Lent CT, Mattson DR, Ewing KE, Johnson PM. A Comparison of the Reversal of Rapacuronium with Neostigmine and Edrophonium. Presented at American Association of Nurse Anesthetists Foundation's Annual Meeting, San Francisco, CA, USA, August 2001.

Department of Obstetrics/Gynecology

Apodaca CC, Pierce BT, Rossignol TM, DeHart MJ, Napolitano PG, Hume RF, Calhoun BC. Comparison of Adrenomedullin and Adrenomedullin Receptor mRNA Expression in Placenta from Normal and Complicated Pregnancies. Presented at Society for Maternal Fetal Medicine Meeting, Reno, NV, USA, February 2001.

Bergemann JL, Hibbert ML, Harkins G, Narvaez JC, Asato AJ. Omental Herniation Through a 3-mm Umbilical Trocar Site: Unmasking a Hidden Umbilical Hernia. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Brizuela MA, Bush MR, Perez RP, Hibbert ML. Acute Pelvic Pain at Time of Menarche: A Syndrome of Uterus Didelphys, Obstructed Hemivagina, and Ipsilateral Renal Agenesis. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Brizuela MA, Hernandez SL, Nielsen PE, Apodaca CC. Chronic Myelogenous Leukemia in Pregnancy. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Burney RO, Bush MR, Brizuela MA. Laparoscopic Trocar Insertion at the Left Upper Quadrant: A Case Series and Description of Technique. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Burney RO, Hibbert ML, Bush MR. Thiazolidinediones in the Management of Insulin Resistant Polycystic Ovary Syndrome. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Burney RO, Ladwig M, Hibbert ML. Appendiceal Carcinoid Tumor in a Patient with Chronic Pain. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Dainty LA, Carlson JW, Nielsen PE, Bush MR. Gestational Trophoblastic Neoplasm After an Uncomplicated Term Spontaneous Vaginal Delivery. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Foglia LM, Dance VD, Hancock EG, Nielsen PE, Calhoun BC, Pierce BT. Intravascular Adenosine Administration via Cordocentesis for Treatment of Fetal Supraventricular Tachycardia. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Hancock EG. Longitudinal Assessment of Lipid Profile Values in a Heterogeneous Population of Pregnant Women and the Correlation with Hypertensive Disorders of Pregnancy. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Hancock EG, Hume RF, Calhoun BC, Martin LS, Patience TH, Treadwell MC, Zador IE, Evans MI. Maternal Age and Ultrasound Detection of Non-Aneuploid Fetal Structural Anomalies. Presented at American College of Medical Genetics & Soc. of Inborn Errors in Metabolism Meeting, Miami, FL, USA, March 2001.

Hancock EG, Hume RF, Patience TH, Pierce BT, Abadie JM, Calhoun BC. Lipid Profile Values in a Heterogeneous Population of Pregnant Women and the Correlation with Hypertensive Disorders of Pregnancy. Presented at Society of Maternal-Fetal Medicine Meeting Meeting, Reno, NV, USA, February 2001.

Hibbert ML, Woodman PJ, Peterson AC, Allen RC, Ruiz HE, Davis GD. Renewal of Idealism in Rsidents and Fellows: Humanitarian Surgical Mission to Honduras. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Hibbert ML, Woodman PJ, Seymour SD, Davis GD, Perez RP. Intraoperative Cystoscopy for the Evaluation of Urinary Tract Injury (Video Presentation). Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Holland RHB, Foglia LM, Nielsen PE. Evaluation of an Outpatient Clinical Skills Orientation Program for Interns and Residents. Presented at APGO/CREOG Meeting, Orlando, FL, USA, March 2001.

Holland RHG, Fugate S, Payne JF, Hibbert ML. Persistent Ectopic Following Complete Salpingectomy. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Holland RHG, Nielsen PE, Pierce BT. Large Placental Chorioangiomas: A Case Series and Review of the Literature. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Kovac C, Brown J, Hume RF, Apodaca CC, Pierce BT, Napolitano P, Nielsen P, Patience TH. Maternal Ethnicity and Second-Trimester Fetal Femur Length Variation. Presented at American Institute of Ultrasound in Medicine Meeting, Orlando, FL, USA, March 2001.

Larsen W, Vara T, Ricks RE, Hawley-Bowland C, Flynn D, Lancaster A, Nielsen P, Phillips D. Female Soldier Readiness: Leader's Guide - Utility Validation Survey. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Misko CA, Dunn JS, Foglia LM, Calhoun BC, Brost B. Evaluation of Clinical Risk Factors of Delivering a Macrosomic Fetus. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Narvaez JC, Asato AJ, Davis GD, Hibbert ML. Fallopian Tube Prolapse Through the Vaginal Cuff: Combined Vaginal and Laparoscopic Management. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Nielsen PE. Female Soldier Readiness: A Leader's Guide - Implementation Phase. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Parker J, Broberg J, Napolitano PT. Maternal Arnold-Chiari Type 1 Malformation and Syringomyelia: A Labor Management Dilemma. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Pierce BT, Calhoun BC, Lau A, Matej LA, DeHart MJ, Pierce LM. Connexin 43 mRNA and Protein Expression in Normal and Dysfunctional Labor. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Pierce BT, Napolitano P, Pierce LM, Apodaca CC, Hume RF, Calhoun BC. The Effects of Hypoxia and Hyperoxia on Fetal-Placental Vascular Tone and Inflammatory Cytokine Production. Presented at Society for Maternal Fetal Medicine Meeting, Reno, NV, USA, February 2001.

Pierce LM, Pierce BT, Hume RF, Napolitano PT, Calhoun BC. Vascular Endothelial Growth Factor and Placenta Growth Factor are not Acutely Produced by the Placenta During Fetal Hypoxia or Fetal Hypoperfusion. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Ricks RE, Walker RO, Kelly PC, Nielsen PE, Chow GE, Calhoun BC, Martin LS, Flynn DM. Mentoring for the New Millennium: Enhanced Scholarly Activity, Professional Development, and Personal Satisfaction for Future Academics Through the Successful Implementation of a Mentor System. Presented at APGO/CREOG Meeting, Orlando, FL, USA, March 2001.

Rodriguez-Falcon W, Pierce BT. Complication and Comorbidities affecting Pregnancy of the Morbidly Obese Patient. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Vara T, Ricks RE, Hawley-Bowland C, Larsen W, Flynn D, Lancaster A, Nielsen P, Phillips D. Female Soldier Readiness: Leader's Guide Update 2000. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Wood RA, Battaglia MG, Vara T, Remmenga S, Potter B, Calhound BC, Hume RF, Ricks RE. U.S. Navy Female Servicemember Readiness: A Leader's Guide-Implemenation Phase: Utility Validation Survey. Presented at Armed Forces District Meeting, American College of Obstetricians/Gynecologists Meeting, Cincinnati, OH, USA, October 2000.

Department of Pathology

Abadie JM. Can a Strategy be Developed for More Cost-Effective Ordering of Cardiac Injury Marker Assays?. Presented at American Federation for Medical Research Meeting, New Orleans, LA, USA, March 2001.

Vos JA, Coad JE, Brissette MD, Myers JB. Phenotypic Variations in the Mucosal Lymphoid Tissue of Celiac Disease. Presented at Experimental Biology, 2001 Meeting, Orlando, FL, USA, April 2001.

Department of Pediatrics

Martin LS, McGrannahan M, Millar W, Barfield W, Everett M, Schreckhise C, Divelbiss D, Kelly P, Hume RF. DoD Newborn Screening System: Cost Benefit Analysis of Best Practice Model for DoD. Presented at American College of Medical Genetics Meeting, Miami, FL, USA, March 2001.

Preventive Medicine Service

Battle SE, Shanka D, Gunzenhauser JD. Description of a Tuberculosis Epidemic on Kenyan Tea Estates. Presented at Preventive Medicine 2001 Meeting, Miami, FL, USA, February 2001.

Parker ME, Gunzenhauser JD. Rates of Health Care Utilization by Smokers, Smokeless Tobacco Users and Non-tobacco Users in a Population of Young, Active Duty Soldiers. Presented at Preventive Medicine 2001 Meeting, Miami, FL, USA, February 2001.

Department of Radiology

Cote MG. Myocardial FDG SPECT Imaging with High Energy Collimators. Presented at 2001 Annual Spring conference, Pacific Northwest Chapter, Society of Nuclear Medicine Meeting, Quinault Beach Resort, Ocean Shores, WA, USA, March 2001.

Fuller GM, Toft C, Gallucci B, Carter P, Myers MA. Breast Cancer Clinical Pathway: A Multidisciplinary Approach & Diagnostic Pathway. Presented at Seeking Excellence in Breast Cancer Care Meeting, Baltimore, MD, USA, November 2000.

Fuller GM, Toft CK, Gallucci BJ, Myers MA. Diagnostic Breast Pathway: Multidisciplinary Approach. Presented at Seeking Excellence in Breast Cancer Care Meeting, Baltimore, MD, USA, November 2000.

Wright SC, Youngberg RA. Indirect Magnetic Arthrography of the Shoulder Compared with Arthroscopy. Presented at American Roentgen Ray Society Meeting, Seattle, WA, USA, April 2001.

Department of Surgery

Gagliano RA, Reinschmidt JP, Murray SP, Casha LM, Tracy DP, Collins GJ. A Novel Method of Transthoracic Lung Nodule Localization. Presented at Gary P. Wratten Surgical Symposium Meeting.

General Surgery Service, Department of Surgery

Sebesta JA, Brown T, Williard WC, DeHart MJ, Aldous WK, Kavolius J, Azarow K. Specificity and Sensitivity of Telomerase in Thyroid FNAs for the Detection of Thyroid Cancer. Presented at North Pacific Surgical Association Meeting, Coeur D'Alene, ID, USA, November 2000.

Ophthalmology Service, Department of Surgery

Anderson R, Brady SM, Parmley VC. LASIK Corneal Surgery with Good Results Despite Abnormal Endothelium Associated with Posterior Polymorphous Dystrophy. Presented at American Society of Cataract & Refractive Surgery Meeting, San Diego, CA, USA, April 2001.

Carroll RB, Mazzoli RA, Otto CS, Ainbinder DJ, Hansen EA, Raymond WR. Late Retrobulbar Hemorrhage with Visual Loss Complicating Displaced Orbital Floor Fractures: A Report of Two Cases. Presented at NANOS Conference Meeting, Palm Springs, CA, USA, February 2001.

Otto CS, McMann MA, Parmley VC, Carroll RB. Warm Balanced Salt Solution for Clearing Surface Secretions During Cataract Surgery. Presented at American Society of Cataract and Refractive Surgery Meeting Meeting, San Diego, CA, USA, April 2001.

Otto CS, Raymond WR, Coppitt GL, Mazzoli RA, Nixon KL, Ainbinder DJ, Hansen EA, Grazko MA. Gaze Evoked Amaurosis: A Report of Five Cases. Presented at Amer.Soc.of Ophthalmic Plastic & Reconstructive Surg & Acad. of Ophthal. Meeting, Dallas, TX, USA, October 2000.

Orthopedics Service, Department of Surgery

Gerlinger T, Molinari RW. Functional Outcome of Instrumented Posterior Lumbar Interbody Fusion (PLIF) in Active Duty U.S. Servicemen: A Comparison with Nonoperative Management. Presented at Scoliosis Research Society Meeting, Cairns, Australia, October 2000.

Jones RO, Pitcher JD, Beitler AL, Clark BA. Algorithmic Approach to Diagnosis and Treatment of Soft Tissue Tumors of the Ankle and Foot. Presented at Joint Annual Meeting and Scientific Seminar - Expo 2001 Meeting, New Orleans, LA, USA, February 2001.

Jones RO, Pitcher JD, Beitler AL, Clark BA. Soft-Tissue and Bone Tumors of the Ankle and Foot: A Diagnostic Algorithm and Multimodality Approach. Presented at American College of Foot and Ankle Surgeons Annual Conference Meeting, New Orleans, LA, USA, February 2001.

Jones RO, Vermillion D, Williamson M, Wigboldy J. Positional Assessment of the Maxwell-Brancheau Arthoeresis Implant on the subtalar Joint Using Three-Dimensional Surface Computed Tomography. Presented at Joint Annual Meeting and Scientific Seminar Expo 2001 Meeting, New Orleans, LA, USA, February 2001.

StPierre P. A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus a Cancellous Trough: A Preliminary Report. Presented at Society of Military Orthopedic Surgeons Meeting, USA, December 2000.

Otolaryngology Service, Department of Surgery

Crawford J, Purdom EB, Champeaux A. Seminomatous Testicular Carcinoma Metastatic to the Neck. Presented at American Academy of Otolaryngology--Head and Neck Surgery Meeting, Denver, CO, USA, September 2001.

Cupero TM. The Effects of Functional Septoplasty on the Facial Growth of Ferrets. Presented at American Society of Pediatric Otolaryngology Meeting, Scottsdale, AZ, USA, May 2001.

Hariadi JW, Goco PC. The Full-Body Plethysmograph: A Novel Way to Assess Nasal Patency. Presented at American Academy of Otolaryngology--Head and Neck Surgery Meeting, Denver, CO, USA, September 2001.

Kerr J, Steger J, Sorenson D. Case Report: Medline Maxillary Odontogenic Keratocyst. Presented at American Academy of Otolaryngology--Head and Neck Surgery Meeting, Denver, CO, USA, September 2001.

Kim SY, Reardon RA, Anderson D, Sorenson D. Correlation of Fine Needle Aspiration and Surgical Pathology of the Head and Neck at Madigan Army Medical Center. Presented at Canadian Society of Otolaryngology-HNS Meeting, Vancouver, CAN, USA, May 2001.

Massengill PL, Goco P. Determining Optimal Nonsurgical Treatment for Auricular Cartilage Contouring in a Rabbit Model. Presented at Combined Otolaryngological Spring Meetings Meeting, Palm Springs, CA, USA, May 2001.

Massengill PL, Goco P. Determining Optimal Nonsurgical Treatment for Auricular Cartilage Contouring in a Rabbit Model. Presented at American Academy of Otolaryngology--Head and Neck Surgery Meeting, Denver, CO, USA, September 2001.

Urology Service, Department of Surgery

Pierce LM, DeHart MJ, Poulton TL. The Effect of 1,25 Dihydroxyvitamine D3 (Vitamin D) on Vascular Endothelial Growth Factor Production and Telomerase Activity in Prostate and Bladder Cancer Cell Lines. Presented at 48th Annual James C. Kimbrough Urological Seminar Meeting, San Diego, CA, USA, January 2001.

Pierce LM, Marean AJ, Costabile RA, Lance RS. Detection of Prostate and Bladder Carcinoma Cells in Peripheral Blood. Presented at Western Section: American Urological Association 76th Annual Meeting, Palm Desert, CA, USA, November 2000.

Pierce LM, Marean AJ, Costabile RA, Lance RS. Detection of Micrometastatic Tumor Cells in the Peripheral Blood of Prostate Cancer Patients. Presented at 48th Annual James C. Kimbrough Urological Seminar Meeting, San Diego, CA, USA, January 2001.

Pierce LM, Marean AJ, Lance RS. The Catalytic Component of Telomerase (hTERT) Is Not a Reliable Marker to Detect Circulating Cancer Cells Isolated by Immunomagnetic Enrichment. Presented at 48th Annual James C. Kimbrough Urological Seminar Meeting, San Diego, CA, USA, January 2001.

K. Exempt Protocols

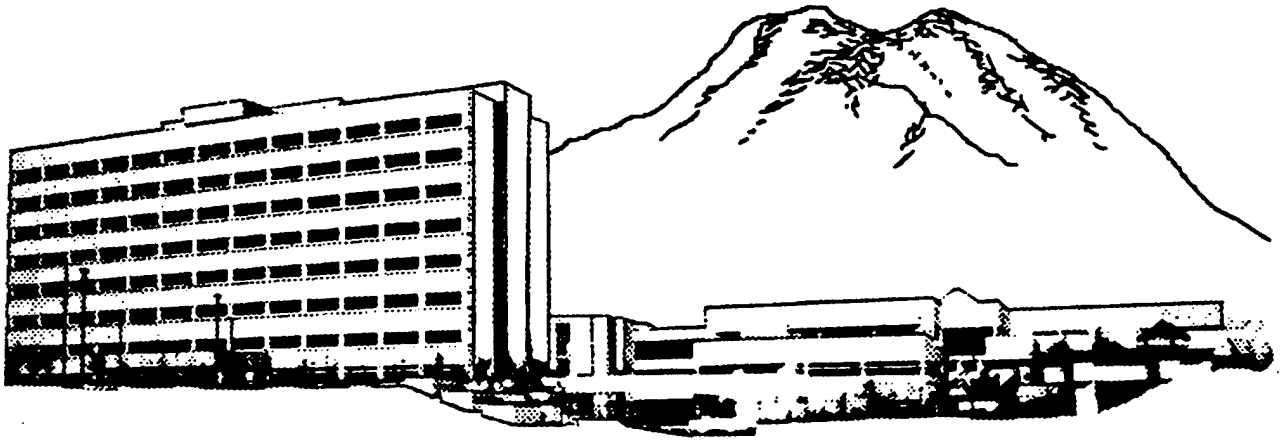
Number	PI	Title
201/092	Bassett C	The Chaplain's Response to Critical Incident Stress in Emergency/Intensive Care Providers
201/105	Carter ER	The Adherence in Children to Two Controller Treatment Regimens for Asthma: Montelukast vs Flucticasone Propionate
201/084	Do NV	The Effect of Using Personal Digital Assistant (PDA) Technology as a Method of Physician Order Entry on Prescribing Practices Among Internal Medicine Resident
201/102	Do NV	The Effectiveness of Referral Guidelines when Implemented on Personal Digital Assistant (PDA)
201/131	Hemman EA	Improving Emergency Medical Technician (EMT) Learning Using a Computer Based 3-D Virtual EMT Training Simulator
201/068	Kennedy RE	Sexual Addiction: Treating the Causes and Effect
201/063	McElroy AJ	A Christian Pastoral Response to Suffering
201/133	McPherson F	An Evaluation of Complimentary and Alternative Health Care Usage Among Patients in a Military Health Care System: A Randomized, Descriptive Study Design
201/103	Organ RJ	Establishment of Primary Myocyte Cell Cultures from Mouse Embryonic Fibroblasts with the DNA Construct pBABEpuroMyoD
201/085	Padden MO	Specialty Preference of Military Medical Students
201/141	Padden MO	Retrospective Evaluation of Glucovance versus Glyburide Plus Metformin in Select Diabetes Populations
201/062	Peterson AC	A Retrospective Study of Plastibell Template Circumcision
201/119	Piesman M	The Impact of the "Buddy Watch" Protocol at Ft. Lewis on the Admission Rates to the Psychiatric Ward and Combat Readiness
201/064	Robison RH	The Effectiveness of a Hospital Chaplain as a Pastor to Patients Claiming No Religious Preference (NRP) Status
201/094	Tillotson-Criss MC	Tick Surveillance and Analysis for Borrelia burgdorferi and Other Potential Pathogenic Borrelia species in Pierce County, Washington
201/124	Wells R	Parental Ability to Correctly Identify the Inpatient Physician Team Member(s) Caring for Their Child

L. Detailed Summary Sheets

Table of Contents

Legend:

Column labeled "S" stands for Status of Protocol, and each protocol is defined as:
C = Completed, O = Ongoing, T = Terminated, S = Suspended



Detail Summary Sheets

Department of Anesthesia & Operative Services

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/046	**Status**: Terminated

Title: An Open-label, Long-term Safety and Tolerability Study of Ziconitide Administered Intrathecally to Patients with Chronic, Severe Pain

Principal Investigator: MAJ Andrew G Kowal, MC

Department: Anesthesia & Operative Services	**Facility**: MAMC

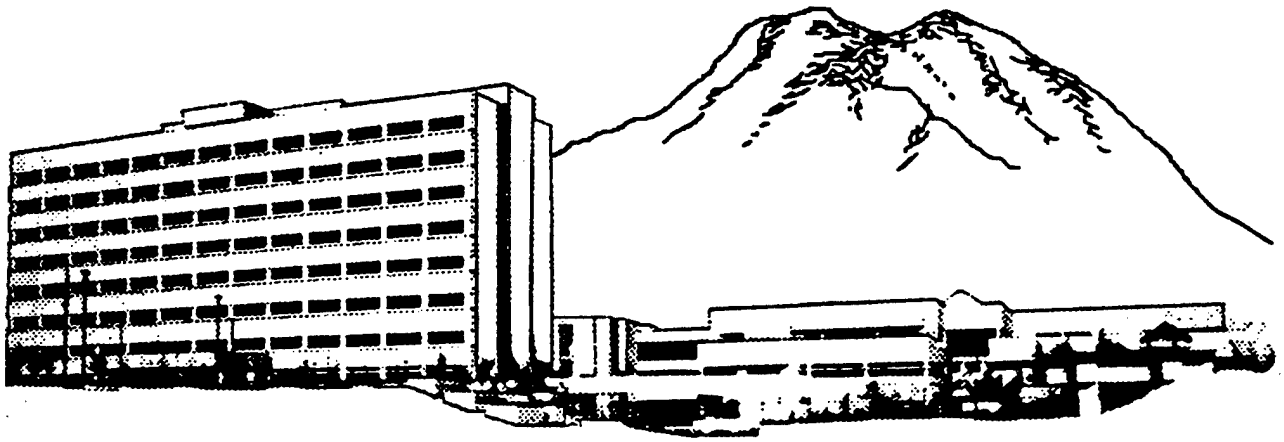
Associate Investigator(s): MAJ Stephen L. Bolt, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Jan 10	1/23/2001

Study Objective: The purpose of this study is to assess the long-term safety and tolerability of ziconotide administered intrathecally to patients with chronic, severe pain.

Technical Approach: This is a Phase IIIB, long term, open-label, multicenter study to assess the safety and tolerability of intrathecally administered ziconotide in up to 700 patients with chronic severe pain. The target population is made up of patients who suffer from chronic, severe pain with intrathecal catheters already in place, or those whose next line of therapy would require placement of such devices. Patients will be seen on an outpatient basis. For the first month, they will come in at least twice a week to have a physical assessment and get their dose adjusted accordingly. After the first month, safety assessments and pump refills will be done monthly on an outpatient basis. Demographics and baseline information will be summarized with descriptive statistics. Descriptive statistics will be used to summarize the changes from baseline to the follow-up scheduled time points for the vital sign measurements, ECG results, the Wechsler Memory Scale subtest, Trail Making, parts A and B, and Function Level Assessment. The study will continue until the drug is FDA approved.

Progress: This study was terminated, 7 Mar 01, per the PI and study sponsor after additional limits and restrictions placed on study enrollment made continuation at MAMC not feasible.



Detail Summary Sheets

Center for Health Promotion & Preventive Medicine, West

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/040	**Status**: Terminated

Title: Ergonomic Interventions in Military Dental Clinics

Principal Investigator: MAJ Thomas C. Delk, MS

Department: CHPPM - West	**Facility**: MAMC

Associate Investigator(s): Mr. John S. Pentikis, BS; LTC Mary S. Lopez, MS; Mr. Mark A. Lucas, MS

Start Date:	**Est. Completion Date:**	**Periodic Review:**
1/23/2001	Jan 02	N/A

Study Objective: To examine the relative effects of training and workstation design on self-reported discomfort (a precursor indicator of musculoskeletal injury) among dental care providers. Specifically the study will (1) compare self-reports of discomfort following ergonomic training to baseline measurements; (2) compare self-reports of discomfort following ergonomic engineering changes to both baseline measurements and post-training measurements; (3) evaluate effectiveness of training in facilitating a behavioral change in dental care providers; and (4) evaluate usability and feasibility of ergonomic engineering changes.

Technical Approach: The study will consist of two basic phases: a descriptive phase to collect baseline discomfort measurements by type of procedure and an intervention phase involving both training and engineering interventions.

Descriptive Phase: All dental providers (dentists and dental hygienists) at Fort Lewis, WA will be invited to participate in this study. Once a consent form is completed, the subjects will be given a brief questionnaire pertaining to general risk exposure and information on age, gender, rank or GS level, length of time in the job, previous injuries (treatments/lost work time (how long), treatments/lost work time (how long) predisposing conditions, current conditions (how long) and injury predictive personal characteristics. Clinic administrative records will be reviewed for information on the types of procedures performed, average workload, injuries, compensation claims, and lost work time over the past 3 years. Worker focus groups will be conducted to determine what changes to the workplace should be made to improve comfort and productivity. A questionnaire on management style will be given to all supervisors.

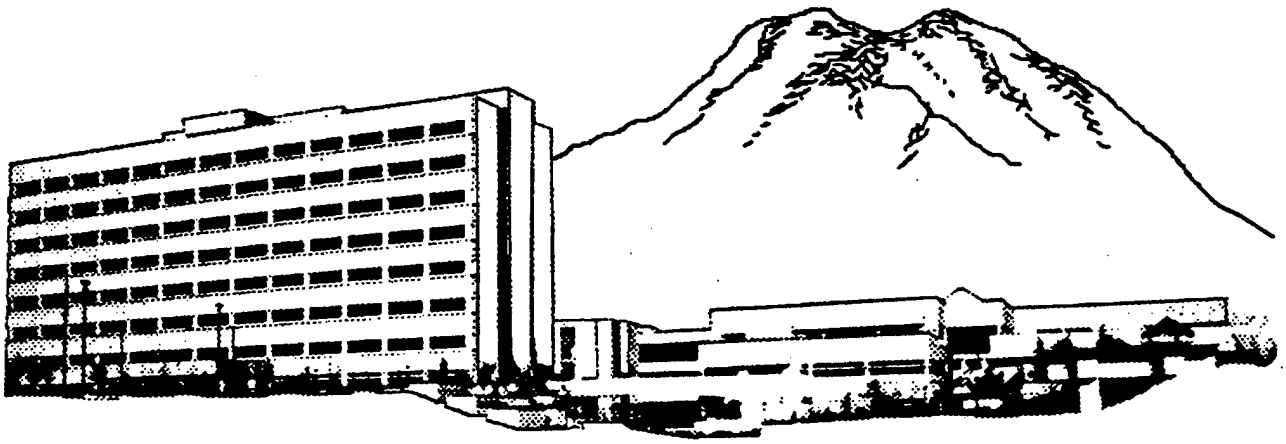
Baseline measures: Each provider will complete sections A-E of the Department of Defense Job Requirements and Physical Demands (JRPD) Survey (Description of Work, Organizational Factors, Physical Effort, Discomfort Factors, and General Questions). Each participating provider will complete a brief questionnaire on discomfort after every procedure for a four-week period.

Study Process: The procedure to collect the discomfort self-report questionnaires; receptionist completes section A of form with provider(s) identification, date, time of day category, attaches form(s) and envelope to patient record, provider(s) complete procedure and completes procedure documentation with patient record and section B of discomfort questionnaire and places in envelope and seals envelope. Provider returns sealed questionnaire to receptionist. Receptionist compiles all sealed questionnaires for the day. Study staff member collects questionnaires at the end of the day.

Intervention Phase: Training; Each participating provider will receive a short training session on dental ergonomics. A question and answer session will follow the training. In addition, each provider will be given contact information to answer specific ergonomic questions as they arise. After the training is completed, each provider will continue to complete the previously described discomfort surveys following every procedure for a period of four weeks. At the end of the four weeks each provider will complete a Training Impact Questionnaire on the training and any behavioral changes that occurred as a result of the training.

Equipment; Provider seating and handtools will either be modified or replaced to meet ergonomic design criteria based on dental tasks. These modifications or replacement decisions will be made by expert ergonomists in consultation with local dental care providers and other dentists throughout the Army. The design changes or replacements decisions will be made to balance both ergonomic concerns and financial realities in order to produce a program template which can be used in other Army dental clinics. Providers will receive training on the design modifications or replacements and the proper use and adjustment of the items. After the ergonomic changes are in place and training completed, providers will continue to complete the previously described discomfort survey after each procedure for a four-week period. At the end of the four-week period, each provider will complete a Usability and Feasibility Questionnaire for the modified or replaced equipment.

Progress: This study has been cancelled due to lack of participation of study group. The study was unable to obtain the appropriate amount of baseline information to progress the study past the baseline phase. Without the baseline information the PI was unable to introduce training and engineering controls to the study and to measure their effectiveness.



Detail Summary Sheets

Madigan Center Judge Advocate

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/059 **Status**: Terminated

Title: A Regional Military Health Care System Response to Expanding Genetic Research; Ethical, Legal, and Social Implication

Principal Investigator: LTC Lanie Olmsted, JA

Department: Center Judge Advocate **Facility**: MAMC

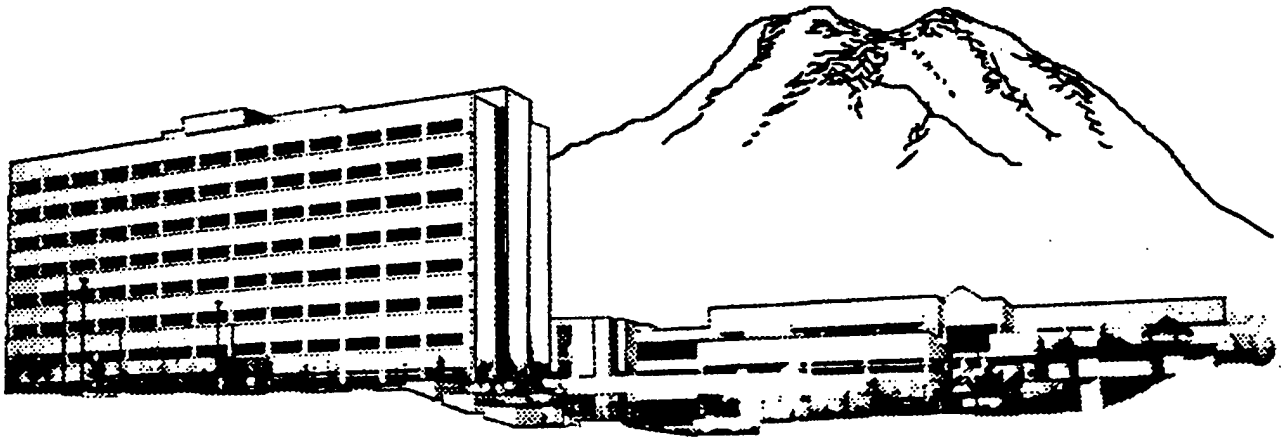
Associate Investigator(s): CPT Melissa W. Hartley, JA; Mr. Richard P. Geib, JA; Ms. Barbara A. Jones, AA; Troy H. Patience, B.S.; Ms. Tammie L. Maple, M.B.A; LTC Kenneth S. Azarow, MC; COL Jerome B. Myers, MC; Laura S. Martin, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Dec 01	N/A

Study Objective: Advances in biotechnology, molecular genetics and informatics demand IRB oversight; these ethical challenges must be integrated (incorporated) in the existing legal framework and regulatory procedures for the protection of research subjects from unintended consequences of unrecognized risks? These require adaptation of IRB policy and Integration convergent policies.

Technical Approach: Policy research, survey of existing IRB approved protocols and the informed consent process. Adaptation of new policy to guide the ethical (legal) conduct of the IRB review and oversight of genetic research.

Progress: This study has been terminated. No work was accomplished on this study due to time constraints of investigators.



Detail Summary Sheets

Admin. Residents/Deputy Commander for Administration

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/038 **Status**: Completed

Title: Clinical Outcomes and Resource Utilization of Well-managed Diabetics in the Military Medical Care System

Principal Investigator: CPT Robert Lenza, MS

Department: DCA/Admin Residents **Facility**: MAMC

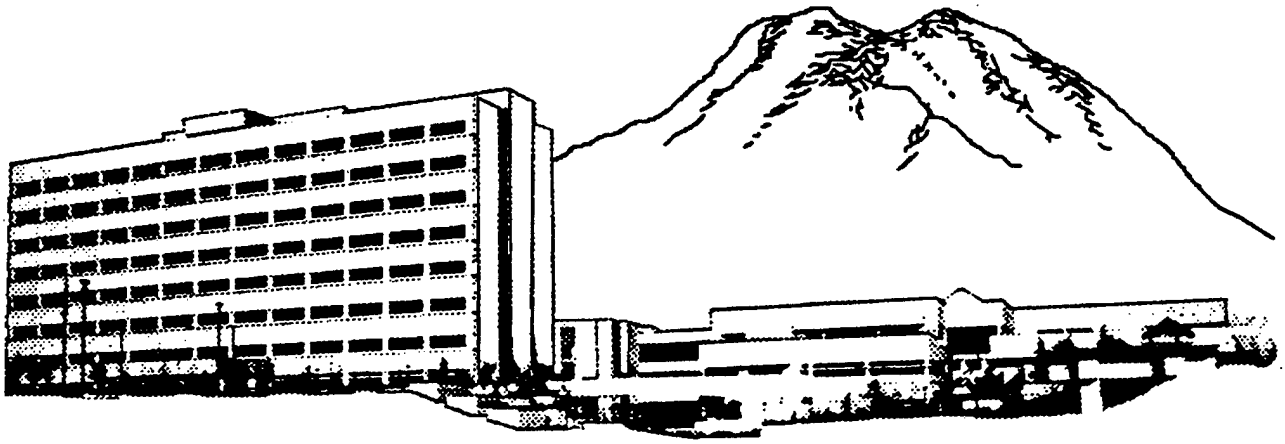
Associate Investigator(s): LTC Margaret Rivera, MS

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Jun 01	N/A

Study Objective: 1) Resource utilization at MAMC related to how well patient is managed (follow cpg), 2) Resource utilization to xrt program

Technical Approach: Use of existing computerized patient health care data to identify MAMC patients with DM. Review of records for adequacy of adherence to DM CPGuidelines. Evaluate outcome variables and resource utilization among subjects and between cohorts. Additionally, assess the attributable benefit of participation in an XRZ program:

Progress: Examination of records for this retrospective chart review has been completed. Conclusions drawn from the study show that implementation of Clinical Practice Guidelines and a Patient Prescription Exercise program can significantly reduce the total resources used by participating patients.



Detail Summary Sheets

Department of Clinical Investigation

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/023 **Status**: Terminated

Title: Cholesterol Transfer in the Term Human Placenta: The Effects of Lipoprotein Cholesterol Infusion in the Dual Perfused Isolated Human Placental Cotyledon Model

Principal Investigator: COL Roderick F. Hume, MC

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): Laura S. Martin, M.D.; MAJ Elizabeth G. Hancock, MC; CPT Todd M. Rossignol, MS; COL Jerome B. Myers, MC; CPT David J. Phillips, MS; MAJ Bardett Fawcette, MC USAF; Robert Steiner, MD; William E. Connor, MD

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Nov 00	10/24/2000

Study Objective: To identify and quantitate the pharmacokinetics of cholesterol transfer in the term human placenta by investigating the effect of lipoprotein cholesterol infusion on the maternal-fetal transfer of cholesterol across the placenta using the dually perfused isolated human cotyledon.

Technical Approach: The placentas will be collected immediately after deliver and transported to the perfusion laboratory. After visual inspection for lacerations or infarcts, the fetal surface will be inspected for a chorionic artery and vein pair supplying a cotyledon. The chorionic artery and vein of the selected cotyledon will be cannulated. This section of the placenta will be clamped into a holder and then the cotyledon will be transferred to a temperature-controlled chamber maintained at 37 degrees C. A second cotyledon will be prepared in an identical manner by a second investigator. All perfusions will be started within 20 minutes of placenta delivery. After establishing baseline perfusion steady states for approximately 30 minutes using Hanks' balanced salt solutions, perfusion pressures and effluents will be obtained. At this time a solution of Hanks' balanced solution with albumin and heparin with various concentrations of cholesterol (100-400 mol/L) will be switched with the perfusate of one of the cotyledons. After a 20 minute steady state period perfusion pressures and perfusates will be collected, goal out of 4-6 hours. Perfusate cholesterol concentrations relevant to natural occurring maternal-placental cholesterol concentrations will be obtained. There will be a total of 4 collection periods. Remaining placental tissue not used in the experiment may be submitted to pathology for evaluation to assure normal placental histology or frozen for further study.

Progress: This bench study has been terminated at MAMC due to the principal investigator's retirement from the military and no new PI identified.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/073	**Status**: Ongoing

Title: Comparative Medical/Surgical Research and Development (Limited)

Principal Investigator: MAJ L. Layne Norlund, VC

Department: Clinical Investigation	**Facility**: MAMC

Associate Investigator(s): None.

Start Date:	**Est. Completion Date:**	**Periodic Review:**
3/8/2000	Mar 03	6/20/2001

Study Objective: (1) To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients; in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC and (2) To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies, and surgical advancement training proposed by MAMC-affiliated medical staff.

Technical Approach: This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) development or refinement of animal models for medical/surgical research or training; b) limited pilot studies (animal) that are preliminary to more extensive research proposals; c) practice of newly described surgical procedures, in animal models, prior to utilization in the MAMC human surgical patient population. Animal use in these investigative pursuits will generally be limited to not more than four (4) animals per co-investigator or procedure, and will be conducted as acute (non-survival) experiments unless animal survival is specifically justified. Details of proposed model development or refinement, pilot studies, or surgical procedure practice will be provided as procedure specific addenda to this standing protocol. This protocol will only be used for preliminary pilot/model development and MAMC surgical care advancement, and will not be used to generate data sufficient for publication in scientific journals.

Progress: This protocol was not utilized during FY 01. The study remains ongoing for pilot animal model protocols.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/146 **Status**: Ongoing

Title: Biomedical Research or Training Using Animal Tissues Only

Principal Investigator: MAJ L. Layne Norlund, VC

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): None.

Start Date:	Est. Completion Date:	Periodic Review:
9/13/2000	Sep 03	12/5/2001

Study Objective: To reduce live animal use in biomedical research or training at MAMC, by facilitating animal tissue use as alternative research/training models, where feasible.

Technical Approach: Animal cadavers or tissues used under this protocol will be derived from MAMC IACUC-approved animal use protocols, other AAALAC accredited research institutions, or from local commercial slaughter houses unless otherwise specified in addenda and approved by the IACUC in advance of procurement. This document will serve as a generic, IACUC-approved protocol providing specifications and assurances for animal tissue use in biomedical research or training, which will be adhered to by all persons using this protocol. Specific activities differing from the generic provisions of this protocol will require description and/or justification by addendum, and IACUC approval, prior to conducting the described research or training.

Progress: This protocol was not utilized during FY01. The study remains ongoing for future animal tissue research protocols.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/091 **Status**: Ongoing

Title: Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra hircus, Pig/Sus scrofa, and Sheep/Ovis aries)

Principal Investigator: MAJ L. Layne Norlund, VC

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): COL William E. Eggebroten, MC; LTC Clifford A. Porter, MC; SFC DiAnn Dansereau, USA

Start Date:	Est. Completion Date:	Periodic Review:
3/14/2001	Feb 04	N/A

Study Objective: To train federally affiliated (e.g. DoD/VA) HCPs in advanced/combat trauma management skills essential to the maintenance of combat medical readiness. More specifically, this protocol encompasses both formal ATLS certification training, and duty/mission-specific combat-relevant trauma management training that is of limited availability to military HCPs in peacetime practice.

Technical Approach: The protocol supports three levels of trauma management training, as follows: 1) Formal Advanced Trauma Life Support (ATLS) training and certification (physicians), recognized and accredited by the American College of Surgeons (ACS). 2) Combat-relevant Trauma Management training for physicians (CTM-P), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 3) Combat-relevant Trauma Management training for ancillary medical personnel (CTM-NP), focusing on "hands-on" training of mission/duty-related trauma intervention procedures selected from levels 1 and 2, above. Training associated with this protocol will utilize both inanimate (e.g. mannequin, cadaver, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. CTM-NP training (level 3, above) will generally be combined with CTM-P training activities (level 2, above), or will utilize animal cadavers in order to minimize the number of live animals sacrificed in support of this protocol. Animal species used for this protocol will include sheep, goat and pig.

Progress: Two standard ATLS courses, and four Combat Trauma Management Training exercises were conducted under this protocol during FY01, providing military-relevant trauma management training to 55 doctors, 10 nurses or PA's, 48 medics, and 5 OR technicians; for a total of 410 training man-hours (see list below).

Date/Event:	Animal Use:	Audience - #:	Tng Man-hours:
29 Mar 01 / ATLS Course	Goat - 4	MD - 20	40
29 Apr 01 / MedRed Conf Combat Trauma Mgt Tng	Goat - 2	MD - 6 Nurse - 6 Medic - 12	72
7 Jun 01 / Ranger Medic Tng Combat Trauma Mgt Tng	Goat - 4 Pig - 4	MD - 2 Medic - 20	86
26 Jul 01 / ATLS Course	Goat - 4	MD - 20	40
1 Aug 01 / 250th Fwd Surg Team, Combat Trauma Mgt Tng	Goat - 3	MD - 3 Nurse - 2 Medic - 4 OR tech - 3	72
7 Sep 01 / 915th Fwd Surg Team & 3/2 ID IBCT, Combat Trauma Mgt Tng	Goat - 4	MD - 4 Nurse/PA - 2 Medic - 12 OR Tech - 2	100

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/032 **Status**: Ongoing

Title: Birth Weight as a Function of Maternal Duty Status and Participation in Mandatory Physical Training Program

Principal Investigator: Troy H. Patience, B.S.

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): COL Robert E. Ricks, MC; COL Byron C. Calhoun, MC, USAF; CPT Melissa V. Terry, MC; LCDR Mary G. Battaglia, NC, USNR; COL Roderick F. Hume, MC; MAJ Katherine M. Opitz, AN; CPT Sandra L. Hernandez, MC; CPT Kim Whittington, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Oct 02	N/A

Study Objective: Conflicting reports have confused the impact of maternal work or phyical activity upon fetal development. The majority of pregnant women work outside the home. Active duty soldiers are a special case of workers. One of the requirements to remain on active duty is maintaining physical fitness standards for gender and age group. Specifically designed exercise programs for pregnant and postpartum soldiers have been ongoing a Ft. Lewis for several years. Voluntary and mandatory participation depends upon active duty unit assignment. All active duty pregnancies are cared for by the OB depart at MAMC, MFM/DCI consults for the PSWP, the vast majority of participants deliver at MAMC. Therefore, we propose to tabulate birthweights and percentile for gestational age at delivery to compare those newborns of active duty who did or did not participate in the PSWP, and matched dependent wives as controls.

Technical Approach: Does maternal work or working out alter birth weight. Existing medical records (CHCS, CIS and Birth Register) will be reviewed to collect pertinent information in coded files (no linkage to person). Current duty status (20- vs 30), maternal age, gestational age at delivery, birth weight and complications are in the Delivery Books. CHCS & CIS maintain the obstetrical records; which will be reviewed by AI (MT, EH) to verify smoking, maternal ponderal index and diabetes status. PSWP participant duty roster is maintained as an EXCEL data sheet. Correlations for each case (AD-+PSWP & AD- not PSWP) will be matched to the next same age, parity and gestational age birth in the record. Data collection will be b y the AI (RFH) on a Filemaker Data record designed for this purpose by the PI. Three cumulative distribution curves of birth weight by gestational age will be generated for 20+,20-, & 30. Confounders include smoking status, parity, race, and gestational diabetes, Materanl ponderal index will be calculated from ht and weight; neonatal percentile will be calculate from birth weight by gestational age at birth reported as a %tile and categorized as LGA (>90th%tile), AGA or SGA (<10th%tile). Major question is does maternal duty status, or mandatory exercise lead to smaller babies, or more perterm or SGA births?

Progress: More than 2000 records have been reviewed. This five year study continues to collect data via birth records which are not kept electronically.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/043 **Status**: Ongoing

Title: Immunohistochemical and Molecular Biotechnicologic Detection of the Human Adrenomedullin Receptor

Principal Investigator: CPT Todd M. Rossignol, MS

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): COL Roderick F. Hume, MC; MAJ Christina C. Apodaca, MC; COL Byron C. Calhoun, MC, USAF; Mr. James R. Wright, M.T.; Mr. Louis A. Matej, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Sep 00	12/10/2001

Study Objective: (1) Produce a polyclonal antibody that recognizes both the native and denatured forms of the human adrenomedullin receptor. This will allow the detection of this receptor in both immunohistochemical assays and western blot analysis. (2) Perform immunohistochemical assays and western blot analysis on various compartments of the human placenta.

Technical Approach: A peptide sequence corresponding to amino acids 5-19 and 244-254 of the human adrenomedullin receptor will be sent to Sigma Genosys to be synthesized and conjugated to KLH. This peptide will then be used to produce polyclonal antibodies. Once the antibodies are produced, preliminary immunohistochemical assays will be run to determine the proper dilution of the antibody. In order to verify that the antibody is recognizing the intended protein, the antibody is pre-incubated with the purified antigen. Upon identifying eligible placentas, the primary investigator will be notified at the time of the delivery. The placenta will be obtained immediately after delivery and placed on ice. Approximately 5 grams each of the placental amnion, cotyledon, umbilical vein and umbilical artery will be dissected and isolated. 1-2 cm2 area of the frozen tissues sections will be mounted on the cryostat using OCT. The tissues will be sliced into 5-10 uM sections. These sections will be probed with the primary antibody (Rabbit Anti-Adrenomedullin Receptor IgG) after being blocked and then after washing they will be probed with the secondary antibody (Mouse Antirabbit IgG) conjugated with Fluorescein Isothiocyanate (FITC). The slides will be viewed using a fluorescent microscope with an excitation wavelength of 450-490 nm and filtered at 520-560 nm.

Progress: Commercial antibody production did not produce any useful antibodies. Investigators are now focusing on a molecular approach to producing the adrenomedullin receptor for use in this protocol.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/006 **Status**: Ongoing

Title: Effect of JP-8 Fuel and Fuel Exhaust on Markers of Inflammation and Immune Function in Exposed Workers Compared to a Non-exposed Cohort

Principal Investigator: CPT Todd M. Rossignol, MS

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): Terri L. Blake, Ph.D.; MAJ Thomas C. Delk, MS; Greg S. Opheim; David N. Weissman, M.D.; Mr. Mark A. Lucas, MS; Mr. James R. Wright, M.T.; Mr. Louis A. Matej, B.S.; Mr. Ernest R. Crutcher; CPT Shannon N. Shaw; CPT Derek J. Licina; Mr. Lynn B. Whittern

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Aug 01	N/A

Study Objective: 1) Analyze nasal lavage and blood samples from JP-8 exposed and non-exposed workers for markers of inflammation and immune function. 2) Collect cells by nasal scraping from these workers for analysis of induction of transcription of specific genes: CYP1A1, AhR, and AhR-NT. 3) Administer a questionnaire focused on pulmonary function and illness in these workers. 4) Collect personal and ambient air samples for analysis.

Technical Approach: This study is a NIOSH funded collaboration with the DOD to describe the exposure of a cohort of Ft. Lewis workers exposed to engine exhaust compared to a cohort of workers not routinely exposed to exhaust. 60 workers in each cohort (120 total) will undergo nasal swabbing to collect cells and nasal lavage for assessment of cytokine levels by ELISA (IL-1, IL-6, IL-8, TNF-alpha, and MIP-1). A 5 ml blood sample will be used to measure serum IG-E. These biomarkers will be used to assess the degree of upper respiratory inflammation and immune response. Personal and worksite area air sampling will also be performed to describe the composition of the fuel exhaust. Members of each cohort will answer a standardized questionnairre about work and smoking history and respiratory symptoms. Study results will be reported to NIOSH and published in peer-reviewed journals in order to direct future research into potenial health effects of engine exhaust exposure.

Progress: 60 volunteers enrolled in this study and samples collected. Study is currently in data analysis.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/060	**Status**: Completed

Title: Re-engineering Placental Perfusion Rings: Formal Focus Group Analysis

Principal Investigator: CPT Todd M. Rossignol, MS

Department: Clinical Investigation	**Facility**: MAMC

Associate Investigator(s): COL Roderick F. Hume, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
2/27/2001	Mar 02	N/A

Study Objective: The methods of placental perfusion have evolved over the past half century. Krantz et al first reported the ex vivo perfusion of the human perfusion in 1962. The first modern device for the perfusion of the human plancenta was reported in the AJOG 1972 and has been modified by Myatt 1983 and Markenson 1993/5. We have experimented with various materials to obtain an optimal system. Our goal is to solicit feedback via a formal focus group survey to assess the utility and critical review of several prototype placental rings.

Technical Approach: Having developed an acceptable prototype with new materials. We plan to distribute sets to several laboratories with experience in placental perfusion. Questionaire explores areas of key interest. We will use this feedback to futher modify the system. We plan to graphically depict our system and the historical development overtime through collaboration with the graphic artist in Medical Illustration. Goal(s): 1. present poster of methods at SMFM or SGI 2002, (2) publish an Instruments & Methods paper in the "green journal", and (3) further refine the methodoligic approach to placental studies.

Progress: Feedback garnered by surveys over the past year lead to several changes to the existing system, especially the materials used for the placental rings (plastic appliance to hold perfused cotyledon). Further modifications were made to the ergonomics of the lab space. Formal teaching using graphical displays was developed to augment the collection of precise placental tissues used for molecular studies, histopathology, and immunochemistry. Refinement software for data coordination allows integration of coded tissue results with abstracted clinical information adhering to ethical constaints of medical information and genetic privacy. Conclusion: The improved system is much easier to learn, yielding more reliable results. This also allows integration with other researcher interests; differential gene expression, apoptosis, and developmental outcomes. The ultimate success will be exportation of progeny laboratories.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/130 **Status**: Ongoing

Title: Production of Anti-Adrenomedullin Receptor Monoclonal Antibodies in Mus musculus

Principal Investigator: CPT Todd M. Rossignol, MS

Department: Clinical Investigation **Facility**: MAMC

Associate Investigator(s): Mr. Louis A. Matej, B.S.; Mr. James R. Wright, M.T.; COL Byron C. Calhoun, MC, USAF; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/11/2001	Jul 04	N/A

Study Objective: To produce a monoclonal antibody that is specific for the human adrenomedullin receptor in order to evaluate the following hypothesis: Preeclamptic human placental tissues express a lower level of the adrenomedullin receptor than do normal placentas.

Technical Approach: This protocol proposes the use of not more than 10, Balb/c mice to produce adrenomedullin receptor protein-sensitized hybridoma cells by injecting purified adrenomedullin antigen into mouse spleens, stimulating non-differentiated B-lymphocytes to replicate and differentiate into anti-adrenomedullin plasmocytes (AAP). Mice will be euthanized four (4) days after spleen injection, and AAPs will be separated from splenic homogenate and fused to commercially available mouse myeloma cells to form anti-adrenomedullin hybridoma cells (AAH). Anti-adrenomedullin hybridoma cells will then be cultured to produce monoclonal anti-adrenomedullin antibody for immunohistochemical detection of adrenomedullin in normal and preeclamptic human placenta tissues.

Progress: Work has not yet been initiated on this bench protocol at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/025 **Status**: Ongoing

Title: The Department of Clinical Investigation's Molecular Biology Short Course for Physicians

Principal Investigator: CPT Todd M. Rossignol, MS

Department: Clinical Investigation **Facility**: MAMC

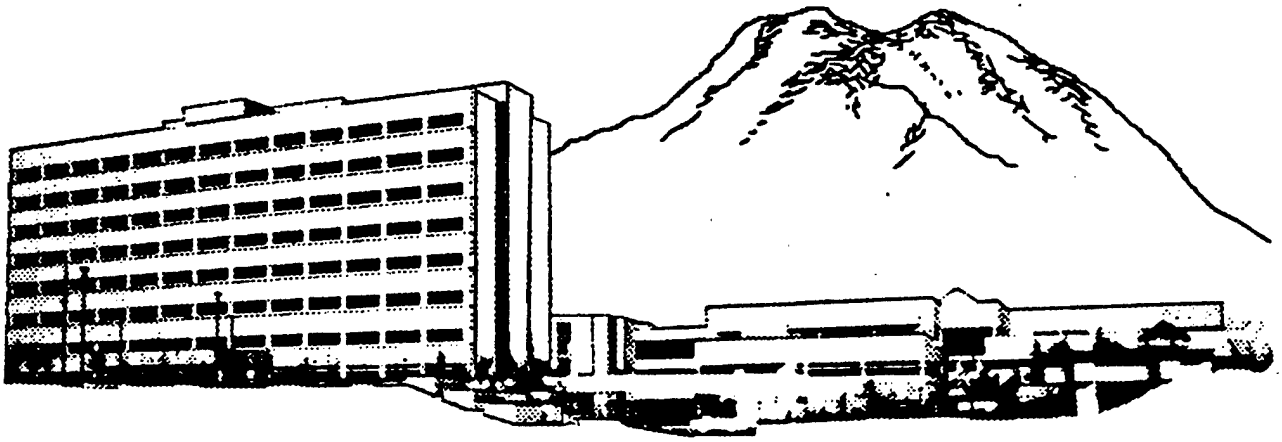
Associate Investigator(s): MAJ Rodger K. Martin, MS; CPT Wade K. Aldous, MS; CPT Aziz N. Qabar, MS

Start Date:	Est. Completion Date:	Periodic Review:
01/20/1995	Jun 96	12/10/2001

Study Objective: To familiarize MAMC residents, fellows, and staff physicians with the research capabilities and resources of the Department of Clinical Investigation. To support MAMC Graduate Medical Education through instruction and research. To foster an appreciation of molecular biology concepts in residents, fellows, and staff physicians and to augment their understanding of the scientific literature. To encourage residents, fellows and staff physicians to develop research protocols incorporating these technologies.

Technical Approach: This course is designed to familiarize physicians with the most commonly encountered molecular approaches in the scientific and clinical literature. It is hoped that this will foster more critical reading of the literature as well as encouraging the development of research protocols employing these technologies. Although six weeks in duration, students will be required to attend two hours of lecture per week in addition to approximately seven hours of laboratory exercises. Topics addressed and used in the course range from DNA isolation to cloning and sequencing of PCR products.

Progress: No courses were taught in FY01.



Detail Summary Sheets

Hospital Dental Clinic

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/035	**Status**: Completed

Title: Low Energy Laser (helium-neon) Biostimulation and Mucosal Wound Healing

Principal Investigator: MAJ Charles E. Middleton, DC

Department: Dentistry	**Facility**: MAMC

Associate Investigator(s): COL Wayne Olsen, DC; LTC Charles R. Weber, DC; LTC Peter Zagursky, DC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
1/25/2000	Apr 00	1/26/2001

Study Objective: To illustrate that the application of low energy laser radiation to mucosal wounds in vivo results in a shortened healing time and that the hand held laser is an effective device to deliver low-energy radiation.

Technical Approach: Fifty patients scheduled for the bilateral surgical extraction of maxillary third molar teeth will have one of two standard vertical releasing incisions lased with a helium-neon hand held laser at time of surgery. The contra-lateral incision will serve as control. The helium-neon laser is a commercially available (laser-pointer) instrument that is highly portable and field ready. This study will attempt to prove that the application of low energy laser radiation to surgical wounds results in a biostimulatory process with resultant shortened healing times. Wound Analysis Index will be secured at 4, 7, 14 and 21 days post-surgery. Lasing energy fluence will be at 1.2 j/cm2. The data will then be analyzed for statistical significance.

Progress: Thirty-three (33) patients requiring the surgical extraction of maxillary right and left impacted third molar teeth had 1 of 2 full-thickness mucogingival flap incisions lased by a handheld He-Ne diode laser. Fifty-seven percent (57%) of the participant's lased incisions had accelerated healing at post-exposure day 4. Accelerated healing peaked at post-exposure day 8 at sixty-eight percent (68%). There was no difference beyond day 14. This study's results tend to support the biostimulatory properties of low-energy laser irradiation as applied to surgical wounds.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/024 **Status**: Terminated

Title: Low Energy Laser (helium-neon) Biostimulation and Wound Healing

Principal Investigator: MAJ Charles E. Middleton, DC

Department: Dentistry **Facility**: MAMC

Associate Investigator(s): COL Wayne Olsen, DC

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Apr 01	N/A

Study Objective: (1) To support or oppose published data on the effectiveness of wound healing and the use of the helium-neon laser, (2) to illustrate that the application of low energy laser radiation to wounds in vivo results in a shortened healing time and (3) to demonstrate that the hand held laser is an effective device to deliver low-energy radiation.

Technical Approach: Twenty-five patients scheduled for BSSO's will have one of two standard percutanious incisions lased with a helium-neon hand held laser at time of surgery. The contra-lateral incision will serve as control. The helium-neon laser (laser-pointer) is a commercially available instrument that is highly portable and field ready. This study will attempt to prove that the application of low energy laser radiation to surgical wounds results in a biostimulatory process with resultant shortened healing times. Wound analysis will be secured at 3, 7, 14, and 21 days post-surgery. Lasing energy fluence will be at 1.2 j/cm2. The data will then be analyzed for a statistical significance in healing rates between the lased and non-lased incision.

Progress: This study was terminated by the PI prior to its initiation at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/005 **Status**: Terminated

Title: Wound Healing Comparison Using Standard Versus Micro-sutures

Principal Investigator: COL Craig C. Willard, DC

Department: Dentistry **Facility**: MAMC

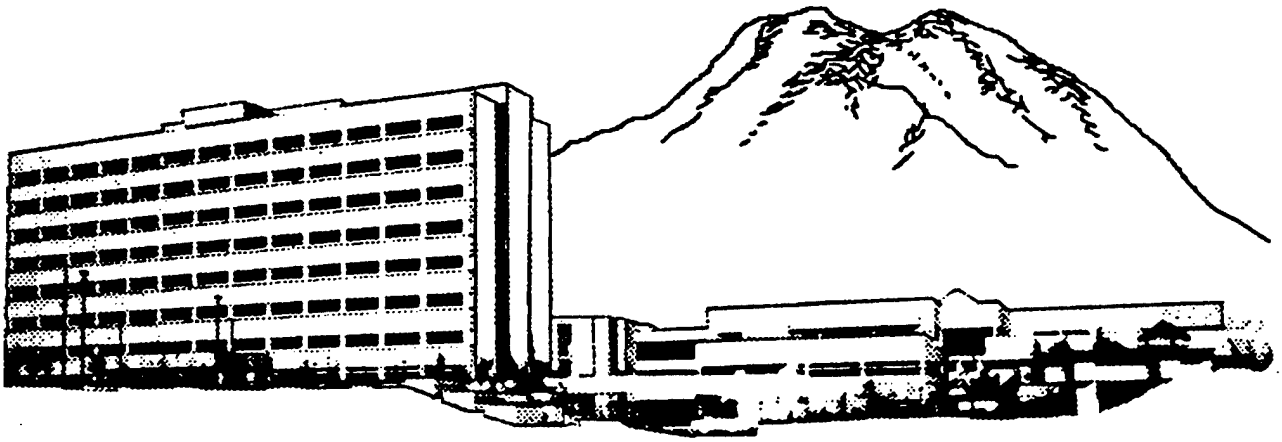
Associate Investigator(s): COL(Ret) Robert B. O'Neal, DMD, MEd, MS; Thomas H. Morton, Jr., DDS, MSD; LTC Alan D. Smith, DC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Dec 00	N/A

Study Objective: To determine the use of a smaller suture size or the closer placement of smaller sutures will result in improved wound healing at 7 days when compared to the use of a larger, standard suture size.

Technical Approach: This is a bench study based on a University of Washington, IACUC approved protocol of the same name. Work to be accomplished at MAMC will be analysis of the slides and/or digitized impages produced by the UW investigators.

Progress: This study was terminated at MAMC, 30 Jan 01, before it could be initiated at MAMC.



Detail Summary Sheets

Department of Emergency Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/070 **Status**: Ongoing

Title: A Survey to Determine the Incidence of Infection in Plantar Puncture Wounds

Principal Investigator: CPT Charles P. Buck, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): CPT Austin W. Burgess, MC; MAJ David A. Della-Giustina, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/22/1999	Jul 99	6/26/2001

Study Objective: To determine the incidence of infection in plantar puncture wounds, and to determine if infection rates are different for healthy vs. immune compromised and aggressive vs. conservative initial management groups.

Technical Approach: All adult ambulatory patients identified by the triage nurse as having a prior plantar puncture wound will be asked to complete an anonymous survey. Investigators will periodically collect the forms and transfer the data to spreadsheets for further analysis. Method of data analysis: Primary is the overall incidence of infection of plantar puncture wounds, with data analyzed at 95% confidence intervals. Secondary is the infection rate for two groups, which will consist of subjects that had aggressive initial treatment vs. conservative treatment, and those who were healthy at the time of injury vs. those with vascular or immuno-compromising diseases. These groups will be analyzed by Chi-Square to determine statistical significance at $p < 0.05$.

Progress: Investigators are currently tabulating the results of the surveys. The study remains ongoing for data analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/135 **Status**: Ongoing

Title: Oral Dexamethasone in the Emergency Department to Prevent Relapse of Acute Migraine Headaches: A Randomized, Placebo Controlled Trial

Principal Investigator: CPT Michael C. Hirsig, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): MAJ David A. Siegel, MC; CPT Brian Ness, MC; CPT Tim Gregory, MC; CPT Brad A. Kilcline, MC; CPT Timothy Talbot, MC; CPT Jeremiah Johnson, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/25/2001	feb 02	N/A

Study Objective: To determine the incidence of recurrence of migraine headaches up to 24 hours after discharge from the emergency department and to determine if oral dexamethasone given in the emergency department will lead to a reduction in patient revisits for headache at 24 hours.

Technical Approach: This study plans to enroll 120 and will include males and females aged 18-65 with known history of migraine headache presenting to the ED with a chief complaint of headache. During initial evaluation patients will be informed of the study and asked to consent. Their migraine will be treated according to study protocol if patient consents. The physician will fill out a questionnaire that asks the patient to rate their headache at presentation and discharge (visual analog scale of 0-10, 0 being no headache, 10 being worst headache of life). Patients will then be asked to take the study drug (which will be randomized in plastic bags). The patient is then discharged from the ED and told they will be contacted in 1-2 days and asked if they had to seek additional medical care for their headache or if they had to use any rescue medications that were prescribed to them in the past 24-48 hours. Patients will also receive a self-addressed stamped envelope with a visual analog scale attached and asked to mail the completed scale back to the investigators. Once the final number is reached, the code of the randomized numbers will be revealed and the data will be tabulated regarding the control group's demographic, pain scale data vs. the treatment groups demographic and pain scale data. Outcome variables are headache at 24-48 hours causing the patient to seek additional medical care and a secondary outcome of use of rescue medication.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/104 **Status**: Terminated

Title: A Randomized, Placebo-Controlled, Study of Intravenous Magnesium in Acute Benign Headaches

Principal Investigator: MAJ Kurtis R. Holt, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): Marvin K. Valrey, MD; Leonard Frank, MD; Laura Fife, MD; CPT Thomas R. Coomes, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Oct 00	10/24/2000

Study Objective: Our purpose is to evaluate the efficacy of IV magnesium in acute headache pain, in a prospective randomized, double blind, placebo-controlled trial. Because of the difficulty of classification, as well as the desire to make this study more applicable to the typical clinical practice of emergency medicine, we will evaluate all patients who present with benign headache pain.

Technical Approach: The Pharmacy will pre-prepare bags of drug and placebo in lots of ten by standard randomization procedures. Each bag will be labeled with a study number, the name of the study, and the date of preparation/expiration. Emergency Department personnel and patients will be blinded to the study treatment. The Pharmacy will hold the randomization code which will only be broken in the event of an emergency. Staff and resident physicians in the Emergency Room will obtain patient consent. Enrolled patients will be assigned the next available treatment number and corresponding treatment. The physician via infusion pump will administer the study treatment. Data collection before, during, and after treatment, may be done by physician or nursing staff. Study data forms will be placed in opaque envelopes labeled "Mg/HA study" and placed in the secure drug cabinet. Study investigators (Coomes and Valrey) will periodically collect the data sheets and compile the data.

Progress: This study has been terminated due to low subject accrual and difficulty obtaining study drug from pharmacy. Data from eleven subjects continues to be analyzed. Data acquired thus far indicates there is no difference in treatment of migrane headaches with the addition of magnesium.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/061 **Status**: Completed

Title: Variations in the Treatment of Primary Headache Disorders in Emergency Medicine

Principal Investigator: CPT Timothy R. Hurtado, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): MAJ David A. Della-Giustina, MC; MAJ James T. Vandenberg, MC; ;

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Mar 01	N/A

Study Objective: To describe the parenteral treatment of adults with primary headache disorders in an Emergency Department setting and to asses the compliance of emergency department physicians with national guidelines for the treatment of headaches.

Technical Approach: A multicenter retrospective descriptive study; descriptive analyses will be performed to address the following issues: what medications are employed in the treatment of benign headache disorders, what is the frequency of polytherapy, what is the frequency of multiple visits and how closely do our treatment patterns conform to the evidence-based guidelines.

Progress: Data analysis for this study was completed during FY01. A total of 629 visitis were reviewed. 58% were diagnosed with migraine, 41% with headache, and 1% with tension headache. Twenty parenteral medications were used: 82% were treated with two or more medications, 25% with three or more. Headache management varied greatly among the different IDs. Opiods showed the widest variation (16% to 72%) though DHE (5% to 16%) and prochlorperazine (32% to 59%) and adjunct diphenhydramine with prochlorperazine also varied (42% to 88%). Compliance with headache guidelines also varied greatly among EDs. First line therapy (prochlorperazine) was used in less than half of the cases (46%). Second line therapy was used infrequently (dihydroergotamine 8% and sumatriptan 3%). Patients who were treated with opiods received them as first line agents. Patients who received opiods during their first visit more commonly returned to the ED for repeated parenteral therapy and this therapy was often repeated opiods (87%).

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/080 **Status**: Ongoing

Title: Impact of Chest Radiography Results on Clinician Decision-making for Young Adult Patients Presenting to the Emergency Department with Non-traumatic Anterior Chest Pain, Normal Vital Signs and a Normal Physical Exam

Principal Investigator: CPT Nicholas Martyak, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): Marcus A. Trione, M.D.; MAJ David A. Della-Giustina, MC; CPT Walter A. Fink, Jr., MC; MAJ Robert K. Lather, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 01	6/26/2001

Study Objective: The purpose of this study is to evaluate the impact of chest radiography on clinical decision-making in young adult patients presenting to an Emergency Department with non-traumatic anterior chest pain, normal vital signs and a normal physical exam.

Technical Approach: This study will be a prospective evaluation of clinical decision making by ED physicians. Physicians will be asked to present a pretest diagnosis and treatment plan with disposition prior to interpreting the chest radiograph. Diagnosis and treatment plan will then be assessed in light of the chest radiograph. Finally, the physician will be asked to assess whether the chest radiograph altered the patient's diagnosis or treatment plan. For both diagnosis and treatment, the physician will be asked to classify the change from pre- to post-interpretation as incidental or major. This study's goal is to assist in the generation of rational, evidence-based guidelines for the use of chest radiography in this low-risk (military) population.

Progress: 32 subjects entered this study in FY00 and 28 subjects in FY01 for a total enrollment at MAMC of 60. Enrollment will continue with the expected goal of 250 patients, extending the previously anticipated end date until possibly 2002.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/020 **Status**: Ongoing

Title: A Model for Prehospital 12-Lead Acquisition Without A Dedicated 12-Lead ECG Machine

Principal Investigator: Steven A. Pace, MD

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): Fritz P. Fuller, N.R.E.M.T.-P; COL Alice M. Mascette, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/21/1997	May 96	12/18/2001

Study Objective: To verify that a 12-lead ECG obtained with a cardiac monitor/defibrillation unit is comparable in accuracy to that of a dedicated 12-lead ECG machine.

Technical Approach: The management of ischemic chest pain and acute myocardial infarction hinges on early diagnosis and treatment with thrombolytic agents if indicated. It has been shown that prehospital recognition of acute MI using 12-lead electrocardiography and interpreted by nurses/paramedics trained in ECG evaluation can result in significantly faster times to thrombolytics compared to patients who did not receive a prehospital ECG. Today there are several portable 12-lead machines with computer assisted diagnosis available, but they have only recently became available and are very expensive. By utilizing a portable 12-lead machine (Lifepak 10) and demonstrating that it can produce diagnostic quality ECG's, we hope to make available to a large group of prehospital providers 12-lead capability without an increased monetary investment.

Progress: A total of 50 subjects enrolled in this study and all data has been collected. The study remains ongoing for data analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/028 **Status**: Completed

Title: Pediatric Intubation Training Utilizing the Ferret (Mustela putorius furo) Model

Principal Investigator: Steven A. Pace, MD

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): CPT Daniel Mcilmail, MC; MAJ Nathan T. Rudman, MC; MAJ James T. Vandenberg, MC; LTC Mary P. Fairchok, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/18/1997	Dec 00	12/18/2000

Study Objective: To improve the skill of physicians and other health care providers in pediatric endotracheal intubation, thereby improving the outcome of pediatric patients they treat.

Technical Approach: Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube. 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.

Progress: This protocol reached trienniel expiration, 18 Dec 00, and is currently being rewritten by LTC Mary Fairchok, Staff, Department of Pediatrics, for submission for IACUC review. There were no training sessions held in FY01 under this protocol prior to the closure date.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/007 **Status**: Ongoing

Title: Is There Any Additional Efficacy in Adding Single Dose Intravenous Antibiotic Therapy to an Oral Antibiotic Regimen for Uncomplicated Cellulitis?

Principal Investigator: MAJ David A. Siegel, MC

Department: Emergency Medicine **Facility**: MAMC

Associate Investigator(s): CPT Thomas R. Coomes, MC; MAJ Danny O. Stene, MC; CPT John Westhoff, MC; Janet H. Shotwell, M.D.; MAJ Robert W. Desverreaux, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Nov 02	10/24/2000

Study Objective: To determine if there is any additional efficacy in adding single dose intravenous antibiotic therapy to an oral antibiotic regimen for uncomplicated cellulitis.

Technical Approach: Subjects with cellulitis will be enrolled and randomly assigned into one of two treatment arms. The first arm will receive intravenous cefazolin, and the second arm will receive a parenteral placebo. All subjects will receive a 10-day course of oral cephalexin. Clinical indicators will be assessed and compared at days 7 and 14.

Progress: Nine subjects enrolled in FY01 for a total enrollment of 27 subjects. No adverse events have been noted by the DEM staff. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 98/002	**Status**: Completed

Title: Emergency Surgical Procedures Laboratory Training Using the Goat (Capra hircus)

Principal Investigator: CPT Wesley G. Zeger

Department: Emergency Medicine	**Facility**: MAMC

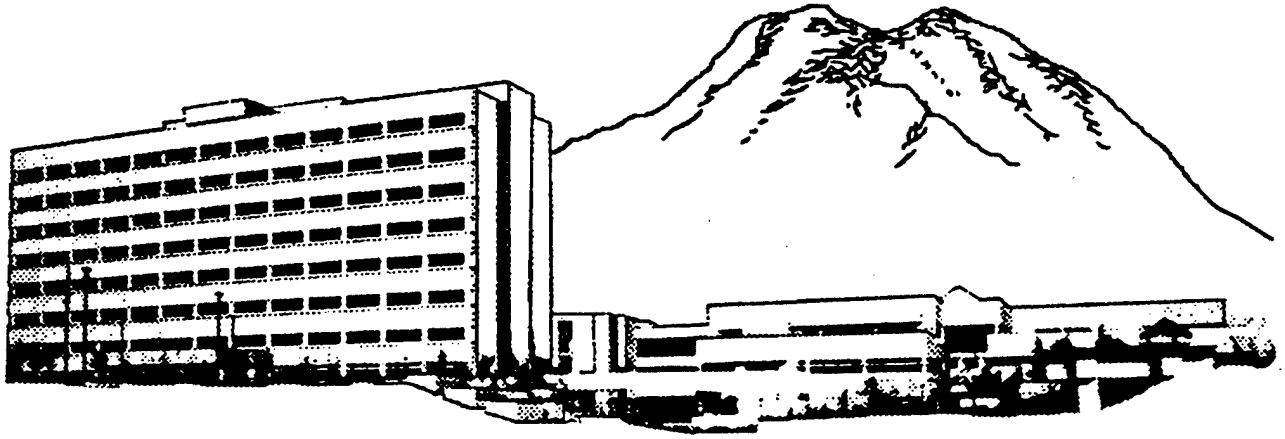
Associate Investigator(s): MAJ Nathan T. Rudman, MC; MAJ James T. Vandenberg, MC; CPT Garrett R. Baer, SP

Start Date:	**Est. Completion Date:**	**Periodic Review:**
10/17/1997	Oct 00	10/28/1999

Study Objective: The objectives of this training exercise are to teach physicians one safe method of performing six life-saving procedures for trauma patients.

Technical Approach: The procedures listed below will be performed under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures. The procedures consist of 1) Chest tube insertion, 2) Thoracotomy, 3) Pericardiocentesis, 4) Diagnostic peritoneal lavage, 5) Venous cutdown, 6) Cricothyroidotomy.

Progress: Protocol reached triennial closure date, 17 Oct 00. This study has been terminated and training has been incorporated into the replacement MAMC protocol #201091.



Detail Summary Sheets

Department of Family Practice

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/107 **Status**: Ongoing

Title: Prevention of Unintended Pregnancy in the Military: A Multicenter Randomized Clinical Trial

Principal Investigator: LTC Diane M. Flynn, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): LTC Jeffrey Clark, MC; COL Jeffrey D. Gunzenhauser, MC; COL Roderick F. Hume, MC; Ann K. Lancaster, CHN; MAJ Wanda A. Barfield, MC; MAJ Sherri Baker, AN

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Dec 04	6/26/2001

Study Objective: To determine if a 3-hour educational class coupled with a system of facilitated access to health care are an effective strategy to: (1) Decrease the rate of unintended pregnancies among military women ages 18-25, (2) Decrease the rate of unintended paternity among military men ages 18-25, and (3) Advance the stage of behavioral change with respect to contraceptive attitudes among military men and women ages 18-25.

Technical Approach: Subjects will be given a questionnaire to determine their attitudes about pregnancy and/or paternity. Subjects will then attend a 3-hour class on reproductive health. After one year, class participants will be again fill out a questionnaire to determine rates of pregnancy/paternity in the previous year and about the outcomes of those pregnancies. Questionnaires will also ask about contraceptive use and behavioral stages of change with regard to contraceptive attitudes.

Progress: Funding has not been obtained for this protocol. The study remains inactive at MAMC pending identification of a possible funding source.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/050 **Status**: Completed

Title: Unintended Pregnancy Prevention Program

Principal Investigator: LTC Diane M. Flynn, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): COL Jeffrey D. Gunzenhauser, MC; COL Roderick F. Hume, MC; Ann K. Lancaster, CHN; LTC Jeffrey B. Clark, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/21/1997	Mar 97	1/23/2001

Study Objective: The purpose of this study is to evaluate the effect of an intervention consisting of education and facilitated access to contraception on the unintended pregnancy rate of active duty US Army soldiers serving at Ft Lewis, WA.

Technical Approach: This research project is a randomized clinical trial designed to determine the effect of education and facilitated access to contraception on unintended pregnancy rates among female soldiers at Ft Lewis. Effectiveness of the intervention will be determined by: 1) Calculating annualized pregnancy rates using SIDPERS data and positive beta-HCG results from the MAMC clinical laboratory; unintended pregnancy rates will be determined from a survey completed at prenatal care orientation. 2) A questionnaire mailed to women in the Intervention Group and the Control Group one year after the intervention designed to assess contraception use, whether the intervention affected contraception use, and the rate of unintended pregnancy.

Progress: Data analysis has been completed for two of three outcomes for the UPPP. (1) Among female soldiers who presented to MAMC for prenatal care one year after program implementation, the rate of unintended pregnancy was compared between women who received the intervention with those who did not, (Relative risk 1.1). (2) Among women who had positive pregnancy tests at MAMC lab, the rate of unintended pregnancy was compared between women from units who received the intervention and those who did not, (No significant difference.) (3) Data analysis remaining includes analysis of responses to mailed surveys administered one year after program implementation.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/018	**Status**: Completed
Title: A Spirituality Curriculum for Family Practice Residency		
Principal Investigator: LTC Colin M. Greene, MC		
Department: Family Practice		**Facility**: MAMC
Associate Investigator(s): David Grembowski, PhD		
Start Date: 11/28/2000	**Est. Completion Date:** Jun 01	**Periodic Review:** N/A

Study Objective: Assess the baseline knowledge, attitudes, and practices involving spirituality and medicine of the residents and teaching staff of the Madigan Family Practice Residency Program. Measure changes in those same categories after the implementation of a new Spirituality Curriculum.

Technical Approach: Baseline questionnaires will be distributed to all DFP residents and staff providers directly associated with residency training. Questionnaires will be numbered, with completed surveys kept separate from any personal data. A code list of names and numbers will be kept in a secure place and used for second or third submissions of the survey and to link paired data with the follow-up study. The identities of responders will be protected from being linked with their answers at all times. Data from the baseline survey will be tabulated and reported as either categorical proportions or as Likert scores, depending on the variable involved. Near the end of the academic year, a follow-up study will be distributed to the same individuals with identical questions to the baseline survey and the addition of queries on lecture and rotation attendance.

Progress: This study was completed prior to PCS of CH Greene. A final abstract of the findings is pending.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/019 **Status**: Completed

Title: Spirituality in Primary Care Residency Training

Principal Investigator: LTC Colin M. Greene, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): Ann Downer, PhED; David Grembowski, PhD

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Jul 01	N/A

Study Objective: Determine the proportion of US family practice and internal medicine residency programs which are incorporating spirituality into their curricula, and the attitudes of the program directors toward religion, spirituality, and their training programs, now and in the foreseeable future.

Technical Approach: Cross-sectional survey; Names and addresses of US family practice and internal medicine residency directors will be obtained from the on-line lists provided by the AAFP and ACP. A code list of addresses and numbers will be created and stored in a secure environment, as needed for activities such as re-mailings. Each participant will receive a survey questionnaire, a self-addressed, postpaid envelope for return of the survey, and a cover letter explaining the purpose of the survey and a request to return the survey blank if he/she chooses not to participate. Three weeks after the first mailing, a second mailing will be sent to all addresses from whom no response has been received. If necessary to achieve the 75% response goal, a third mailing will take place three weeks after the second. Outcome variables will be the proportion of residency programs explicitly teaching spirituality in their curricula, and the mean total, religious, and existential scores on the Ellison Spiritual Well-being Scale for each program director. Data will be tabulated and analyzed using SPSS for Windows 9.0.

Progress: This study was completed prior to PCS of CH Greene. A final abstract of the findings is pending.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/002 **Status**: Completed

Title: Prenatal Breast-feeding Education as a Means to Increase the Rate of Breast-feeding Initiation and Continuation at Six Months Postpartum

Principal Investigator: CPT Mary V. Krueger, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): CPT Irene M. Rosen, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Mar 02	9/25/2001

Study Objective: To determine whether attending a lactation education class significantly increased the rate of Breast-feeding initiation and continuation at 6 months postpartum. Outcomes will be defined by presence of Breast-feeding noted in the nutrition section of the infants' chart.

Technical Approach: This is a retrospective cohort study which will assess the efficacy of lactation education as a tool for increasing the incidence and duration on Breast-feeding . The measure of efficacy will be the Breast-feeding rate at six months postpartum. The mothers' charts will be reviewed for demographic data and Breast-feeding intention. The children's charts will be reviewed for thed presence of Breast-feeding at two weeks, two months, four months and six months. The data will be analyzed using chi-square distribution.

Progress: Data analysis showed a significant increase in Breast-feeding at six months postpartum between those attending classes compared with controls ($p<0.05$). There was no significant difference between rates of Breast-feeding initiation.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/042 **Status**: Ongoing

Title: Identifying Relevant Barriers to Breast-feeding in Active Duty Soldiers Using a Theory of Planned Behavior-based Model

Principal Investigator: CPT Mary V. Krueger, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): CPT Hillary Arnold-Hurtado, DO; COL Thomas C. Michels, MC; CPT(P) Jennifer N. Reynard, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Mar 02	N/A

Study Objective: (1) To use the theory of planned behavior-based structural model for Breast-feeding to determine what factors prevent active duty military females from initiating breast feeding, (2) To use the theory of planned behavior-base structural model for Breast-feeding to determine what factors cause active duty military females to stop Breast-feeding prematurely, (3) To evaluate active duty women's rates of Breast-feeding intention prenatally, initiation at birth and continuation at eight weeks postpartum and compare them to the rates of their employed civilian peers and (4) To determine active duty military female's prenatal and postpartum attitudes towards and knowledge about Breast-feeding .

Technical Approach: Names of prospective subjects will be obtained from a list of patients participating in the Pregnant Soldier Wellness program. This is a program in which all I Corps pregnant soldiers must participate. After giving consent for participation, subjects will complete a survey of infant feeding attitudes at the time of a regularly scheduled OB visit. Survey items will include demographic information as well as questions about work environment and attitudes (reverent beliefs), attitudes toward breast and formula feeding (behavioral beliefs), Breast-feeding knowledge, perception of control (control beliefs) and intent of infant feeding type. At time of delivery, method of feeding will be recorded in the patients' electronic record. This data will be used to determine Breast-feeding initiation rate. At eight weeks postpartum, a second survey will be conducted. This will address the actual barriers that were encountered by the patient, as well as the perceived insufficient milk factor. Information on method of infant feeding will also be obtained.

Progress: 152 active-duty female soldiers completed the surveys. The vast majority of soldiers were pleased to be able to express their thoughts on the study topic. The study will proceed with post-partum data collection as study participants deliver. Data analysis has been hampered slightly by problems with the scanning software, necessitating hand-entry of the questionnaire answers. It is anticipated that data collection will be completed no later than 30 Jun 02, with analysis and write-up completed by 30 Jul 02.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/067 **Status**: Terminated

Title: Effects of the Acetic Acid Wash on the Cytologic Interpretation of the PAP Smear

Principal Investigator: CPT Mary V. Krueger, MC

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): CPT Brian C. Harrington, MC; CPT Robert H. G. Holland, MC; COL Mark E. Potter, MC; CPT Veronica Santee, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/27/1999	Sep 99	4/24/2001

Study Objective: To determine if interpretation of cervical intraepithelial neoplasia is altered by applying acetic acid prior to taking the Pap smear during colposcopic examination.

Technical Approach: Premenopausal, nonpregnant females with abnormal Pap smears (ASCUS or higher grade) presenting for first time colposcopy within 6 months in Family Practice and OB/GYN clinics at Madigan who agree to participate in the study will be stratified based on presenting Pap diagnosis (ASCUS, LGSIL, HGSIL), then randomized to the saline (Group 1) or acetic acid (Group 2) groups. Each group will have a Pap smear done: after saline washing in Group 1, and after acetic acid washing in Group 2. The cytologist will be blinded to the use of saline vs acetic acid for the wash. Cytologic diagnoses will be based on the Bethesda criteria. We will compare the results between the saline and acetic wash groups to assess whether acetic acid changes the diagnosis, specificity, and/or increases the number and/or grade of abnormal slides.

Progress: No work was completed on this study during FY01. The study was terminated as MAMC has changed standard practice regarding PAP smears and gone to utilizing a liquid-based cytology; therefore, the study population is no longer available to continue work on this study.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/039 **Status**: Terminated

Title: Can Distribution of an Educational Interactive CD-ROM Highlighting the Specialty of Family Practice Reverse the Trend of Declining Applications for Residency Training in the Specialty?

Principal Investigator: LCDR Maureen O. Padden, MC, USN

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): COL Joseph F. Yetter III, MC; CDR John R. Holman, MC; CPT Mary V. Krueger, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Nov 04	N/A

Study Objective: To determine whether distribution of an educational interactive CD-ROM highlighting the specialty of Family Practice will lead to, (1) increased participation in family practice clinical clerkships and (2) increased applications for and matriculation into residency training in family practice.

Technical Approach: This is a prospective cohort study aimed at identifying whether distribution of an educational interactive CD-ROM regarding family practice to military medical students will increase interest in the speciality. Increased interest will be assessed by examining participation rates in military family practice clinical clerkships and in increased applications for residency training in family practice at the JSGMEB. Information will be gathered by survey as to how many individuals utilized the CD-ROM and compare these individuals against those who ultimately show increased interest in and entry into family practice.

Progress: This study was terminated, 11 Oct 01, due to lack of grant funding from Uniformed Services Academy of Family Physicians.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/041 **Status**: Terminated

Title: Implementation of the Diabetes Disease Management Program (DDMP) in the Family Practice Clinic at Madigan Army Medical Center: Improved Outcomes?

Principal Investigator: LCDR Maureen O. Padden, MC, USN

Department: Family Practice **Facility**: MAMC

Associate Investigator(s): Larry Green, R.Ph.; CDR John R. Holman, MC; CPT Mary V. Krueger, MC; MAJ Bryan L. Smith, MC; LCDR Patrick H. Ginn, MC, USN; Troy H. Patience, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Feb 02	N/A

Study Objective: To determine whether active disease management applied to a diabetic population within a family practice clinic by a multidisciplinary team can improve health outcomes by several performance measures.

Technical Approach: This is a prospective cohort study involving a high-risk family practice diabetic population to follow outcomes after implementation of an active disease management program. This study will examine hospitalization rates, emergency room visits and continuity of visits with PCM before and after the intervention. Finally, if found to be clinically effective, this study will undertake a cost analysis study of the Diabetes Disease Management Program (DDMP) to measure cost effectiveness.

Progress: This protocol was terminated, 9 Apr 01, before it could be initiated at MAMC. Due to command interest in the project, an expanded version of the study will be submitted for IRB approval.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/073 **Status**: Ongoing

Title: Outcomes of Diabetes Disease Management in a Military Population Using Two Different Models

Principal Investigator: LCDR Maureen O. Padden, MC, USN

Department: Family Practice **Facility**: MAMC

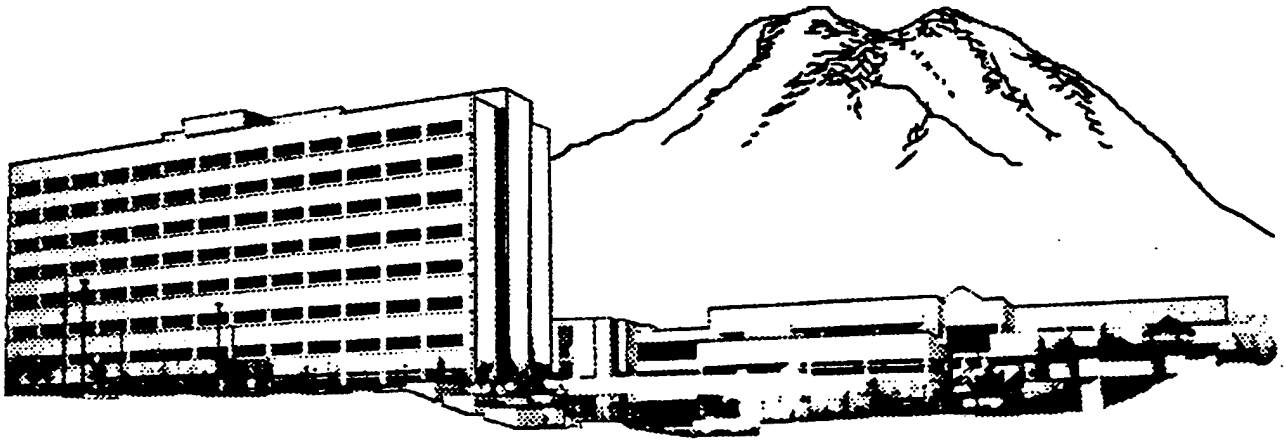
Associate Investigator(s): LCDR Patrick H. Ginn, MC, USN; CDR John R. Holman, MC; Troy H. Patience, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
4/24/2001	May 02	N/A

Study Objective: The specific aims of this proposal are to identify whether each respective disease management program applied to a cohort of high-risk diabetics will: (1) Improve glycemic control as measured by Hemoglobin A1C (HbA1C), (2) Improve compliance with preventative services, (3) Improve continuity of care with assigned provider, (4) Reduce use of inappropriate portals of access to care (emergency room) and (5) Improve patient satisfaction.

Technical Approach: This is a prospective cohort study involving 375 high-risk and 375 low-risk diabetic patients in three separate portals of care being managed by two newly implemented different disease management programs. We will examine emergency room visits and continuity of visits with PCM before and after the intervention.

Progress: 145 subjects enrolled in this study at MAMC in FY01. Subject enrollment expected to be complete by December 2001.



Detail Summary Sheets

Cardiology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/062 **Status**: Ongoing

Title: Substudy 02: The Neurohormone Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction

Principal Investigator: LTC James J. King, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC David T. Schachter, MC; LTC Michael Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	Apr 03	4/24/2001

Study Objective: To determine the effect of valsartan, captopril, and the combination of valsartan and captopril on the levels of neurohormones, measures of oxidative stress, and inflammation (plasa catecholamines, aldosterone, brain natriuretic peptide, aldehydes, adrenomedullin, collagen one telopeptide, procollagen type III, Nterminal propeptide, and C-reactive protein) at baseline, one month and 20 months post infarction, and with each episode of congestive heart failure requiring hospitalization and to assess the relationships between post-infarction neurohormonal activation, cardiovascular risk factors, and clinical outcome and evaluate the effect of valsartan, captopril and their combination on these relationships.

Technical Approach: This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of neurohormones as an indicator of prognosis for patients suffering from myocardial infarction. Blood samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, blood samples will be taken whenever the patient is hospitalized for heart failure. Samples will be sent to a central laboratory for evaluation.

Progress: Two patients were enrolled in this substudy in FY00 at MAMC. No further patient enrollment occurred during FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/063 **Status**: Ongoing

Title: Substudy 04: The Microalbuminuria Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction

Principal Investigator: LTC James J. King, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC David T. Schachter, MC; LTC Michael Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	Apr 03	4/24/2001

Study Objective: To assess the relationship between microalbuminuria and prognosis, and evaluate how valsartan and captopril modify this relationship and whether a correlation between microalbuminuria, neurohormonal activation and gene polymorphisms exists.

Technical Approach: This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of albuminuria as an indicator of prognosis for patients suffering from myocardial infarction. Spot urine samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, urine samples will be taken whenever the patient is hospitalized for heart failure. Urine samples will be sent to a central laboratory for evaluation.

Progress: Two patients enrolled in this substudy in FY00 at MAMC. No patients enrolled during FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/099 **Status**: Terminated

Title: A Phase IIIb, Randomized, Open Label Trial with 3 Parallel Groups, Full Dose TNK-tPA Together with Heparin Sodium, Full Dose TNK-tPA Together with Enoxaprin and Half Dose TNK-tPA with Abciximab and Heparin Sodium in Patients with Acute Myocardial Infarction, Protocol 1123.10

Principal Investigator: LTC James J. King, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; MAJ Rosemary P. Peterson, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/27/2000	Apr 01	

Study Objective: The objective of this study is to evaluate the safety and efficacy of full dose TNK-tPA with heparin sodium (Group A), full dose TNK-tPA combined with enoxaparin (Group B), and half dose TNK-tPA combined with abciximab and heparin sodium (Group C).

Technical Approach: After obtaining informed consent, eligible subjects will be randomized into one of three groups; Group A will receive TNK-tPA (full dose) and heparin sodium (unfractionated heparin, Group B will receive TNK-tPA (full dose) and enoxaparin (low molecular weight heparin) and Group C will receive TNK-tPA (half dose) and abciximab and low dose heparin sodium (unfractionated heparin). Subjects will be contacted or return to the hospital for follow-up at 30 days for vital status and clinical outcome. One year after randomization, subjects will be contacted by phone or mail to check their vital status. The satellite study will not be initiated at MAMC.

Progress: This study was reported terminated at MAMC, 20 Feb 01, by the study sponsor, as drug was needed at other enrolling sites. No patients enrolled at MAMC.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 99/042	**Status**: Ongoing

Title: The Coreg Heart Failure Registry: COHERE

Principal Investigator: LTC James J. King, MC

Department: Medicine/Cardiology	**Facility**: MAMC

Associate Investigator(s): MAJ James P. Olson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
02/23/1999	Jun 99	1/4/2002

Study Objective: (1) To collect clinically pertinent outcome data (e.g., mortality, need for hospitalization, use of concomitant medications, patient global assessment, NYHA class in patients with heart failure) receiving Coreg under the care of a broad population of community physicians, (2) To compare the clinical characteristics of the patients treated in the US Phase III and early extended physician use programs with those treated in the community and to assess outcome differences in major subpopulations, (3) To characterize the experience with initiation of Coreg in the community, and (4) To compare patient characteristics and management approaches between cardiologists and internists.

Technical Approach: The Coreg Heart Failure Registry will document the relationship of selected patient characteristics to outcomes, such as morbidity, mortality, need for hospitalizations, quality of life and change in clinical status as well as tolerability. By the year 2000, COHERE will contain the most up-to-date information on the natural history of, and effect of B-Blockade in CHF. COHERE will involve approximately 600 participating physicians, and will enroll 6,000 patients with heart failure receiving Coreg. The live portion of the registry will take place over 30 months, and patients will be assessed over a period of 24 months.

Progress: 18 subjects enrolled in FY00, 2 in FY99, for a total of 20 subjects enrolled at MAMC. This registry closed to subject enrollment, however the study remained ongoing in FY01 to continue data collection on the 20 subjects enrolled at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/053 **Status**: Ongoing

Title: Multinational, Multicenter, Double-Blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-Term Treatment with Valsartan, Captopril, and Their Combination in High-Risk Patients After Myocardial Infarction

Principal Investigator: LTC James J. King, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): COL Alice M. Mascette, MC; MAJ James P. Olson, MC; LTC David T. Schachter, MC; CPT Kenneth M. LeClerc, MC; MAJ Steven E. Miller, MC; LTC Michael J. Wilson, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Apr 03	2/27/2001

Study Objective: (1) To demonstrate that long-term administration of valsartan is more effective than captopril in reducing total mortality after acute myocardial infarction, (2) To demonstrate that long-term administration of the combination of valsartan with captopril is more effective than captopril alone in reducing total mortality after acute myocardial infarction, and (3) If valsartan as monotherapy cannot be shown to be superior to captopril as in objective 1, to demonstrate that long-term administration of valsartan given as monotherapy is at least as effective as captopril given as monotherapy in reducing total mortality after acute myocardial infarction.

Technical Approach: VALIANT is a prospective multinational, multicenter, double-blind, randomized, active-controlled phase III study with three parallel treatment groups. The three treatment groups are 1) Captopril monotherapy (active control drug). The target dose is 50 mg three times daily; 2) Valsartan monotherapy (investigational drug). The target dose is 160 mg twice daily; 3) The combination of captopril and valsartan (investigational regimen). The target doses are 50 mg three times daily and 80 mg twice daily, respectively. The study consists of two phases: 1) a study medication initiation and titration phase and 2) maintenance phase. The duration of these two phases depends upon the patient's status and response to study medication. Randomization and initiation of study medication will occur at Visit 1 on Day 1. For most patients, this will occur in hospital. Dose titration and maintenance will occur at Visits 2-16. Visit 2 will occur on Day 15 or at hospital discharge, whichever is first. For patients not in hospital at the time of randomization, Visit 2 will occur on Day 15. Visits 3-16 are planned as outpatient visits, but depending on the patient's status, may occur in hospital. They are to be performed at specified time points but some flexibility is allowed. During the first year, visit may take place up to 15 days before or after the protocol-scheduled visit. Telephone follow-up is permitted if the patient cannot come for follow-up visits. The study will end when the required number of primary endpoints has been reached. This may occur prior to or after Month 48. If the study ends prior to Month 48, the procedures listed for Visit 16 will be completed for all patients. If the study is extended beyond Month 48, the procedures listed for Visit 15 will be completed every 4 months until study end, at which point the procedures listed for Visit 16 will be completed.

Progress: Eight patients enrolled in this study in FY00 at MAMC. No patients enrolled during FY01. All serious adverse events have been reported to the IRB; none occurred at MAMC. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/300	**Status**: Ongoing

Title: Jostent Coronary Stent Graft (HUD)

Principal Investigator: LTC David T. Schachter, MC

Department: Medicine/Cardiology		**Facility**: MAMC

Associate Investigator(s): None.

Start Date:	**Est. Completion Date:**	**Periodic Review:**
9/25/2001	Sep 10	N/A

Study Objective: Humanitarian Use Device

Technical Approach: The Jostent Coronary Stent Graft is approved as an HUD for the indication of arterial perforation. Physicians trained to deploy the stent will be added as associate investigators upon receipt of documentation of training. Use of the device will be tracked per 21 CFR 814.124(a).

Progress: This HUD recently received IRB approval for use at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/013 **Status**: Terminated

Title: Magnesium in Coronaries (MAGIC): A Study of the Effect of Magnesium Administration in Patients with Acute Myocardial Infarction

Principal Investigator: LTC David T. Schachter, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC James J. King, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/15/1998	Mar 01	11/28/2000

Study Objective: To determine if administration of intravenous magnesium within 6 hours of symptom onset in high-risk patients with suspected acute MI reduces all cause and 30-day mortality.

Technical Approach: Subjects will be randomly assigned study drug or placebo in a double-blinded fashion. Subjects will be stratified by site, and by whether the subject is eligible for reperfusion therapy or not. Stratum I will include subjects who are 65 years or older and are eligible for reperfusion therapy. Stratum II will include patients of any age who are not eligible for reperfusion therapy. Subjects will receive either magnesium sulfate or placebo by bolus followed by 24 hour continuous infusion. Follow-up evaluation by telephone or clinic visit will be performed by the PI. The primary endpoint is 30-day all cause mortality. Secondary endpoints include (1) use of intravenous inotropic therapy and/or vasopressors and/or mechanical support for a failing circulation (IABP,LVAD), (2) electrical reversion of ventricular fibrillation or sustained ventricular tachycardia, and (3) placement of an external or transvenous pacemaker.

Progress: This study was terminated Oct 01 by the investigator. No new subjects enrolled in this study in FY01 due to an inability to find subjects that meet entry criteria. While the study was ongoing, three subjects entered in FY99, two in FY00, for a total of 5 patients enrolled at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/110 **Status**: Ongoing

Title: Efficacy and Safety Study of the Oral Direct Thrombin Inhibitor H 376/95 Compared with Dose-adjusted Warfarin (Coumadin) in the Prevention of Stroke and Systemic Embolic Events in Patients with Atrial Fibrillation (SPORTIF V)

Principal Investigator: LTC Michael J. Wilson, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC David T. Schachter, MC; LTC James J. King, MC; MAJ Rosemary P. Peterson, MC; COL Frederick G. Flynn, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Sep 02	6/26/2001

Study Objective: (1) To determine whether H 376/95 is non-inferior compared to dose-adjusted warfarin aiming for an INR 2.0-3.0 for the prevention of all strokes (fatal and nonfatal) and systemic embolic events in patients with chronic non-valvular AF, (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for an INR of 2.0-3.0 for the combined endpoint of prevention of death, nonfatal strokes, nonfatal systemic embolic events and nonfatal acute myocardial infarction (AMI), (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for INR 2.0-3.0 for the combined endpoint of prevention of ischemic strokes, TIAs and systemic embolic events, and (3) To assess the safety of H 376/95 compared to dose-adjusted warfarin aiming for INR 2.0-3.0 with an emphasis on major and minor bleeding events and any treatment discontinuations.

Technical Approach: This is a multicenter, randomized, double-blind, two arm, parallel group study comparing the effects of H 376/95 versus dose-adjusted warfarin. Subjects will be followed for at least one year, up to 2 1/2 years. Eligible patients will be randomized and stratified according to current low dose aspirin use and previous stroke or TIA history. Subjects will complete a 2 week screening period prior to randomization to receive either H 376/95 36 mg bid (and placebo for warfarin) or to dose-adjusted warfarin (and placebo for H 376/95). Screening will include consent process, medical history, vital signs, ECG, blood/urine samples and physical examination. Upon randomization, a second ECG will be performed, and the Stroke Symptom Questionnaire will be completed. Study visits will be performed at weeks 1, 4, 6, and then months 2, 3, 4, 5, 7, 8, 10, 12 and then every 3 months thereafter until the study treatment is completed. At study visits, study medication will be returned and new drug will be dispensed, concomitant medications and adverse events will be reviewed, safety blood samples and melagatran samples will be obtained. INR samples will be obtained as necessary. At months 6, 12, 18, and 24 visits subjects will undergo the above tests in addition to ECGs and the Stroke Symptom Questionnaire. Subjects will be contacted by telephone at months 7, 9, and 11 and will be required to return to the clinic for in-clinic INR evaluation as necessary. At the end of the study subjects will have a complete PE, vital signs, ECG, blood tests, INR samples, and the Stroke Symptom Questionnaire will be obtained. Following treatment withdrawal, the subjects will be followed an additional 2 weeks until satisfactory conversion from blinded study therapy to normal active treatment has been made. Subjects will return to the clinic for INR draws using a sponsor provided CoaguChek System. INR values will remain blinded to the investigator and study coordinator utilizing the CoaguChek System and the IVRS system.

Progress: Three subjects enrolled in this study at MAMC during FY01. There have been 30 SAE's reported. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/055 **Status**: Ongoing

Title: A Six-Month, Multi-Center, Double-Blind, Placebo-controlled, Parallel-group Design Clinical Study to Assess the Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride for the Treatment of Atrial Fibrillation in Patients Who Require Electrical Cardioversion with an Open-label Follow-up Phase to Assess the Long -term Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride.

Principal Investigator: LTC Michael J. Wilson, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC James J. King, MC; LTC David T. Schachter, MC; MAJ Rosemary P. Peterson, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
1/23/2001	Dec 04	N/A

Study Objective: Primary: to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in prolonging the time from the start of the efficacy period to the first symptomatic or asymptomatic AFib, AFlut, or PSVT event. The efficacy period begins following a three day, twice daily oral dose of study medication after sinus rhythm has been documented as a result of successful cardioversion (DC or Spontaneous) on Day 4 (+2 days). An event is defined as: AFib, AFlut, or PVST <24 hours duration for which the patient is readmitted to the hospital or requires DC cardioversion, or AFib, AFlut, or PVST of >= 24 hours duration. Secondary: to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo: (1) On successful DC cardioversion from AFib (Day 4, +2days), (2) On "symptom frequency load," during the first AFib, AFlut, or PSVT event, (3) On the quality-of-life measure referred to as physical functioning on the SF-36, (4) On individual symptoms from the Brignole Atrial Fibrillation Symptom Checklist, (5) On the number of days spent in-hospital or as emergency room visits due to AFib, AFlut, or PVST events following initial discharge on day four. Open Label, Follow-up Phase: Assess the safety of outpatient once-daily initiation of 125mg of Azimilide Dihydrochloride in placebo patients who complete the double-blind, placebo-controlled study, assess the long-term safety of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study, assess the efficacy of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study.

Technical Approach: This is a randomized, double-blind, placebo-controlled, six-month, multi-center, parallel group design study, followed by an open-label, follow-up phase to assess the efficacy and safety of 125mg of daily oral Azimilide Dihydrochloride. Approximately 440 patients will be enrolled at 60-80 sites. The number of patients per site is to be assessed on an ongoing basis by the sponsor. Recruitment is expected to last 9-12 months. Patients who are in AFib and in need of a DC cardioversion will be hospitalized and randomized to receive a twice weekly oral dose of 125mg Azimilide Dihydrochloride or placebo for 3 consecutive days. Beginning on Day 4, patients will receive a once-daily oral maintenance dose of their assigned treatment until they complete or withdraw from the double-blind study. During the hospitalization, patients will be monitored by telemetry. A 12-lead ECG will be obtained prior to the first dose on all days while in the hospital. All patients will be re-assessed by 12-lead ECG on Day 4 (or within the following 2 days) prior to taking study medication that day. Patients who are in sinus rhythm prior to DC cardioversion on day 4 (+2 days) will be considered to have spontaneously cardioverted (after sinus rhythm has been documented by two 12-lead ECGs taken at least one hour apart). Patients who have not cardioverted to sinus rhythm by Day 4 (+2 days) will undergo a DC cardioversion. On the day of cardioversion, all study medication will be withheld until successful cardioversion has been documented. Patients who have not achieved successful cardioversion on Day 4 (+2 days) will be

withdrawn from the study. Once the patient is successfully cardioverted, AFib, AFlut, or PVST recurrences must be documented electrocardiographically (12-lead ECG preferred). The duration of the recurrence will be documented by the patient's own recollection and subsequent follow-up. At all visits in the treatment period of the double-blind, study (except day 4), patients will be asked if they have been hospitalized or required an emergency room visit for any reason. For patients to remain in the study, sinus rhythm should be restored within 8 weeks of their event. Documentation must be obtained by any means of electrocardiograph tracing immediately after cardioversion and again by 12-lead ECG at least one hour later. If sinus rhythm is not restored within 8 weeks, patients must be withdrawn from the study. Patients will have additional scheduled visits during the double-blind study at weeks 2, 4, 6, 8, 10, 12, and 26. The coordinator/investigator should instruct the patient to return to the site for unscheduled visits if they experience symptoms of their arrhythmia, or any unusual symptoms, infection, nonspecific fevers, pharyngitis, or influenza-like symptoms. Patients will complete the Short Form 36 (SF 36) quality-of-life questionnaire and the Brignole Atrial Fibrillation Symptom Checklist. Patients will be considered to have completed the double-blind portion of the study upon documentation of the second AFib, AFlut, or PVST event or after they complete 26 weeks. Patients who complete the double-blind study will be given the opportunity to enter the open label follow-up phase. Open Label, Follow-up Phase: Patients may begin this phase of once-daily oral dose of 125mg of Azimilide Dihydrochloride the day following their completion of the double-blind study. Upon entry into the open label phase, patients will be given sufficient Azimilide Dihydrochloride for 8 days. Patients will return to the study site after 7 days (1 day) for a 12-lead ECG. Patients who are in sinus rhythm will undergo scheduled evaluations, return home, and continue routine follow-up care. Patients who choose to enter the open label phase will have visits at weeks 1, 2, and every 2 weeks for the remainder of the first 12 weeks; they will then return at weeks 26, 38, 52, and then every 26 weeks (6 months) thereafter until approximately 2 years from the time the patient completes the double-blind study. Patients who complete or withdraw from the either phase will return to the clinic for followup visits 7 and 30 days post-treatment.

Progress: No subjects have been enrolled at MAMC during FY01 and no SAE's reported. This study remains ongoing to subject enrollment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/056 **Status**: Ongoing

Title: A Multi-Center, Six-Month, Double-Blind, Placebo-controlled, Parallel-group design Clinical Study to Assess the Efficacy and Safety of a Daily Oral Dose of 125 mg of Azimilide Dihydrochloride for the Prophylactic Treatment of Atrial Fibrillation and an Open-label follow-up Clinical Phase to Assess the Long -term Efficacy and Safety of a 125 mg Daily Oral Dose of Azimilide Dihydrochloride

Principal Investigator: LTC Michael J. Wilson, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): LTC James J. King, MC; LTC David T. Schachter, MC; MAJ Rosemary P. Peterson, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Dec 04	N/A

Study Objective: Primary: to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo n prolonging the tachycardia-free period in 2 patient strata separately in: Patients with CHF and/or IHD and, Patients with neither CHF nor IHD. Secondary: (1) To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the total number of symptoms (among 6 pre-specified symptoms from the Event Symptom Severity Checklist) reported during the first symptomatic event, (2) to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the frequency of symptomatic events (i.e., an assessment of efficacy that allows for multiple events per patient), (3) to assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the total SVA burden in patients. The SVA burden includes the frequency, duration, and severity of AFib, AFlut, or PSVT events, (4) to assess the impact of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in patient quality-of-life, specifically, on the physical functioning subscale of the SF-36 at week 4, and (5) To assess the number of days in?hospital and number of emergency room visits due to AFib, AFlut, or PSVT events following initial discharge for patients hospitalized for the loading period, and beginning on Day 1 for all other patients.

Additional Objectives: To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in prolonging the tachycardia-free period in patients with and without CHF/IHD (i.e., and assessment of efficacy that combines time to first symptomatic event information from both strata) To assess individual symptoms from the Brignole Atrial Fibrillation Symptom Checklist (week 4) To assess the efficacy of a daily oral dose of 125mg of Azimilide Dihydrochloride versus placebo in reducing the number of asymptomatic events To assess the safety of 125mg of Azimilide Dihydrochloride in patients both with and without CHF/IHD (strata combined). Safety will be assessed by examining the type and incidence of AEs, ECG parameters, and type and severity of laboratory abnormalities and chest x-ray results

Open Label, Follow-up Phase: Assess the safety of outpatient once-daily initiation of 125mg of Azimilide Dihydrochloride in patients who received placebo and who complete the doubleblind, placebo-controlled study Assess the long-term safety of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study Assess the long-term efficacy (i.e.: frequency of SVA events) of once daily oral dosing of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind, placebo-controlled study.

Technical Approach: This is a randomized, six-month, double-blind, placebo-controlled, multi-center, parallel group design phase, to assess the efficacy and safety of 125mg of daily oral dose of Azimilide Dihydrochloride in maintaining sinus rhythm in patients who have had symptomatic AFib documented by TTM or ECG during the 1 month screening period. An open label phase, designed to evaluate the long-term safety of 125mg of Azimilide Dihydrochloride in patients who complete the double-blind portion follows. Approximately 660 patients will be enrolled at 80-100

sites. Patients will be stratified according to whether or not they have a history of CHF and/or IHD, then randomly assigned to the 2 treatment groups of 2 strata. Enrollment will be stopped once 440 patients with CHF/IHD have been randomized. Enrollment of patients without CHF/IHD will be stopped once 220 of those patients are randomized or enrollment of CHF/IHD patients has been completed. A separate randomization schedule will be used for patients with NYHA Class III CHF. This is being done to ensure as much as possible that an equal number of patients with Class III CHF receive of Azimilide Dihydrochloride and placebo. Patients will be evaluated at Baseline/Day 1, day 4, and weeks 2, 4, 6, 8, 10, 12, and 26. Throughout the double-blind phase, patients will use a TTM device to transmit their ECGs: If they experience symptoms that they believe are indicative of an arrhythmia, and daily thereafter until they return to sinus rhythm and when contacted weekly by the central monitoring service.

Patients will complete the Short Form 36 (SF 36) quality-of-life questionnaire and the Brignole Atrial Fibrillation Symptom Checklist. These forms will be completed at the day 1 visit prior to dosing in the hospital (baseline), and for weeks 4, 12 and 26 visits.

Patients will only be allowed to enter the screening period while in sinus rhythm. Females of childbearing age will be given the special issues leaflet regarding pregnancy.

Patients will be asked to record and send a transmission to the central TTM service any time they experience symptoms they believe are indicative of an arrhythmia. This monitoring will occur over a 1-month period, and patients may continue their antiarrhythmic medications at the investigator's discretion. Patients may be randomized into the double-blind phase upon return to sinus rhythm from their qualifying event of AFib. Patients who fail the 1-month screening period and who are taking their antiarrhythmic medications may discontinue those medications and repeat the 1-month screening period one time. Patients may qualify during the screening period with any ECG-documented symptomatic AFib. The qualifying ECG will be forwarded to the central facility if it was not obtained by TTM. Patients must have their Day I visit within 30 days of the onset of the documented symptomatic AFib event of the screening phase. The Base line visit must occur within 7 days prior to the first dose of study drug. Loading period in patients with (inpatient) and without (outpatient) CHF/1HD: Patients with CHF or IHD will be monitored in the hospital during the 3-day loading period. After all Baseline and Day 1 procedures have been completed and the patient is confirmed to be in sinus rhythm, patients with and without CHF/IHD will take the first dose of the 3-day, twice daily, loading regimen in the presence of study staff. For the remainder of the 3 days, patients will take the study medication twice daily. Thereafter for the remainder of the study, all patients will take study medication once daily at the same time every day. Patients will be considered to have completed the double-blind portion of the study when they have a sinus rhythm-containing day after their second confirmed occurrence of symptomatic AFib, AFlut, or PVST event or after they complete 26 weeks. Patients who complete the double-blind study will be given the opportunity to enter the open label follow-up phase. Open Label, Follow-up Phase: Patients may begin this phase of once-daily oral dose of 125mg of Azimilide Dihydrochloride the day following their completion of the double-blind study. Patients will have visits every 2 weeks for the first 12 weeks. After that, patients will return at weeks 26, 38, 52, and every 26 weeks thereafter, for approximately 2 years. During the open label phase, the TTM will not be used to transmit ECGs, but patients may return to the clinic if they experience symptoms of their arrhythmia. Patients will return to the study site after 7 days (1 day) for a 12-lead ECG. Patients who are in sinus rhythm will undergo scheduled evaluations, return home, and continue routine followup care. Patients who choose to enter the open label phase will have visits at weeks 1, 2, and every 2 weeks for the remainder of the first 12 weeks. They will return at weeks 26, 38, 52 and then every 26 weeks thereafter until approximately 2 years from the time the patient completes the double-blind study. Patients who complete or withdraw from the double blind or open label phases will return to the clinic for follow-up visits and 30 days post-treatment.

Progress: No subjects have been enrolled at MAMC during FY01 and no SAE's reported. This study remains ongoing to subject enrollment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/069 **Status**: Ongoing

Title: Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

Principal Investigator: LTC Michael J. Wilson, MC

Department: Medicine/Cardiology **Facility**: MAMC

Associate Investigator(s): MAJ Patrick A. Cambier, MC; COL Roger F. Chamusco, MC; COL Alice M. Mascette, MC; MAJ Herman E. Collier III, MC; LTC Karl C. Stajduhar, MC; MAJ Michael D. Eisenhauer, MC; CPT John A. McHenry, MC; MAJ Maureen A. Arendt, MC; CPT Thomas M. Roe, MC; MAJ James P. Olson, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/16/1996	Mar 01	1/8/2002

Study Objective: 1) To compare whether optimized antiarrhythmic drug therapy administered to attempt to maintain sinus rhythm has an impact on total mortality when compared to optimized therapy which controls the heart rate. 2) Since stroke is such an important endpoint in trials of patients with atrial fibrillation, composite endpoints will include the following: total mortality, disabling stroke or anoxic encephalopathy, major bleeding and cardiac arrest; cost; quality of life.

Technical Approach: This is a multi center trial sponsored by the National Heart, Lung, and Blood Institute. The purpose is to compare the effect on survival of two different treatment plans in patients with atrial fibrillation. One treatment is aimed at rate control and the other at maintaining a normal sinus rhythm. The primary physician will choose which drug or drugs are used to obtain each treatment objective. The physician will initially determine the treatment to convert patients to normal sinus rhythm after which the patient will be randomized to one of the treatments described above. Patients will be followed at month 2 and 4 and then at least every 4 months until the year 2001. Patients will complete a quality of life questionnaire and have an assessment of their functional status completed at various time points. Patients who fail their assigned treatment or are intolerant will continue to be followed regardless of crossover to another therapy. We anticipate enrolling 15 patients at Madigan Army Medical Center.

Progress: 32 patients enrolled in this study at MAMC, with 28 continuing to be followed. This study closed to enrollment, 31 Oct 99.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/140 **Status**: Completed

Title: A Double-Blind, Placebo-Controlled, Parallel Design Study to Determine the Effect of 100 mgs of Orally Administered Azimilide Dihydrochloride versus Placebo on Survival in Recent Post-Myocardial Infarction Patients at Risk of Sudden Death (ALIVE)

Principal Investigator: LTC Michael J. Wilson, MC

Department: Medicine/Cardiology **Facility**: MAMC

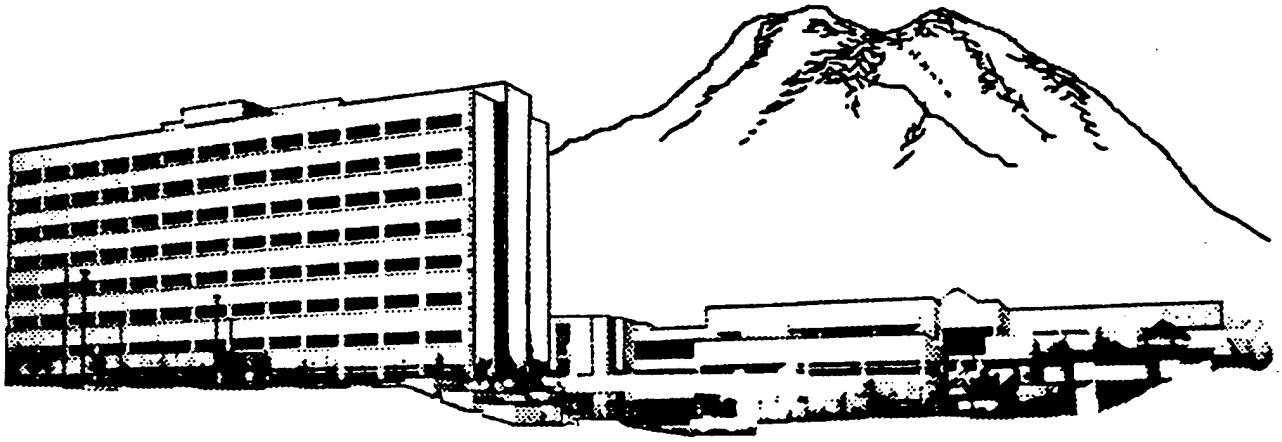
Associate Investigator(s): MAJ Maureen A. Arendt, MC; MAJ Karen A. Hicks, MC; MAJ James P. Olson, MC; LTC James J. King, MC; LTC David T. Schachter, MC; CPT Kenneth M. LeClerc, MC; CPT Allan B. Wicks, MC; MAJ Steven E. Miller, MC; MAJ Theresa A. Horne, AN; COL Alice M. Mascette, MC; MAJ Michael L. Yandel, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/19/1997	May 99	8/28/2001

Study Objective: To evaluate the effects of 75 mg of azimilide dihydrochloride versus placebo or 100 mg of azimilide dihydrochloride versus placebo on all-cause mortality, based on longitudinal intent-to-treat observations in patients with a recent (within 6 to 21 days) acute MI, low left ventricular ejection fraction (15 to 35%), and low heart rate variability (<= 20 U). These patients are defined as "at high risk" of sudden death.

Technical Approach: This is a randomized, double-blind, placebo-controlled, multi-national study at approximately 500 study centers. A treatment regimen consisting of daily oral doses of 75 or 100 mg of azimilide dihydrochloride will be compared to a placebo group in a parallel design. Patients will be equally randomized across all 3 treatment groups. Patients who have recently experienced an acute MI and meet other study entrance and screening criteria will receive their first dose of study medication within 6-21 days of that MI. Once-daily treatment will be administered for approximately one year. No specific hospitalization is required for treatment. Screening procedures (to include a 24 hour Holter monitor) will be done to determine the group "at high risk" of sudden arrhythmic death. Evaluations during the treatment period will take place at Week 2, and at Months 1, 4, 8, and 12. Monthly serum pregnancy tests will be performed on females of childbearing potential who are not surgically sterile. Patients who complete 365 days of dosing will be followed for one month after completion of their participation in the study. Patients who withdraw from the trial early will return within 4 weeks for study exit procedures and furthermore, will be followed to assess survival status until the time at which they would have completed 365 day of dosing had they remained in the trial. Safety monitoring will include but is not limited to, clinical laboratory test results, 12-lead ECG measurements and frequency and severity of adverse events.

Progress: This study was closed, 10 Jul 01, as all patient visits had been completed. A total of five patients enrolled at MAMC with three completing the study. Two patients had been withdrawn from the study, one due to death not considered related to study participation and the other due to a serious adverse event prior to drug administration.



Detail Summary Sheets

Geriatrics Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/021 **Status**: Ongoing

Title: Reading Level, Cognitive Test, and Functional Task Performance in Cognitively Intact Elders

Principal Investigator: Ann L. Hightower, M.D.

Department: Medicine/Geriatrics **Facility**: MAMC

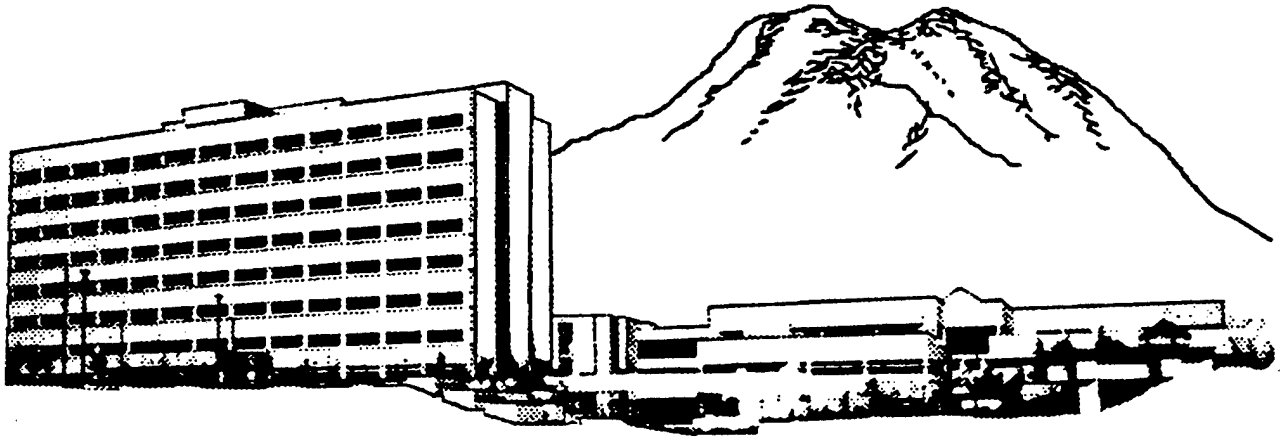
Associate Investigator(s): None.

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Oct 02	N/A

Study Objective: The primary objective of the proposed study is to characterize the relationship between education (using reading level as a proxy), cognition and function in cognitively intact elders. The objectives have been divided into the following: Specific Aim I: (1) To determine if reading level is correlated with cognitive test performance in African American and White elders, (2) to describe the relationship between reading level and cognitive test performance across a range of reading levels, (3) to determine if there is a main effect for race in the correlation between reading score and cognitive test performance, (4) to determine if ethnic differences in cognitive test performance exist at a given reading level. Specific Aim II: (1) To determine if there is a correlation between reading level and performance on a structured independent activity of daily living functional task, the Medication Management Test (Gurland, et al, 1994). (This test provides information about cognitive ability as it relates to an important functional task; the ability to manage one's own medications)

Technical Approach: Instruments used to measure cognition and function in this study include the following: Mini-Mental State Exam (MMSE), Blessed Memory Information and Concentration Test (BMICT, which is part of the Blessed Dementia Rating Scale), Mini-Cog, Wide-Range Achievement Test-3 (WRAT-3), Geriatric Depression Scale (short-version), Boston Naming Test, Paragraph Recall (also known as Logical Memory, a subtest of the Wechsler Memory Scale), Category Naming Test, Trails A and B Test and the Medication Management Test. Because this is a correlative study, I will not be using or reporting standard scores but will be using raw scores.

Progress: 49 subjects enrolled in this protocol during FY01. Data collection remains ongoing.



Detail Summary Sheets

Gastroenterology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/031 **Status**: Ongoing

Title: The Use of a Nutritional Supplement as an Antimicrobial in Helicobacter pylori Eradication

Principal Investigator: LTC Jonathan P. Kushner

Department: Medicine/Gastroenterology **Facility**: MAMC

Associate Investigator(s): Mr. James R. Wright, M.T.; LTC Spencer S. Root, MC; MAJ William K. Hirota, MC; Janet C. Chilton

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Dec 01	2/27/2001

Study Objective: To assess the antimicrobial action of garlic on Helicobacter pylori: to attempt to eradicate Helicobacter pylori with the combination of garlic and a proton-pump inhibitor in a double-blinded, placebo-controlled trial; also, to assess changes in symptoms, endoscopic appearance, histology, quantitative cultures, quantitative unrease activity (by breath test) and serum and gastric tissue cytokines following the eradication attempt.

Technical Approach: After screening up to 500 candidates with H. pylori serology, as well as a standarized GI Likert (17) scale dyspepsia sysmption questionnaire and a food freqency questionnaire, two 7 mL red top blood tubes (one for H pylori serology and one for cytokine assays) and one complete blood count will be drawn at the time of the initial screening. Those with positive serology will be asked to discontinue PPI, and if possible, non-steroidal antiinflammatory medications. Active H. pylori infection will be confirmed in patients with positive serology by the presence of either positive H. pylori on histology and a positive rapid urease test. At endoscopy, after aspiration of gastric juice, seven biopsies will be obtained from the antrum, and seven from the body of the stomach. One biopsy from each will be used for the RUT test, with two for histology and two for H. pylori culture. The sixth biopsy will be frozen in liquid nitorgen for cytokine mRNA expression and the seventh biopsy, as well as the gastric aspirate, assayed for cytokine protein. Patients positive for h. pylori infection will be stratified into either a low/normal habitual garlic consumption. Patients will be blocks of 15 Those in the treatment blocks will receive three garlic supplement capsules twice daily while those in the placebo blocks will recive six identically appearing capsules. Patients will refrain from antibiotic, PPI, bismuth, and if possible, NSAID use during this period. Blood work and endoscopy will be repeated for purposes of research and data collection.

Progress: Total of 27 patients enrolled in study. Total of 12 patients endoscopically positive for H pylori and randomized to study therapy. 11 patients completed study therapy. 10 of these 11 have completed follow up endoscopy and studies. The remaining subject refused any form of follow up study after completing the therapeutic trial. One subject is beginning study therapy at this time and will be scheduled for follow up. One additional subject has agreed to participate in study and will undergo first endoscopy shortly. Still recruiting additional subjects, with a goal of 60 total randomized subjects between MAMC and WRAMC. (At last count WRAMC had randomized 14 or 15 subjects with recruitment still ongoing).

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/144 **Status**: Ongoing

Title: A Randomized, Double-blind, Placebo-controlled, Dose Finding, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Tegaserod Given Orally at Three Dose Levels and Placebo in Patients with Functional Dyspepsia and Documented Delayed Gastric Emptying

Principal Investigator: COL Amy M. Tsuchida, MC

Department: Medicine/Gastroenterology **Facility**: MAMC

Associate Investigator(s): MAJ Robert K. Durnford, MC; MAJ Eric J. Ormseth, MC; LTC Jonathan P. Kushner

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Oct 01	9/25/2001

Study Objective: (1) To determine in patients with symptoms of dyspepsia and documented delay in gastric emptying rate the efficacy of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo as measured by satisfactory relief of meal related upper stomach problems and (2) to rate the effects of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo; (3) patient's assessment of symptoms of functional dyspepsia; (4) patient's quality of life and (5) the safety and tolerability.

Technical Approach: This is a multicenter, Phase II dose-finding trial with a parallel group design in patients with functional dyspepsia and delayed gastric emptying as measured by scintigraphy. Following a one week screening and a two week washout period, eligible subjects will be randomized to receive either placebo tid or daily doses of 1.5 mg, 6 mg or 18 mg Zelmac (tegaserod) given orally tid for 8 weeks. Data will be collected on patient symptoms of dyspepsia and quality of life. Drug compliance, concomitant medications and adverse events will be monitored.

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/145 **Status**: Completed

Title: A Randomized, Double-blind, Placebo-controlled, Dose Finding, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Tegaserod Given Orally at Three Dose Levels (1.5 mg, 6 mg, 18 mg) and Placebo in Patients with Functional Dyspepsia (FD) and Documented Normal Gastric Emptying (Protocol CHTF919D2204)

Principal Investigator: COL Amy M. Tsuchida, MC

Department: Medicine/Gastroenterology **Facility**: MAMC

Associate Investigator(s): MAJ Robert K. Durnford, MC; MAJ Eric J. Ormseth, MC; LTC Jonathan P. Kushner

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Oct 01	9/25/2001

Study Objective: (1) To determine in patients with symptoms of dyspepsia and documented normal gastric emptying rate the efficacy of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo as measured by satisfactory relief of meal related upper stomach problems and (2) to rate the effects of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo; (3) patient's assessment of symptoms of functional dyspepsia; (4) patient's quality of life and (5) the safety and tolerability.

Technical Approach: This is a multicenter, Phase II dose-finding trial with a parallel group design in patients with functional dyspepsia and normal gastric emptying as measured by scintigraphy. Following a one week screening and 2 week washout period, eligible subjects will be randomized to receive either placebo tid or daily doses of 1.5 mg, 6 mg or 18 mg Zelmac (tegaserod) given orally tid for 8 weeks. Data will be collected on patient symptoms of dyspepsia and quality of life, and drug compliance, concomitant medications and adverse events will be monitored.

Progress: Seven patients have been consented in this study at MAMC; however, none have been randomized. This study closed to patient entry, 10 Aug 01, and is no longer actively recruiting and enrolling patients.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/164 **Status**: Ongoing

Title: Epidemiology of Gallbladder Sludge and Stones in Pregnancy

Principal Investigator: COL Amy M. Tsuchida, MC

Department: Medicine/Gastroenterology **Facility**: MAMC

Associate Investigator(s): Sum P. Lee, M.D., Ph.D; MAJ Kazunori Yamamoto, MC; COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF; Scott J. Schulte, M.D.; Beth W. Alderman, M.D., MPH; Dr. Gerard Schellenberg, M.D.; Edward J. Boyko, M.D., Ph.D.; Gail Jarvik, M.D.; Katherine H. Moore, Ph.D.; MAJ Janice C. Stracener, MC; COL Dawn E. Light, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/20/1996	Sep 02	9/26/2000

Study Objective: The primary objective of this NIH-funded study is to determine the incidence of gallstones and sludge during pregnancy. Other objectives are to: 1) identify behavioral and genetic risk factors for the development and regression of sludge and stones; 2) elucidate the mechanism by such risk factors may induce gallstones; and 3) predict the development and regression of sludge and stones.

Technical Approach: This cohort study will include serial ultrasound tests of the gallbladder during pregnancy and post-partum. All women presenting for prenatal care will be eligible unless they: (1) do not speak English; (2) have had gallbladder surgery; (3) are over 20 weeks pregnant; (4) do not expect to deliver at MAMC; and (5) are less than 18 years of age. Eligible women who agree to participate will complete Participation and Consent Forms and under waist and hip circumference measurements. the ultrasonographers will test participants for evidence of sludge and stones at 10, 18, and 28 weeks of gestation and 6 weeks postpartum. For each ultrasound test, the study radiologist will review selected ultrasound images saved by the ultrasonographer. Participants who have stones or sludge at 6 weeks postpartum will return in 12 year for a follow-up ultrasound. At her time of each ultrasound, participants will be asked to complete a one-hour questionnaire and interview. They will also be asked to give an extra fasting blood sample at 128 weeks of gestation. Medical data from the CIS and CHCS will be downloaded and linked to study data.

Progress: 569 subjects enrolled in this study at MAMC in FY01 for a total enrollment of 4903. The final subject recruitment date was 18 Apr 01. The last projected subject delivery is November 2001, with the final subject follow-up ultrasounds due to be completed by December 2001.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/012 **Status**: Ongoing

Title: A Pre-Clinical Research and Development Study to Evaluate Stool Specimens for the PolyStat CRC Test

Principal Investigator: COL Amy M. Tsuchida, MC

Department: Medicine/Gastroenterology **Facility**: MAMC

Associate Investigator(s): LTC Robert H. Sudduth, MC; MAJ Kazunori Yamamoto, MC; MAJ John G. Carrougher, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/15/1996	Oct 97	10/23/2001

Study Objective: Evaluate the clinical utility potential of the PolyStat CRC Test strip assay in detecting basement membrane complexes in individuals with or without colorectal cancer, respectively. And to isolate sufficient amounts of colon BMC for additional antibody production and antigen characterization using the PolyStat CRC Teststrip assay and other antibody tests.

Technical Approach: This is a multicenter trial with MAMC providing stool specimens from patients undergoing colonoscopy. Following colonoscopy, eligible participants will be instructed to collect a stool specimen after their stools have returned to normal and prior to any other intestinal procedures. The specimen will be shipped directly to Alidex Diagnostic Sciences, Inc.

Progress: Since initial approval, 160 patients have enrolled, with 87 enrolled during FY01. Subject recruitment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/004 **Status**: Ongoing

Title: Epidemiology of Barrett's Esophagus

Principal Investigator: COL Amy M. Tsuchida, MC

Department: Medicine/Gastroenterology **Facility**: MAMC

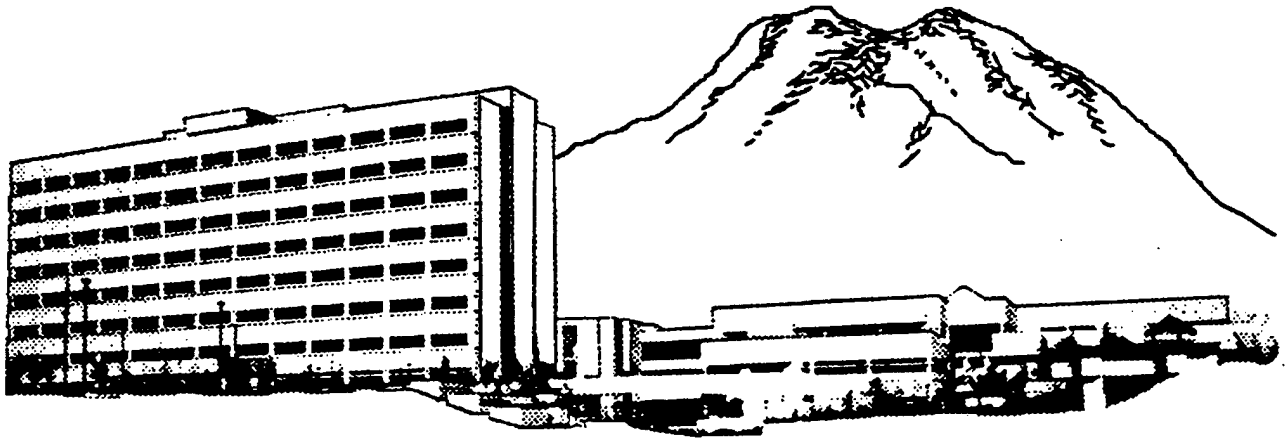
Associate Investigator(s): Diana C. Farrow, Ph.D.; MAJ William K. Hirota, MC; LTC Spencer S. Root, MC; LTC Robert H. Sudduth, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/17/1997	Jun 01	10/23/2001

Study Objective: To determine whether there are any specific environmental, dietary, or personal factors which increase the risk of developing Barrett's Esophagus.

Technical Approach: Patients who are undergoing an upper endoscopy for evaluation of their heartburn complaints will have four biopsies and a small amount of stomach fluid taken for research purposes. Information from the endoscopic findings will be abstracted from medical records.

Progress: As of October 2001, 116 subjects have enrolled in this study at MAMC. Subject enrollment continues through 31 Mar 02, with data collection continuing through 30 Jun 02. Statistical analysis will begin when the data analysis is complete.



Detail Summary Sheets

Hematology/Oncology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/057 **Status**: Completed

Title: A Phase III, Double-blind, Placebo Controlled Trial of Gemcitabine plus Placebo versus Gemcitabine plus R115777 in Patients with Advanced Pancreatic Cancer

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ Matthew P. Jones, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
3/28/2000	Dec 05	

Study Objective: (1) This study will determine whether the addition of R115777 to standard gemcitabine therapy improves overall median survival time by 36% in comparison to gemcitabine plus placebo, (2) compare quality of life (QOL) between the two arms, (3) compare the objective response rate, progression free survival and duration of objective response, (4) estimate 6 month and one-year survival rates of the two arms, (5) assess the safety of the two arms based on laboratory and clinical parameters, and (6) determine the incidence of ras mutations in patients with tissue blocks available for analysis.

Technical Approach: This is a randomized, double-blind, placebo controlled Phase III study for patients with pancreatic cancer. All participating patients will receive gemcitabine and be randomized to R115777 versus placebo. Gemcitabine , 1000 mg/m2 will be administered intravenously weekly for 7 consecutive weeks followed by one week of rest. The study drug, R115777, or placebo will be given orally, 2 dosage units, twice daily, continuously. Treatment will be given until progression or the development of unacceptable toxicity. All patients will be followed indefinitely.

Progress: This study closed to further patient enrollment, 15 Jan 01. One patient consented and screened at MAMC, but was not eligible for study participation. No patients received study medication at MAMC. Multiple SAEs were reported to the IRB and are on file in DCI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/086 **Status**: Terminated

Title: A Phase II Study of Herceptin, Taxol, and Paraplatin in Hormone Refractory Prostate Cancer that Overexpresses HER2-neu

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines Sanchez-Rivera, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Jan 02	5/22/2001

Study Objective: (1) To determine the response rate in HRPC to weekly administration of Herceptin, paclitaxel and Carboplatin. Response rate is defined as the percentage of enrolled patients who achieve a best response of complete or partial response. Rates of complete response, partial response, stable disease and progressive disease will be reported, (2) To assess the relative toxicity of adding Herceptin to the chemotherapy regimen.

Technical Approach: This is a Phase II, multicenter trial with a primary outcome variable of response rate to weekly administration of Herceptin, paclitaxel and carboplatin. Subjects with hormone refractory prostate cancer (HRPC) will be eligible for entry into the study. All subjects will have tissue biopsy of a metastatic site. That site will be analyzed for HER2 over expression. Patients with HRPC who over express HER2 will be treated with weekly Herceptin, paclitaxel and carboplatin and followed for response. Other endpoints will be median survival, median time to progression, and the rate of toxicity to this treatment.

Progress: Development of this protocol was terminated 12 Oct 01 due to funding issues. Grant funding from two industry clinical trial sponsors had been offered to support this study; however final CRDA agreement to allow acceptance of this funding could not be negotiated with these sponsors.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/097 **Status**: Completed

Title: A Randomized, Double-blind, Phase III Comparative Trial of 2 Doses of ZD1839 (IRESSA) in Combination with Gemcitabine and Cisplatin Versus Placebo in Combination with Gemcitabine and Cisplatin in Chemotherapy Naive Patients with Advanced (Stage III or IV) Non-small Cell Lung Cancer, Protocol 1839IL/0014 COV-1935

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; LTC James J. King, MC; LTC David T. Schachter, MC; LTC Michael Wilson, MC; COL Kevin J. Chismire, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 02	6/26/2001

Study Objective: (1) To demonstrate an increase of 35% in the 1-year survival rate for ZD1839 compared to placebo, (2) To demonstrate a statistically significant improvement in time to worsening of disease-related symptoms based on the FACT-L lung cancer subscale (LCS) for ZD1839 compared to placebo, (3) to demonstrate a statistically significant improvement in progression free survival for ZD1839 compared to placebo, (4) to demonstrate a higher symptom improvement rate based on the FACT-L LCS for ZD1839 compared to placebo, (5) to demonstrate an improvement in the overall objective response rate (complete + partial response) for ZD1839 compared to placebo, (6) to provide an estimate of the duration of response (complete + partial response) for each treatment arm, (7) to demonstrate an improvement in the disease control rate (complete + partial response) for ZD1839 compared to placebo, (8) to demonstrate a quality of life for ZD1839-treated patients that is as good as or better than that for placebo-treated patients, (9) to establish a manageable safety profile of ZD1839 in combination with chemotherapy that is compatible with chronic use, (10) to assess the correlation of Epidermal Growth Factor Receptor (EGFR) expression with survival, adjusted for dose and baseline chemotherapy, using data from trials 1839IL/0017 and 1839IL/0014, (11) to compare the adverse event profile and survival of 2 doses of ZD1839 given with and following chemotherapy and (12) to investigate the demographic and pathophysiological factors of patients affecting exposure to ZD1839.

Technical Approach: This is a randomized, parallel-group, double-blind, placebo-controlled, multicenter trial. All eligible patients will receive standard of care (gemcitabine and cisplatin), and will be randomized to one of the following three treatment groups; (1) ZD 1839, 250 mg/day, (2) ZD 1839, 500 mg/day or (3) placebo. Subjects will be further stratified by weight loss in previous 6 months, disease State III versus disease Stage IV, performance status 0-1 versus 2 and measurable disease versus non-measurable disease. The medication will be taken twice (about 12 hours apart) on Day 1 to assure rapid achievement of steady state levels. The study drug will be taken once a day from Day 2 onwards. All subjects will receive gemcitabine, IV, 1000 mg/m2 on days 1, 8, and 15 and cisplatin IV, 100 mg/m2 on days on Day 1 only with 3 liters of fluids. The chemotherapy cycles will be repeated every 4 weeks for a maximum of 6 cycles.

Study drug or matching placebo will be taken daily until disease progression, or 6 months after the last subject has been recruited. Subjects continuing to show evidence of response or clinical benefit from the study drug may continue to receive ZD 1839 under a separate protocol.

Progress: Two subjects enrolled in this study at MAMC; however, both experienced serious adverse events requiring hospitalization. Both subjects were removed from study treatment and subsequently died of progressive disease. Enrollment into the study was voluntarily suspended by Dr. McCune, 4 Nov 00, due to extensive SAEs reported and pending notification of interim safety analysis report, Dec 00. The study was reactivated 27 Mar 01, following IRB approval of Amendment #4 which addressed recommendations of the interim safety report; however, the study closed to further enrollment, 17 May 01 before enrolling more subjects at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/114 **Status**: Ongoing

Title: A Phase III, Multicenter, Randomized, Active-controlled Clinical Trial to Evaluate the Efficacy and Safety of rhuMAb-VEGF (BEVACIZUMAB) in Combination with Standard Chemotherapy in Subjects with Metastatic Colorectal Cancer (AVF2107g)

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Sep 04	7/24/2001

Study Objective: To evaluate the efficacy of multiple administrations of rhuMAb-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer, as measured by duration of survival and to evaluate the safety of multiple administrations of rhuMAb-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer.

Technical Approach: rhuMab-VEGF (Bevacizumab) is an experimental, humanized monoclonal antibody using recombinant DNA technology, directed against vascular endothelial growth factor, or VEGF. Following a 28 day screening period, eligible subjects will be randomized into one of three treatment arms, (1) 5-FU/leucovorin/CPT-11 plus placebo, (2) 5-FU/leucovorin/CPT-11 plus study drug, or (3) 5-FU/leucovorin plus study drug. The treatment period will last approximately 23 months with a 14 day follow-up. Subjects will be asked to periodically complete Quality of Life Questionnaires and blood samples will be sent to an outside lab for pharmacokinetic testing. Second-line treatment options will be offered under this protocol if there is disease progression, depending on the treatment arm originally assigned. Subjects will be removed from the study if the disease progresses further following second-line treatment. A safety analysis will be conducted after the first 50 patients treated with the study drug and CPT-ll. At the conclusion of the study, if the tumor is stable or smaller and if subjects received rhuMab-VEGF, they may be eligible to continue to receive the study drug under an extention study.

Progress: This multicenter study was opened at MAMC Hematology and Oncology Clinic in March 01. Protocol Amendments 1 and 2 were issued, submitted, and approved by MAMC IRB in FY 01. Amendment 2 incorporates results of preliminary safety analysis by the sponsor company, closing enrollment of subjects to the 1 of 3 treatment arms that did not include the study drug. In July, an 80% FTE RN Clinical Research Coordinator was identified to work with investigators on all HJF oncology clinical trials in the clinic, and to assist with locating and coordinating new oncology protocols. The position is funded by the Henry M. Jackson Foundation for the Advancement of Military Medicine MAMC oncology accounts. Eligible subjects have not been identified for this metastatic colorectal cancer treatment protocol to present date. Coordination with other MAMC clinics and services has been set in motion to enhance screening of new patient consultations for possible eligibility. Subject recruitment continues. The protocol was approved for continuation by MAMC IRB in July 01.

Adverse Reactions: None at MAMC

Non-MAMC IND Safety Reports FY 01: 3 serious adverse events reported to investigators in FY 01. An update of the Investigator Brochure was issued 10 September 2001. The Principal Investigator has requested that additional risk information be included in the MAMC Informed Consent form relating to adverse events reported in August and September 2001.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/007 **Status**: Terminated

Title: A Multicenter, Double-blind, Randomized Study to Compare the Safety and Efficacy of Levofloxacin with that of Cefepime in the Treatment of Fever and Neutropenia

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; LTC Joseph T. Morris III, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Oct 01	N/A

Study Objective: Evaluate whether monotherapy with Levofloxacin given intravenously is at least as safe and effective as monotherapy with a cefepime intravenous drug regimen in the treatment of hospitalized subjects with fever and neutropenia (ANC<500) who are anticipated to remain hospitalized up to the end-of-therapy visit. The regimens to be compared are Levofloxacin 750 mg IV once daily versus Cefepime 2g IV given q8 hours.

Technical Approach: This is a multicenter, double-blind, placebo controlled, phase IIIB study, which will enroll hospitalized patients who have a diagnosis of febrile neutropenia. Patients will be randomized and statified by study center to receive 1 of the 2 treatment regimens, which will be compared for safety and efficacy. Duration of participation will be up to 14 days or until the patient has been afebrile for 48 hours (oral temp below 99 degrees F and has recovered to an ANC >500 cells/ul or sever days after defervescence (abatement of fever) and ANC >100.

Progress: This study was terminated, 22 Aug 01, per the study sponsor due to difficulty enrolling subjects. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/008 **Status**: Terminated

Title: A Multicenter, Randomized Study to Compare the Safety and Effiacacy of Oral Levofloxacin vs. Parenteral Ceftriaxone and Amikacin with the Potential of Conversion to Oral Ciprofloxacin and Amoxicillin/Clavulanate in the Treatment of Subjects with Talcott Group IV Febrile Neutropenia

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; LTC Joseph T. Morris III, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Oct 01	N/A

Study Objective: This non-inferiority trial will evaluate the safety and efficacy of oral antimicrobial treatment of Talcott group IV patients who develop fever while neutropenic or anticipated to develop neutropenia. The study will attempt to define that oral monotherapy with levofloxacin is at least as effective as an i.v. or i.v. p.o. combination drug regimen. Secondary Objectives: This trial will evaluate the association of C.pneumoniae, an organism uncommonly identified from clinical specimens, with fever in the neutropenic patient. A further secondary objective will be to compare the resource utilization of both treatment arms.

Technical Approach: This is a multi-center, randomized, phase IIIB study, which will enroll patients who have a diagnosis of febrile neutropenia. The patients will be randomized (and stratified by study center) to receive 1 of the 2 treatment regimens, which will be compared for safety and efficacy. Patients receiving oral Levofloxacine will take one 250mg tablet and one 500mg tablet by mouth once daily, preferably in the morning. (Levofloxacine 750mg IV may be substituted for patients who cannot subsequently tolerate oral therapy [e.g., patients with nausea/vomiting] until oral therapy can be reinitiated). Patients to receive the comparator, will be given Ceftriaxone 2gm and Amikacin 15mg/kg intravenously q24h. After receiving at least one day of IV therapy, patients who, in the opinion of the investigator, are candidates for conversion to oral therapy may receive Amoxicillin/Clavulanate one 875mg tablet to be taken twice daily in accordance with the manufacturer's instructions as described in the package insert. One Ciprofloxacin 750mg tablet shall also be taken twice daily.

Patients will take medication by mouth or IV for up to 14 days, or until he/she is afebrile for 48 hours and has regained an Absolute Neutrophilic Count (ANC) in excess of 500 cells per ul. Therapy of up to 28 days can be approved by the medical monitor. The duration of the therapy will be up to 14 days as clinically indicated or until the patient has been afebrile for 48 hours and has recovered to an Absolute Neutrophilic Count (ANC) >500 cells/ul. Rate of relapse will be determined by clinical and microbiologic response at the post-study visit; Clinical response and microbiologic response will be assessed by the investigator based on the same parameters as the original infection. The rate of new infections will also be evaluated at this time.

Note: Response to IRB stipulation #1: Modified Talcott IV Group- these criteria differ slightly from the original paper used by Talcott, which allows for the inclusion of patients above the age of 65 who may have otherwise been excluded under the original Talcott criteria.

Progress: This trial was closed by the sponsor, Ortho-McNeil, 6 Sep 01, due to poor subject enrollment at all sites. No patients have been screened or randomized for this trial at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/025 **Status**: Ongoing

Title: A Multicenter, Phase III Randomized Trial for Stage IIIB or IV NSCLC Comparing Weekly Taxol (Paclitaxel) and Carboplatin (Paraplatin) Regimen Versus Standard Taxol and Carboplatin Administered Every Three Weeks, Followed by Weekly Taxol (TAX/MEN.12)

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Feb 02	N/A

Study Objective: The primary objective of this study is to determine the overall patient survival rate for each of the two treatment regimens outlined in this study. The secondary objectives are to determine the time to disease progression for each regimen, to determine the objective response rate of the two treatment regimens, and to evaluate the safety and toxicity of the treatment regimens.

Technical Approach: This is a Phase III, multicenter, randomized, open-label trial to further investigate the safety and efficacy of weekly 1-hour infusions of paclitaxel (Taxol) and carboplatin for stages IIIB and IV NSCLC compared with a 3-hour infusion of the standard Taxol and carboplatin regimen administered every three weeks. During the induction phase, patients will be randomized to two treatment combination regimens of Taxol and carboplatin, followed by a maintenance phase that will consist of cycles of weekly Taxol for 3 weeks followed by a week of rest. Approximately 60 sites will participate in this study in the United States.

The primary efficacy endpoint will be the overall patient survival rate. The survival rate will be evaluated at 1,2,3,4, and 6 months and at 1 year for each of the dosing arms during the induction phase and for the maintenance phase. The secondary efficacy endpoints will be the objective response rate and the median time to disease progression. The response rate is defined as the percentage of patients that achieved a complete or partial response. The response rate for each treatment arm of the induction phase will be tested for equality to a 25% historical control rate. The time to progression will be evaluated during the induction phase and the maintenance phase. The time to progression data will be characterized by Kaplan-Meier curves and summarized using descriptive statistics

Progress: This multicenter study was initially opened at MAMC Hematology and Oncology Clinic in May 01. Protocol Amendment #1 was issued, submitted, and approved by MAMC IRB in July 01. Also in July, an 80% FTE RN Clinical Research Coordinator was identified to work with investigators on all HJF oncology clinical trials in the clinic, and to assist with locating and coordinating new oncology protocols. The position is funded by the Henry M. Jackson Foundation for the Advancement of Military Medicine MAMC oncology accounts. Two patients have since been enrolled to this Non-small Lung Cancer chemotherapy trial. The first enrolled subject has completed 4 treatment cycles without disease progression. The second has recently completed the first treatment cycle. A third patient was identified in September who remains in screening for enrollment. Collected data for this clinical trial is reported by fax and express mail delivery to central data managers, and this process is up to date. Subject recruitment continues.

Adverse Reactions: None at MAMC. Non-MAMC IND Safety Reports FY 01: 2 serious adverse events reported to investigators in FY 01, of occurrences in FY 99 and 00. These were reported to MAMC IRB, and did not require consent form changes in the opinion of the MAMC investigator.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/114 **Status**: Ongoing

Title: A Double-Blind Clinical Study to Compare Single IV Doses of Palonosetron, 0.25 mg or 0.75 mg, and Dolasetron 100 mg IV, in the Prevention of Moderately Emetogenic Chemotherapy-Induced Nausea and Vomiting, Protocol No. PALO-99-04

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Dec 02	N/A

Study Objective: Primary: To compare the efficacy of single IV doses of palonosetron 0.25 mg or 0.75 mg to dolasetron 100 mg IV in preventing moderately emetogenic chemotherapy induced nausea and vomiting. Secondary: To evaluate the safety and tolerability of palonosetron and its relative safety in comparison with dolasetron and to evaluate the effect of anti-emetic control with palonosetron or dolasetron on the quality of life of patients receiving moderately emetogenic chemotherapy.

Technical Approach: This clinical trial is a multicenter, Phase III, randomized, balanced, controlled, double-blind, parallel, stratified, and active comparator study of a new long acting antiemetic 5-HT3 receptor antagonist medication with a currently available and approved antiemetic treatment for prevention of nausea and vomiting in patients receiving moderately emetogenic chemotherapy. Approximately 65 investigative sites will participate in this study with the number of patients estimated to be 567, distributed in 3 groups of 189 men and women. At MAMC there are expected to be 10 to 20 patients enrolled to the PALO-99-04 protocol during approximately one year. Eligible patients must be 18 years or older, and able to provide written informed consent. Subjects at this clinical trial site will be identified from the MAMC Hematology/Oncology Clinic male and female patient population with histologically or cytologically confirmed malignant diseases, and who are scheduled on Day 1 of this study to receive a single dose of at least one of several protocol-listed moderately emetogenic chemotherapy agents as their major chemotherapeutic agent.

A subgroup of enrolled patients in the PALO 04 and -05 trials (16-17% of the total randomized) will be randomized to receive and consented for a period of continuous ECG recording by Holter Monitor as part of the safety evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location. A separate consent form will be utilized for patients randomized to the Holter monitoring subgroup for each of these studies. Efficacy data and quality of life data for the periods between clinic/study visits will be collected using the tools of 1) a 5-day Patient Diary to record emetic episodes, rescue medication, severity of nausea, and evaluate patient satisfaction with antiemetic therapy, and 2) the FLIE (Functional Living Index-Emesis) Patient Questionnaire which will be completed twice during the study.

General Procedures: On Study Day 1, randomized patients will receive a single IV dose of 0.25 mg or 0.75 mg of palonosetron OR of dolasetron 100mg at 30 minutes prior to start of scheduled chemotherapy. For patients receiving Holter ECG monitoring, a 12 lead ECG will be performed 15 minutes after study drug is given, and single blood draw for PK analysis will be performed on selected study days. Patients return for follow up to the clinic at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will make telephone contact with the patient for follow up data. All patients have the option of continuing in the study after day 15 by enrolling

to an open-label extension protocol that permits them to receive the study drug with up to 9 more cycles of chemotherapy if other inclusion and exclusion criteria continue to be met. Please refer to protocol submission for PALO-99-06. These patients return to the clinic for a 5th visit on day 21-28.

Progress: These three multicenter clinical trial protocols each use the antiemetic study drug Palonosetron in comparison with Dolasetron or Ondansetron or alone in patients receiving chemotherapy. The three protocols and the first 4 Protocol Amendments for each have received MAMC IRB and CIRO approval, and a CRDA is in place. The studies are scheduled for initiation at MAMC Hematology and Oncology Clinic 12 October 01. Study drug and supplies have been received and FDA regulatory requirements met to date. Following the October initiation meeting, active subject recruitment may begin. Protocol Amendment #5 for each protocol in the series was issued, submitted, and approved by MAMC IRB in September 01. The Clinical Research Coordinator has been identified to work with investigators on these and all oncology clinical trials in the clinic, and to assist with locating and coordinating new oncology protocols.

Serious Adverse Events: None at MAMC-Not open to patient enrollment in FY 01 at MAMC. Non-MAMC IND Safety Reports FY 01: 2 reported to investigators in FY 01, and were reported to MAMC IRB. The patients recovered with treatment. Both events required discontinuation of study drug.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/115	**Status**: Ongoing

Title: A Double-Blind Clinical Study to Compare Single IV Doses of Palonosetron, 0.25 mg or 0.75 mg, and Ondansetron, 32 mg IV, in the Prevention of Highly Emetogenic Chemotherapy-Induced Nausea and Vomiting, Protocol No. PALO-99-05

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology	**Facility**: MAMC

Associate Investigator(s): MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/26/2001	Dec 02	N/A

Study Objective: Primary: To compare the efficacy of single IV doses of palonosetron 0.25 mg or 0.75 mg to ondansetron 32 mg IV in preventing nausea and vomiting induced by highly emetogenic chemotherapy. Secondary: To evaluate the safety and tolerability of palonosetron and its relative safety in comparison with ondansetron and to evaluate the effect of anti-emetic control with palonosetron or ondansetron on the quality of life of patients receiving moderately emetogenic chemotherapy.

Technical Approach: This clinical trial is a multicenter, Phase III, randomized, balanced, controlled, double-blind, double-dummy, parallel, stratified, and active comparator study of a new long acting antiemetic 5-HT3 receptor antagonist medication with a currently available and approved antiemetic treatment for prevention of nausea and vomiting in patients receiving highly emetogenic chemotherapy. Approximately 65 sites will participate in this study and the number of patients to be included in this study is estimated to be 669, distributed in 3 treatment arms of 223 men and women. At MAMC there are expected to be 2 to 5 patients enrolled to this protocol during approximately one year. Eligible patients must be 18 years or older, and able to provide written informed consent. Subjects at this clinical trial site will be identified from the MAMC Hematology/Oncology Clinic male and female patient population with histologically or cytologically confirmed malignant diseases, and who are scheduled on Day 1 of this study to receive a single dose of at least one of five protocol-listed highly emetogenic chemotherapy agents as their major chemotherapeutic agent.

12-lead ECG testing is indicated by the protocol for patients at screening, at study drug treatment (for patients randomized to Holter ECG monitoring), at study day 2 and study day 8. The investigator is asked to review the ECG on site, and original ECG strips will be further evaluated by a cardiologist at a central location. A subgroup of enrolled patients in the PALO 04 and -05 trials (16-17% of the total randomized) will be randomized to receive and consented for a period of continuous ECG recording by Holter Monitor as part of the safety evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location. A separate consent form will be utilized for patients randomized to the Holter monitoring subgroup for each of these studies. Efficacy data and quality of life data for the periods between clinic/study visits will be collected using the tools of 1) a 5-day Patient Diary to record emetic episodes, rescue medication, severity of nausea, and evaluate patient satisfaction with antiemetic therapy, and 2) the FLIE (Functional Living Index-Emesis) Patient Questionnaire which will be completed twice during the study.

General Procedures: On Study Day 1, randomized patients will receive a single IV dose of 0.25 mg OR 0.75 mg of palonosetron OR of ondansetron 32mg at 30 minutes prior to start of scheduled chemotherapy. In double-dummy blinded fashion, a 5ml IV bolus and a 50ml IV infusion will both be administered. At the investigator's discretion, and if so determined at the time of

randomization, a single dose of dexamethasone or appropriate substitute medication may be given at 15 minutes before chemotherapy is started. For patients receiving Holter monitoring, a 12 lead ECG will be performed 15 minutes after study drug is given, and single blood draw for PK analysis will be performed on selected study days. Patients return at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will make telephone contact with the patient for follow up data. All patients have the option of continuing in the study after day 15 by enrolling to an open-label extension protocol that permits them to receive the study drug with up to 9 more cycles of chemotherapy if other inclusion and exclusion criteria continue to be met. Please refer to protocol submission for PALO-99-06. These patients return to the clinic for a 5th visit day 21-28.

Progress: These three multicenter clinical trial protocols each use the antiemetic study drug Palonosetron in comparison with Dolasetron or Ondansetron or alone in patients receiving chemotherapy. The three protocols and the first 4 Protocol Amendments for each have received MAMC IRB and CIRO approval, and a CRDA is in place. The studies are scheduled for initiation at MAMC Hematology and Oncology Clinic 12 October 01. Study drug and supplies have been received and FDA regulatory requirements met to date. Following the October initiation meeting, active subject recruitment may begin. Protocol Amendment #5 for each protocol in the series was issued, submitted, and approved by MAMC IRB in September 01. The Clinical Research Coordinator has been identified to work with investigators on these and all oncology clinical trials in the clinic, and to assist with locating and coordinating new oncology protocols.

Serious Adverse Events: None at MAMC-Not open to patient enrollment in FY 01 at MAMC. Non-MAMC IND Safety Reports FY 01: 2 reported to investigators in FY 01, and were reported to MAMC IRB. The patients recovered with treatment. Both events required discontinuation of study drug.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/116 **Status**: Ongoing

Title: A Multicenter, Open-Label Study to Assess the Safety and Efficacy of IV Palonosetron for the Prevention of Chemotherapy-Induced Nausea and Vomiting in Repeated Chemotherapy Cycles, Protocol No. PALO-99-06

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Dec 02	N/A

Study Objective: To assess the safety of single dose IV palonosetron used in up to a maximum of 10 consecutive chemotherapy cycles, to assess the safety of single dose IV palonosetron plus dexamethasone used in a maximum of 10 consecutive chemotherapy cycles and to assess continued efficacy of palonosetron and palonosetron plus dexamethasone in repeated cycles of chemotherapy.

Technical Approach: This clinical trial is a multicenter, Phase III, uncontrolled, open-label, repeat-cycle safety study designed to assess the safety and efficacy of single IV doses of Palonosetron, 0.75mg, in the prevention of CINV in repeated chemotherapy cycles. Palonosetron is a new long acting antiemetic 5-HT3 receptor antagonist medication. PALO-99-06 is an extension study to PALO-99-04 and PALO-99-05. Approximately 65 sites will participate in this study. At MAMC there are expected to be a maximum of 12 to 25 patients enrolled to the PALO-99-06 protocol. Enrollment in PALO-99-06 will remain open and patients will be allowed to continue in the protocol until at least 1200 additional chemotherapy cycles have been evaluated, and for as long as enrollment is ongoing in the PALO-99-04 and PALO-99-05 protocols, up to a maximum of 1700 cycles. Screening/baseline procedures may be performed on the same day as Study Day 1 and chemotherapy administration if feasible. On Study Day 1 patients will receive a single IV dose of 0.25 mg palonosetron as a 5-mL IV bolus at 30 minutes prior to administration of the major chemotherapeutic agent. For those patients who participated in PALO-99-05, a single dose of dexamethasone, 20mg IV, may be administered 15 minutes prior to chemotherapy. Dexamethasone will not be administered to PALO-99-06 patients who previously participated in PALO-99-04. Patients return to the clinic at Study Day 2 and Day 6. On Day 5 and Day 15, the study coordinator will contact patients by telephone for follow up data and progress. Patients who did NOT receive Holter ECG Monitoring in the PALO-04 and -05 trial they participated in have the option to take part during this study in evaluations to determine if clinically significant changes in the ECG occur between 2 hours before until 24 hours after study drug administration. Patients in this extension study may elect Holter participation for one of their PALO-99-06 plus chemotherapy treatment cycles. Holter monitoring equipment and related supplies are provided by the study sponsor. Holter Monitor recordings will also be evaluated by a cardiology consultant in a central location.

Patient Visit Procedures through Study Day 15 will be performed in the same way for each repeat chemotherapy cycle up to 9 additional cycles. Efficacy data collection will include a 5-day Patient Diary to record emetic episodes, rescue medication, and severity of nausea on study days 1 to 5.

Progress: These three multicenter clinical trial protocols each use the antiemetic study drug Palonosetron in comparison with Dolasetron or Ondansetron or alone in patients receiving chemotherapy. The three protocols and the first 4 Protocol Amendments for each have received MAMC IRB and CIRO approval, and a CRDA is in place. The studies are scheduled for initiation at MAMC Hematology and Oncology Clinic 12 October 01. Study drug and supplies have been received and FDA regulatory requirements met to date. Following the October initiation meeting, active subject recruitment may begin. Protocol Amendment #5 for each protocol in the series was

issued, submitted, and approved by MAMC IRB in September 01. The Clinical Research Coordinator has been identified to work with investigators on these and all oncology clinical trials in the clinic, and to assist with locating and coordinating new oncology protocols.

Serious Adverse Events: None at MAMC-Not open to patient enrollment in FY 01 at MAMC. Non-MAMC IND Safety Reports FY 01: 2 reported to investigators in FY 01, and were reported to MAMC IRB. The patients recovered with treatment. Both events required discontinuation of study drug.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/093 **Status**: Ongoing

Title: Phase II Trial of Gemcitabine and Herceptin in HER2 Overexpressing Metastatic Breast Cancer

Principal Investigator: MAJ David E. McCune, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

Associate Investigator(s): MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Jul 01	7/24/2001

Study Objective: 1) To response rates of complete response, partial response, stable disease and progressive disease. 2) To document the median time to progression and median survival of disease. 3) To monitor toxicities of Grades 3 or higher to be reported (toxicities graded based on the NCI common toxicity grading scheme).

Technical Approach: This is a Phase II multicenter trial conducted in military medical centers experienced in the treatment of breast cancer. The study will investigate the response rate, time to treatment failure, overall survival and toxicity/safety profile of a novel combination of Gemcitabine and Herceptin in patients with metastatic breast cancer. Both of the drugs will be administered weekly in patients whose breast cancer overexpresses the BER2 proto-oncogene.

Progress: This protocol has not yet received final IRB approval and remains inactive at MAMC due to time contraints of its investigators. The PI plans to comply with IRB stipulations and open this study to enrollment during FY02.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/085 **Status**: Ongoing

Title: A Phase II Trial of Recombinant-Human Granulocyte-Macrophage Colony Stimulating Factor (rhu-GM-CSF, Leukine) in Chronic Diabetic and Venous Stasis Wounds

Principal Investigator: MAJ Patrick Williams, MC

Department: Medicine/Hematology & Oncology **Facility**: MAMC

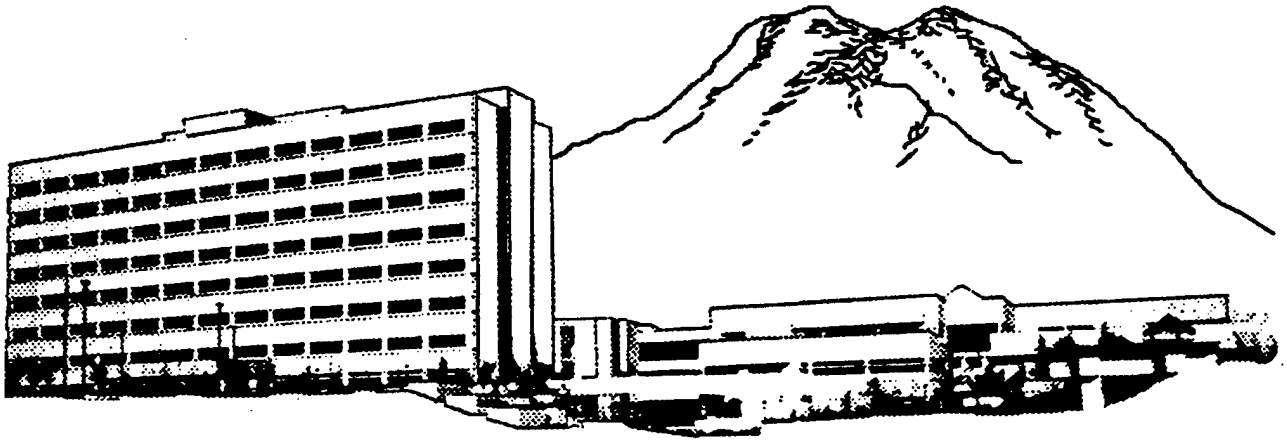
Associate Investigator(s): MAJ David E. McCune, MC; Vickie R. Driver, DPM; CPT Amy L. Young, DO

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Jan 02	5/22/2001

Study Objective: (1) Assess the efficacy of applying rhu-GM-CSF peri-lesionally to chronic diabetic and venous chronic wounds at a dose of 500mcg twice weekly to decrease time to wound healing and (2) Assess the safety, as an adjunct to standard wound care, of peri-lesional rhu-GM-CSF to improve time to wound healing.

Technical Approach: This study is an open, single-arm pilot study. 30 male/female eligible patients, over 18 years-old, with chronic wounds as a result of the verifiable diagnosis of diabetes or venous stasis will receive rhu-GM-CSF (Leukine) twice weekly through peri-lesional injection in a four-points-of-the-compass fashion of their wounds for a total of twenty weeks. Wound size will be measured at entry, at each visit, and at the conclusion of therapy. The change in the cross-sectional area of the wound will be recorded for each patient and reported as the primary endpoint of the study. Patients will be sequentially enrolled with interim analysis at twenty patients. The secondary endpoint of the study is the incidence of toxicity with the study drug. Toxicity will be assessed at every visit, and recorded according to the NCI Common Toxicity Criteria. Efficacy will be measured by comparison to historical records and safety monitored throughout the study. This data will be used to initiate a phase III trial to develop and utilize a topical gel formulation of rhu-GM-CSF.

Progress: This study has not yet been initiated at MAMC, awaiting a Nursing Impact Statement.



Detail Summary Sheets

Infectious Disease Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/122 **Status**: Terminated

Title: A Phase II Randomized, Double-blind Controlled Study to Evaluate the Safety and Immunogenicity of MEDI-516 with MF59C.1, an E. Coli Pilus Vaccine, in Adult Women at Risk for Recurrent Urinary Tract Infections

Principal Investigator: LTC Joseph T. Morris III, MC

Department: Medicine/Infectious Disease **Facility**: MAMC

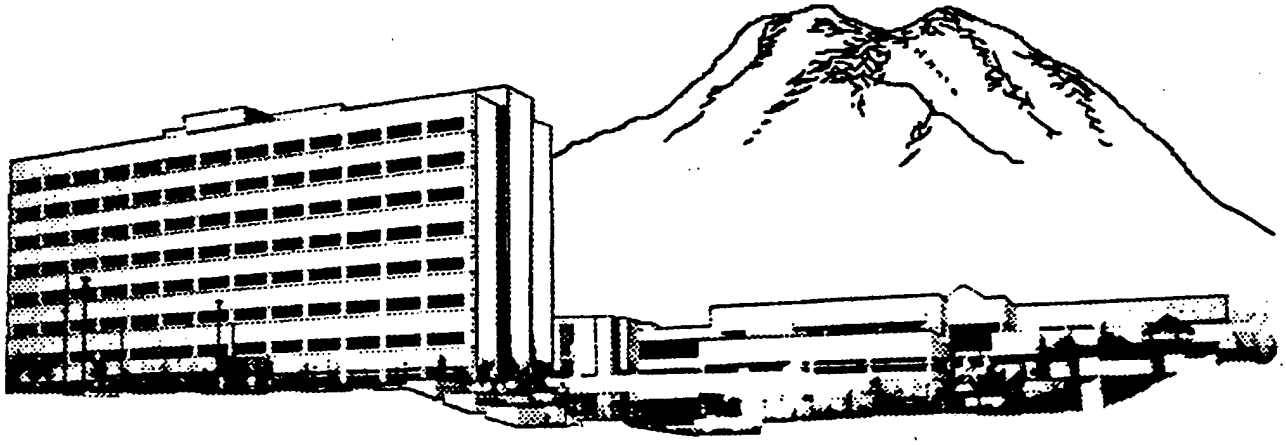
Associate Investigator(s): MAJ Kristie Lowry

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Nov 02	7/24/2001

Study Objective: The primary objective of this study is to describe the safety and reactogenicity (serum and urine antibody responses) of three doses of MEDI-516 formulated in MF59C.1 in healthy adult women with a history of recurrent urinary tract infection (UTI). Describe and analyze the occurrence of UTIs in volunteers receiving at least one dose of vaccine.

Technical Approach: This randomized, double-blind, controlled Phase II study is designed to gather additional safety and immunogenicity data in healthy, sexually active female volunteers age 18-45 who have experienced symptomatic urinary tract infections (UTI) within the preceding 12 months. Volunteers will be monitored to describe local and general safety, reactogenicity, and immunogenicity of three doses of either 25 micrograms of MEDI-516 with MF59C.1 or adjuvant control administered on study days 0, 28, and 180.This study will also describe the occurrence of symptomatic UTI and asymptomatic bacteriuria caused by E. coli and other uropathogens, as these events are important in defining clinical endpoints that are critical to the design of Phase III Efficacy studies.

Progress: This study closed to patient entry, 9 Apr 01, upon recommendation of the study sponsor. One subject enrolled in this study at MAMC and received a single dose of study vaccine per protocol. However, the vaccine was discontinued following notification of positive pregnancy test results prior to receiving the second scheduled dose. The subject was withdrawn and subsequently reported a miscarriage and her decision to discontinue all study participation. Subject continues to receive prophylactic antibiotic therapy for her recurrent urinary tract infections and has been reported as stable on this treatment. This study was reported as terminated at MAMC, 25 Jul 01.



Detail Summary Sheets

Internal Medicine Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/032 **Status**: Completed

Title: Cost Analysis of Prescreening for Hepatitis A Before Immunization in Patients with Chronic Liver Disease

Principal Investigator: CPT Marten B. Duncan, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): MAJ William K. Hirota, MC; COL Amy M. Tsuchida, MC; LTC Spencer S. Root, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Feb 01	1/23/2001

Study Objective: To define the prevalence of hepatitis A virus (HAV) in a population of patients with chronic liver disease (CLD) and to characterize demographic features of previously exposed patients. To perform a cost analysis of immunization for hepatitis a virus in those with CLD by comparing three strategies.

Technical Approach: 100 subjects with CLD will be recruited to clarify the prevalence of prior hepatitis A exposure. Subjects will complete a survey to identify which risk factors are most common among patients with CLD. Hepatitis A serology will then be determined using an anti-HAV elisa. Subjects will be asked to report for vaccination only if they are seronegative for prior exposure to the virus. A cost analysis will be done to identify the least costly way to provide immunity against the virus in this subgroup of patients using the prevalence of prior infection determined by this study. These strategies include: (1) to determine seropositivity and vaccinate only those without evidence of prior exposure, (2) to immunize all persons with CLD, or (3) determine antibody status and vaccinate in one visit with follow-up vaccination at 6 months only if the patient was seronegative for anti-HAV.

Progress: Study with follow-up serology has been completed. 100 patients screened. Seroprevalence of hepatitis A in those with chronic liver disease was 53%. Cost analysis revealed that prescreening for hepatitis A prior to immunization is cost-saving. This method should be applied to achieve current vaccination guidelines.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/125	**Status**: Ongoing

Title: The Effect of Montelukast on the Methacholine Challenge

Principal Investigator: CPT Thomas C. Hattan, MC

Department: Medicine/Internal Medicine	**Facility**: MAMC

Associate Investigator(s): CPT David Y. Gaitonde, MC; LTC John C. Walker, MC; COL Jerry L. Pluss, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
8/28/2001	Jun 01	N/A

Study Objective: Investigate the effect of the leukotriene receptor antagonist (LTRA), montelukast, on airway hyperresponsiveness to inhaled methacholine.

Technical Approach: The goal of this small study is to investigate the effect of montelukast on inhaled methacholine challenge in 30 subjects with positive or borderline positive methacholine challenges. Clinical significance is whether the subject reacts to the methacholine challenge at an increased concentration, ie. does the change in reactivity bump a subject from the severe to the mild category of BHR? Subjects will be eligible to participate if they have a positive methacholine challenge (20% decline or more in FEV1 at concentrations of methacholine up to 16 mg/ml) and do not meet any of the exclusion criteria. Study subjects will be given 2 to 3 weeks of therapy with montelukast 10 mg or placebo orally once a day, then undergo a second methacholine challenge. After a two week wash out period they will perform the opposite arm of the study and undergo a third methacholine challenge. Comparison to baseline results will be made with each subject serving as his/her own control. Primarily, the concentration of methacholine required to decrease the FEV1 by 20% (PC20) before and after 2- 3 weeks of montelukast and placebo will be analyzed on an individual participant basis.

Progress: Two subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/072 **Status**: Ongoing

Title: The Effectiveness of Outpatient Management of Hyperlipidemia Using Internet Technology, a Randomized, Controlled Trial

Principal Investigator: CPT Patricia A. McKay, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Jul 01	N/A

Study Objective: (1) Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patient with hyperlipidemia using Internet technology, (2) Show that patient compliance can be improved through personalized patient education and through meaningful interactions with their providers using the Internet as the medium for communication and delivery of information.

Technical Approach: The study design for this pilot study is a randomized non-blinded study. The study population are patients with hyperlipidemia who are enrolled in the Adult Primary Care Clinic Cascade team. The clinicians on the Cascade team will manage both the control and study group. Patients in the placebo group will have their hyperlipidemia managed the traditional method which includes routine office visit and phone calls. The study group will be managed with routine office augmented by VPCC e-health system. The primary end point is the change in LDL cholesterol from baseline. Secondary endpoints will include patient and provider's satisfaction, effectiveness of patient and provider education, clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and logistic regression. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/078 **Status**: Ongoing

Title: A Comparison of Electronic Consults to Telephone Consults for Workload, Satisfaction, and Clinic Efficiency, A Randomized, Controlled Trial (VPCC Substudy)

Principal Investigator: CPT Patricia A. McKay, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): CPT Samara Rutberg, MC; LTC Gary A. Wheeler, MC; MAJ Nhan V. Do, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Jan 02	N/A

Study Objective: (1) Evaluate the effects of secured Internet messaging as a means for communication on efficiency and quality of care in an outpatient clinic, (1) Evaluate the impact on patient and provider satisfaction and (3) Evaluate the impact on demands for office visits.

Technical Approach: This protocol is designed to measure acceptance by the health care team of patient, provider, and nursing to facilitate delivery of health care. Measure of satisfaction with electronic communication by each member of this team will be compared to traditional telephone consultation. Sub-analysis of type of communication (advice, refills, acute medical need, appointment request, etc.) will demonstrate whether e-consultation is particularly conductive or poorly suited to certain types of patient-provider communications. Also measured will be the potential shift of health care from the traditional face-to-face visit to electronic consultation visit. Such virtual visits may be particularly well suited for dissemination of information and patient education The Military Healthcare System (MHS) currently does not recognize or endorse the use of electronic communication for workload purposes. Adoption of an e-con communications system could therefore represent a significant cost-shift from the military treatment facility if current policy is not appropriately amended. This protocol will give an estimate of that cost. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/101 **Status**: Ongoing

Title: Adjuvant Therapy with Folate and Vitamins B6 and C in Patients with Anemia of Chronic Renal Failure Undergoing Epoeitin Therapy

Principal Investigator: CPT Robert M. Perkins, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): COL Howard M. Cushner, MC; MAJ Christopher J. LeBrun, MC; SSG Janice White, NC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
5/22/2001	May 02	N/A

Study Objective: To determine whether epogen dosing requirements can be reduced through supplementation with vitamins B6, C and folate in pre-dialysis patients undergoing epoeitin therapy for their anemia of chronic renal failure.

Technical Approach: This study is a group-sequential design to determine the effect of adjuvant therapy with pyridoxine, ascorbic acid, and folate on epogen dosing. Patients enrolled in the epogen clinic who meet inclusion criteria and are not excluded by our criteria will be eligible, and patient recruitment will take place during routine evaluation in the epogen clinic before and during the stabilization period. After their target hematocrit is achieved, and weekly epogen dosing has stabilized over an eight-dose period (as determined by two monthly CBCs), patients who choose to enroll in our study will receive adjuvant therapy with pyridoxine, folate, and ascorbic acid at standard doses. For patients who enroll, we will then compare weekly epogen doses required over the next two months with those doses required during the pre-vitamin, stabilization period. The primary endpoints are epogen dose required to maintain the target hematocrit and the target hematocrit itself.

Progress: Seven subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/076 **Status**: Ongoing

Title: The Effectiveness of Outpatient Management of Hypertension Using Internet Technology, a Randomized, Controlled Trial (VPCC Substudy)

Principal Investigator: CPT Richard Reed, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC; MAJ Jerald W. Rumph, MC; LTC Gregory A. Gahm, MS

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Jul 01	N/A

Study Objective: (1) Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patients with hypertension using Internet technology, (2) Show that patients' compliance can be improved through personalized patient education and through meaningful interactions with their providers using the Internet as the medium for communication and delivery of information.

Technical Approach: The study population will include both male and female patients from the APCC Cascade team with hypertension but without advanced cardiovascular complications and age range from 18 to 75. Study design is a randomized non-blinded study. The physicians on the Cascade team will manage both the control and study group. Patients in the control group will have their hypertension managed in the traditional method, which includes routine office visits and phone calls. The study group will be managed with routine office visit but with electronic communications and a limited computer clinical support system. Since no previous study exist, this study will be considered a pilot study to determine power for additional studies if needed. The primary endpoint is the change in systolic blood pressure from baseline. Secondary endpoints will include patient and provider's satisfaction, effectiveness of patient and provider education, clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and logistic regression. Patient will be recruited using informational flyers and form letters. Information about rules and regulation of the VPCC will be made available for patient to review and sign prior to enrollment. There is neither medical risk nor deviation from standard of care. There is a potential privacy risk due the nature of electronic communication and storage however standard precautions will be taken with industry standard encryption methods.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/117 **Status**: Ongoing

Title: Serum Cardiac Troponin Levels After Positive Cardiac Stress Tests

Principal Investigator: CPT Samara Rutberg, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

Associate Investigator(s): LTC James J. King, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Jun 01	N/A

Study Objective: To determine if positive cardiac stress tests lead to elevated serum troponin levels.

Technical Approach: Patients who present to the MAMC emergency room with chest pain and are presumed to have cardiac ischemia by history or a positive EKG for ischemia (1 millimeter ST segment depressions in two consecutive EKG leads), yet a negative initial serum troponin level, will be admitted to the inpatient ward to be ruled out for an acute myocardial infarction. Once the workup for an acute myocardial infarction is negative the patient will undergo a cardiac stress test in the Cardiology treadmill room. Twenty patients with positive cardiac stress tests will be consented for the study. All patients entered in the study will remain in the hospital and a serum troponin level will be drawn within 6 to 12 hours after their cardiac stress test. Any patient, who has ST segment elevations on their EKG during their cardiac stress test, or show concern for persistent cardiac ischemia, will be readmitted to the inpatient ward and immediately assessed by the cardiology service.

Progress: This study has not yet been initiated at MAMC due to its potential impact on nursing staff and in-patient services. A revised protocol is pending.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 90/099 **Status**: Ongoing

Title: Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure

Principal Investigator: CPT Samara Rutberg, MC

Department: Medicine/Internal Medicine **Facility**: MAMC

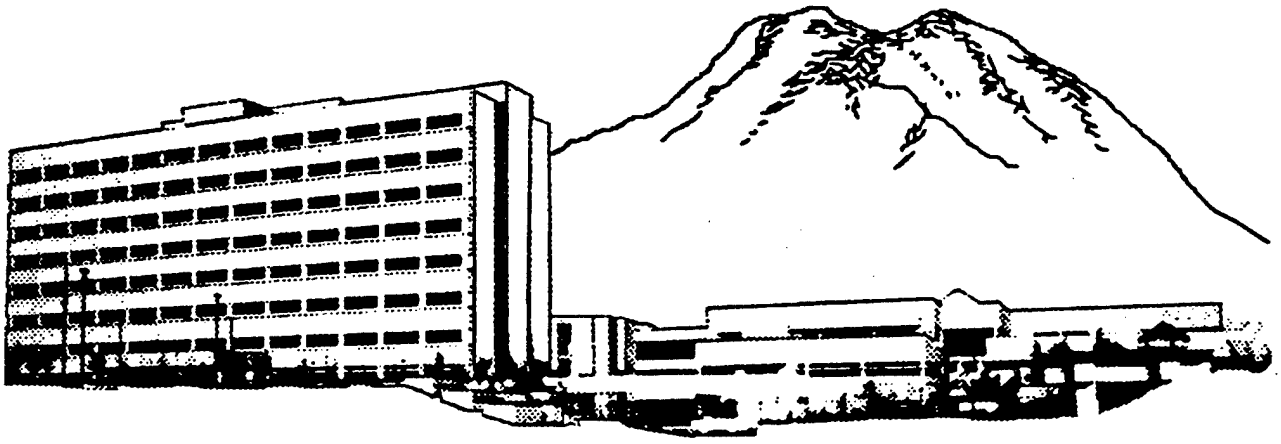
Associate Investigator(s): LTC William H. Cragun, MC; CPT Stephen M. Salerno, MC; CPT Donald M. Collins, MC; LTC Bernard J. Roth, MC; CPT Jennifer E. Jorgenson, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/17/1990	Jun 96	8/28/2001

Study Objective: To determine if the albumin gradient is a more effective criterion than Light's criteria to distinguish transudates from exudates in patients with congestive heart failure that have been treated with diuretics.

Technical Approach: Fifteen patients with clinically suspected congestive heart failure and chest radiograph evidence of pleural effusion will be studied. A thoracentesis to remove 50 cc of fluid will be performed and the following laboratory tests will be done on the fluid: albumin, total protein, glucose, LDH, bilirubin, cell count with cytospin differential, gram stain, and routine culture. A simultaneous sample of serum will be measured for albumin, total protein, LDH, bilirubin, and glucose. After three to five days of therapy for the congestive heart failure a repeat chest radiograph with bilateral decubitus view will be done. If pleural fluid persists, a repeat thoracentesis and laboratory tests will be done. If no fluid persists after three to five days, then the patient will be dropped from the study. Bilirubin ratio will also be assessed. The classification of the patients as exudate or transudate by serum effusion, bilirubin ratio, and Light's criteria will be compared between the two thoracentesis. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria.

Progress: No subjects enrolled in this study at MAMC in FY01. Twelve subjects have been enrolled in previous years. Subject enrollment continues.



Detail Summary Sheets

Nephrology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/061 **Status**: Completed

Title: A Study Evaluating the Initiation and Titration of Fixed Doses of Novel Erythropoiesis Stimulation Protein (NESP) Therapy in Subjects with Chronic Renal Insufficiency

Principal Investigator: MAJ Christopher J. LeBrun, MC

Department: Medicine/Nephrology **Facility**: MAMC

Associate Investigator(s): None.

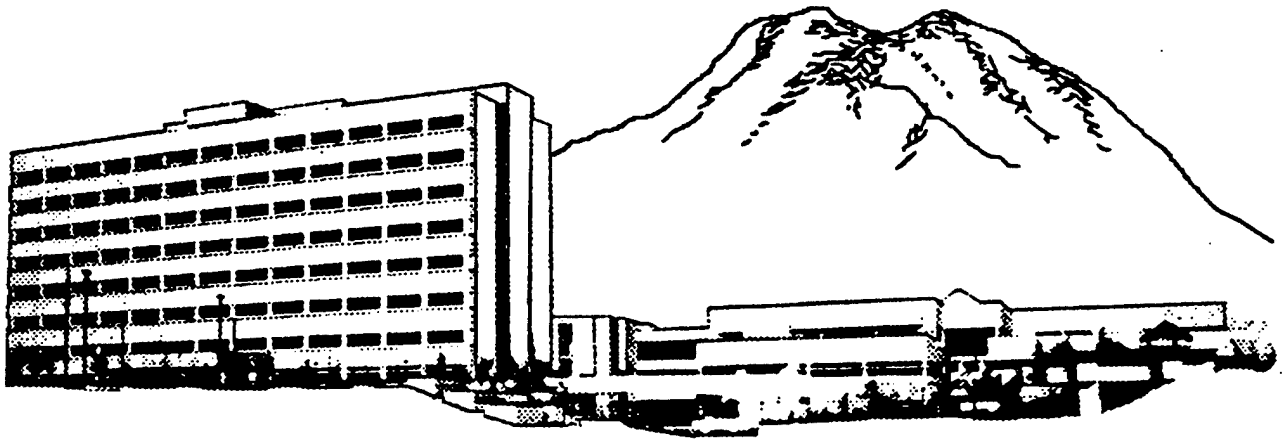
Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	May 01	4/24/2001

Study Objective: To assess the use of NESP, when initiated and titrated as a fixed dose, necessary to achieve and maintain the hemoglobin (Hb) concentration within a target range (11.0 to 13.0 g/dL) in subjects with chronic renal insufficiency (CRI) and the safety and tolerability of chronic NESP therapy in subjects with CRI.

Technical Approach: This is a multicenter, open-label study designed to assess the use of NESP, when initiated and titrated as a fixed dose, necessary to achieve and maintain Hb with a target range (11.0 to 13.0 g/dL) in subjects with chronic renal insufficiency (CRI). The duration of the study for an individual patient is 27 weeks. After an initial 2-week screening/baseline period and 1-week baseline period during which time additional laboratory assessments will be performed, eligible subjects with CRI will initiate therapy with NESP. The initial dose of NESP will be based on the subjects' body weight. Each subject will receive a SC injection of NESP once weekly for a period of 24 weeks. The study concludes with a 1-week post treatment observation and evaluation period.

Progress: During the period 1 Oct 00 to 1 Oct 01, 5 subjects were consented and screened for possible enrollment to the NESP CRI study. One subject met all eligibility criteria and enrolled in the study in Feb 01. Multicenter study enrollment was discontinued on 15 Feb 01 due to complete accrual. The MAMC subject received study medication dosages according to results of tests to monitor response of blood hemoglobin and hematocrit to the study treatment, and did experience improvement of anemia while on study. Serum chemistry values, weight and blood pressure data were followed, and the subject continued non-study visits and follow up care in the MAMC Nephrology clinic for Chronic Renal Insufficiency (CRI). The subject remained on study through week 17 of 24, when the PI withdrew the subject due to progression of CRI and preparation for off-site Nephrology referral and renal dialysis. The patient's withdrawal was reported to MAMC IRB. Last dose of study drug was received on 11 June 01. All study data for the subject was reported to central study personnel and all data queries have been answered. All study activities are complete. Study site closeout visit by clinical trial project management is pending for early FY 02.

Serious Adverse Events: None at MAMC. Non-MAMC IND Safety Reports FY 01: The study drug continues clinical trials in many and international centers for multiple disease indications: Anemia in Chronic Renal Failure, CRI, Oncology, and Chronic diseases. From 1 Oct 00 to 1 Oct 01, 68 Serious Adverse Events (SAE) were reported in IND Safety Letters to investigators in all NESP clinical trials. In December 00, additional risks were listed in the MAMC Informed Consent Document at request of the PI, based on review of IND Safety Reports.



Detail Summary Sheets

Neurology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/123 **Status**: Ongoing

Title: Carpal Tunnel Syndrome in Pregnancy: A Prospective Study on its Natural History

Principal Investigator: MAJ John Hartmann, MC

Department: Medicine/Neurology **Facility**: MAMC

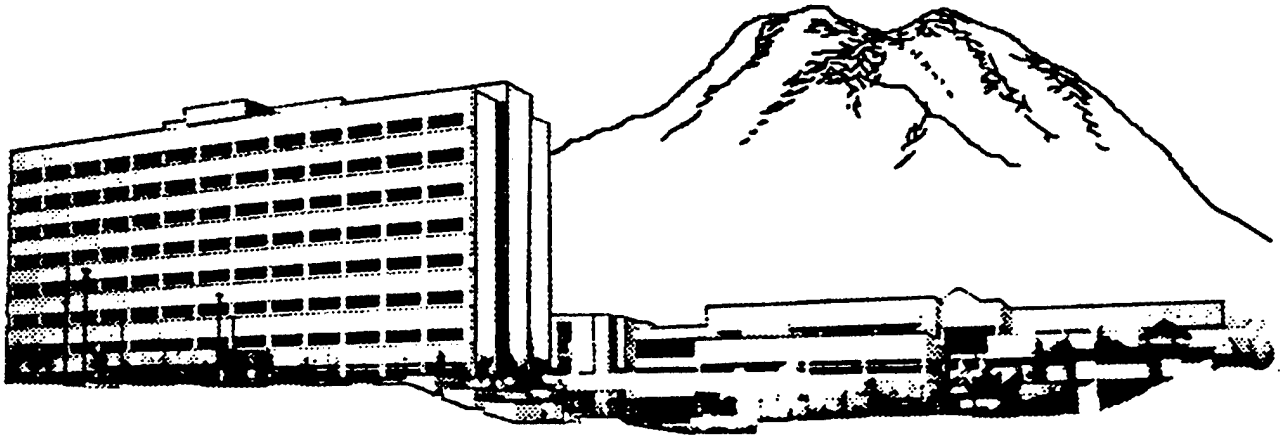
Associate Investigator(s): MAJ Wendy Ma, MC; CPT Paul J. Walting, MC; CPT Anna M. Hohler, MC; COL Giorgio S. Turella, MC; LTC Beverly R. Scott, MC; MAJ Traci D. Ryan, MC; CPT Trenton James, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Sep 02	8/28/2001

Study Objective: This study will try to determine the incidence of Carpal Tunnel Syndrome (CTS) during pregnancy in a prospective manner. Secondary objectives of this study will try to determine: (1) the incidence of CTS in each trimester of pregnancy; (2) potential risk factors for developing CTS in pregnancy such as Gestational Diabetes, preeclampsia, CTS in prior pregnancies, history of CTS prior to current pregnancy, excessive weight gain during pregnancy, nulliparous vs. multiparous pregnancies, single vs. multigestation pregnancies, concurrent hypothyroidism, and particular occupations; (3) the persistence of signs and symptoms of CTS after delivery and (4) pilot test a survey assessing Restless Leg Syndrome in pregnant women.

Technical Approach: This protocol will survey women seen in the Obstetric Clinic at MAMC for the development of CTS during each trimester and postpartum. Women will be enrolled at their first antepartum check and given a biographical sheet and questionnaire to complete, and an initial physical exam for the evaluation of CTS administered. The examiner will test the patient's ability to feel light touch, pinprick and 2 point discrimination at the points outlined. The examiner will then test muscle strength in the Abductor Pollicis Brevis, Opponens, Adductor Digiti Minimi, and Extensor Indicis Proprious. A Tinel's sign will be tested at each wrist, and Phalen's sign will be positive if sensory changes are reproduced in a median nerve distribution within 20 seconds of wrist flexion. At each evaluation, the presence of possible, probable, or definite CTS will be determined. Possible CTS will be defined as follows: Sensory changes to the hand, with nocturnal symptoms. Probable CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Localization by physical exam would be defined as consistent sensory findings over areas supplied by branches of the median nerve traversing through the carpal tunnel (via pinprick and light touch). Definite CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Motor findings, such as atrophy and weakness of median innervated muscles would be defined as Definite CTS. The Obstetrician will review the chart to complete the data for other obstetrical information. For the pilot study of RLS, the patient will answer questions on this topic during each of the sessions. Serial questionnaires and physical exams would be performed at the following intervals: 20-24 weeks gestation, 34-36 weeks gestation, and 6-10 weeks postpartum.

Progress: Currently, 283 women have been enrolled in this study. Data collection remains ongoing. The plan will be to continue the study until 500 women are enrolled and complete follow up as outlined in the original protocol.



Detail Summary Sheets

Pulmonary Disease & Critical Care Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/033 **Status**: Completed

Title: A Multicenter, Randomized, Open-Label Study Comparing the Efficacy and Safety of Once Daily ORG 31540/SR90107A Versus Adjusted-Dose Intravenous Unfractionated Heparin (UFH) in the Initial Treatment of Acute Symptomatic Pulmonary Embolism (PE)

Principal Investigator: LTC William E. Caras, MC

Department: Medicine/Pulmonary&Critical Care **Facility**: MAMC

Associate Investigator(s): COL John M. Bauman, MC; LTC Bernard J. Roth, MC; LTC George N. Giacoppe Jr., MC; LTC Leonard E. Deal, MC; Erleen Spitsnoble, Pharm D; COL Dennis R. Beaudoin, MS; COL Thomas A. Dillard, MC; MAJ Stacia L. Spridgen, MS

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Dec 01	1/23/2001

Study Objective: To demonstrate that an o.d. subcutaneous (s.c.) injection of ORG31540/SR90107A is at least as effective as adjusted-dose (aPTT, 1.5-2.5 x control) i.v. UFH in the initial treatment of patients with a confirmed diagnosis of acute symptomatic PE.

Technical Approach: This study treats acute pulmonary embolism with 2 different medications to determine if one medication is just as good as the other. After the patient has a confirmed diagnosis of acute pulmonary embolism (APE) and signs a consent form, that patient will be randomized to either standard therapy (UFH) or ORG31540/SR90107A. Patients will be treated with appropriate doses of either medication depending on the study arm to which they have been randomized, followed by a 90-day period of monitoring. The primary efficacy endpoint is the recurrence of a venous thromboembolism (VTE).

Progress: One patient enrolled in this study at MAMC during FY01. This study was reported as complete at MAMC, 25 Sep 01. Data analysis is not yet available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/143 **Status**: Terminated

Title: A Phase I Safety, Tolerability, Acceptability and Microbial Kinetic Study of Topical IB-367 Gel and Rinse in Orally Intubated Patients Receiving Mechanical Ventilation (Protocol No. 09-001)

Principal Investigator: LTC George N. Giacoppe Jr., MC

Department: Medicine/Pulmonary&Critical Care **Facility**: MAMC

Associate Investigator(s): LTC Leonard E. Deal, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Mar 01	

Study Objective: Part I: To compare the tolerability of IB-367 Gel and Rinse and to determine the antimicrobial response following a single 9 mg and a single 30 mg oral administration of IB-367 Gel or Rinse in orally intubated patients receiving mechanical ventilation. Part II: To determine the most favorable regimen of IB-367 (safety, tolerability, dosage, and frequency of administration) that reduces the bacterial burden of the aerodigestive tract in orally intubated patients receiving mechanical ventilation.

Technical Approach: This is a multicenter, randomized clinical trial with two parts. Part I will not be initiated at MAMC. Based on the safety data and antimicrobial effect seen in both the Gel and Rinse formulations in Part I and the information obtained from nurses and patients regarding the acceptability, one formulation will be chosen for administration during Part II. Part II will evaluate the safety, tolerability, and antimicrobial effect of up to 4 IB-367 Study Drug Administration Regimens . Regimens are designed so that individual administrations of IB-367 will not exceed 30 mg, the total daily dose will not exceed 60 mg, and the interval between doses will be no less than every 4 hours. Part II of the trial will enroll up to 4 cohorts of 8 patients each. In each cohort 6 patients will receive up to 5 days of IB-367 administration and 2 patients will receive equal volumes of placebo. Each cohort will receive a different Study Drug Administration Regimen. Enrollment in each cohort will begin after the safety and antimicrobial data has been evaluated from the previous cohort. Each cohort will be monitored for AEs, particularly vasovagal and gastrointestinal events. Oral, oropharyngeal, and tracheal secretions will be collected and evaluated for antimicrobial effect. Secretion collection will occur around the first Study Drug Administration and then every 24 hours thereafter. The schedule of secretion collection will vary depending on the regimen. Antimicrobial response will be evaluated by comparing the number of CFUs in all samples before and after the Study Drug administration. If any patient develops pneumonia or other significant infections (e.g.: urinary tract infections, wound infections, and bacteremias) attempts will be made to clearly identify the causative organism.

Progress: This study was terminated, 29 Nov 00, per the study sponsor, due to a disagreement with IRB stipulations for final approval at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/129 **Status**: Ongoing

Title: Osteoporosis in Patients with Obstructive Lung Disease Who Are on Non-continuous Oral Steroid or Inhaled Steroid Therapy

Principal Investigator: LTC Bernard J. Roth, MC

Department: Medicine/Pulmonary&Critical Care **Facility**: MAMC

Associate Investigator(s): CPT Todd C. Bennett, MC; Suzette Gagnon-Bailey, RN

Start Date:	Est. Completion Date:	Periodic Review:
8/28/2001	Jun 01	N/A

Study Objective: To determine if there is an association between intermittent systemic glucocorticoid therapy or inhaled steroid therapy and secondary osteoporosis in patients with obstructive lung disease.

Technical Approach: This pilot descriptive cross-sectional study will identify patients managed in the Pulmonary clinic for COPD or asthma who have received intermittent doses of oral corticosteroids within the last 6 months. Patients with COPD or asthma who have not been treated with intermittent oral steroids but are on inhaled steroids will be compared to this group. A third group of patients with COPD or asthma on chronic oral steroids will be identified and will serve as a comparison group of patients at known high risk for osteoporosis. Dual energy X-ray bone absoptiometry will be performed on all patients. The bone density of patients with intermittent oral steroid use will be compared to control patients and to patients with chronic oral steroid use.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/132 **Status**: Ongoing

Title: Respiratory Care Team to Decrease the Misuse of Metered Dose Inhalers in Hospitalized Patients

Principal Investigator: LTC Bernard J. Roth, MC

Department: Medicine/Pulmonary&Critical Care **Facility**: MAMC

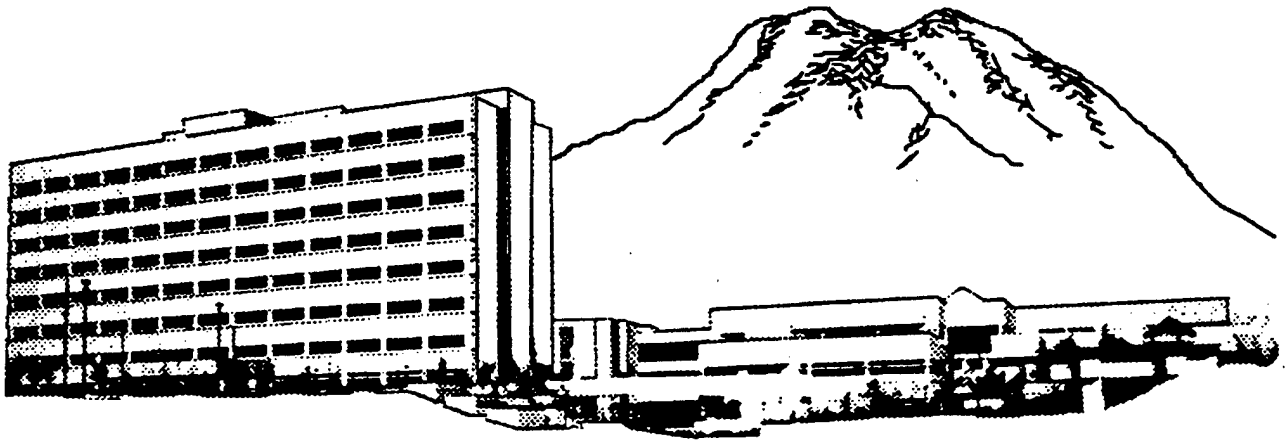
Associate Investigator(s): COL Thomas A. Dillard, MC; Michael G. Winter, RRT; Nora A. Regan; CPT John J. Mullon, MC; CPT Michael W. Quinn, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
09/19/1997	Mar 96	8/22/2000

Study Objective: To determine if a respiratory team teaching proper metered dose inhaler (MDI) use to inpatients will improve the observed rate of proper MDI use at Madigan Army Medical Center (MAMC).

Technical Approach: In this study, a pulmonologist will interview 60 inpatients prescribed an MDI and observe their MDI technique to establish a baseline rate of misuse. Then a respiratory care team will receive a daily list from Pharmacy on all patients newly prescribed an MDI. They will provide direct teaching to the patients on correct use of their MDI. After the teaching program has been in place for 2- 6 weeks the same pulrnonologist will interview 60 more patients and observe their MDI technique to establish the rate of misuse after the intervention. The patient will be asked if they have received education and this will be correlated to the chart documentation of education by the Respiratory Therapist. The major endpoint will be the change in the rate of MDI misuse observed.

Progress: 90 patients have been enrolled in this study at MAMC. This study is halfway through the second phase. Patient enrollment continues.



Detail Summary Sheets

Rheumatology Service, Department of Medicine

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/078 **Status**: Completed

Title: A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Prograf (Tacrolimus) in the Treatment of Rheumatoid Arthritis in Patients Who Have Failed One or More Disease-Modifying Antirheumatic Drugs

Principal Investigator: MAJ Leslie W. Jackson, MC

Department: Medicine/Rheumatology **Facility**: MAMC

Associate Investigator(s): LTC Thomas L. Irvin, MC; MAJ David R. Finger, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/22/1999	Jun 00	8/22/2000

Study Objective: This protocol is designed to evaluate the efficacy and safety of the immunosupressant tacrolimus in RA patients who are either resistant or intolerant of one or more DMARDs.

Technical Approach: This will be a 6 month multi-center, randomized, double-blind, placebo controlled study of adult patients, of either gender, with a diagnosis of rheumatoid arthritis for at least 6 months. Eligible patients will have demonstrated either resistance to or intolerance of one or more DMARDS. A total of 450 patients from approximately 50 centers will be randomized, with a maximum of 36 patients per center. Patients will be assigned to either the DMARD resistant or the DMARD intolerant stratum prior to randomization. Randomization to the three treatment arms will be at 1:1:1, tacrolimus (2 mg/day), tacrolimus (3 mg/day), or placebo respectively within each stratum at each center. The primary efficacy endpoint will be the composite American College of Rheumatology (ACR) 20 success at six months for the combined 2 mg and 3 mg tacrolimus groups as compared to placebo. If the combined treatment group response is statistically significantly different from the placebo group response, then the pairwise comparisons between the placebo and the individual tacrolimus groups will be performed. Secondary efficacy endpoints are the ACR 20, 50, and 70 response rates at the end of the treatment, and the evaluation of change from baseline for the individual components of the ACR composite at end of treatment.

Progress: The study was reported as completed, July 01. A total of five subjects were screened. Three subjects did not complete the study due to screen failure or loss to follow-up. Two subjects were randomized, both completed study treatment and continued to receive treatment on the open-label trial. Of these two patients, one patient responded well to the medication with regards to joint count and global assessment. The other patient continued to have fairly active disease during the study. At this time a full report of data from other centers and statistical analysis is not available from Fujisawa Healthcare (sponsor of the study) in order for conclusions to be adequately drawn.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/079 **Status**: Completed

Title: An Open-Label, Long-Term Study to Evaluate the Safety of Prograf (tacrolimus) for the Treatment of Rheumatoid Arthritis

Principal Investigator: MAJ Leslie W. Jackson, MC

Department: Medicine/Rheumatology **Facility**: MAMC

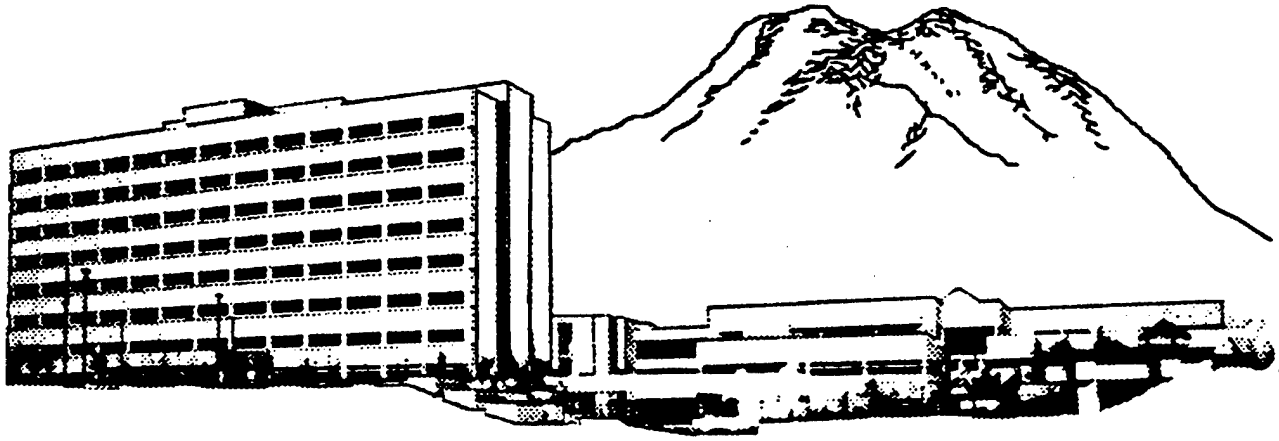
Associate Investigator(s): MAJ David R. Finger, MC; LTC Thomas L. Irvin, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/22/1999	Jun 02	7/24/2001

Study Objective: The primary objective of this study is to evaluate the long-term safety of Prograf in rheumatoid arthritis patients. A secondary objective of the study is to evaluate long-term efficacy of Prograf in RA patients.

Technical Approach: This will be a 12 month open-label, non- comparative, multi-center study. Eligible patients will have an RA diagnosis of at least six months duration and, in the investigator's opinion, require the use of a DMARD. A total of approximately 300 patients who have participated in previous Fujisawa protocols and approximately 500 patients who are entering this study directly will be enrolled at approximately 80 centers. All patients will receive a total daily dose of 3 mg of tacrolimus. Adverse events, including clinically significant laboratory abnormalities, will be recorded on the Case Report Forms. Treatment emergent adverse events during the 12 months of the open-label treatment will be determined and will be the primary assessment of risk. ACR 20, 50, and 70 will be assessed at 3, 6, 9, and 12 months as secondary endpoints of the study.

Progress: The study was a multi-center randomized, double blind placebo controlled trial that moved into an open label study after 6 months. The study was completed July 01. Patients who completed the six month of double blind therapy were eligible for treatment with open label tacrolimus. During FY01, one subject enrolled in the randomized study and three subjects enrolled in the open label protocol. Of these one patient was removed from the open study at month after 6 months of the randomized study due to severe hypothyroidism with impaired renal function. The other two patients followed both arms of the study to completion. Of these two patients, one patient responded well to the medication with regards to joint count and global assessment. The other patient continued to have fairly active disease during the study. At this time a full report of data from other centers and statistical analysis is not available from Fujisawa Healthcare (sponsor of the study) in order for conclusions to be adequately drawn.



Detail Summary Sheets

Department of Ministry and Pastoral Care

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/022	**Status**: Completed

Title: A Study on the Role of Spirituality in the Lives of Incarcerated Persons

Principal Investigator: CPT Allen W. Staley, CH

Department: Ministry & Pastoral Care	**Facility**: MAMC

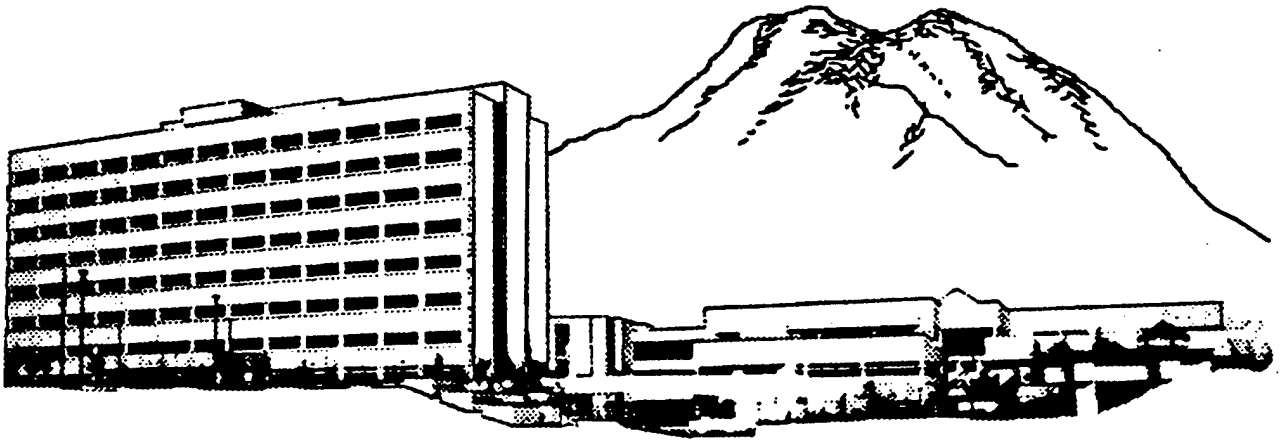
Associate Investigator(s): SGT Victoria Acree, USA; CPT Randal H. Robison, CH

Start Date:	**Est. Completion Date:**	**Periodic Review:**
11/28/2000	Apr 01	N/A

Study Objective: To enable chaplains and the RCF leadership to develop programs that will help inmates grow spiritually, cope with incarceration, and adjust to life after incarceration.

Technical Approach: Approximately 130 to 140 inmates from the Regional Correctional Facility (RCF), Fort Lewis, WA, this number based on the approximate number of inmates that will be incarcerated at the RCF by spring 2001 will be asked to complete 30 survey questions. Instructions to each group of inmates will be given by the PI. Each inmate will be ensured of his confidentiality, his right not to participate in the survey, how this information will be utilized and that it will be presented to the command and persons attending the Specialization Project. The inmate will read the questions and answer them by filling in the answer that most correctly fits him. The information collected will provide insight into the inmates' thoughts, feelings, and religious convictions or the lack of them. Analysis will entail observing current issues, prevailing beliefs, feelings held, and current social trends that are reported by other chaplains.

Progress: This study was completed at MAMC in April 2001. Evidence uncovered in this study validates that spirituality can help incarcerated persons cope with issues of incarceration. Measurement of attitudes towards crime can only be accurately determined from the perspective of time, which is a limitation of this study. Fairly clear correlations were discovered between spirituality before and after incarceration, which would suggest a faith that precedes incarceration is more likely to continue or be returned to.



Detail Summary Sheets

Department of Nursing

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/116	**Status**: Completed

Title: Publishing Practices and Perceptions by Registered Nurses at a Military Medical Center

Principal Investigator: LTC Wynona M. Bice-Stephens, AN

Department: Nursing	**Facility**: MAMC

Associate Investigator(s): LTC Elizabeth A. Mittelstaedt, AN

Start Date:	**Est. Completion Date:**	**Periodic Review:**
8/22/2000	Mar 01	7/24/2001

Study Objective: (1) To describe publishing practices by Registered Nurses as a military medical center, (2) To identify perceptions of aspects of publishing by Registered Nurses at a military medical center, and (3) To identify whether nurses are encouraged to publish by internal or external motivators.

Technical Approach: This study will survey registered Nurses to determine their perceived barriers to publication. Based on results of the questionnaires, a publication workshop will be designed for Department of Nursing personnel.

Progress: 415 surveys were collected. Data collection is complete and the study is currently in the data analysis phase.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/126 **Status**: Completed

Title: The Effect of Marshmallow Consumption on the Quantity of Effluent During an Appliance Change in Individuals with an Ileostomy

Principal Investigator: LTC Wynona M. Bice-Stephens, AN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): LCDR Kerri S. Pegg, NC, USN

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Mar 01	7/24/2001

Study Objective: To compare the effect of consumption of marshmallows versus non-consumption of marshmallows to the quantity of effluent expressed in individuals with an ileostomy during a simulated appliance change.

Technical Approach: Each of the 10 subjects will collect the effluent four times during simulated appliance changes. For two of the simulations, they will collect effluent as "control", meaning that they will not eat marshmallows prior to changing the appliance. For two simulations, subjects will eat the marshmallows prior to changing the appliance, and collect the effluent during the appliance change. Results from the "control" versus "intervention" will be evaluated to determine if there was more or less efluent when marshmallows were consumed prior to appliance change simulation.

Progress: This protocol enrolled 7 subjects during FY 01. This study demonstrated that some individuals that have an ileostomy may benefit from consuming marshmallows prior to an appliance change. The intervention has the potential, in some individuals, to decrease the volume of effluent during appliance change. Additionally, this intervention has the benefit of being easy to administer, non-objectionable to the individual, and of negligible cost. In conclusion, this practice has the potential to advance an individual's efficiency in appliance changes, increase the confidence in one's proficiency in self-care, which is directly related to one's quality of life. This study is completed. An abstract is on file in DCI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/136 **Status**: Completed

Title: Prevention of Hypertension in the United States Army: A Descriptive Correlational Study on Dietary Habits of Junior Enlisted Soldiers Living at Fort Lewis, WA

Principal Investigator: LTC Wynona M. Bice-Stephens, AN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): CPT Jean Jones, AN; Susanna Cunningham; CPT Michelle D'Amico, SP

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Jan 01	

Study Objective: (1) To document the macronutrient and micronutrient intake of soldiers living at Fort Lewis, WA, specifically sodium, Vitamin C, omega 3 fatty acids, and the number of fruits and vegetables per day, (2) To compare intake of soldiers with a diet that decreases the risk of developing hypertension and (3) To document the general dietary habits of soldiers living at Fort Lewis, Washington.

Technical Approach: Subjects will be recruited to participate in the study as their unit participates in the Corporate Wellness Program. Subjects will complete three questionnaires including demographic data, dietary habits, and food frequency.

Progress: This study surveyed 175 subjects during FY 01. Conclusions are that the sample's diet was not consistent with a diet that lowers the incidence of HTN. Per day, the majority consumed: greater than 30% of calories from fat and greater than 2400 mg of sodium; consumed less than 7 servings of fruit and vegetables, less than1200mg of calcium, and less than 280mg of magnesium. The sample did not meet the recommendations for potassium intake. The overall nutritional health of the sample was poor. The protocol is Completed at MAMC. An abstract is available in DCI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/137 **Status**: Completed

Title: Development and Evaluation of the Military Nursing Moral Distress Scale

Principal Investigator: LTC Wynona M. Bice-Stephens, AN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Ann Hurley, AN; Sara Fry; COL Barbara Jo Foley, AN

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	May 01	9/25/2001

Study Objective: The ultimate objective of this program of research is to minimize moral distress in military nurses during crisis military deployments. Crisis deployment refers to that time when the officer has been ordered to support an operation off station (and perhaps out of country) to provide nursing care during a military operation, humanitarian and/or peacekeeping mission. This project will develop and evaluate an instrument to measure the moral distress (MMDS) of nurse officers in the US Army. Moral Distress in defined as the negative balance between a nurse's moral judgment and the opportunity to implement that judgment in nursing actions.

Technical Approach: Subjects in this study will be asked to complete a series of questionnaires indicating their levels of moral distress.

Progress: Approximately 170 anonymous surveys were distributed during FY01. Analysis of returned surveys is underway. An abstract has been written, but is not yet available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/074 **Status**: Ongoing

Title: E-Health Demand Management for Frequent Medical System Utilizers (VPCC-FMU Substudy)

Principal Investigator: Pamela S. Birgenheier, RN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Nancy A. Woolnough, AN; LTC Gregory A. Gahm, MS; Deland Peterson, Ph.D.; MAJ Nhan V. Do, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	May 01	N/A

Study Objective: (1) Utilize the Virtual Primary Care Clinic (VPCC) infrastructure to support demand management of frequent medical system utilizers (FMU) who are presently enrolled in TRICARE Senior Prime (TSP) (2) Evaluate the effects of regular electronic communication (messages reflecting concern for patient health and health promotion information) on medical system utilization frequency for TSP patients identified as frequent medical system users and (3) Evaluate the workload requirements and appropriateness of having nursing staff implement this process.

Technical Approach: This study utilizes nursing staff to implement a demand management program for TRICARE Senior Prime(TSP) patients enrolled in the APCC at MAMC. Participants will include 150 (50 treatment condition, 50 standard VPCC, 50 control) TSP patients previously identified by MAMC Utilization Management and the Northwest Lead Agent as frequent system users (10 or more outpatient visits [Specialty care, Primary care, AIC, or ER]). Control I - TSP APCC patients receiving standard care with no VPCC; Control II - TSP APCC patients receiving VPCC access without specific focused health concern or health promotion interaction; Control III - previous personal history of treatment group TSP APCC patient utilization prior to initiation of the VPCC. Nursing staff can appropriately implement this procedure. The workload requirements for nursing staff to implement this process will be more than offset by the decreased medical system utilization by patients.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/012 **Status**: Ongoing

Title: In-Home Urinary Incontinence Therapy for Female Soldiers

Principal Investigator: Kathleen A. Clary, RN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Lori A. Loan, PhD; COL Gary D. Davis, MC; LTC (Ret) Richard A. Sherman, MS; LTC Ann M. V. Bianchi, AN

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Oct 02	N/A

Study Objective: The study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for exercise-induced urinary incontinence in the home setting with those receiving similar biofeedback treatments in the Troop Medical Clinic or medical center environment. This aim will be accomplished by adding a third group (in-home biofeedback) to the two groups already enrolled (TMC & Medical Center) in the MAMC approved study, Improving Soldier Access to Urinary Incontinence Therapy (Loan, 98-053).

Technical Approach: This proposed study represents the investigation of an innovative evidence-based health care delivery intervention that may be successful in alleviating some of the problems related to access to care for female soldiers with exercise-induced urinary incontinence. This will be accomplished by providing portable, in-home biofeedback equipment and a 12-week nurse run biofeedback program to 62 female soldiers with exercise induced urinary incontinence. The study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for urinary incontinence in the home setting with results from those who previously received biofeedback treatments in the troop medical clinic or medical center environment. Data from 62 prospective and approximately 124 retrospective female soldiers treated with biofeedback for urinary incontinence will be used to address the following hypotheses:

For female soldiers with exercise-induced urinary incontinence: (1) treatment obtained in the home environment will significantly increase realized access to care compared to treatment obtained at the troop medical clinic or the medical center; and (2) patient satisfaction will be significantly higher when treatment is received in the home environment and lower when treatment is received at the troop medical clinic or the medical center. Descriptive statistics will be used to summarize central tendency and data dispersion. Pretreatment differences in demographic and descriptive information will be compared using ANOVA or Kruskal-Wallis ANOVA for Ranks as appropriate.

Progress: Preliminary Results: As of 24 Oct 01, screening tools were sent to 671 female soldiers on Ft. Lewis with 290 returned. Thirty-nine women indicated that they wanted treatment for urinary incontinence, 8 were eligible and consented, and 6 female soldiers started the intervention. Five female soldiers have completed the intervention. A second mailing of the screening tool is underway.

Study findings to-date from the screening, of the 290 female soldiers responding to the screening tool: 154 (53%) had leaked urine; 100 (65%) had leaked urine during physical fitness training (PT); 135 (90%) take precautions before PT to prevent leakage or minimize embarrassment; 80 (52%) restrict fluids during field exercises to prevent leaking urine; 18 (12%) had urine leakage problems significant enough to impact regular duties; 62 (40%) of those wanting treatment for leaking urine thought they would be hassled or embarrassed by their supervisor while getting permission to get an appointment for treatment; 43 (28%) indicated urine leakage was enough of a problem for them to want treatment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/047 **Status**: Ongoing

Title: Prone Position and the Pattern of Oxygenation in Acute Lung Injury Patients

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Janet R. Harris, AN; Kathleen Vollman; LTC George N. Giacoppe Jr., MC; Mary S. McCarthy, RN, MN, CNSN

Start Date:	Est. Completion Date:	Periodic Review:
3/28/2000	Dec 03	2/27/2001

Study Objective: To examine the pattern of oxygenation in 60 patients with acute lung injury (ALI)/adult respiratory distress syndrome (ARDS) who undergo a 4-hour prone positioning trial and to develop evidence-based guidelines for a prone positioning protocol regarding safety, timing, and frequency of the intervention for patients with ALI or ARDS.

Technical Approach: Informed consent will be obtained from the patient or surrogate prior to participation in the study. Patient ventilator settings, positive end-expiratory pressure (PEEP) and inspired oxygen fraction (FiO2), will be established by the patient's physician according to the clinical needs of the patient. During the data collection periods for this study, the ventilator settings will remain unchanged. An Acute Lung Injury Score (Murray et al., 1988) will be assessed for each subject to further delineate the severity of acute pulmonary damage. Prior to data collection all equipment will be calibrated according to the manufacturer's recommendations. The arterial line will be calibrated and leveled to the subject's phlebostatic axis (Boggs & Wooldridge-King, 1993). Baseline supine measurements will occur after the subject has been in the supine position for at least one hour and just prior to turning the subject to the prone position. Following site visits to both facilities by the Consultant who is the developer and an expert in the device to be used for the intervention, trained teams will be identified. The subject will be turned to the prone position. PaO2/FiO2 will be measured every hour for the 4 hours the subject is in the prone position. The subject will remain in the prone position for 4 hours unless the subject does not tolerate the prone position or has an emergency (loss of airway or central access, cardiopulmonary resuscitation, hemodynamic instability). Following initial measurements in the baseline supine position, measurements will be conducted at 1 hour intervals while the subject is in the prone position and 1 & 2 hours after returning to the supine position.

Subject demographics that will be collected include: age, gender, diagnoses, etiology of acute lung injury, parenteral and enteral nutrition, date of admission to ICU, duration of time since first diagnosed with ALI, days of mechanical ventilation before initial prone trial, Acute Lung Injury Score, and severity of illness as measured by the APACHE II scoring tool.

Progress: This study required several revisions to meet stipualations of two additional sites for subject recruitment (BAMC, WHMC). Revisions have been approved. Anticipate recruitment will begin NLT 22 Oct 01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/095 **Status**: Ongoing

Title: Expectations of Military Health Care: An Inductive Analysis

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Bonnie M. Jennings, AN; Debra DePaul, RN

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 02	5/22/2001

Study Objective: To acquire empirical evidence for use in reforming military health care, for the purpose of improving patient satisfaction and quality.

Technical Approach: Focus groups consisting of active duty personnel and family members of active duty personnel, will be utilized in this study to present customer satisfaction/expectation questionnaires to recipients of military medical care and use the results to analyze both real and perceived strengths and weakness of the Military Health System. Focus groups specific to health care personnel will also be conducted to explore differences between consumer expectations and health care personnel perceptions of the care delivery process.

Progress: Eight focus groups have been conducted, four at Ft. Lewis and four at Ft. Bragg. Transcripts from these focus groups are in the process of being coded. Expectation themes from the content are being developed. Models regarding the relationship between first line treatments for soldiers at the unit level and TRICARE were drafted.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/011 **Status**: Ongoing

Title: The Effects of Postoperative Supplemental Oxygen on Tissue and Wound Healing

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Kathleen A. Clary, RN; LTC Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Jerome B. Myers, MC; MAJ Jeannie M. Muir-Padilla, MC; JoAnne D. Whitney, Ph.D., RN

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Oct 01	N/A

Study Objective: The specific aims of this study are to: (1) Compare the effects of 36 hours of supplemental oxygen therapy provided postoperatively to patients having cystectomy and nephrectomy surgery, to management without supplemental oxygen on: (a) wound healing in test wound tissue samples obtained on the 7th postoperative day including: (1.) hydroxyproline accumulation determined by high performance liquid chromatography; and (2.) mRNA for Pro a 1(I) collagen as measured by in situ hybridization (3.) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation and (b) subcutaneous tissue oxygen tension (PscO2) in test wound sites on postoperative days 0, 1 and 2 using a subcutaneous tonometer/electrode system. (2) Compare the incidence of wound complications between the two groups evaluated in the surgical wound on the 2nd and on the 7th postoperative day using a wound registry scoring tool. (3) Compare clinical healing outcomes (satisfactory/not satisfactory), and describe complications that occurred in the two groups during the 30 days post surgery.

Technical Approach: The study utilizes a randomized, two group, experimental repeated measures design. Eight subjects with a need for cystectomy and nephrectomy surgery, ages 18 and above, will be recruited for the study. Subjects will be randomly assigned to receive only room air (control group) or supplemental oxygen at 28% via nasal cannula (n/c) for 36 hours postoperatively (treatment group). PscO2 will be measured at Hour 1, 18, and 36 using a tonometer/sensor system. Wound healing is evaluated by analysis of tissue cellularity and hydroxyproline from a tissue sample obtained from a small, polytetrafluoroethylene tube place subcutaneously and removed on the 7th postoperative day. Wound complications/infections will be evaluated using the Wound Registry. Differences between groups will be tested using Analysis of Variance for repeated measures, Wilcoxon Rank Sum test, and Chi-square.

Progress: Preliminary Results: This pilot study utilizes a randomized, two groups, and experimental repeated measures design. Eight subjects currently scheduled for surgery, ages 18 and above, will be recruited for the study. Subjects will be randomly assigned to receive only room air (control group) or supplemental oxygen at 28% via nasal cannula for 36 hours postoperatively (treatment group). PscO2 will be measured at Hour 1, 18, and 36 using a tonometer/sensor system placed in the subjects upper arm. Wound healing is evaluated by analysis of tissue cellularity and hydroxyproline from a tissue sample obtained from a small, polytetrafluoroethylene tube place subcutaneously in the upper arm and removed on the 7th postoperative day. Wound complications/infections will be evaluated using the Wound Registry. Differences between groups will be tested using Analysis of Variance for repeated measures, Wilcoxon Rank Sum test, and Chi-square. As of 24 Oct 01, four subjects have been consented. Two subjects were started on the protocol and one was completed. No adverse reactions have been noted.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/027 **Status**: Completed

Title: The Relationship Between Patient and Unit Level Acuity and Intrapartum Nursing Interventions

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Rebecca S. Miltner, RNC, MS; LTC Laura R. Brosch, AN

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Nov 01	N/A

Study Objective: The purpose of this study is to examine the specific nursing interventions provided to women in the intrapartum period and begin to explore whether higher patient medical acuity and/or unit acuity level have an effect on the actual processes of nursing care.

Technical Approach: This prospective, descriptive study will use observational techniques to collect data about specific nursing interventions provided in a 90 two-hour episodes of care involving registered nurses in Labor and Delivery assigned to term women in labor. This study will use the Quality Health Outcomes Model (Mitchell, Ferketich, & Jennings, 1998) as the framework to examine the process of intrapartum nursing practice. here are three independent (predictor) variables in this study; two related to patient medical acuity, minutes of non-reassuring fetal heart rate and number of six specified medical treatments/interventions, and one related to concurrent unit level acuity, adjusted nurse patient ratio. A total of twenty-three specific nursing interventions within three broad categories of interventions which were identified by intrapartum nurses as having the most effect on childbirth outcomes comprise the outcome variables. The primary dependent (outcome) variable is the broad category of labor support time spent providing labor support interventions (13 specific nursing interventions). Support interventions include three subcategories, emotional support (4 interventions), physical comfort (4 interventions), and informational support (5 interventions). Secondary dependent variables include the broad categories of surveillance interventions (6 interventions) and indirect care management interventions (4 interventions). The nurse will be observed and his/her activities will be recorded at one-minute intervals during the episode of care.

Data analysis will consist of descriptive statistics, including frequencies, measures of central tendency, and measures of dispersion, calculated for all variables. Correlational statistics will be run on all study variables. Standard multiple regression analysis will be used to examine how the combination of specific unit acuity levels and individual patient high risk care needs explain variance in the frequency of and time spent providing each category of nursing activities.

Progress: Since 1 Oct 00, data collection for this study was implemented and completed. All 24 RNs employed in the setting agreed to participate, and no patient approached refused to participate. Data analysis and interpretation has been conducted. Results of the study indicate that the patient's acuity, as operationalized by the number of medical interventions required and fetal well-being, and unit level acuity, as operationalized by the actual RN staffing minus the recommended RN staffing based on patient acuity, does predict 17.3% of the variance in the amount of time that the RN spends with a patient, and 19.1% of the variance in the amount of time that the RN spends in non-patient care activities. However, these patient and unit acuity variables do not predict the types of interventions that the RN provides to the labor patient, suggesting that variation in intrapartum nursing practice is related to other, as yet unidentified, factors.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/070 **Status**: Ongoing

Title: The Use of Body Fat Analysis and Severity of Illness to Determine Energy Expenditure in the Obese Critically Ill Patient

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Mary S. McCarthy, RN, MN, CNSN; Janet C. Fabling, CNSD

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Dec 02	N/A

Study Objective: The specific objectives of this study are: (1) to formulate a predictive equation for energy expenditure (EE) to be used in the nutritional assessment of the obese, critically ill patient, (2) to utilize a state-of-the-art, portable, body composition analyzer to measure body fat for inclusion into the equation, (3) to document APACHE II scores for inclusion into the equation, and (4) to perform indirect calorimetry on all study patients to obtain the measured resting energy expenditure (MREE).

Technical Approach: This study is intended to evaluate the benefit of percent body fat and severity of disease to a predictive equation of energy expenditure in the obese, critically ill patient. The study involves the collection of patient data during routine nutritional assessment. A predictive correlational design will be used to derive a regression equation that is + 10% of measured resting energy expenditure obtained via indirect calorimetry. A convenience sample of the first 70 adult ICU patients who meet the National Heart, Lung, and Blood Institute criteria for overweight (BMI 25.0 - 29.9 kg/m2) and obesity (>30.0 kg/m2) will be used for data collection. It is anticipated that enrollment will take about 18 months. The associate investigator, a registered dietitian with duties in the ICU, will identify subjects during their routine admission nutritional assessment. The PI makes rounds regularly with the ICU team and she too will identify candidates for the study. The PI will perform body fat analysis and indirect calorimetry on two separate occasions. Chart review will provide the data for APACHE II score and the other equation predictors of age, gender, actual weight, and ventilatory status. A regression equation will be derived using multivariate correlation analyses. The equation will correlate within + 10% of the measured resting energy expenditure to be considered acceptable in this population.

Progress: This project is temporarily on hold while the metabolic cart reliability and validity is established. Too much variance has been detected when performing indirect calorimetry. Recruitment is expected to begin NLT 29 Oct 01. All other equipment has been purchased and the research team is ready to initiate this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/044 **Status**: Ongoing

Title: Physical Activity and Exercise in AD Female Soldiers

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Debra DePaul, RN; LTC Laura R. Brosch, AN; COL Melissa A. Forsythe, AN

Start Date:	Est. Completion Date:	Periodic Review:
02/20/1998	Oct 98	12/18/2001

Study Objective: To examine the physical activity levels and habitual exercise patterns of active duty female soldiers and to identify factors that influence those habits in hopes of producing information to be used to improve the health of female soldiers.

Technical Approach: Each subject will complete an initial survey and APFT scores will be obtained for each service member consenting to be in the study. Focus groups will then explore the issues among subjects identified as belonging to subgroups at risk for low exercise participation.

Progress: 1103 subjects in FY99, with data analysis continuing on surveys collected. Four focus groups were conducted, content analysis of focus group themes continues. As three of the study investigators recently PCS'd to the east coast, final analysis of study findings has been delayed. Descriptive statistics for the survey portion of the study and psychometric properties for the instruments employed have been calculated. A structural equation model to identify relationships among the study variables has been calculated. The qualitative analyses of focus group data is in its final stages and the study team is in the process of writing the study final report.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 98/053	**Status**: Ongoing

Title: Improving Soldier Access to Urinary Incontinence Therapy

Principal Investigator: Lori A. Loan, PhD

Department: Nursing	**Facility**: MAMC

Associate Investigator(s): LTC Ann M. V. Bianchi, AN; LTC (Ret) Richard A. Sherman, MS

Start Date:	**Est. Completion Date:**	**Periodic Review:**
01/16/1998	Sep 98	11/27/2001

Study Objective: This study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for exercise-induced urinary incontinence in the troop medical clinic environment with those receiving similar treatments at a medical center.

Technical Approach: All subjects interested in participating in the study will be screened for evaluation of the lower urinary tract. If inclusion criteria is met, the subject will be randomized to treatment at either the TMC or MAMC and be scheduled for treatment visits every 2 weeks for 12 weeks. During the first visit, demographic and descriptive information will be gathered and subjects will learn how to do Kegel exercises using biofeedback. Subjects will be asked to keep daily logs and to practice the Kegel exercises for twenty minutes two times a day. Subsequent visits to the treatment center will be to encourage continuation and the keeping of daily logs. At the final visit more demographic and descriptive information will be asked and a Patient Satisfaction Questionnaire will be filled out by each subject. The portable biofeedback equipment will be used to evaluate Kegel performance during this final visit.

Progress: Preliminary Results: As of 24 Oct 01, screening tools were sent to 3,703 female soldiers on Ft. Lewis with 1,238 returned. One hundred and seventy three women indicated that they wanted treatment for urinary incontinence, 83 were eligible and consented, and 81 female soldiers started the intervention. Thirty-two female soldiers have completed the intervention. A fifth mailing of the screening tool is underway. Study findings to-date from the screening, of the 1,195 female soldiers responding to the screening tool: 639 (53%) had leaked urine; 417 (65%) had leaked urine during physical fitness training (PT); 575 (90%) take precautions before PT to prevent leakage or minimize embarrassment; 332 (52%) restrict fluids during field exercises to prevent leaking urine; 79 (12%) had urine leakage problems significant enough to impact regular duties; 252 (40%) of those wanting treatment for leaking urine thought they would be hassled or embarrassed by their supervisor while getting permission to get an appointment for treatment; 177 (28%) indicated urine leakage was enough of a problem for them to want treatment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/107 **Status**: Completed

Title: Nurses Influence on Patient Outcomes in US Army Hospitals

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Barbara Jo Foley, AN; Dr. Carolyn C. Kee; Dr. Ptlene Minick; Dr. Susan Harvey; COL Bonnie M. Jennings, AN; LTC Laura R. Brosch, AN

Start Date:	Est. Completion Date:	Periodic Review:
09/15/1998	Sep 99	8/22/2000

Study Objective: To describe patient outcomes in active duty personnel, military retirees, and military dependents, associated nursing organizational structures and processes; and hospital characteristics.

Technical Approach: Interviews, questionnaires and short answer surveys will be used to gather information on (1) patient outcomes while in the hospital to include the occurrence of adverse events such as injury-sustaining falls, length of stay, and severity-adjusted mortality; (2) following discharge from the hospital, outcomes include patient satisfaction with nursing care, satisfaction with how symptoms were managed, and functional health status. (3) Nursing organizational structures include factors such as nursing practice model, nursing skill mix, and the education and experience level of registered nurses (RN);and (4) nursing organizational processes include RN job satisfaction, the degree of autonomy in nursing practice or the discretionary judgement accorded nurses in the work environment, the level of RN and physician collaboration, the degree of clinical expertise, and the extent to which an ethical work environment is present.

Progress: All work on this study has been completed. All work on this study has been completed. More than 400 medical records and 200 patient surveys were completed, slightly exceeding target sample size goals. Both chief nursing administrators and all eight unit heads responded to the interviews and questionnaires. Staff nurse response rate was 56%.

Patient outcomes were good with few adverse events. Patients were highly satisfied with nursing care and with symptom (pain) management. Functional health status shortly after discharge was lower than that reported for myocardial infarction patients hospitalized sometime within the past year. Scores on the mental health subscale were fairly high, however, and mental status has been associated with positive overall health outcomes.

Nursing organizational structures promoted good communication, and units used an array of nursing practice models. Educational and experiential differences were found between military and civilian nurses.

Nursing organizational processes demonstrated that nurses were satisfied with their jobs overall. Scores on nurse-physician relationships were particularly high. Scores on the MER and the EEQ were also good. Differences between mixed bed and specialty units were found for autonomy, control over practice, and the MER but not always in the expected direction.

Overall, the hospitals and the units were quite similar on a number of variables. The implication here is that quality of care is fairly evenly distributed across hospitals and units. The differences found between the military and civilian nurses may be complementary for each group. The finding of excellent nurse-physician relationships is a finding that should be beneficial in terms of recruitment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/028 **Status**: Ongoing

Title: Factors Associated with Preventable Hospitalization in Older Military Retirees

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): COL Bonnie M. Jennings, AN; Suzanne K. Wilson, MSN, RN; LTC Laura R. Brosch, AN; Rebecca S. Miltner, RNC, MS

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Jun 01	12/18/2001

Study Objective: To prospectively assess the relationship between patient-specific characteristics and the likelihood of preventable hospitalization for Tricare Senior Prime enrollees.

Technical Approach: All 3,620 Madigan Army Medical Center Tricare Senior Prime enrollees will be surveyed to obtain baseline predisposing (age, gender, race, education, living arrangements), enabling (income, tangible social support, perceptions of regular source of care, transportation, transportation time) and need factor (perceived physical health status, perceived mental health status, perceived functional limitations, chronic illnesses, past hospital use) data. These data will subsequently be liked to hospitalization data prospectively collected for the 12 month period following the survey. Each study participants hospital use will be classified into one of three categories: (1) no hospital admissions, (2) at least one potentially preventable hospitalization, or (3) hospitalized, but not for a potentially preventable condition. Descriptive statistics will be used to profile the sample in terms of the factors under study and summarize the frequency of occurrence of each type of hospital use. Multivariate polytomous logistic regression will be used to identify predisposing, enabling and need factors associated with the likelihood of potentially preventable hospitalization.

Progress: Data collection for the 3620 participants who have agreed to be in this study was completed in May 2001. Data analysis remains ongoing. No abstract is available at this time.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/110 **Status**: Completed

Title: The Effects of Using Four Different Missing Data Imputation Methods on the Psychometric Property of the SF36

Principal Investigator: Lori A. Loan, PhD

Department: Nursing **Facility**: MAMC

Associate Investigator(s): Qiuping Zhou, MS, RN; LTC Laura R. Brosch, AN; 1LT Janet L. Hyers, AN

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Jun 01	8/28/2001

Study Objective: The purpose of this study is to determine the effects of using four different missing data imputation methods on the psychometric property of SF36, for different sample sizes, different length of the questionnaire, and different percentage of missing data.

Technical Approach: This is a secondary data analysis. An existing data set with SF36 items included will be used to perform the simulations. The outcomes include the reliability and factor structure of the SF36 measure. Variables manipulated include (1) imputation methods (person mean, item mean, regression, and EM algorism replacement), (2) length of the instrument (36 versus 12 items), (3) percentage of missing data (0%, 5%, 10%, 20%, and 30%) and (4) sample sizes (large, medium, and small).

Data collected from 2800 patients in a military organization. SPSS 8.0 will be employed to analyze the data. Reliability and factor analysis will be performed on data sets with varying conditions. The results will be compared and summarized. Replacing methods with the minimum effect on the psychometric performance of the SF36 will be identified.

Progress: This study was completed during FY01. There were differences in performance of the imputation methods regardless of the data conditions. Item means substitution (IMS) was consistently the worst in terms of accuracy and bias for all but two parameters. Person mean substitution (PMS) was the second worst in parameter estimates. In contrast, expectation maximization algorithm (EM) andstochastic regression imputation (SRI) produced more accurate estimates for most parameters considered. EM ranked the best for the estimation of item mean and intercorrelations among items and scales while SRI ranked the best for item SD, alpha, and goodness-of-fit statistics. The two methods were equivalent for other parameters. Further, their performance was less influenced by the missing data conditions. In terms of reducing bias, SRI was better for most of the parameter than EM.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 98/063	**Status**: Completed

Title: Improving ALI/ARDS Patient Outcomes with Metabolic Support

Principal Investigator: Mary S. McCarthy, RN, MN, CNSN

Department: Nursing	**Facility**: MAMC

Associate Investigator(s): CPT Maginia S. Morales, AN; Janet C. Chilton

Start Date:	**Est. Completion Date:**	**Periodic Review:**
03/20/1998	Sep 00	2/22/2000

Study Objective: 1) What are the differences in nutritional and physiologic responses between ARDS patients who receive a special formula (Oxepa) versus ARDS patients who receive a standard formula (Osmolite HN)? (2) What are the differences in patient outcomes between ARDS patients who receive a special formula (Oxepa) versus ARDS patients who receive a standard formula (Osmolite HN)?

Technical Approach: Subjects will be randomized to receive either immune-enhanced formula (Oxepa) or a standard stress formula (Osmolite HN) for a minimum of 4 days. Nutritional outcomes will be based on prealbumin values, nitrogen balance, and % caloric goal achieved. Physiologic outcomes will be measured by the oxygenation ratio respiratory quotient, and plasma interleukin-6 levels.

Progress: A total of 19 subjects were recruited prior to completion of this study in FY01. Over a 7-day period of enteral feeding, subjects randomized to receive either an immune-modulated formula or a standard "house" formula demonstrated improvement in achieving caloric goal, decreasing their cytokine levels, and minimizing mechanical ventilatory support. While clinically significant, there were no statistically significant differences in nutritional or physiologic outcomes, or in patient outcomes between the two groups. Fifty three percent of the subjects were dispositioned home or to a skilled nursing facility.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/075 **Status**: Ongoing

Title: E-Health Management of Fibromyalgia Pain (VPCC Substudy)

Principal Investigator: LTC Fujio McPherson, AN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): LTC Gregory A. Gahm, MS; Deland Peterson, Ph.D.; John Allison, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	May 01	N/A

Study Objective: (1) Evaluate the effects of using regular electronic communication that includes content information about specific patient health concerns, cognitive behavioral therapy, medication, exercise, lifestyle changes, complimentary/non-traditional health care and health promotion information via the internet, in the treatment of patients with fibromyalgia, (2) Evaluate the workload requirements and appropriateness of having primary care providers working in collaboration with a clinical psychologist to implement supportive psychotherapy into this process, and (3) Identify the use of complimentary/non-traditional medical practices among patients with fibromyalgia and their impact on patient outcomes.

Technical Approach: The study will involve a random assignment of patients with a diagnosis of fibromyalgia/myalgia. An enrollment questionnaire will then be forwarded to them which provides inclusion and exclusion criteria. Those who meet the inclusion criteria and agree to be included in the study will be divided into two groups. The first group (experimental group) will be subject to the interventions designed in the study (being provided information and access to the VPCC via the internet), the second group (control group) will continue to receive care thorough the primary care portal without access to e-health. Although the control group will not be restricted from using their Internet servers to access non-VPCC sources of information. The experimental group will then be given a group presentation to instruct them on the study parameters, specifically how to access the VPCC system using their Internet interfaces. From that time until the conclusion of the study, information will be provided electronically to and from the experimental group using the VPCC. The control group, minus the Internet briefing will receive the same questionnaire via routine postal service. Retrospective and prospective data will be collected from both groups prior to the study, three months after the study and at the conclusion of the study, projected at six months.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/045	**Status**: Ongoing

Title: Determining the Need for a Bereavement Program at a Military Medical Center

Principal Investigator: LTC Elizabeth A. Mittelstaedt, AN

Department: Nursing	**Facility**: MAMC

Associate Investigator(s): LTC Wynona M. Bice-Stephens, AN; CPT Carie G. Bussey, AN; Kathi M. Hamilton

Start Date:	**Est. Completion Date:**	**Periodic Review:**
2/27/2001	Jan 02	N/A

Study Objective: To determine the level of MAMC nursing staff knowledge regarding patient death, dying and grief.

Technical Approach: The study will occur at Madigan Army Medical Center. Potential participants will include nursing staff members. The survey will include demographic questions and a self-assessment regarding grief, death, and dying. The survey will also address information about current facility activities regarding death and dying. The survey is voluntary, and distributed to each individual in person or via their unit mailboxes/Head Nurse. The surveys will be distributed and collected within a 14-day timeframe. Social security numbers, addresses or other identifying data will not be requested. Descriptive statistics will be applied to quantitative and demographic data; qualitative data will be categorized. The responses to this survey will provide invaluable information regarding current aspects of grief support at the Medical Center. Respondents will also provide key information regarding their grief support needs. The implications of this study will assist the Hospital Bereavement Committee to develop educational programs, support systems and services to meet the needs of staff, students, and patients at Madigan Army Medical Center.

Progress: The Nursing Bereavement Instrument was sent to 842 nurses (RNs, nurse practitioners, LPNs/91Cs, operating room technicians, CHNs, nursing assistants/91Bs, and inpatient unit clerks) working at MAMC. Responses to the qualitative questions were annotated and major themes identified. Analysis of the data by the research committee is awaiting the intital analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/077 **Status**: Ongoing

Title: The Relationship Between Health Locus of Control, Self-Care Agency, Health Promoting Behaviors and Glycemic Control in Adults with Type 2 Diabetes and Internet Use: A Randomized, Controlled Trial (VPCC Substudy)

Principal Investigator: LTC Mary A. Schwenka, AN

Department: Nursing **Facility**: MAMC

Associate Investigator(s): MAJ Nhan V. Do, MC; LTC Gregory A. Gahm, MS

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Jan 02	N/A

Study Objective: Show that efficiency and quality of care can be improved without excessive operational cost when managing a population of patient with Type 2 Diabetes using Internet technology and that integrating Internet Healthcare tools with traditional clinical practice can improve Health Promoting Behaviors, Health Locus of Control, and Self-Care Agency scores in patients with Type 2 Diabetes.

Technical Approach: Our study population will include both male and female patients from the APCC Cascade team with diabetes but without advanced or severe complications from diabetes and age range from 18 to 75. Study design is a randomized non-blinded descriptive correlational study. The providers on the Cascade team will manage both the control and study group. Patients in the study group will have their diabetes managed the traditional method which includes routine office visit and phone calls. The study group will be managed with routine office visit but with electronic communications and a limited computer clinical support system. The primary endpoint is the change in hgbA1c from baseline. Secondary endpoints will include scores from Health Locus of Control, Self-Care Agency, and Health Promoting Behaviors instruments, patient and provider's satisfaction, and clinic resource utilization as determined by number of office visits, T-Cons, and e-mails. Data analysis will comprise of descriptive analysis, t-test, and scoring of instruments per published protocols.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/067 **Status**: Ongoing

Title: Weight and Body Fat Percentage Gain or Loss at ROTC Advanced Camp 2000

Principal Investigator: LTC Joan K. Vanderlaan, AN

Department: Nursing **Facility**: MAMC

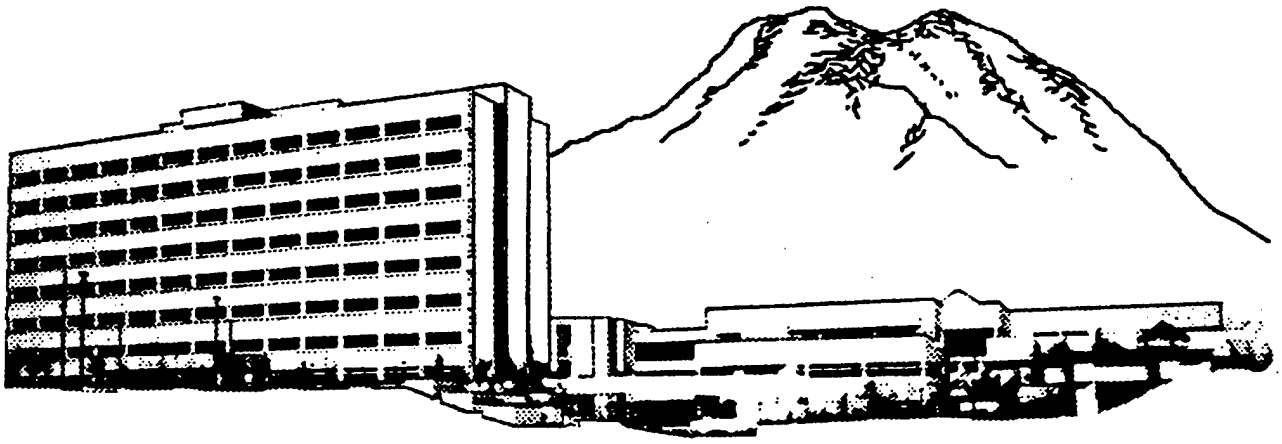
Associate Investigator(s): CPT Nicole L. Kerkenbush, AN; CPT Corina Barrow, AN

Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	Nov 00	4/24/2001

Study Objective: To answer the following questions: (1) Do Cadets lose or gain weight at camp? (2) If so, how much weight (in lbs.) do they gain or lose? (3) Are there gender and racial variables to the weight change? (4) If weight loss does occur, is there a difference between Cadets who are trying to lose weight versus those who don't care about weight loss? (5) Does the weight loss affect tape results utilizing the Army system? That is, can weight loss be correlated to change in % body fat? and (6) If Cadets are minimally overweight or overtape at the beginning of camp, would they lose enough weight or % body fat during camp to justify the time and expense of retaining them at camp as a means of improving ROTC officer commission production?

Technical Approach: Cadets will be informed of the purpose and procedures of the study and given the option to participate or not. During the commissioning physical, they will answer a brief questionnaire and their height and weight will be recorded as per Army APFT standards. For one platoon per Regiment, consenting cadets will also be taped according to the Army taping procedure as described in AR 600-9. This occurs on day 2 of the 35 day camp cycle. On day 34 of the camp cycle, cadets will again be weighed and those previously taped will be taped again. The paired T-test was used to determine the pre and post weight gain or loss (lbs) by each individual and changes in body fat percentages.

Progress: The entire target population of cadets (3757) was asked to participate in the weight change portion of the study. Of these 3196 (85%) volunteered. One Platoon from each Regiment was randomly selected to participate in the body fat measurement (taping) portion of the study. The size of the taped group (346) had to be limited to prevent disruption of concurrently scheduled camp activities. Those who departed camp prior to day 34, or moved between Regiments were excluded from final data analysis. FINDINGS: As a group, the mean difference between weights was 1.6 lbs. ($p<0.0001$). Body fat changes were 1.1% ($p< 0.0001$). Secondary findings included a mean difference between gender of 3.36 lbs. ($p<0.0001$) in weight change and 1.6% ($p<0.0001$) in body fat. Females gained 1.04 lbs while males lost 2.32 lbs. These weight changes were supported by the body fat changes, with females having a mean increase of 0.1% and males having a decrease of 1.6%. There was no difference related to ethnicity. CONCLUSIONS/RECOMMENDATIONS: Male cadets lose weight and body fat during Advanced Camp, however females gain. Further studies to determine why differences exit between genders are recommended. IMPLICATIONS: These finding have been used to change policy on cadet eligibility to attend ROTC Advanced Camp. Cadets exceeding their required body fat percentage by less than 2% at the start of camp may be permitted to remain at camp, but must meet AR 600-9 standards by the end to qualify for camp credit. Despite the secondary findings on gender, this standard is applied equally to all cadets in order to prevent gender discrimination. During Camp 2001, only 2 (1 male, 1 female) of the 63 cadets permitted to attend under this new policy did not successfully meet body fat percentage standards by the end of camp.



Detail Summary Sheets

Anesthesia Students, Department of Nursing

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/135 **Status**: Terminated

Title: A Comparison in the Early Reversal of Rapacuronium with Neostigmine and Edrophonium

Principal Investigator: CPT Brock M. Smith, AN

Department: Nursing/Anesthesia **Facility**: MAMC

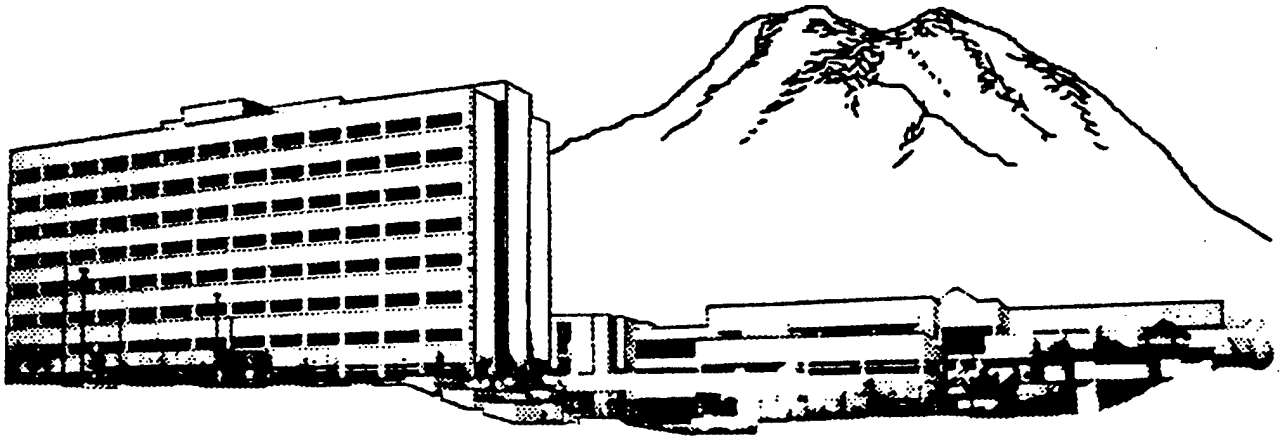
Associate Investigator(s): CPT Charles T. Lent, AN; CPT Daniel R. Mattson, AN; CPT Kyle E. Ewing, AN; CPT Paul M. Johnson, AN

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Jun 01	

Study Objective: The purpose of this study is to determine whether endrophonium or neostigmine produces a faster return of the trail-of-four (TOF) ratio to 0.7 following an intubating dose of rapacuronium.

Technical Approach: The purpose of this double-blind, randomized, Phase IV drug study is to determine the fastest means of reversing rapacuronium. A convenience sample size of 100 subjects undergoing general anesthesia for surgery will be used. Subjects will be randomized to receive either neostigmine 0.07 mg/kg with glycopyrrolate 0.01 mg/kg diluted with 0.9% sodium chloride solution or endrophonium 1.0 mg/kg with atropine 0.01mg/kg diluted with 0.9% sodium chloride. Following the reversal of rapacuronium data will be collected on onset, recovery of Tl to 25% and 75%, TOF ratios of 0.7 and 0.8.

Progress: Received notification by the PI, 2 Apr 01, the protocol had to be terminated due to recall of rapacuronium by manufacturer. There were not enough patients enrolled to perform data analysis.



Detail Summary Sheets

Nutrition Care Division

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/132	**Status**: Ongoing

Title: Army Weight Control Program - Identifying Predictors of Success

Principal Investigator: CPT Michelle D'Amico, SP

Department: Nutrition Care	**Facility**: MAMC

Associate Investigator(s): 2LT Hillary Harper, SP

Start Date:	**Est. Completion Date:**	**Periodic Review:**
9/26/2000	Jun 01	10/23/2001

Study Objective: The aims of this study are to (1) identify factors that predict the ability of Active Duty soldiers in the AWCP to successfully achieve the standards and (2) specifically, identify the motivators, attitudes and practice behaviors related to successful achievement of AWCP standards.

Technical Approach: Soldiers enrolled in the Active Duty Weight Control Program, Fort Lewis, WA, will complete an initial and 6 month follow-up questionnaire. Questionnaires will be anonymous and information will be reported in aggregate form only with no participant identifiers.

Progress: 49 soldiers enrolled in this study at MAMC during FY01. Questionnaires continue to be collected for this multi-center study. No findings or conclusion have yet been reached.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/111 **Status**: Terminated

Title: An Evaluation of UPBEAT Weight Management Program

Principal Investigator: 1LT Joseph T Frost

Department: Nutrition Care **Facility**: MAMC

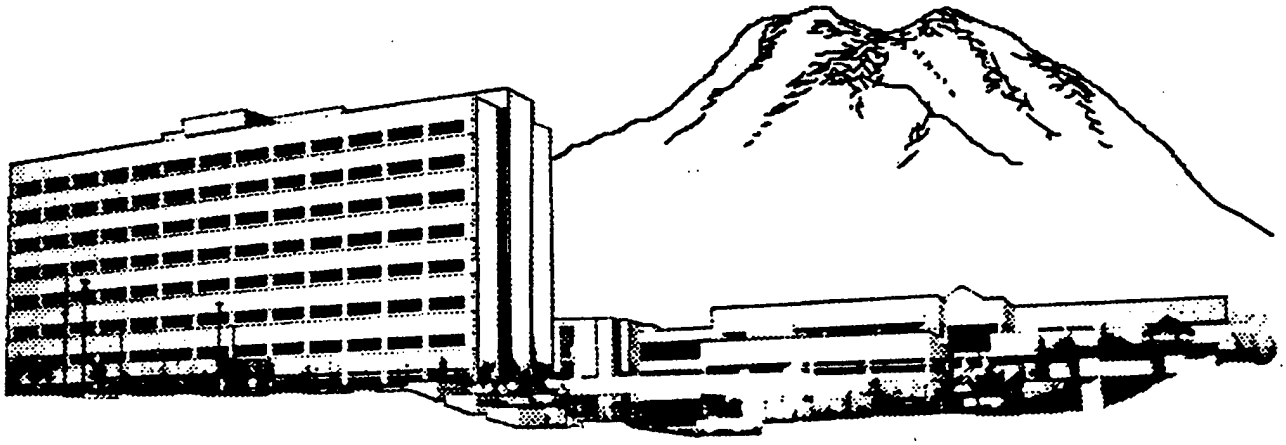
Associate Investigator(s): 1LT Susan Ann Jordan, SP

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Nov 99	1/23/2001

Study Objective: (1) To educate soldiers about the mind and body drives that lead to overeating and inactivity, (2) To increase soldier readiness through sustained improvement in overall health and fitness, and (3) To decrease losses in personnel due to AR 600-9.

Technical Approach: UPBEAT Program will consist of 4 phases: orientation/testing, personal interviews, Skill Training, Partnering for Change, and Maintenance and Relapse Prevention. This first phase will assess the soldiers' readiness to change, and develop individualized goals and outcomes. This phase will also identify if a soldier has an eating disorder. Based on the efforts of phase 1, the second phase will involve commanders and UPBEAT staff partnering for soldier success. The third phase will involve a 12- week intervention aimed at identifying the mind and body cues that will lead to permanent lifestyle changes and improved overall health. The fourth phase will focus on the maintenance of these skills and behaviors. This phase is essential in working through any relapses and is considered crucial in long term success. This phase will extend out to a full year.

Progress: 46 subjects enrolled onto this protocol during FY00. However, the study has been terminated due to poor enrollment during FY 01.



Detail Summary Sheets

Department of Obstetrics/Gynecology

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/068 **Status**: Ongoing

Title: The Role of Methergine in the Management of Spontaneous Abortion

Principal Investigator: CPT Jodi L. Bergemann, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): LTC Gregory E. Chow, MC; CPT Robert W. Chalmers, MC; CPT Jannifer A. Brown, MC; CPT Sandra L. Hernandez, MC; CPT Kimberly Devore, MC

Start Date:	Est. Completion Date:	Periodic Review:
4/25/2000	Mar 01	4/24/2001

Study Objective: (1) Comparison of failure rates of conservative therapy in management of spontaneous abortions. Failed conservative management is defined as requiring a dilation and curettage; (2) Amount of blood loss; (3) Duration to completion of spontaneous loss (# days until quantitative BHCG<5); (4) Pain scale (control vs. methergine).

Technical Approach: Patients presenting with the clinical and laboratory diagnosis of spontaneous abortion and desiring conservative therapy will be randomized to methergine or placebo treated groups. Each group will be asked to take their medication for 24 hours. On Day #1, laboratory data including CBC and quantitative B-HCG will be obtained. B-HCG values will be followed on Days #4 and #7, then weekly until values are below 5 (indicating uterine evacuation). At this time, a CBC will be evaluated and the patient will complete a pain scale to measure amount of pain associated with the treatment.

Progress: Two subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/106	**Status**: Ongoing

Title: Tubal sterilization with the Ligasure Vessel Sealing System

Principal Investigator: CPT Lisa M. Foglia, MC

Department: OB/GYN	**Facility**: MAMC

Associate Investigator(s): CPT Louis A. Dainty, MC; LTC Peter E. Nielsen, MC; COL Milo L. Hibbert, MC; CPT Ruth A Reardon, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/27/2000	Jul 01	7/24/2001

Study Objective: To determine whether the Ligasure Vessel Sealing System may be used to effectively seal fallopian tubes as evidenced by gross and histological examination.

Technical Approach: Subjects will have a preoperative evaluation that will include obtaining a history, physical examination, preoperative anesthesia visit, and laboratory studies (CBC, hCG). Subjects will be randomized on a 1:1:1 basis to three different treatment groups - 1 seal per Fallopian tube, 2 seals per Fallopian tube, 3 seals per Fallopian tube with the Ligasure device. A laparoscopic tubal ligation will performed. A mid-isthmic segment of the right Fallopian tube will be identified. The Ligasure device will be inserted through the suprapubic port, and a mid-isthmic segment of Fallopian tube will be grasped with the Ligasure device. It will be sealed one, two or three times depending upon which group the patient was assigned to. The Ligasure device will be removed and then a laparoscopic Pomeroy will be performed where the ligated segment of tube is excised and removed. The length of the tubal segment removed will not be altered by the Ligasure procedure.

The segments of Fallopian tube will be submitted to Pathology, as per usual for the Pomeroy procedure. The tubal diameter (lumen and external diameter), length of tubal occlusion, and length of tissue damage beyond the length of tubal occlusion will be measured in millimeters. The tubal segments will be examined histologically for extent of spread of tissue damage. Presence or absence of tubal occlusion will be determined by ability to cannulate the tubes with a lacrimal duct probe and then by histologic examination of the tube. The presence/absence of tubal occlusion will be compared by group. The length of tubal occlusion and length of tissue damage beyond the length of tubal occlusion will be compared by group, using the ANOVA.

Progress: No work was initiated on this study in FY01 as investigators continue to seek funding for supplies.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/129 **Status**: Completed

Title: An Introductory Training Program for New PGY-1, PGY-2, and PGY-3 Obstetrics & Gynecology Residents

Principal Investigator: CPT Lisa M. Foglia, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): CPT Lisa M. Foglia, MC; LTC Peter E. Nielsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Aug 01	7/24/2001

Study Objective: Demonstrate that an initial training process improves the performance and knowledge base of new interns and residents.

Technical Approach: This is an educational intervention study. A series of 20 minute lectures and/or demonstrations on basic obstetric , gynecologic, and infertility topics will be given to all new PGY-1 and PGY-2 residents, with curriculum pretest, immediate posttest, delayed posttest and a qualitative survey on performance, confidence and competence. Pretests and posttest results will be compared and evaluations will be compared to determine both subjectively and objectively whether this training appears to benefit this group of residents.

Progress: Study has been completed and presented as a podium presentation. No abstract is available at this time.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/023 **Status**: Ongoing

Title: Delayed Maternal Pushing with Labor Epidural Analgesia: Effects on Operative Vaginal Delivery

Principal Investigator: LTC Peter E. Nielsen, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): CPT Richard O. Burney, MC; MAJ Brian T. Pierce, MC; MAJ Christina C. Apodaca, MC; MAJ Richard K. Wagner, MC; LTC (Ret.) Sylvia Wood, RN; Thomas W. Overly; COL Byron C. Calhoun, MC, USAF; Kathleen M. Judge; CPT Robert W. Chalmers, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/26/1999	Feb 00	1/23/2001

Study Objective: To determine the effect of delayed maternal pushing on the rate of operative vaginal delivery.

Technical Approach: Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects will be randomized into one of two treatment groups after the placement of epidural analgesia; early pushing and delayed pushing. Early pushing group: Subjects will be allowed to push at the first maternal urge once the cervix is completely dilated. Delayed pushing group: Subjects will begin pushing when the vertex is distending the perineum. The subjects in this group will be given o.25% bupivacaine epidural boluses to delay the maternal urge to push. Cervical examinations in both groups will occur at either maternal urge to push, or at 2 hours following complete cervical dilation. If no maternal urge to push at 2 hours, and the decent of the vertex is >= 1 cm/hr, then continue management as randomized. If decent < 1 cm/hr, then begin oxytocin infusion per protocol for hypo tonic contractions and reexamine cervix in 2 hours, or at the onset of urge to push. If uterine activity is adequate, then begin pushing in both groups. Reexamine cervix in 2 hours and evaluate for arrest of decent. This management may allow the length of the second stage to be extended to approximately 5 hours, exceeding the generally accepted length of 3 hours in nulliparas and 3 hours in multiparas with epidural analgesia. The type of operative intervention (forceps, vacuum or cesarean delivery) will be the decision of the attending physician to ensure a safe and effective delivery.

Progress: 10 subjects enrolled during FY01 for a total enrollment of 56 overall. Enrollment remains ongoing. Investigators are considering the addition of another study site to help with accrual.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/024 **Status**: Ongoing

Title: Extending the Duration of Active Phase Arrest: Effects on Cesarean Delivery

Principal Investigator: LTC Peter E. Nielsen, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): CPT Amy J. Asato, MC; MAJ Brian T. Pierce, MC; MAJ Christina C. Apodaca, MC; MAJ Richard K. Wagner, MC; Thomas W. Overly; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
01/26/1999	Feb 00	1/23/2001

Study Objective: To determine the effect of extending the length of active phase arrest of dilation from 2 to 4 hours on the rate of cesarean delivery.

Technical Approach: Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects with active phase arrest, despite 2 hours of adequate uterine activity and continuous labor epidural analgesia, will be randomized to either cesarean delivery or 2 additional hours of labor. All subjects at the end of this 2 hour study period who fail to demonstrate cervical change (< 1 cm progress in 2 hours) will be delivered by cesarean section. All other patients will continue the labor process. Cesarean delivery for non reassuring fetal heart rate tracing will be performed based on routine obstetric indications.

Progress: 5 subjects enrolled during FY01 for a total enrollment of 12 subjects overall, with no adverse events reported. Enrollment remains ongoing.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/031 **Status**: Ongoing

Title: Relationship of Cesarean Delivery for Arrest of Descent and Station at Onset of Maternal Pushing: A Case Control Study

Principal Investigator: LTC Peter E. Nielsen, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): CPT Craig Frayer, MC; LTC (Ret.) Sylvia Wood, RN; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Apr 99	2/22/2000

Study Objective: To determine the effect of station at onset of second stage on the rate of cesarean delivery in primiparous patients with epidural anesthesia.

Technical Approach: Using the 1996/1997 labor and delivery records of deliveries at MAMC, a case control study will be performed. All primiparous patients with epidural anesthesia who required a cesarean section for arrest of descent will be identified and labeled as cases. For each case, two primiparous patients with epidural anesthesia who progressed to spontaneous delivery will be identified and labeled as controls. For each case, respective controls will be matched for maternal age, gestational age, fetal weight and use of oxytocin in labor. During this period of labor management, all patients began pushing efforts at the onset of the second stage, which was defined as cervical progression to complete effacement and complete dilation irrespective of fetal station. The fetal station at the onset of second stage will be determined for all cases and controls. A chi-square analysis will be performed to compare cases and controls with second stage maternal pushing efforts begun at fetal station 0 and higher. This will be conducted so as to allow the determination of an odds ratio for operative delivery when maternal pushing efforts are begun at fetal station higher or equal to 0. Additionally, each station will be assigned a value to allow for the performance of the Mann-Whitney Rank Sum Test in the comparison of cases and matched controls.

Progress: 30 records were reviewed during FY00. No additional information was collected during FY 01. Study remains ongoing for data collection.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/046 **Status**: Ongoing

Title: Outcome of Infants Born at 22-28 Weeks Gestation: A Retrospective Review in Military Care Facilities

Principal Investigator: LTC Peter E. Nielsen, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): LTC Michael K. Yancey, MC; LTC Gary C. Sharpe, MC, USAF; LTC Peter G. Napolitano, MC; MAJ Wanda A. Barfield, MC; MAJ Gregory A. Marinkovich, MC; MAJ Christina C. Apodaca, MC; MAJ Richard K. Wagner, MC; COL Byron C. Calhoun, MC, USAF; MAJ Brian T. Pierce, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Feb 00	2/27/2001

Study Objective: To analyze and report neonatal morbidity and mortality in early gestation in military care facilities.

Technical Approach: All neonates born between 22 and 28 weeks EGA, inclusive, will be identified through hospital coding systems. A chart review will be performed on both the mother and neonate. Data will be collected to include: Gestational age at delivery, delivery weight antepartum betamethasone administration, neonatal surfactant administration, maternal age and race, and specific neonatal complications to include: death, RDS, WH (grade 3 and 4), periventricular leukomalacia, NEC, hyperbilirubinemia requiring phototherapy or exchange transfusion, retinopathy of prematurity, hypoglycemia, and sepsis. Maternal medical problems and ante/intrapartum complications will also be recorded. A follow-up study is planned to report long term follow up in these premature infants, specifically at 2 years of age and 5 years of age. The data will be collected on a separate date sheet (attached), with the patient being identified by a code number. The principle investigator will be the sole keeper of the names of the patients as well as the code to which they are assigned.

Progress: No work was completed on this study during FY01. Chart review is expected to begin early in FY02.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/084 **Status**: Completed

Title: Team Performance in Labor & Delivery: L&D MedTeams: Concept Phase

Principal Investigator: LTC Peter E. Nielsen, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): COL Matthew M. Rice, MC; Kathleen M. Judge; Robert Simon, EdD; CDR Ron Dommermuth, MD; LCDR Mike Bidus, MD; LT Deidra Parker, MD

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Oct 00	2/27/2001

Study Objective: The proposed study, Concept Phase, is intended to develop an educational initiative in teamwork training (MedTearns) for Labor Delivery. Observational Study to determine components of curriculum and optimal training curriculum. Culmination in Experimental Phase pending successful Grant Application FY2000.

Technical Approach: This study is intended to demonstrate that an educational initiative in teamwork training (MedTeams) can be instrumental in improving labor & delivery caregiver performance and job satisfaction while reducing error patterns that are potentially dangerous to patients, mother and child. This initiative has its beginnings in the aviation community through team coordination training entitled "Cockpit Resource Management". Cockpit Resource Management in essence are rules of engagement that crew members abide by when communicating with one another, (i.e., check back, challenge, etc). This simple innovation was found to be a powerful one within the last several years and has contributed to a decrease in both civilian and military aviation mishaps. The successful multicenter educational trial involving the ETCC has proven that a similar initiative in medicine can reduce medication errors and other actions that are potentially harmful to patients. MedTeams has been funded by DA through ARL under a MOA with DRC and collaborating Medical Centers to test this hypothesis in emergency departments. A suite of both objective and subjective measures will be developed at MAMC under this expedited review protocol to pilot an L&D MedTeam educational initiative at MAMC. This program will serve as the core for the next phase, experimental phase, of a multicenter educational interventional trial which will parallel the ETCC trial. The Program will involve an eight-hour MedTeams didactic training, frequent refresher and reinforcement sessions, in addition to the administration of anonymous caregiver and patient survey tools. Commonly available continuing improvement and risk management data will be monitored to follow trends of error patterns, medication error, patient complaints, etc. Goal to develop Grant Proposal and Multicenter Trial by Oct 2000. CRDA with DRC, MAMC/CIRO through Geneva will develop concurrently.

Progress: 21 charts were reviewed with the following results: Teamwork failures were primary contributors to adverse events in 57% of reviewed cases. In 91% of cases where primary teamwork failures existed, there were other teamwork failures present. Improvement in teamwork related functions may reduce adverse events and improve patient outcome.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/077 **Status**: Ongoing

Title: Misoprostol for the Medical Management of Non-viable First Trimester Pregnancies

Principal Investigator: CPT Jason D. Parker, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): COL Milo L. Hibbert, MC; LTC Peter E. Nielsen, MC; Troy H. Patience, B.S.; CPT Louis A. Dainty, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/22/1999	Mar 01	3/28/2000

Study Objective: The purpose of this study is to examine the effectiveness of misoprostol for the management of non-viable first trimester pregnancies. Specifically, misoprostol (15-S-15-methyl PGE1) will be compared to a placebo with expectant management in who have documented non-viable gestations. We will examine the following outcome variables: time to resolution, number of patients requiring dilation and curettage, change in hematocrit, cost to the institution, patient satisfaction, and reported side effects.

Technical Approach: Patients presenting to the OB/GYN clinic with a nonviable gestation will be considered potentially eligible to participate in the study. The diagnosis of non-viable gestation will be documented by endovaginal ultrasound. Those patients entering the study will be directed to the OB/GYN clinic for evaluation, exam, counseling and to watch the video giving explanation of purpose of the study and the planned procedure, but also expected side effects and possible complications. An anembryonic gestation will be diagnosed in any patient with an irregularly shaped gestational sac and mean sac diameter of 16 or greater without an embryonic pole. Additionally any patient with an intrauterine fetal pole between 5 and 14 mm with no cardiac activity will be considered non-viable and will be considered for acceptance into our study. Ultrasonic findings will be verified by two of the resident staff from OB/GYN. After explanation of the study, verification that the patients meet the inclusion criteria, patients will be offered participation in the study and asked to view a short video to ensure consistency of counseling. Upon conclusion of the counseling and video, patients will be asked to sign a consent form for participation in the study. Complete history and physical will be performed and initial laboratory will be obtained to include CBC, BUN, creatinine, quantitative BHCG and blood type to include Rh status. Patients will be randomized into two groups: receiving misoprostol or placebo. Subjects will be issued an envelope and asked to report to the pharmacy where they will pick up their study medication, which will be blinded to them and the provider administering the medication. Additionally, they will be given Motrin and Phenergan to help alleviate undesired side effects. Subjects will have four 200 ug tablets of misoprostol in the posterior fornix of the vagina using a speculum under the direct visualization of the provider. Patients will be asked to return in 24 hours for re-examination to include a pelvic ultrasound using a vaginal probe. If no evidence of an intrauterine pregnancy remains (i.e. gestational sac, fetal pole etc.), patients will be informed that their miscarriage was complete, given precautions and asked to make an appointment for follow-up in 4 weeks in addition to weekly visits to the lab for quantitative BHCG. All patients will be followed until the quantitative BHCG has fallen zero to ensure resolution of the pregnancy event. Those patients with evidence of a gestational sac will be given a second dose of misoprostol or alternatively a D&C if they choose to withdraw from the study or surgical intervention is deemed clinically indicated by the attending staff. Again, the subjects will be given appropriate counseling and precautions and asked to follow up in an additional 24 hours for re-evaluation. Surveys will be given at each visit and follow up to evaluate patient satisfaction and also to query for unintended side effects and complications.

Progress: 18 patients enrolled in this study at MAMC with no adverse outcomes or reactions occurring to date. Anticipate completion of the study by early of 2002.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/127 **Status**: Completed

Title: Mentoring for the New Millennium: Enhanced Scholarly Activity, Professional Development, and Personal Satisfaction for Future Academics Through the Successful Implementation of a Mentor System

Principal Investigator: COL Robert E. Ricks, MC

Department: OB/GYN **Facility**: MAMC

Associate Investigator(s): COL William O. Walker, Jr., MC; COL Patrick C. Kelly, MC; LTC Peter E. Nielsen, MC; LTC Gregory E. Chow, MC; COL Byron C. Calhoun, MC, USAF; Laura S. Martin, M.D.; LTC Diane M. Flynn, MC; COL Romeo P. Perez, MC; COL Roderick F. Hume, MC; CPT Lisa M. Foglia, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Mar 01	8/28/2001

Study Objective: How do you teach mentors? How do you provide the increased faculty and fellow time during downsizing? What are the optimal parameters for the mentoring process?

Technical Approach: Multidimensional system of educational intervention with use of MENTOR TOOL to track scholarly activity, realistic time-management tools, directive advice and goal setting for novices. Use of CREOG & ABOG scores, number of IRB approved protocols, abstracts, publications, visiting speaker, and personal satisfaction survey to measure outcome of formal mentor process. Now formal and informal focus group methodologies (survey) and review of existing GME files used to document scholarly productivity.

Progress: Emphasis on faculty development among the fellows and junior faculty can increase medical student and resident scholarly activity. This augments the recruitment of exceptional junior housestaff who become excellent teachers. The Program Coordinator is essential to this success, often serving as the mediator of mentors for the student (medical student, resident or fellow). Mentoring is an active process involvinghigher professional development through experience, feedback and effort. Tormentors (toxic mentors) must be identified for formal mentoring to redirect efforts toward institutional goals. Mentorship works best when formal education is sustained by use of formal feedback tools for both the mentor and protege synergy - MAPS. Senior mentos, program coordinators and program difectors can then focus on the specific faculty development issues of their junior faculty.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/128 **Status**: Completed

Title: US Navy Female Service Member Readiness: A Leader's Guide-Implementation Phase: Utility Validation Survey

Principal Investigator: LCDR Robin E. Wood, MC, USN

Department: OB/GYN **Facility**: MAMC

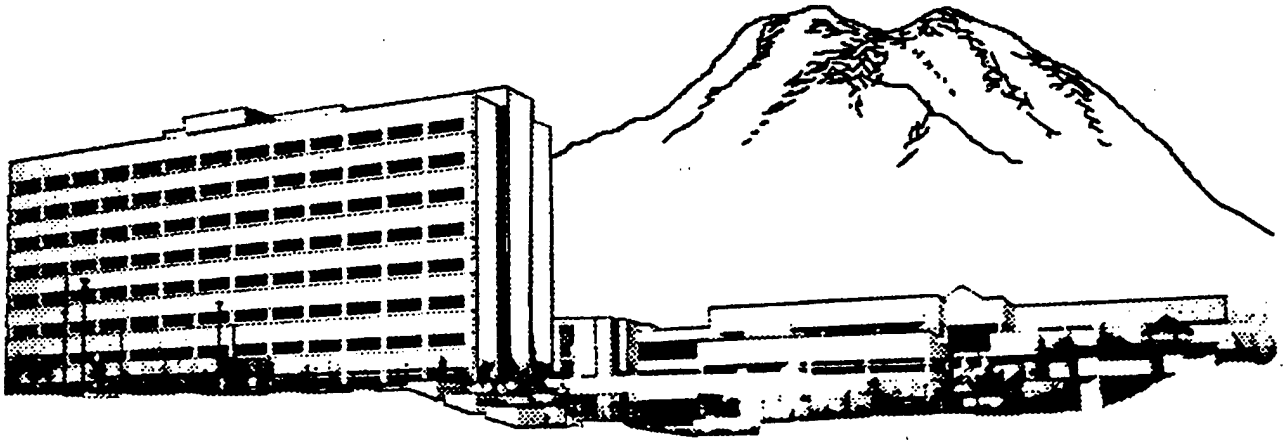
Associate Investigator(s): CPT Tiffany Vara, MSC; LCDR Mary G. Battaglia, NC, USNR; COL Byron C. Calhoun, MC, USAF; COL Robert E. Ricks, MC; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Sep 01	7/24/2001

Study Objective: Development of the FSRG for the AD US Army and US AF female service member has been successful. WRMC also serves USN. Cultural literate translation of FSRG for USN complete, and now survey for formal and informal focus group feedback needed to validate tool.

Technical Approach: Publication and distribution of GUIDE to line (fleet) unit leadership for formal and informal focus group feedback.

Progress: USN Guide Development completed and presented for approval by USN OG OTSG Consultant. Impact with BNH Obstetrical Naval personnel to field trial just as was done on Ft. Lewis for Female Soldier Readiness Guide. 180 subjects participated during FY01. Work on the study has been completed.



Detail Summary Sheets

Maternal-Fetal Medicine, Department of Obstetrics/Gynecology

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/002 **Status**: Terminated

Title: Early Test for Preeclampsia Using Fetal Cells in Maternal Blood

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): COL Roderick F. Hume, MC; MAJ Elizabeth G. Hancock, MC; MAJ Christina C. Apodaca, MC; MAJ Brian T. Pierce, MC; ; ; ;

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Jul 00	8/28/2001

Study Objective: To test whether there are increased numbers of fetal erythroblasts in patients at risk for severe preeclampsia.

Technical Approach: This protocol seeks to enroll 150 singleton, uncomplicated nulligravida patients at 16-20 weeks in a prospective cohort study. Patients will be selected on the basis of uterine artery Doppler flow abnormalities. A cohort of normal, uncomplicated, nulligravida patients with normal uterine artery Dopplers will serve as controls. Presently anatomy surveys are performed on virtually all pregnant women at 16-20 weeks at this time and the examinations will add only 10-15 minutes per exam. All patients will have 20 ccs of maternal blood drawn at 16-20 week ultrasound and 4-6 weeks later and sent to our co-investigators (at their expense) for analysis of fetal erythroblasts. The co-investigators will be blinded to the uterine artery Doppler studies and demographics until after completion of the study when correlation between uterine Doppler studies, fetal erythroblasts, and preeclampsia will be done. For analysis will be done using Mann-Whitney test for non parametric data (SPSS Statistic package).

Progress: This study was reported as completed without participation from MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/015 **Status**: Ongoing

Title: Myometrial Gap Junctions and Their Importance in Obstetric Patients with Chorioamnionitis

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; Alan F. Lau, Ph.D.; MAJ Christina C. Apodaca, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Oct 00	10/23/2001

Study Objective: The purpose of this study is to investigate whether decreased conexin 43 mRNA and/or protein levels and the decreased formation of gap junction plaques in the myometrium is responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

Technical Approach: Myometrial tissue will be obtained during cesarean section from laboring patients with and without chorioamnionitis, and from those patients requiring cesarean section prior to the onset of labor (without chorioamnionitis). Cx43 messenger RNA and protein levels will be compared among these patients and immunohistochemistry will be performed to examine the presence of gap junction plaques. Decreased Cx43 mRNA and protein levels and decreased gap junction formation in the myometrium of chorioamnionitis patients may lead to decreased gap junctional communication (GJC) in the myometrium. This decreased GJC may be responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

Progress: Myometrial biopsies were obtained from 21 patients with dysfunctional labor undergoing cesarean section: 11 with chorioamnionitis, 10 without. Northern and Western analyses were performed to determine Cx43 mRNA and protein expression, respectively. Localization of Cx43 protein was determined by immunohistochemistry and graded as absent, mild, moderate, or dense. Results: There was no difference in Cx43 MRNA expression, protein expression, or degree of immunohistochemical staining between the groups.

Conclusions: Chorioamnionitis may increase a woman's risk for cesarean section due to dysfunctional labor, however it is not associated with aberrant Cx43 mRNA and protein expression, nor with altered presence of gap junction plaques.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/024 **Status**: Completed

Title: The Effects of Shear Stress on Placental Production of Vascular Endothelial Growth Factor (VEGF), Placental Growth Factor (PLGF), and Tumor Necrosis Factor (TNF-alpha) in the Isolated Dually Perfused Placental Cotyledon

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; MAJ Christina C. Apodaca, MC; LTC Peter G. Napolitano, MC; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Dec 00	11/27/2001

Study Objective: To determine the effects of shear stress on placental production of vascular endothelial growth factor (VEGF), placenta growth factor (PlGF), and tumor necrosis factor-a (TNF-a).

Technical Approach: Placental effluents from a prior study are available for evaluation of placental response of these molecules. The effluents were collected in the following manner: Paired cotyledons from 5 placentas obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery were used. A perfusate consisting of Hank's balanced salt solution, bovine albumin, heparin, and gentamicin was used to perfuse both the maternal and fetal circulations of the cotyledons. One cotyledon had the fetal circulation infused at 1 cc/min. The other cotyledon had the fetal circulation perfused at 10 cc/min. After establishing perfusion of an intact fetoplacental circuit, effluents were collected at hourly intervals for four hours. These samples were stored for determination of IL-6 levels by ELISA. The fetoplacental vascular tone was continuously monitored throughout the experiment and recorded at 10-min intervals. Data was analyzed using repeated measure analysis of variance.

Progress: All placenta work on this protocol occurred during FY00 and the study has been completed at MAMC. Five placentas were divided into two cotyledons each. One cotyledon was perfused at a high perfusion rate (10 cc/min), the other at a low perfusion rate (1 cc/min). Fetal effluents were collected hourly for four hours and VEGF, P1GF, and TNF concentrations were determined by ELISA. Results: VEGF and P1GF were not detected in the fetal effluents under either condition. TNF was significantly elevated under the low perfusion rate conditions. Conclusion: VEGF and P1GF are not acutely produced by the placenta during hypoperfusion. Hypoperfusion may be related to cerebral palsy, in that elevated inflammatory cytokines are a hallmark of the fetal inflammatory response syndrome, and placental pathology is a common finding in fetuses who subsequently develop CP.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/029 **Status**: Completed

Title: The Effects of Hypoxia and Hypoxia with Acidemia on Placental Production of Vascular Endothelial Growth Factor and Placenta Growth Factor in the Isolated Dually Perfused Placental Cotyledon

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; LTC Peter G. Napolitano, MC; MAJ Christina C. Apodaca, MC; MAJ Elizabeth G. Hancock, MC; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Dec 00	12/14/2001

Study Objective: To determine the effects of hypoxia and hypoxia with acidemia on placental production of vascular endothelial growth factor (VEGF), placenta growth factor (PlGF), and tumor necrosis factor-a (TNF-a).

Technical Approach: Paired cotyledons from 20 placentas will be obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery. A perfusate consisting of Hank's Balanced Salt Solution, bovine albumin, heparin, and gentamicin will be used to perfuse both the maternal and fetal circulations of the cotyledons. The first 10 placentas will be divided into 2 cotyledons, one perfused with a hypoxic solution, the other (control) perfused with a physiologic solution. The next 10 placentas will also be divided into 2 cotyledons, one perfused with a hypoxic and acidemic solution, the other (control) perfused with a physiologic solution. After establishing perfusion of an intact fetoplacental circuit, effluents will be collected at hourly intervals for four hours. These samples will be stored for determination of VEGF, PlGF, and TNF-a protein levels by ELISA. The fetoplacental vascular tone will be continuously monitored throughout the experiment and recorded at 10 minute intervals. Data will be analyzed using repeated measure analysis of variance.

Progress: Five placentas were divided into two cotyledons each. One cotyledon was perfused under hypoxic conditions and the other was perfused under hyperoxic conditions. Fetal effluents were collected hourly for four hours and VEGF and P1GF were determined under ELISA. Results: VEGF and P1GF were not detected in the fetal effluents under either condition. Conclusion: VEGF and P1GF are not acutely produced by the placenta during fetal hypoxia. An abstract for this protocol is available in DCI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/094 **Status**: Ongoing

Title: Hispanic Ethnicity and the Relationship of Ultrasound Criteria for Attributable Risk for Aneuploidy

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): CPT Jannifer A. Brown, MC; MAJ Elizabeth G. Hancock, MC; CPT Lisa M. Foglia, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Mar 01	5/22/2001

Study Objective: To determine ultrasound growth curves from the database presently in place from the MAMC IRB approved protocol #96164 (Natural History of Gallbladder Disease in Pregnancy) and develop ethnic specific growth curves with attributable risk for aneuploidy based ultrasound derived criteria.

Technical Approach: This retrospective study of previously existing files will look at fetal measurements at varying times during gestation. Measurements obtained on Hispanic patients will be compared to those of Asian, Caucasian, and Black patients to determine what is considered normal growth for Hispanic patients. Predictions of aneuploidy will be evaluated against birth records as well as prenatal chromosomal analysis by amniocentesis when available. This information will allow comment on the accuracy and applicability of femur length as a minor ultrasound risk adjustment for aneuploidy specific to a Hispanic population.

Progress: The study subgroups consisted of 63 Asian mothers, 142 black mothers, 60 Hispanic mothers, and 718 white mothers. The mean values of the variance from the expected femur length by biparietal diameter +/- 1 standard deviation were: for Asian mothers: -1.720 +/- 2.03; for the fetuses of black mothers: -0.468 +/- 1.98; for fetuses of Hispanic mothers: -0.59 +/- 6.819; and for fetuses of white mothers: -0.899 +/- 2.80. The femurs of the fetuses of the Asian, Hispanic, and black mothers were compared to white mothers: Asian versus white, P=0.0398, for the Hispanic versus white mothers, P=0.0398, and for the black versus white mothers, P=0.1221. Conclusions: There is a significant difference in the mean expected femur lengths by biparietal diameter among fetuses in the second trimester with regard to maternal ethnicity. Shorter femurs were noted among the fetuses of Asian and Hispanic mothers compared to the fetuses of white and black mothers. This study demonstrates further data is required for the genetic sonogram for femur length as a screening ultrasound tool.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/026 **Status**: Ongoing

Title: Differential mRNA Expression in the Preeclamptic vs. Normal Human Placenta

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; Laura S. Martin, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Dec 01	N/A

Study Objective: To identify genes differentially expressed in placentas from patients with preeclampsia compared to placentas from normal pregnancies.

Technical Approach: Prospective case-controlled observational study with placental tissue collection. Placental samples will be collected immediately after delivery and rinsed in physiological saline.The basal plate (cotyledon) excluding the large vessels will be sectioned into approximately 0.5 g pieces, snap frozen in liquid nitrogen, and stored at -70oC until mRNA analysis. Maternal age, gestational age at delivery, and birth weight will be recorded for each placenta. An anonymously coded clinical data sheet will be used to identify cases and controls.

Differential gene expression: Placental tissue from a preeclamptic patient and a normal pregnancy will undergo differential gene expression analysis using the AtlasTM cDNA Expression Array technology (AtlasTM Custom Hybridization and Analysis Service, Clontech, Palo Alto, CA). Frozen specimens (approximately 0.5 g tissue each from one preeclamptic placenta and one normal placenta) will be mailed to Clontech for analysis. RNA will be isolated from these placental samples, and cDNA probes will be prepared using a gene-specific primer mix and hybridized to a nylon array of 1,176 human genes involved in a wide range of biological pathways. Computer analysis of phosphorimages by Clontech's AtlasImageTM software will compare expression signals to generate a gene expression profile mailed to us by Clontech. Differential expression of identified genes will be confirmed at the Department of Clinical Investigations Laboratory via Northern analysis (below) if cDNA probes are available. If cDNA probes cannot be obtained, reverse transcriptase polymerase chain reaction (RT-PCR) using gene-specific PCR primers obtained from Clontech will be performed using PCR conditions as per the manufacturer's instructions. This analysis to confirm differential expression will be performed on 10-25 placentas from pregnancies complicated by preeclampsia and 10-25 placentas from normal pregnancies, including tissue from the placentas used to obtain the original gene expression profile. Of note is that this is not considered a genetic study because we are not linking the results to the family. This study is for research purposes only. Patients will not be contacted with their differential expression profiles.

Northern analysis: Total cellular RNA will be isolated from the placental tissue using the method of Chomczynski and Sacchi (26). Frozen tissues will be placed into 3 ml of Solution D (26) in a 50 ml tube on dry ice and will be minced with a scalpel. Samples will then be homogenized at room temperature with a Polytron hand-held tissue homogenizer and allowed to sit at room temperature for 15 min. One-tenth volume of 2M sodium acetate (pH 4.0), one-fifth volume of chloroform-isoamyl alcohol mixture (48:1), and an equal volume of diethyl pyrocarbonate (DEPC)-treated water-saturated phenol will be added to each homogenate with thorough mixing by inversion after the addition of each reagent. The final suspension will be shaken vigorously, transferred to a 15 ml tube, and cooled on ice for 20 min. Samples will be centrifuged at 4oC for 20 min. at 9,500 rpm in a Beckman GS-15R tabletop centrifuge. The aqueous layer will be removed and placed into 1.5 ml microcentrifuge tubes in 600 ml aliquots. An equal volume of isopropanol will be added and samples will either be frozen overnight at -70oC or on dry ice for 15 min. Samples will be centrifuged at 15,300 rpm for 20 min., and the resulting RNA pellets will be

dissolved in 600 ml of Solution D, precipitated again with an equal volume of isopropanol either overnight at -70oC or on dry ice for 15 min., centrifuged for 20 min., and washed in 80% ice cold ethanol. RNA pellets will be centrifuged for 10 min., resuspended in 75 ml DEPC-treated water, and quantitated using a UV spectrophotometer.

Total RNA (30 mg/lane) will be denatured, resolved in a 1.2% agarose-formaldehyde gel, transferred to a GeneScreen (NEN, Boston, MA) membrane in 10X saline sodium citrate (SSC), and UV cross-linked to the membrane. Probes will consist of complementary DNAs for differentially expressed genes identified by hybridization with the AtlasTM cDNA Expression Arrays (Clontech, Palo Alto, CA) and 18S ribosomal RNA (Ambion, Inc., Austin, TX) as an internal loading standard. Probes will be labeled by random priming (Amersham, Arlington Heights, IL) with [a-32P]dCTP (3000 Ci/mmol, Amersham, Arlington Heights, IL) and the Klenow fragment of E. coli DNA polymerase. Unincorporated counts will be removed using STE push columns (Stratagene, La Jolla, CA). Prehybridization and hybridization will be performed at 55oC using the SuperTM Hybridization Buffer System (DNA Technologies, Inc., Rockville, MD) following the manufacturer's instructions. Blots will be washed 3 x 5 min. in 2X SSC at room temperature before images will be obtained with a BioRad GS-505 Molecular Imager System. Blots which will be stripped and reprobed with the18S complementary cDNA will be washed in the buffers supplied in the SuperTM Hybridization Buffer System kit (DNA Technologies, Inc., Rockville, MD) following the manufacturer's instructions. Densitometry will be used to measure the relative quantity of mRNA (of the putative differentially expressed gene being investigated) present in the samples (calculated as the differentially expressed gene:18S ratio).

Progress: Placental tissue from both severe preeclampsia and normal pregnancy underwent differential gene expression analysis using the AtlasTM cDNA Expression Array technology (Clontech). Initial analysis identified several genes involved in cell cycle regulation, signal transduction, and cell growth to be differentially expressied in placental tissues from preeclamptic compared to normal pregnancy. The expresion of the gene encoding the katanin p80 subunit, an ATPase that disassembles microtubules (necessary for the rapid reorganization of the microtubule cytoskeleton during the cell cycles, differentiation, and cell migration) was 18-fold decreased in preeclampsia. The early growth response protein 1 was downregulated 3-fold in preeclampsia. Expression of teratocarcinoma-derived growth factor 1, which activates components of the ras/raf/MEK/MAPK signal transduction pathway, was decreased in preeclampsia almost 7-fold (correlates with Hannke-Lohmann 2000 finding of MAPK signaling pathway downregulation in preeclamptic placentas). Genes upregulated in preeclampsia included insulin-like growth factor binding protein 1 (increased 10-fold), which may inhibit the action of insulin-like growth factors at the endometrial-trophoblastic interphase, and pregnancy-associated major basic protein (increased 4.5-fold), a potent cytotoxin. Preliminary results show promise for the discovery of differentially expressed genes that may be involved in critical cellular pathways for the pathogenesis of preeclampsia.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/068 **Status**: Completed

Title: The Expression of Adrenomedullin and Its Receptor in the Human Placenta

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Richard K. Wagner, MC; Katherine H. Moore, Ph.D.; MAJ Christina C. Apodaca, MC; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Sep 98	3/28/2000

Study Objective: To elucidate the expression of adrenomedullin (ADM) and its receptors in specific tissue components of the human placenta. This will be investigated by using placental tissue from both uncomplicated pregnancies and pregnancies complicated by chronic hypertension and pregnancy induced hypertension. Western blot analysis will be used to identify adrenomedullin expression. Reverse transcriptase-polymerase chain reaction will be used to identify the expression of adrenomedullin messenger ribonucleic acid for ADM and to identify presence of the ADM receptor. Immunocytochemical analysis will also be used to establish the expression of ADM in specific placental tissues.

Technical Approach: Adrenomedullin is a potent vasoactive peptide, whose vasoactive properties have been extensively described. It has been isolated from various human tissues, including pheochromocytoma, lung, heart and pancreas. Its presence in human plasma suggests that it functions as a circulating hormone, influencing the perfusion of various organs. The presence of adrenomedullin has recently been described in fetal membranes and amniotic fluid, suggesting its role in fetal perfusion. Increases of adrenomedullin in pathologic states have been described, including renal failure and hypertension in non-pregnant individuals, and in pregnant women with preeclampsia. To date there exist no studies demonstrating the isolation of adrenomedullin and its receptor in specific placental tissues. We will isolate samples of amnion, cotyledon, umbilical artery and umbilical vein from women with uncomplicated pregnancies and pregnancies complicated by pregnancy induced hypertension. Western blot analysis will be used to identify the presence of the adrenomedullin protein. Reverse transcriptase-polymerase chain reaction will be used to isolate total messenger ribonucleic acid for adrenomedullin and its receptor. Histochemical staining will be used to identify adrenomedullin in the tissue samples. Categorical analysis will be performed describing the distribution of adrenomedullin and its receptor in both normal placentas and the placentas from patients with chronic hypertension and pregnancy induced hypertension.

Progress: 8 placentas were examined, (5 from normal pregnancies, 3 from pregnancies complicated by oligohydramnios). Adrenomedullin and adrenomedullin receptor mRNAs were identified in all tissue components of the placentas tested. Within the normal placentas, the expression of adrenomedullin mRNA and adrenomedullin receptor mRNA did not differ statistically between the tissue components. Within the placentas from patients with oligohydramnios, the expression of adrenomedullin and adrenomedullin receptor mRNA did not differ statistically between the tissue components. However, when comparing normal to oligohydramnios placentas, there was a five-fold increase in adrenomedullin mRNA and a three-fold increase of adrenomedullin receptor mRNA in placentas from patients with oligohydramnios. Adrenomedullin immunoreactivity was present in all tissues studied. The increased adrenomedullin mRNA in the umbilical artery and elevated adrenomedullin receptor mRNA in the cotyledons of placentas from patients with oligohydramnios may represent a local fetoplacental physiologic adaptive response to vascular compromise. This study has been completed at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/100 **Status**: Terminated

Title: Comparison of First and Second Trimester Screening for Prenatal Detection of Down Syndrome and Other Birth Defects (FASTER)

Principal Investigator: COL Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Christina C. Apodaca, MC; MAJ Brian T. Pierce, MC; LTC Peter E. Nielsen, MC; Laura S. Martin, M.D.; COL Roderick F. Hume, MC; V Souter

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Jul 01	8/28/2001

Study Objective: (1) To determine the effectiveness of first trimester screening in detection of fetal chromosome abnormalities as well as other birth defects and to compare the accuracy of first trimester screening with second trimester screening, and (2) to evaluate patient assessment of perceived risk compared to calculated risk of fetal Down syndrome and other birth defects.

Technical Approach: Patients will be enrolled between 10.5 and 14 weeks. They will be asked to complete a questionnaire to evaluate their perceived risk of fetal Down's syndrome and their attitudes toward patient screening. First trimester ultrasound with maternal-blood sampling in will be performed 10 3/7 weeks and 13 6/7 weeks looking for nuchal (neck thickness) with a follow-up ultrasound in the second trimester between 15 and 20 weeks.

First trimester laboratory testing will include maternal-serum for free Beta-human chorionic gonadotropin and pregnancy associated plasma protein-A (PAPP-A). The second trimester testing will include alpha-fetoprotein (AFP), unconjugated estriol (uE3), and human chorionic gonadotropin (hCG) as well as inhibin-A. Further, the patients who screen positive in either first or second trimester analyte screening will have maternal blood sent to be included in the "National Institute of Child Health and Human Development Fetal Cell Isolation Study (NIFTY). This study seeks to explore the ability to extract fetal cells from maternal blood for possible detection of abnormal chromosomes.

Progress: This study was terminated at MAMC, 28 Aug 01, with no patients enrolled. The study objectives were met by enrollment in other centers without requiring our patient population.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/091 **Status**: Completed

Title: Magnesium in Preeclampsia: Plasma (maternal & fetal) and Placental Levels of Ionized Magnesium (iMg)

Principal Investigator: MAJ Elizabeth G. Hancock, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF; CPT Todd M. Rossignol, MS; Melinda MacKenzie, PA-S; Cynthia Standely, Ph.D.; Jennifer Hubbart, PA-S

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Mar 01	5/22/2001

Study Objective: To determine maternal blood levels of ionized magnesium (IMg) before and after delivery, fetal (umbilical) blood levels of IMg at delivery and placental IMg levels at delivery.

Technical Approach: Maternal venous blood, placental samples, and umbilical blood will be collected from the following subjects during labor and delivery: 25 preeclamptic patients, 25 patients in preterm labor, and 25 patients in uncomplicated term labor. Sodium, potassium, ionized calcium, and ionized magnesium will be measured. Results will be analyzed to determine if there is a significant deviation in levels of blood chemicals for different pregnancy conditions.

Progress: This study was completed during FY01. Results are that mean maternal ionized magnesium levels tended to be lower in preeclamptic and preterm labor patients versus controls. Furthermore, ionized magnesium levels in fetal and postpartum blood and placental tissue tended to be higher in preeclamptics and preterm patients versus controls. However, none of the electrolyte values examined reached statistical significance. This study supports previously published literature with preeclamptic and preterm labor patients exhibiting lower ionized magnesium levels. In addition, placental and fetal ionized magnesium levels tended to be higher in preeclamptic patients suggesting the placenta may contribute to the development of hypomagnesemia in pregnancy.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/131 **Status**: Completed

Title: Comparative Study of US Detected Fetal Anomalies and Maternal Age in Two Healthcare Systems (Referral versus Routine Screening)

Principal Investigator: MAJ Elizabeth G. Hancock, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): Laura S. Martin, M.D.; Mark I. Evans, Proffessor; COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Mar 01	7/24/2001

Study Objective: What if any effect does maternal age play in prenatal detection of fetal anomalies? Is there a difference between two healthcare delivery systems in the detection rates for fetal anomalies according to maternal age or type of anomaly (minor, major, multiple)?

Technical Approach: Epidemiologic comparative analyses of existing data of US findings stratified by maternal age and type of fetal anomaly, fetal or neonatal karyotype, and neonatal confirmation of findings when available (+MAMC,-WSU).

Progress: 1,003 cases with ultrasound detected fetal structural anomalies were identified at WSU among the 16,992 prenatal ultrasound cases; (detection rate of 59:1000). 98 cases with ultrasound detected fetal structural anomalies were identified at MAMC among the 17,875 prenatal ultrasound cases; (overall detection rate of 54:1000).

Statistical analysis of MAMC data revealed an apparent association of NAFSA and advancing maternal age (>35 yo (2%); p=0.001) and the significant but lower risk for younger age (<20 yo (0.08%); $p < 0.01$). Comparisons between centers showed a 10-fold increased risk for aneuploidy or US anomaly in the WSU referral-based cohort relative to the MAMC routine screening cohort.

The MAMC cohort reveals the clinically signficant contribution of prenatal detection in a screened population. Despite the statistical differences, US screening should not be based solely upon maternal age. Further, the evolving demographics and expanding ethnic diversity in US populations demands evidence based approaches to individual genetic risk assessment relevant to each unique healthcare delivery system. Complete abstract available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/029 **Status**: Terminated

Title: Differential Effect of Betamethasone versus Dexamethasone on Cytokine Production by the Reperfused Human Placental Cotyledon

Principal Investigator: MAJ Elizabeth G. Hancock, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): COL Byron C. Calhoun, MC, USAF; MAJ Brian T. Pierce, MC; Lisa M. Pierce, D.Sc.; COL Jerome B. Myers, MC; CPT Christine M. Kovac, MC; Laura S. Martin, M.D.; COL Roderick F. Hume, MC; Troy H. Patience, B.S.; CPT Todd M. Rossignol, MS

Start Date:	Est. Completion Date:	Periodic Review:
12/8/2000	Dec 01	N/A

Study Objective: To determine whether a difference in placental cytokine production occurs when the perfusate contains betamethasone or dexamethasone.

Technical Approach: TNF-a, IL-6, lipid peroxide concentrations will be determine on stored placental effluents. The effluents will be collected by the following methods: Plase I-At least 6 placentas from uncomplicated term pregnancies will be utilized from both vaginal and cesarean deliveries. Uncomplicated pregnancies will be defined as those without clinical risk factors for uteroplacental insufficiency, no corticosteroid administration in pregnancy, and no evidence for chorioamnionitis. Pregnacy must have completed at least 36 weeks with neonatal birthweight above the 10th percentile for gestational age. This information will be obtained from the maternal outpatient and inpatient record. Phase II-Approximately 24 placentas from complicated pregnancies will then be utilized for the same procedure, and/or with hypoxia (Hoeldtke or Pierce) or lactic acidosis (4mM/L) in perfusion circuit.

The placentas will be collected immediately after deliver and transported to the perfusion laboratory. After visual inspection for lacerations or infarcts, the fetal surface will be inspected for a chorionic artery and vein pair supplying a cotyledon. The artery and vein selected will each be cannulated. A circular section of the placenta, which inlcudes the cotyledon, will be excised. This portion of the placenta will then be clamped into a holder and then the cotyledon will be transferred to a temperature-controlled chamber maintained at 37 degrees C. A second cotyledon from the same placenta will be prepared in a similar manner by a second investigator. All perfusions will be established within 20 minutes of placenta delivery. Maternal and fetal circulations of the cotyledons will be perfused with a solution of Hank's Balanced Salt Solution, bovine albumin, heparin and gentamicin. The solution will be divided into four separate containers. To one of these volumes Betamethasone will be added and this will be perfused to the intervillous space of one cotyledon to mimic the therapeutic levels in Maternal Circulation. Although not physiologic, in some placental runs Betamethasone will be added and perfused through fetal artery of the same cotyledon to mimic fetal levels. Dexamethasone will be added to the third volume of perfusate and will be administered to the intervillous space of the second cotyledon to mimic the therapeutic levels reported in Maternal Circulation. The fourth volume of perfusate will contain Dexamethasone to mimic fetal levels. The combination of these perfusates should mimic the steady state (peak) level of corticosteroid as administered in clinical circumstances in which preterm delivery is anticipated. Alternatively, drug (Betamethasone-A and Dexamethasone-B) will be infused (piggy back) into the maternal circuit. Goal is to attain levels comparable to peak dose in the circuits to mimic the clinical situation.

Progress: This study was terminated when betamethasone became unavailable.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/031 **Status**: Completed

Title: Prenatal Maternal Serum Analyte Screening Within the WRMC of the DoD MHS: Microeconomic Analysis of Various Models of Screening - or the Additional Burden of Unintended Cost Shifts of a 'Cheaper' Laboratory Test

Principal Investigator: MAJ Elizabeth G. Hancock, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): Laura S. Martin, M.D.; COL Roderick F. Hume, MC; LCDR Robin E. Wood, MC, USN; LT Mark L. Everett, USCG, CAAMA; Troy H. Patience, B.S.; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
10/1/99	Jun 01	N/A

Study Objective: A Military Health System-wide pathway for prenatal screening involving the combination of Materanl Serum Analyte Screeing and Fetal Anatomic Surveillance would simplify the process, lessen unintended risks while enhancing the cost effectiveness of prenatal screening in the Department of Defense. What is the optimal approach?

Technical Approach: The methodolies used in the current study would parallel that policy research approach with the augmentation of the existence of several years data within our region with two different approaches. This existing data will be analyzed using microeconomics to evaluate the cost cosequence of the variance between pathway. The initial phase, {pursued as continuing improvement policy research effort using evidence based data from MHS archived within Lead Agent (Health care delivery and epidemiology) involves the assessment of current state of the art regarding prenatal screening pregrams. Primary Methods in current study are: (1) Refine model of optimal prenatal screening program, (2) Microeconomic analysis of Model Systems in literature: cost analysis/theoretical cost consequence study comparison of optimal program, existing program, and other proposals, (3) Microeconomic analysis of existing data within the WRMC (recapitulates #2), (4) Transfer optimal version across WRMC, spread to other RMC with DoD and MHS, and (5) Measure improvement after introduction of Optimal Newborn Screening Pathway.

Progress: 5,000+ MAMC cases were reviewed as were 2,000+ cases at Bremerton. Cost-benefit analysis finds the maternal serum analyte screening protocol which requires informed consent following informed consent and basic obstetrical ultrasound prior to blood testing as the most efficient and cost-effective. While either method is good prenatal practice, the apparent cost-savings of the cheaper laboratory test is not realized in actual practice due to the increased cost of repeated tests.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/034 **Status**: Ongoing

Title: Return to Fitness After Implementation of Formal PSWP AD OB Focus Interdisciplinary Clinic and Discharge Education

Principal Investigator: MAJ Elizabeth G. Hancock, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): LCDR Amy L. O'Boyle, MC, USNR; LCDR Mary G. Battaglia, NC, USNR; COL Roderick F. Hume, MC; CPT Kim Whittington, MC; CPT Sandra L. Hernandez, MC; CPT Melissa V. Terry, MC; COL Byron C. Calhoun, MC, USAF; COL Robert E. Ricks, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Nov 01	N/A

Study Objective: Focussed Obstectrical care has proven beneficial for teen pregancy and enlisted pregnant soldiers by our group. We have re-introduced the concept of an interdisciplinary clinic whose focus is the active duty pregnant soldier (servicemember). All AD pregnancies will be offered streamlined access to this clinic for NOB, NOB limited US, Pelvic FLoor evaluation, COntinuing Obstetrrical care, Coordination of Ob Profile and PSWP participation. At Delivery individualized education for postpartum recovery and return to fitness help and return to duty clinics will be coordination specfically addressing the unique challenges facing the new soldier mom.

Technical Approach: Re-engineering of existing clinical resources into a focused interdisciplinary team approach to the obstetrical care for soldiers. Educational interventional trial for the imact of the PSWP OB Clinic upon the Ob Outcome and Return to Fitness for soldiers who participate compared to those who do not. (Historical controls and Non I Corps AD).

Progress: A list of active duty female soldier who delivered during FY01 has been generated; however, data collection for this study has not yet been initiated.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/013 **Status**: Completed

Title: The Effects of Hypoxia and Hypoxia with Acidemia on Placental Production of Interleukin-6 in the Isolated Dually Perfused Placental Cotyledon

Principal Investigator: CPT Christine M. Kovac, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; LTC Peter G. Napolitano, MC; MAJ Christina C. Apodaca, MC; MAJ Elizabeth G. Hancock, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Oct 00	12/10/2001

Study Objective: To determine the effects of hypoxia and hypoxia with acidemia on placental production of interleukin-6 (IL-6).

Technical Approach: This protocol will isolate and study 2 cotyledons from the placentas of 10 uncomplicated term pregnant patients. One cotyledon will have the maternal and fetal circuit perfused with a hypoxic and non-acidemic Hanks Balanced Solution at physiologic rate (4 cc/min). The other cotyledon will have the maternal and fetal circuit perfused with both a normoxic and non-acidemic Hanks Balanced Solution, also at physiologic rate. Effluents for IL-6 determination will be collected from the fetal circulations at hourly intervals. Perfusion will be maintained for four hours. Vascular tone in the fetal compartment will be continuously monitored throughout the experiment and recorded at 10-min intervals. These results will be compared to existing data from prior perfusion studies.

The second part of this study will also study 2 cotyledons each from 10 uncomplicated term pregnancies. One cotyledon perfused with a hypoxic and acidemic Hanks Balanced Solution at physiologic rate (4 cc/min). The other cotyledon will have the maternal and fetal circuit perfused with both a normoxic and non-acidemic Hanks Balanced Solution, also at physiologic rate. Again, effluents for IL-6 determination will be collected from the fetal circulations at hourly intervals. Perfusion will be maintained for four hours. Vascular tone in the fetal compartment will be continuously monitored throughout the experiment and recorded at 10-min intervals.

These results will be compared to existing data (both IL-6 concentrations and pressure recordings) from prior perfusion studies involving physiologic conditions and different perfusion rates.

Progress: Five placentas were studied. Conclusions: Fetal-placental vasodilation may be a compensatory mechanism to improve acidemic conditions. Unlike fetal hypoperfusion or fetal hyperoxia, fetal acidemia does not result in elevated placental cytokines. This suggests that the increased rate of cerebral palsy observed in acidemic fetuses is not due to placental production of the inflammatory cytokines IL-6 and TNF-a.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/096 **Status**: Ongoing

Title: The Effects of Hypoxia and Hypoxia With Acidemia on Placental Production of Adrenomedullin in the Isolated Dually Perfused Placental Cotyledon

Principal Investigator: CPT Christine M. Kovac, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; MAJ Christina C. Apodaca, MC; LTC Peter G. Napolitano, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Oct 00	5/22/2001

Study Objective: To determine if adrenomedullin levels are increased in placental cotyledons exposed to hypoxic and acidemic conditions.

Technical Approach: Cotyledons from a total of 20 placentas will be obtained from patients with uncomplicated term vaginal and caesarian deliveries. Maternal and fetal circulations of the cotyledons will be perfused with a solution of Hank's Balanced Salt Solution, bovine albumin, heparin and gentamicin. The 2 cotyledons from the first 10 placentas will be perfused, one with hypoxic solution and the other (control) with physiologic solution. Two cotyledons each from the next 10 placentas will be perfused, one with hypoxic and acidemic solution and the other (control) with physiologic solution. After perfusion of an intact fetoplacental circuit has been established, effluents will be collected at hourly intervals for four hours. These samples will be batched and stored for adrenomedullin quantitation, using an ELISA. Fetoplacental vascular tone will be continuously monitored throughout the experiment and will be recorded at ten-minute intervals. Data will be analyzed using repeated measure analysis of variance.

Progress: Fetal artery acidemia resulted in lower placental venous Adrenomedullin concentrations compare to the physiologic arterial pH with a significant difference noted at 4 hours ($p=0.05$). There was no difference in adrenomedullin concentration when comparing hypoxic conditions ($p=0.05$). There was no significant change over time for MMP-9 concentrations from baseline values for any of the conditions studies ($P>0.05$). Conclusions: While fetal acidemia and fetal hypoxia may cause fetal-placental vasodilation, it is not due to increased adrenomedullin, at least in the acute setting.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/030 **Status**: Ongoing

Title: Effect of Angiotensin II on Fetal Placental Perfusion Pressures in Preeclampsia Ex Vivo Cotyledon

Principal Investigator: CPT Christine M. Kovac, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; MAJ Elizabeth G. Hancock, MC; LTC Peter G. Napolitano, MC; COL Byron C. Calhoun, MC, USAF; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/8/2000	Dec 01	N/A

Study Objective: To use the dual perfused placental cotyledon model to investigate perfusion pressure changes induced by angiotensin II in fetoplacental vasculature of preeclamptic placentas pretreated with low dose acetylsalicylic acid, compared to controls.

Technical Approach: We will obtain 10 placentas from patients who meet strict criteria for preeclampsia, and 10 patients without preeclampsia who otherwise meet our inclusion and exclusion criteria. We will perfuse a cotyledon in our placental perfusion lab and measure the baseline perfusion pressure as well as the response of the cotyledon to a low and high dose of angiotensin II with and without treatment of low dose acetylsalicylic acid.

Progress: Three normal placentas have been run in this bench study with data collected from the last placenta. No preeclamptic placentas have been used in this study to date.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/065 **Status**: Ongoing

Title: Effect of Low-Dose Acetylsalicylic Acid and Angiotensin II on Fetal Placental Perfusion Pressures in the Preeclamptic Ex Vivo Cotyledon

Principal Investigator: CPT Christine M. Kovac, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; MAJ Elizabeth G. Hancock, MC; LTC Peter G. Napolitano, MC; COL Byron C. Calhoun, MC, USAF; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Jul 01	N/A

Study Objective: To use the dual perfused placental cotyledon model to investigate perfusion pressure changes induced by angiotensin II in fetoplacental vasculature of preeclamptic placentas pretreated with low dose acetylsalicylic acid, compared to controls.

Technical Approach: This study will obtain 10 placentas from patients who meet strict criteria for preeclampsia, and 10 patients without preeclampsia who otherwise meet our inclusion and exclusion criteria. Investigators will perfuse a cotyledon in the MAMC placental perfusion lab and measure the baseline perfusion pressure as well as the response of the cotyledon to a low and high dose of angiotensin II with and without treatment of low dose acetylsalicylic acid.

Progress: This study is currently collecting and running placentas for data collection. Three placentas have been run with data collected from the last placenta. Preeclamptic placenta data has not yet been collected.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/051 **Status**: Ongoing

Title: The Use of Transvaginal Sonography in Predicting Preterm Delivery in Patients with Preterm Contractions

Principal Investigator: CPT Christine M. Kovac, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): CPT Lisa M. Foglia, MC; MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF; Troy H. Patience, B.S.; MAJ Christina C. Apodaca, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Aug 99	2/27/2001

Study Objective: Primary: To investigate the accuracy of transvaginal cervical ultrasound in predicting the occurrence of preterm delivery, in patients presenting to Labor and Delivery with complaints consistent with preteen contractions. Secondary: We will also compare the abilities of transvaginal sonography and digital cervical exam in predicting preterm delivery within one week from examination.

Technical Approach: Despite recent advances in modem obstetric care, the incidence of preterm delivery has not decreased, and remains a leading cause of neonatal morbidity and mortality. Due to the refractory nature of preterm labor to effective management, early diagnosis is essential. Definitive diagnosis of legitimate preterm labor remains difficult, however, and results in over-diagnosis and treatment of what is most likely innocuous preterm contractions. Early cervical effacement and dilation may be subtle changes that may not be identified on digital examination. Transvaginal cervical ultrasonography is a precise, reproducible, modality that can provide an objective means by which to evaluate the cervix for early effacement and dilation. While studies have identified the utility of transvaginal cervical sonography in predicting preterm delivery, its role in assessing patients with preterm contractions is less clear. We propose to evaluate the utility of transvaginal cervical sonography in predicting subsequent preterm labor and delivery. We will also compare the efficacy of cervical sonography with digital examination in predicting the incidence of preterm delivery. We hope to identify a cervix length in a patient with preterm contractions, at which a physician can feel comfortable sending her home, with a 98 to 100 percent assurance that she will not deliver within the next week (eg, that cervical length which yields a 98 to 100 percent negative predictive value for preterm delivery within a week).

Progress: Seven subjects enrolled in this study at MaMC in FY01 for a total of eleven subjects enrolled. A review of literature shows this is still a good project to pursue. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/035 **Status**: Ongoing

Title: Comparison of Elective Labor Induction and Spontaneous Labor: A Randomized, Controlled Clinical Trial

Principal Investigator: CPT Penny L. Larson, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): CPT Robert H. G. Holland, MC; COL Paul N. Smith, MC; MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF; COL Romeo P. Perez, MC; Kathleen M. Judge; Roxanne Piecek; CPT Miguel A. Brizuela, MC; MAJ Christina C. Apodaca, MC; MAJ Bobby C. Howard, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Feb 00	11/27/2001

Study Objective: The purpose of this study is to compare cesarean section rates between patients delivered at term with a favorable cervix by elective induction with patients allowed to enter labor spontaneously. Additional maternal and neonatal outcomes will also be compared between the two groups.

Technical Approach: Between 38 and 39 weeks, subjects presenting with a favorable cervix and consenting to be in the study, will be randomized into either the labor induction group or the spontaneous labor group. Labor induction will follow MAMC Labor and Delivery protocol. Those subjects assigned to labor induction will be scheduled within 72 hours for admission including routine admission labs, establishment of intravenous access and fetal monitoring. Subjects in the control group will continue in the Obstetric Clinic until the onset of spontaneous labor. Their labor will also follow MAMC Labor and Delivery protocol. Subject information sheets for the health care providers managing the subjects will capture complete documentation of labor and delivery information. These data will be entered into a computer database for analysis and the data sheets will not be part of the subjects medical record. Subjects will also be asked to fill out a questionnaire, the Labor and Delivery Satisfaction Index, to assess satisfaction with their labor and delivery. Chi-square analysis will be used to assess for differences in nominal variables (epidural use, oxytocin use, chorioamnionitis, postpartum complications, NICU admissions, meconium stained amniotic fluid, neonatal or maternal complications, neonatal or maternal birth trauma). The paired Students t-test will be used to compare groups of continuous variables (cesarean section rate, vaginal delivery rate, operative vaginal delivery rate, duration of first and second stage of labor, maternal and neonatal lengths of stay, birth weight, Apgar scores).

Progress: 80 subjects enrolled during FY01 for a total enrollment of 156 overall, with no adverse events reported. Enrollment remains ongoing. Investigators are working on an interim data analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/055 **Status**: Ongoing

Title: Fetal Growth Curves in a Military Population

Principal Investigator: LTC Peter G. Napolitano, MC

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; MAJ Elizabeth G. Hancock, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC; COL Byron C. Calhoun, MC, USAF; MAJ Christina C. Apodaca, MC; CPT Dawn E. Elliot, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/28/2000	Dec 00	2/27/2001

Study Objective: To determine the range of in utero fetal weight throughout pregnancy using actual data, including birth weights, for a cohort at sea level using a database presently in place from the MAMC IRB approved protocol #96164 (natural history of gallbladder disease in pregnancy) and develop specific growth curves relevant to our population.

Technical Approach: Retrospective review of previously existing files and medical records. Data collected will include sonographic measurements of active duty women and military health care beneficiaries, plus maternal age, ethnic origin, smoking status, monthly income, neonatal gender and neonatal birth weight.

Progress: Ultrasound measurements were reviewed of over 1200 women longitudinally throughout their pregnancies. This data was used to compare with 6 different major ultrasound growth curves. Results: The Hadlock growth curve most closely matched that of our racially mixed, culturally diverse military community. The protocol was amended Feb 01 to include collection of ultrasound data already collected on these patients when admitted in labor. To date, data has been collected on only 18 patients. With the addition of a dedicated associate investigators, data collection should be completed under this amendment within the next six months.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/033 **Status**: Ongoing

Title: Train the Trainers Program: Introduction of Formal Curriculum and Exercise Program for Instructors I Corps/MAMC PSWP

Principal Investigator: MAJ Katherine M. Opitz, AN

Department: OB/GYN, MFM **Facility**: MAMC

Associate Investigator(s): MAJ Elizabeth G. Hancock, MC; COL Robert E. Ricks, MC; COL Roderick F. Hume, MC; SGT Steffie Castillo, USA; LCDR Mary G. Battaglia, NC, USNR; CPT Kim Whittington, MC; CPT Sandra L. Hernandez, MC; CPT Melissa V. Terry, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Sep 01	N/A

Study Objective: Introduction of formal curriculum of education and instructional preparation will enhance the motivation of PSWP participants, increase attendance and improve performance. This is team building and soldier development for an existing mandatory exercise program for active duty pregnant soldiers at Ft. Lewis. Goal is to enhance the training of soldier instructors (PSWP Trainers) and provide teaching aides to facilitate the PSWP.

Technical Approach: Formalize the exisiting training into modern photoimages of exercise program, instructors handbook, and learning aides. Train sets of instructors and monitor attendance, satisfication and performance (return to fitness) as measures of success.

62nd Med Group Ft. Lewis is primary agent for the Ft. Lewis/I Corps PSWP. MAMC Female Soldier Readiness Group supports with MFM Consultants and weekly PSWP Focus OB Clinics. Training program has been in existence for 16 years as an informal instructional package for the Female Fitness Volunteer Project (BAMC 82-84), (97th Gen Hosp 84-87, Duke Univesity Medical Center - Rational Approach to Exercise During Pregnancy for Postpartum Recovery (87-89), and MAMC (95-present). The PSWP is now entering its 3rd year. The soldiers have requested the opportunity for more formal instruction, certification and support to self-improve the PSWP program. Education interventional trial. Trainers will be instructed formally beginning December 2000. Formal Publication goal fro March 2001. Attendance records, formal and informal focus group methodologies will be used for satisfaction, and return to fitness will serve as outcome measures.

Progress: PSWP mandated program of I Corps; FSRG and D,MUT have reorganized a PSWP Clinic and 62nd Med Group, Fort Lewis, has requested support for formal instruction. Goal is publication and dissemination of program Investigator team. 183 Trainers received formal instruction under this protocol in FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/004 **Status**: Completed

Title: Correlation Between Maternal Height and Fetal Femur Lengths

Principal Investigator: MAJ Brian T. Pierce, MC

Department: OB/GYN, MFM **Facility**: MAMC

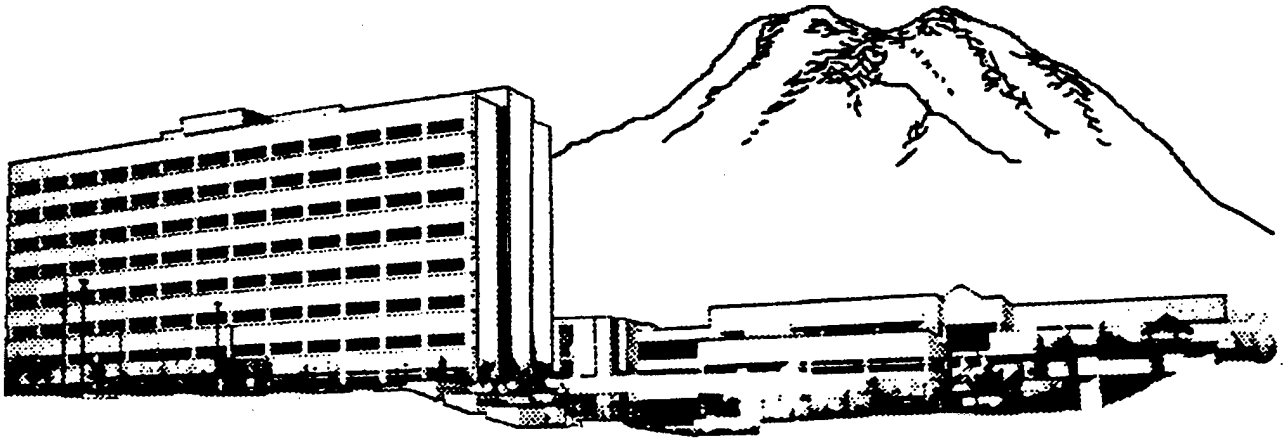
Associate Investigator(s): MAJ Elizabeth G. Hancock, MC; CPT Christine Kovac, MC; COL Roderick F. Hume, MC; LTC Peter G. Napolitano, MC; LTC Peter E. Nielsen, MC; COL Byron C. Calhoun, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Oct 01	N/A

Study Objective: To determine if a correlation exists between maternal height and fetal femur length for a cohort at sea level using a database presently in place from the MAMC IRB approved protocol #96/164 (natural history of gallbladder disease in pregnancy).

Technical Approach: Review previously existing files: American Institute of Ultrasound in Medicine accredited ultrasound clinic database, natural history of gallbladder disease protocol #96-164 and medical records to compare maternal height to fetal femur length in the second trimester of pregnancy in order to clarify the impact of maternal stature on the femur lengths.

Progress: Results from this study demonstrated an increased risk assessment for fetal Down Syndrome for women at earlier gestational ages, as well as for shorter women. The data was published in Obstetrics and Gynecology.



Detail Summary Sheets

Urogynecology, Department of Obstetrics/Gynecology

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/095 **Status**: Ongoing

Title: Voiding Patterns in Asymptomatic Military Women

Principal Investigator: COL Gary D. Davis, MC

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; Mary P. FItzgerald, MD

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	Feb 02	N/A

Study Objective: For a racially diverse sample of American military women without lower urinary tract symptoms, our study aims to determine normal ranges for the following micturition parameters: (1) Daytime voids, (2) Nighttime voids, (3) Fluid intake (cc), (4) Largest voided volume (cc), (5) Mean voided volume (cc), (6) Daytime hourly diuresis (cc/hour), (7) Nighttime hourly diuresis (cc/hour), and (8)Voids per liter fluid intake.

Technical Approach: At informational lectures on "female urinary health" given during periodic female utilization training sessions, we will ask 200 female active duty soldiers to volunteer to participate in a study to determine voiding patterns in asymptomatic military women. Active duty female soldiers, ages 18-65, will be asked to volunteer for the study if they consider themselves to have "normal lower urinary tract function" (i.e. they believe they neither retain or leak urine, are not troubled by the number of times they void daily, nor by the degree of urinary urgency they experience before voiding). Volunteers will be asked to complete a questionnaire about their bladder symptoms and relevant medical history. We will also record information about subjects' age, race, MOS (job description), parity, and hormonal status. We will ask that subjects record the time and amount of any fluids they drink for 24-hours. We will also give subjects a "top-hat" to place in their toilets and ask them to record the volume of urine they pass when they visit the bathroom. We will ask subjects that they do not alter their usual intake and voiding routine during the 24-hour study period. We will then ask subjects to put the "diary" into a supplied envelope and place it in the mail. The voiding diaries will be analyzed to determine subjects' total fluid intake, number of daytime and nighttime voids, largest voided volume, mean voided volume, diuresis per hour and voids per liter fluid intake. Demographic data will also be recorded, described and compared to subjects who did not return the voiding diary.

Progress: The original PI, MAJ Woodman, transferred to another institution following final approval of this study. The new PI, COL Davis, has not initiated work on this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/103 **Status**: Suspended

Title: Prevalence of Anal Incontinence in New Mothers Trial (PAINT)

Principal Investigator: COL Gary D. Davis, MC

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; James M. Nelson; LTC Ronald J. Place, MC; CPT Vanessa D. Dance, MC; COL Romeo P. Perez, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Aug 00	3/27/2001

Study Objective: To discover ways to prevent recognized and occult anal sphincter rupture and improve long-term primary closure outcome; thereby helping to prevent the development of future fecal and flatus incontinence.

Technical Approach: This study will investigate the occult anal sphincter disruption rate as a result of a variety of delivery types in primigravid women. The predominant method of episiotomy at MAMC is midline, which may affect the occult anal sphincter disruption rate. Primigravid women will be recruited from the OB/GYN clinic population and asked to participate postpartum. They will fill out a questionnaire, which will ask about their deliveries, their medical, surgical, colorectal histories and some randomization information. The investigator, who is blinded to the type of delivery, whether the patient had an episiotomy or tear, and other pertinent history, will perform an endoanal ultrasound of the anal musculature at approximately 6 weeks postpartum. Thickness and morphology of the internal and external sphincter and perineal body will be performed and recorded on a data sheet (attached). Those patients in which defects are found will be asked to return at approximately 6 months for repeat examination. At a later date, a second investigator will compare and verify the information requested in the patient questionnaire and obtain information about diagnoses, malposition, degree of episiotomy and extension, and labor augmentation. This will be recorded on the verification sheet. The patients will be identified by coded numbers, cross-classified to FMP/SS#. All data will be entered and analyzed using SPSS, Primer of Biostats, or similar statistical package. A small group of women (approximately 10) will be recruited to participate in an investigation on how the anal sphincter musculature morphology changes during the three trimesters of pregnancy. Each woman will undergo a series of three anal ultrasonographic examinations, one per trimester. These subjects would also the patient questionnaire, and the same data points would be obtained: Thickness and morphology of the internal and external anal sphincter and the perineal body. At the end of the trial, each woman will be asked if she would like to continue with the main study protocol, which would require a separate consent form.

Progress: During continuing review, the PI requested this protocol be suspended pending a possible change in study methods. Work on this study has not been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/016 **Status**: Ongoing

Title: The Degree of Pelvic Relaxation in a General Population of Female Subjects

Principal Investigator: LCDR Amy L. O'Boyle, MC, USNR

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; Steven E. Swift, M.D.; Susan Jackson, M.D.; Margie A. Kahn, M.D.; Val Y. Vogt, M.D.; Michelle M. Germain, M.D.; Michael T. Valley, M.D.; Mary Milner, Project Manager; Joseph Schaffer, M.D.; Marie Fidela R. Paraiso, M.D.; Deirdre R. Bland, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Sep 01	10/23/2001

Study Objective: To describe the degree of pelvic organ support in subjects presenting to nine geographically separate Obstetrics and Gynecology clinics requiring, as part of their visit, a routine pelvic exam to meet the requirements of annual gynecological health care and to evaluate the correlation of pelvic support to specific symptomatology associated with severe pelvic organ prolapse.

Technical Approach: Once subjects consent to be part of the study, during the standard pelvic exam a series of measurements to determine degree of pelvic relaxation will be performed as the subject performs a Valsalva or cough. These measurements will be recorded on a data collection sheet. Various biographical data will be collected and subjects will be asked 20 questions regarding their symptoms associated with pelvic prolapse. Data collected from this study will be used as an initial step in documenting the degree of pelvic organ support in a general population and analyze various suspected etiologic factors for the development of severe pelvic organ prolapse.

Progress: Thirty-nine subjects enrolled in this study at MAMC in FY01, for a total enrollment of 101. Data analysis has not yet begun as recruitment goals for MAMC are for 200/250 subjects. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/058 **Status**: Ongoing

Title: The Effect of Prenatal Pelvic Floor Exercises on Postpartum Pelvic Floor Function: A Two Phase Study

Principal Investigator: LCDR Amy L. O'Boyle, MC, USNR

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; LTC (Ret) Richard A. Sherman, MS; CPT Vanessa D. Dance, MC; CPT Lisa M. Foglia, MC; COL Robert E. Ricks, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/28/2000	Dec 01	3/27/2001

Study Objective: To determine whether the performance of pelvic floor strengthening and control exercises (Kegel exercises and electromyographic biofeedback from the pelvic floor) prior to giving birth for the first time (primiparous) can (1) effect pelvic floor function (as measured by POPQ and transanal sonography) and urodynamic testing (UCMG - urocystometrogram (2) decrease the occurrence and intensity of common pelvic floor problems occurring after delivery including pelvic organ prolapse, urinary incontinence, and fecal incontinence. Within this overall objective, to determine whether addition of home-use surface electromyographic (muscle tension) biofeedback devices to standard Kegel exercises will decrease the rate and intensity of problems.

Technical Approach: The first phase of this study will be a ten-subject open pilot to refine techniques. Each participant will perform the exercises for at least one month prior to delivery and at lease two months afterwards. Feedback about the procedures and patient attitudes will be evaluated. The second phase will recruit a total 60 first-delivery mothers to three different arms of the study. Each participant will randomly be assigned to: no prescribed pelvic floor exercises in addition to standard counseling (normal treatment control group), instructed Kegel exercises (practiced at home for at least one month prior to delivery) in addition to standard counseling, or instructed Kegel floor exercises and use of the Persist Pelvic Floor trainer (a biofeedback device) at home in addition to standard counseling.

Data from all three groups will be compared to determine the effect of supplemented instruction on postpartum pelvic floor function.

Progress: Ten subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/096 **Status**: Ongoing

Title: The Effects of Pregnancy and Delivery on Pelvic Organ Support in Nulliparous Pregnant Females

Principal Investigator: LCDR Amy L. O'Boyle, MC, USNR

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Elizabeth G. Hancock, MC; COL Byron C. Calhoun, MC, USAF; COL Gary D. Davis, MC; COL Robert E. Ricks, MC; CPT Melissa V. Terry, MC; LCDR Mary G. Battaglia, NC, USNR

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	Sep 03	N/A

Study Objective: The purpose of this study will be to measure the degree of pelvic organ support in nulliparous pregnant females throughout gestation and following delivery, and to assess the affect of obstetric variables on pelvic organ support.

Technical Approach: Consenting subjects will undergo an exam to assess stage of pelvic support as measured by the POPQ (Pelvic Organ Prolapse Quantification), and 3-D ultrasound of the pelvic floor anatomy will be performed in the first and third trimesters and post-partum visit (approximately 8 weeks). The POPQ is performed at the same time as a pelvic examination. Nine points in the vagina are measured, in centimeters, relative to the hymen, at the same time that the pelvic exam is performed. These nine points are as follows (GH, PB, Aa, Ba, Ap, Bp, C, D, TVL). GH and PB correspond to the genital hiatus and perineal body. These are measured immediately prior to the pelvic exam. Points Aa, Ba, Ap and Bp correspond to points on the anterior and posterior vaginal walls. Points C refers to the cervix, D to the posterior culdesac and TVL is the total vaginal length. Once derived, a stage is assigned 0, I, II, III or IV. Endoanal ultrasound involves inserting a small probe into the external anal canal. The presence of a break or defect of the circumferential internal and external anal sphincters is measured and quantified by degrees of separation. POPQ is routinely performed at the time of pelvic exam in the Pregnant Soldier Wellness Clinic. Endoanal ultrasound, and 3-D ultrasound are not routinely performed. Endoanal is routinely used however in evaluating patients post-partum who have had traumatic deliveries, and in all patients with symptoms of anal incontinence. At each evaluation, patients will answer questionnaires pertaining to symptoms of pelvic organ support, urinary symptoms and fecal symptoms.

Progress: 93 subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/106 **Status**: Ongoing

Title: MAMC Clinical Investigation Protocol: The Evaluation of Procedural Skills in the Repair of Episiotomy and Obstetrical Lacerations

Principal Investigator: LCDR Amy L. O'Boyle, MC, USNR

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): COL Gary D. Davis, MC; COL Robert E. Ricks, MC; LTC Peter E. Nielsen, MC; LTC George B. McClure, MC; LCDR John D. O'Boyle, MC, USN; MAJ Stephen D. Seymour, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	May 02	N/A

Study Objective: To evaluate the progress of Residents and Fellows in the practical repair of obstetrical lacerations by an objective Cumulative Sum Analysis (CUSUM), and to determine the number of repairs needed to attain competence.

Technical Approach: Fifty patients at Madigan Army Medical Center who have sustained third or fourth degree obstetrical lacerations will be asked to participate in the study. Second year residents will be instructed in the repair of these lacerations by senior faculty who will critique the residents technique according to protocol. Residents will be given a Cumulative Sum Analysis Score (CUSUM) at the conclusion of each R2 year, or the end of the study period. The number of repairs required to achieve acceptable performance as indicated by the CUSCM score will be tabulated for each resident. All subjects will be given detailed pelvic floor evaluation at their six weeks follow up evaluation to include Pelvic Organ Prolapse Quantification (POPQ) scoring, symptom score and evaluation of and sphincter integrity by transaral sonography. Residents will be given feed back from their examinations as to the integrity of their repairs.

Progress: Work on this study has not yet been initiated at MAMC due to time constraints of investigators.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/102 **Status**: Ongoing

Title: Comparison of Tolterodine and Oxybutinin for the Treatment of Urinary Incontinence Among Female Soldiers

Principal Investigator: LCDR Amy L. O'Boyle, MC, USNR

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; COL Milo L. Hibbert, MC; CPT Vanessa D. Dance, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; CDR (Res) Dennis A. Kelly, Ph.D.; LTC (Ret) Richard A. Sherman, MS; COL Gary D. Davis, MC; COL Robert E. Ricks, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Sep 01	9/25/2001

Study Objective: (1) To determine the relative effectiveness of Tolterodine and Oxybutinin in the treatment of urinary urge incontinence in female soldiers during exercise, (2) to determine incidence and severity of anticholinergic side effects of Tolterodine and Oxybutinin in female soldiers, (3) to determine whether Tolterodine and Oxybutinin have significant cognitive effects on work performance tasks, and (4) to determine changes in quality of life and work performance during treatment of urinary urge incontinence with Tolterodine and Oxybutinin.

Technical Approach: Sixty active duty female soldiers with urge incontinence will be recruited through a letter sent to all female soldiers at Fort Lewis, Washington. Each subject will initially undergo a standard evaluation of the lower urinary tract. The urodynamic evaluation will include uroflometry, with post-void residual urine volume measurement, retrograde provocative water cystometry, resting and stressed urethral axis determination, and direct visualization testing of fluid loss with stress. Urethral pressure profilometry with urethral closure pressures will also be performed. The subjects will then be evaluated one week later with ambulatory cystometric recordings. The subjects will be fitted with the UPS 2020 ambulatory measurement system. The intravesical and intravaginal pressures will be recorded with flexible 3mm microtip inserted 6cm from the urethral meatus and above the levator plate vaginally. The subjects will be given instructions to record events on the keyboard of the UPS 2020 ambulatory urodynamic recording system as they occur, and to proceed with the work or exercise which commonly produce their urinary incontinence. All subjects will be asked to complete a standard questionnaire which will assess the number and severity of the incontinent episodes they are experiencing. In addition they will complete a standard questionnaire which will assess job satisfaction and a standard quality of life survey. Once baseline values for the number and magnitude of detrusor contractions have been obtained, the subjects will be randomly assigned to one of three groups: Group I - Twenty subjects will receive placebos (one tablet twice a day), Group II - Twenty subjects will receive Oxybutinin (5mg twice a day), Group III - Twenty subjects will receive Tolterodine (1 mg twice a day). All subjects will be re-tested after one week of therapy by both stationary and ambulatory urodynamic studies. Comparison will be made among the groups as to the reduction of the amplitude and frequency of uninhibited detrusor contractions. The subjects will repeat the standard questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise. All subjects who still complain of urinary urge incontinence at the end of one week of therapy will have their medication increased as follows: Group I - Increased to two tablets twice a day, Group II - Oxybutinin increased to 5 mg three times a day, Group III - Tolterodine 2mg twice a day. All subjects will be re-tested at the end of the second week of therapy by both stationary and ambulatory urodynamics as well as with the cognitive test battery and the questionnaires. Comparisons will be made among the groups as to the reduction of the amplitude

and frequency of inhibited detrusor contractions. The subjects will repeat the standard questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise.

Progress: One subject enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/067 **Status**: Ongoing

Title: Outcomes of Overlapping Anal Sphincteroplasty in a Military Medical Center

Principal Investigator: MAJ Stephen D. Seymour, MC

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; LTC Ronald J. Place, MC; LTC George McClure, MC; MAJ Andrew Walter, MC, USAF; LCDR Shawn Menefee, MC, USN; Lt Col John R. Fischer, MC, USAF

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Jan 02	N/A

Study Objective: (1) Review the colorectal surgery literature to determine the patient population, pre-operative work-up, efficacy and complications associated with overlapping anal sphincteroplasty (OAS), (2) Comparison of the findings in the above literature review with what is seen in a cohort of patients evaluated in military urogynecology and colorectal practices and (3) Determine if adding OAS to complete, site-specific urogynecologic surgical repair affects outcome of OAS in terms of effectiveness or complications.

Technical Approach: The investigators have reviewed surgical logs over the investigative period and determined that approximately 60 overlapping sphincteroplasties have been performed at MAMC with or without adjunctive Urogynecologic procedures between 1JUL98 to 30JUN00. These patients' inpatient and outpatient charts will be scrutinized to allow the investigators to fill out patient data sheets. The individual patients that meet inclusionary criteria will be sent a patient questionnaire, starting 1FEB2001 which includes a validated patient symptom and satisfaction questionnaire. If not returned, the questionnaire will be sent again on 1MAR2001. Responders and nonresponders will be compared to determine if there are any differences between the groups. When the questionnaires are returned, the symptom data will be compared to the chart-derived patient data sheets. Step-wise logistical regression will be used to identify factors associated with poor outcome, early and late complications. his will be done for non-responders, Urogynecology and Colorectal primary surgeons, and military branch, as well, to identify any associated factors.

Progress: 32 subjects enrolled in this study at MAMC during FY01. Subject recruitment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/087 **Status**: Ongoing

Title: Retropubic Urethrolysis for the Management of Post-Urethropexy Urinary Retention and Voiding Dysfunction

Principal Investigator: MAJ Stephen D. Seymour, MC

Department: OB/GYN, UG **Facility**: MAMC

Associate Investigator(s): MAJ Patrick J. Woodman, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Feb 04	N/A

Study Objective: To describe objective and subjective symptomatologic and functional improvement in patients undergoing an abdominal approach to urethrolysis, when their obstructing procedure was a retropubic urethropexy (such as a Burch or Marshall-Marchetti-Krantz colposuspension). The data derived from our cohort will be compared to historical data published in the literature.

Technical Approach: Sequential women meeting selection criteria for partial bladder outlet obstruction with post-operative urinary retention (>100mL PVR), voiding dysfunction, and/or persistent de novo irritative voiding symptoms after urethropexy will be considered candidates for the study. Every portion of this study is the current standard of practice at Madigan. The fact that we will be testing people pre- and post-operatively makes this study an outcomes study for scientific merit, but not for human use concerns since we are already doing the following procedures and they are standard practice.

Demographic data will be collected, a comprehensive history and physical performed, as well as obtaining information about the obstructing procedure from the patient. This will be confirmed by retrospective inspection of all in-patient and out-patient notes pertinent to her complaint. A symptom survey will be obtained from the subject. Interventions will be recorded (medications, biofeedback, CISC, previous surgical attempts at urethrolysis).

Pre-surgical evaluation will consist of provocative multi-channel or video urodynamics, voiding pressure study, urethral profilometry, cystourethroscopy voiding diary and symptom questionnaire. If the clinical diagnosis of iatrogenic bladder outlet obstruction is made, the subject will be ask to enroll in the study. Technique of retropubic urethrolysis has been described elsewhere21. An omental fat pad, when available, or SeprafilmTM (Genzyme Surgical Products; Cambridge, MA) will be interposed between the urethra and pubic bone, to limit reformation of post-surgical scarring. All patients will be counseled of the possibility that urethral hypermobility could return after urethrolysis.

Post-surgical evaluation will consist of cystourethroscopy, voiding diary, symptom questionnaire and serial post-void residual measurements. Each subject will also be given a patient satisfaction questionnaire (Madigan Urethrolysis Questionnaire (Attachment #2)). This patient satisfaction questionnaire is the only thing that will be done differently when subjects are compared to patients who do not participate in the study. Interval pre- and post-operative variables will be analyzed using the paired-t test.

Symptom/quality-of-life questionnaire (IIQ-7 & UDI-6) data will be analyzed by Wilcoxson signed ranks test. Demographic data and parameters measured either only pre- or only post-operatively will be analyzed by descriptive statistics.

Progress: Ten subjects enrolled in this study at MAMC during FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/088 **Status**: Ongoing

Title: Incidence of Occult External and Internal Anal Sphincter Defects in Patients Presenting with Rectocele

Principal Investigator: MAJ Stephen D. Seymour, MC

Department: OB/GYN, UG **Facility**: MAMC

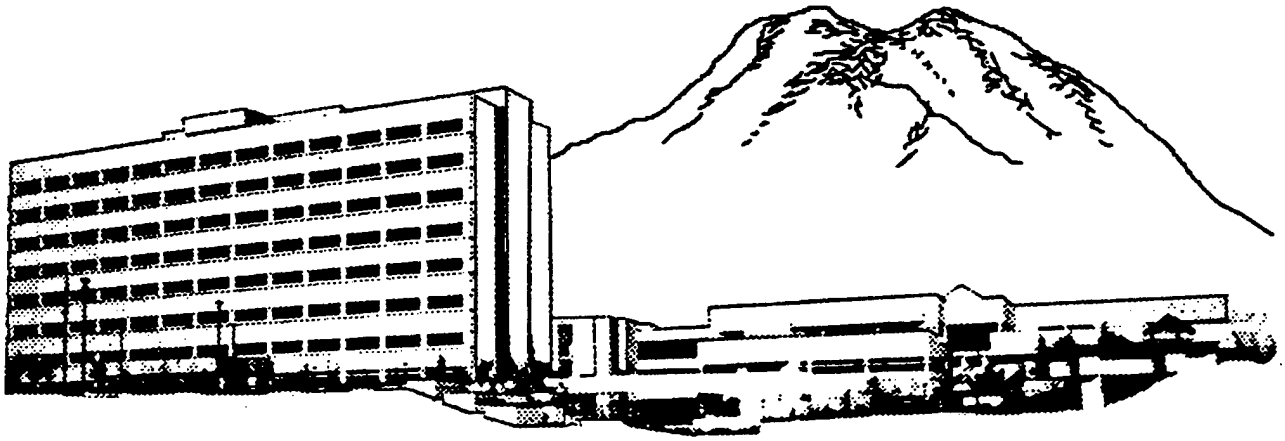
Associate Investigator(s): LTC Ronald J. Place, MC; COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; LCDR Amy L. O'Boyle, MC, USNR

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Jun 01	N/A

Study Objective: To determine the incidence of unrecognized internal and external anal sphincter defects in patients evaluated for rectocele.

Technical Approach: Patients will be identified and asked if they desire to participate in the study. A thorough medical history will be obtained with emphasis on anal incontinence. Study participants will undergo thorough physical examination according to the International Continence Society's system for grading pelvic organ prolapse. Patients will then have an endoanal ultrasound performed to determine the status of anal sphincters. Results of the endoanal ultrasound will be evaluated on the basis of the incidence of occult anal sphincter defects in patients found to have a rectocele on examination. This information will then be related to the stage of pelvic organ prolapse, type of anal incontinence if present, gravidity, parity, the number of vaginal deliveries, fetal weights and other factors associated with delivery in an attempt to determine any correlations.

Progress: Eight subjects enrolled in this study at MAMC during FY01. Subject enrollment continues.



Detail Summary Sheets

Department of Pathology

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/003 **Status**: Completed

Title: Can a Strategy be Developed for More Cost-effective Ordering of Cardiac Injury Marker Assays, Part II

Principal Investigator: CPT Jude Abadie, MS

Department: Pathology **Facility**: MAMC

Associate Investigator(s): None.

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Feb 01	9/25/2001

Study Objective: To develop a cost-effective strategy and outline criteria for ordering cardiac injury marker (CIM) assays in patients that present with chest pain.

Technical Approach: This study is a retrospective comparison of MAMC's CIM ordering patterns before and after institution of the newly developed algorithm, initiated 1 Jul 00. 16,935 CIM assays performed on 2,386 patients during 1999 will be compared to CIM assays performed during theassessment period of 1 Jul 00 through 1 Feb 01. Pre- and Post-algorithm graphical data will be compared to assess cost per patient, number as well as type of CIM assay conducted per patient, and overall expenditure.

Progress: Proper assessment of Cardiac Injury Markers can lead to rapid and accurate diagnosis of AMI and subsequently save lives. Based on CIM testing analysis and on reviews of several prospective studies, this retrospective study outlines a specific strategy to make CIM testing more cost-effective.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/132 **Status**: Ongoing

Title: Methylmalonic Acid (MMA) Level in Serum of Normal population: Important Diagnostic Tool for Evaluation of Cobalamin (Vitamin B12) Deficiency at Tissue Level

Principal Investigator: LTC David K. Turgeon, MC

Department: Pathology **Facility**: MAMC

Associate Investigator(s): CPT Ileana Hauge, USAF; Mark Wener, MD; COL Jerome B. Myers, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/25/2001	Nov 01	N/A

Study Objective: Evaluate MMA serum levels in a normal female population by GC/Mass/Spec. Compare these results to breast cancer patients positive for CA27-CA29 markers that have had their MMA levels measured by standard ELISA techniques.

Technical Approach: In this study only the gender (females, for example) and the age group (35-45 year old female population, for example) will be included. Frozen serum leftovers, previously tested for breast cancer tumor markers CA27-CA29 from the Immunology laboratory at the University of Washington in Seattle, will be tested for the MMA level in the same manner. Results obtained from the random normal population study will be compared with the results from the CA27-CA29 random population to see if there is any major difference between the two groups. Because methylmalonic acid is a validated indicator of tissue level of vitamin B12, the high CA27-CA29 results should test high for MMA. This study expects to obtain higher levels of MMA in the CA27-CA29 population than the normal random one. The serum samples will be tested only after the method is validated as acceptable at the University of Washington Medical Center, Seattle, WA.

Progress: This study recently received approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/134 **Status**: Completed

Title: Detection of Genotypic/Phenotypic Abnormalities in the Mucosal Lymphoid Tissue of Celiac Disease

Principal Investigator: CPT Jeffrey A. Vos, MC

Department: Pathology **Facility**: MAMC

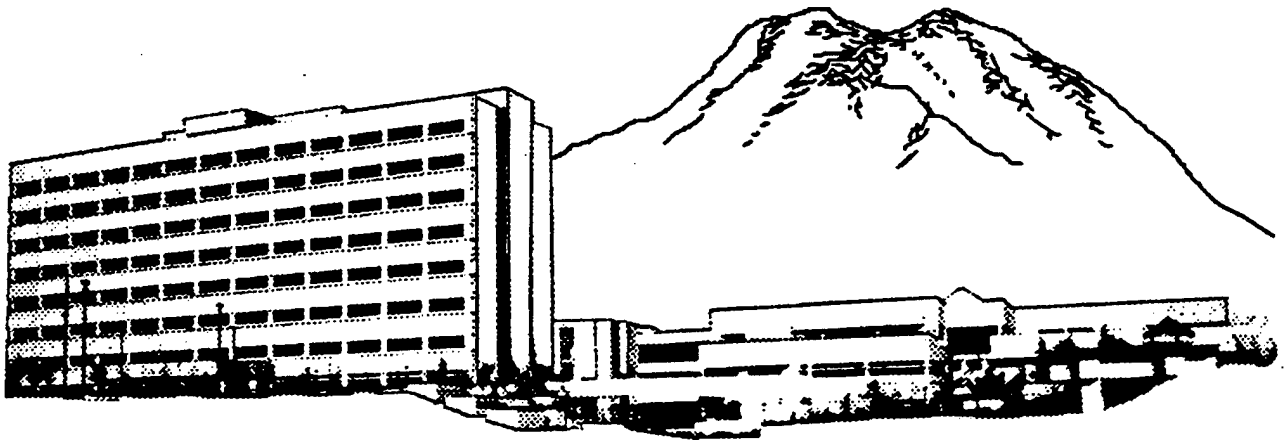
Associate Investigator(s): James E. Coad, M.D.; LTC Mark D. Brissette, MC; COL Jerome B. Myers, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Dec 00	8/28/2001

Study Objective: To determine if immunophenotypic aberrations and/or clonality (findings that would suggest the presence of a low grade lymphoma) can be identified in the T lymphocytes of small bowel biopsies of patients with celiac disease.

Technical Approach: This retrospective, descriptive study will look at paraffin-embedded tissue blocks from patients who have had duodenal biopsies with a histologic interpretation of "celiac sprue" or "changes consistent with celiac sprue". Biopsied tissues from the confirmed "celiac sprue" subjects will be compared to normal tissues by doing an immunohistochemical analysis and a T cell gene rearrangement analysis. Conclusions may be used to help establish markers for the detection of low-grade malignant conditions in celiac disease.

Progress: The project essentially found that celiac sprue, or at least the patients labeled with this disease, based on small bowel biopsy findings, is a heterogeneous disease with respect to the inflammatory cells seen in the mucosa. Intent of this study was to attempt to find those patients that were more prone to have some of the late complications of the disease, namely lymphoma, by looking at the phenotype and genotype of the T cells in the small bowel biopsies. While evidence was not found that would definitely predict lymphoma (ie. no genetypic abnormalities), variations in the T cell phenotypes were found: the majority were consistent with what would be expected for celiac disease, a few were essentially normal (as if they did not have any disease at all), a few had a variant phenotype which mimicked the phenotype most commonly seen in the lymphoma that occurs in the setting of celiac disease (ie. Enteropathy-associated T-cell lymphoma). The implications of these findings are not certain until they are compared to the clinical data and patient outcomes, however they are a step toward better understanding the pathogenesis of this disease and hopefully will supply useful prognostic information or therapeutic guidance when these patients are first diagnosed and biopsied.



Detail Summary Sheets

Department of Pediatrics

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/126 **Status**: Ongoing

Title: Ibuprofen Oral Provocation Challenge in Children with Asthma

Principal Investigator: COL Edward R. Carter, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): CPT Mitchell Moffitt, MC; COL Donald R. Moffitt, MC; ;

Start Date:	Est. Completion Date:	Periodic Review:
8/28/2001	Sep 02	N/A

Study Objective: To estimate the prevalence of ibuprofen-induced bronchoconstricition in children with mild to moderate asthma (please see Appendix E for definitions of mild and moderate asthma) and identify those clinical variables or characteristics that may correlate with ibuprofen-induced bronchoconstriction, to include age, sex, history of nasal polyps, history of sinusitis, history of eczema, history of allergic rhinitis, asthma medications, history of prior NSAID use, and asthma severity.

Technical Approach: This study will be performed jointly by investigators at the Pulmonary Division of Children's Hospital, Seattle and the Department of Pediatrics at Madigan Army Medical Center. The study is designed to determine the prevalence of ibuprofen-induced bronchospasm in children with mild or moderate asthma. Approximately 50 children with asthma, ages 6-18 years, will be enrolled at Madigan and another 150 at the Seattle Children's Hospital in this prospective, double-blind, placebo control, crossover study. The inclusion criteria are: a diagnosis of mild or persistent asthma, a baseline FEV1 > 70% of the predicted value, and the ability/willingness of the patient to swallow capsules; exclusion criteria are: not being able to swallow capsules, taking a leukotriene inhibitor for their asthma, and experiencing increased asthma signs/symptoms. Patient's asthma must be stable and well controlled. Children who have mild or moderate asthma, based on standard criteria, will be asked to fill out an asthma questionnaire and participate in two separate pulmonary function test sessions, each lasting approximately 4.5 hours. During these study sessions patients will perform baseline spirometry and then ingest by mouth either capsules containing 100mg of ibuprofen (10 mg/kg up to a maximum dose of 600 mg) or identically appearing placebo capsules. Patients will then perform spirometry at , 1, 2, and 4 hours post-ingestion of the capsules. Patients will return to the laboratory 2-7 days later for the second session. The order of administering placebo and ibuprofen will be randomized. Patients will be monitored and examined by a physician during all study time points. Precautions will be taken to ensure prompt and effective treatment of bronchospasm. Once patient's FEV1 decreases to < 80% of the baseline value, on that study day sessions will be stopped, and no further testing will be done. Primary outcome measure is the proportion of patients who meet the criteria for ibuprofen-induced bronchospasm. The criteria to be used to determine this is a decrease in FEV1 post-ibuprofen ingestion of 20% from baseline without a decrease in FEV1 on the placebo study day.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/035	**Status**: Completed

Title: Neurodevelopmental Concerns About NICU Graduates: A Parental Needs Assessment

Principal Investigator: LTC Beth E. Davis, MC

Department: Pediatrics	**Facility**: MAMC

Associate Investigator(s): Rebecca S. Miltner, RNC, MS

Start Date:	**Est. Completion Date:**	**Periodic Review:**
1/1/2001	Nov 01	N/A

Study Objective: Parental Needs Assessment of Neurodevelopmental concerns about NICU graduates. Ability to focus care directed to parental needs.

Technical Approach: Survey tool to be mailed by NICU Secretary to all NICU Graduates with letter explaining voluntary nature of completion of anonymous needs assessment.

Progress: This study mailed out 100 surveys during FY01, with 70 returned. Findings: Parents have concerns about neurological development regardless of NICU course. Parents feel their concerns can be met by their child's primary care physician. Some parents are interested in further developmental assessment and/or attending a hi-risk neonatal clinic.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/086 **Status**: Completed

Title: Age of Acquisition for Adolescent Autonomy Skills in Individuals with Myelomeningocele

Principal Investigator: LTC Beth E. Davis, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): COL William O. Walker, Jr., MC; David Shurtleff, MD

Start Date:	Est. Completion Date:	Periodic Review:
4/24/2001	Jul 01	N/A

Study Objective: The specific aim of this study is to describe age of acquisition timelines for normal adolescent autonomy skills in a MM population aged 12- 21 years, stratified by severity of lesion.

Technical Approach: The existing data from 165 adolescents with a primary diagnosis of myelomeningocele (MM) attending a regional multidisciplinary clinic between 12/90 and 12/99 will be reviewed from a prospectively collected clinical data base of 1054 children with MM. All subjects will be assigned to a severity group based on their MM motor lesion level based on physical and neurologic exam findings. SPSS will be used to analyze descriptive data (severity level of lesion and timing of specific skill achievement)and for Generalized Estimation Equation, a form of regression analysis, to provide 20th%ile, 50%ile, and 80%ile ages of acquisition for each autonomy skill stratified by severity groups. The ultimate goal of this analysis is to describe age of acquisition timelines for typical adolescent autonomy skills in a regional cohort of adolescents with myelomeningocele, aged 12 to 21 years, stratified by severity of lesion.

Progress: Adolescents with myelomeningocele acquire autonomy skills significantly later than their non-disabled peers. When adjusted for hygiene independence, adolescent autonomy skill progression is not related to degree of physical impairment. Future studies should include qualitative analysis of participants who consistently acquire skills at earlier ages to identify factors associated with successful transition through adolescence.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/042 **Status**: Completed

Title: Does Breast-feeding Decrease Amount of Antibiotics or the Exposure to Second and Third Line Antibiotics in Infants Less Than a Year of Age?

Principal Investigator: LTC Mary P. Fairchok, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): CPT Michelle S. Flores, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 01	1/23/2001

Study Objective: To determine if breast-feeding in infancy decreases the amount of antibiotics prescribed or number of second and third line antibiotics prescribed in the first year of life.

Technical Approach: This study will gather information on healthy infants and whether or not the mode of feeding (breast versus bottle) has any effect upon the number of days on antibiotics or the use of second and third-line antibiotics. A preliminary pilot will be done to determine sample size. At the 6 month and 12 month well child visits parents will be questioned as to modes of feeding and use of antibiotics. Other possible confounding variables will also be assessed to include daycare use and smoking. CHCS will then be searched for antibiotics prescribed and charts will be reviewed for any emergency room or spectrum clinic visits. Infants will be compared at the 6 month and 12 month periods, and chi square tests will be used to determine if differences in number of days of antibiotics are significant. In addition, the types of antibiotics will be recorded to determine if mode of feeding affects the number of second and third-line antibiotics prescribed. Infants will be grouped into exclusively breast fed (less than one bottle per day for greater than or equal to 13 weeks), exclusively bottle fed (no breast feeding), and partially breast-fed (termination of breast-feeding prior to 13 weeks and initiation of bottle feeding or any combination of breast-feeding and bottle). Antibiotic use will be determined via reviewing the CHCS system and number of days and type of antibiotic prescribed will be recorded. In addition, charts will be used to look for any antibiotic use which may have been prescribed via the emergency room or spectrum clinic since these often are not entered into the CHCS system. Charts will also be randomly reviewed to determine if parental recall is reliable. Groups will be compared statistically at the 6 month period and 12 mos. Comparisons of number of days on antibiotics and number of second and third line antibiotics will be made between groups using chi-square. ANOVA analysis will then be used to assess affects of confounding variables such as daycare use and smoking. A preliminary pilot prior to initiation of study will be done with about 30 subjects for purposes of determining what amount of days and what sample size will be necessary for statistical significance with p values less than 0.05. Sample size will then be determined and study will be adjusted as necessary.

Progress: Data collection for this study was completed during FY00. Analysis and presentation were done during FY01. Overall, antimicrobial use among infants was high with 47% having had at least one course of antimicrobials. Antimicrobial use, second line antimicrobial use, and mean number of days on antimicrobials all showed a statistically significant difference at both the 6 month and the 12 month visits between breastfed and non-breastfed infants. Breastfed infants at both of these ages had fewer courses and less second-line antimicrobials. These findings suggest that breast-feeding decreases exposure of infants to antimicrobial therapy throughout the first year of life. In addition, breast-feeding also decreases use of second-line andimicrobials in these infants.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/100 **Status**: Completed

Title: Prevalence of Undiagnosed Chlamydia in ROTC Cadets

Principal Investigator: LTC Mary P. Fairchok, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): LTC Thomas M. Martinko, MC; CPT Thomas Sutton, MC; MAJ Thomas J. Duncan, MC; COL James E. Cook, MC; Mr. Steven Hale, P.A.

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	Jul 02	N/A

Study Objective: To detect the prevalence of unsuspected chlamydia infection in a population of healthy young active duty adult males, determine risk factors for unsuspected infection with chlamydia, and to conduct a cost assessment of routine chlamydia screening in this population.

Technical Approach: The study will address the prevalence of genital chlamydia trachomatis infection in healthy adult male ROTC cadets presenting for summer camp to Fort Lewis. The study will also determine the cost effectiveness of a screening program for chlamydia trachomatis infection in this population, and risk factors associated with the infection. Upon arrival to MAMC for their scheduled physical exam, subjects will be recruited to the study. When a subject decides to enter the study, they will be consented and requested to provide 30cc of first void urine (with at least an hour interval since the last urination) in a provided container. Subjects will fill out a brief questionnaire. The urine sample and questionnaire will be identified by a secure coded number only. Urine will be frozen in the MAMC lab shipping section until it can be sent by courier (Mon, Wed and Fri) to the Washington State Dept of Health Lab in Shoreline, WA for DNA amplification by ligase chain reaction assay for chlamydia trachomatis. Subjects with a positive test for chlamydia trachomatis will be notified and arrangements made for them to be seen by Mr. Steve Hale at the Preventive Medicine clinic at old MAMC. They will have a contact interview at that time, evaluation for other sexually transmitted diseases as warranted, and be treated with 1 gram of azithromycin. Subjects intolerant of or allergic to azithromycin will be treated with doxycycline at 100 mg po bid for 7 days. Age, number of sexual partners and prior history of STD will be analyzed using Chi -square analysis and Fisher's exact test to determine risk factors for infection.

Progress: 1443 cadets enrolled in the study and completed questionnaires. 1252 urine samples were available for analysis. 31 samples were positive yielding a 2.48% (1.6-3.3% 95% CI) prevalence rate of chlamydia infection. Only 2/31(6.4%)reported any symptoms. There were no significant differences between infected and uninfected cadets in age,recent new partners, number of partners in past 12 months, prior history of STD, geographic location or reported condom use. There were significant differences between infected and uninfected groups related to racial background (5.7% prev in African Americans vs 1.5% Caucasian, p=0.001),and partner with a history of having an STD (8.1% prev with history versus 2.1% without, p=0.001).

Conclusions: This is the largest prevalence study to date of chlamydia infection in male college students.The prevalence rate in our population was lower than in other studies. 93.6% of the infections were asymptomatic, which is much higher than previously suspected. College based health programs targeting STDs might benefit from increased effort in targeting male students with one of these risk factors and in aggressive contact tracing of students diagnosed with an STD, rather than relying on symptomatic presentations.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 90/092 **Status**: Ongoing

Title: Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

Principal Investigator: LTC Mary P. Fairchok, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): COL James S. Rawlings, MC; MAJ Thomas A. Perkins, MC; LTC Joanna C. Beachy, MC; COL Marvin S. Krober, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/20/1990	Sep 91	7/25/2000

Study Objective: To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

Technical Approach: Technical Approach: This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children. This analysis will be done in 120-150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

Progress: No patients enrolled in FY01. This protocol remains open to patient enrollment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/118 **Status**: Completed

Title: The Efficacy of Duct Tape versus Cryotherapy in the Treatment of Verruca vulgaris (the common wart)

Principal Investigator: CPT Dean Focht, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): LTC Mary P. Fairchok, MC; Carole A. Spicer

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	July 01	9/25/2001

Study Objective: To determine if application of duct tape is an effective treatment of common warts in comparison to standard treatment with cryotherapy.

Technical Approach: This study will enroll approximately 100 subjects to one of two treatment arms: cryotherapy or duct tape. Subjects who receive cryotherapy will have their warts frozen and be instructed to debride the wart between visits. The subjects will return every two weeks to assess progress and receive further cryotherapy. If the wart is not gone within four months, subjects will be referred to dermatology for further treatment.

The duct tape will be applied in the clinic and left on for six days at which time the tape will be removed and the wart debrided. The next morning, duct tape will once again be applied to the wart. Cryotherapy will be initiated in the clinic and if the wart is not gone in four months, the subject will be referred to dermatology. Results will be compared to assess relative efficacies.

Progress: This study has been reported as completed, 10 Oct 01. 61 children enrolled in this study at MAMC during FY01. 10 children who were not available for follow-up were dropped from the study. Of the children who completed the study, 25 were in the cryotherapy arm and 26 in the duct tape arm. Results: There was no statistical difference in the mean ages, baseline size of the warts, and location of the warts between the two groups. Effectiveness of the therapy was statistically significant between the two groups with 22/26 (84.6%) of the duct tape arm having complete resolution of their warts versus 15/25 (60%) of the cryotherapy arm ($p=0.048$). The majority of warts that resolved with tape occlusion disappeared within 28 days of initiating therapy (16/22, 72.7%). No major complications were noted, with the most frequent complaints being difficulty in keeping the tape on and minor skin irritation. Conclusions: Based upon our data, occlusion therapy with duct tape was more effective than standard cryotherapy in the treatment of verruca vulgaris. Cryotherapy is also more labor intensive for nursing personnel, requires multiple clinic visits, and can be anxiety provoking for young children. This study indicates that duct tape is a safe, inexpensive, and readily available therapy for the treatment of the common wart.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/043	**Status**: Completed

Title: Public Knowledge of Current American Fat and Cholesterol Nutritional Guidelines

Principal Investigator: CPT Monica D. Murdoch-Cuenca, MC

Department: Pediatrics	**Facility**: MAMC

Associate Investigator(s): LTC Robert A. Puntel, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
2/27/2001	Mar 01	N/A

Study Objective: Determine public knowledge of the current fat and cholesterol guidelines as outlined by the National Cholesterol Education Program.

Technical Approach: This is a descriptive study utilizing anonymous surveys. Approximately 1000 questionnaires will be distributed to parents and adolescents greater than 12 years old in the Pediatric and Adolescent Clinics.

Progress: 321 questionnaires were completed by parents in the pediatrics clinic and returned during FY01. Conclusion: The majority of people do not understand the NCEP fat and cholesterol guidelines for the Nutrition Facts labels nor do they follow the food guide pyramid for themselves or their children. Simplification of the Nutrition Facts label should be considered as the majority of people surveyed cannot interpret the information on packaged foods.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/028 **Status**: Completed

Title: Localization and Quantification of Apoptosis in Human Placental Tissue

Principal Investigator: CPT Robert J. Organ, MC

Department: Pediatrics **Facility**: MAMC

Associate Investigator(s): Steven X. Skapek, MD; MAJ Mark P. Burton, MC, USAF; Laura S. Martin, M.D.; COL Byron C. Calhoun, MC, USAF; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Nov 01	N/A

Study Objective: The purpose of the current study design is to adopt an already established immunohistochemical technique used for the study of apoptosis, and determine if it is possible to apply this same technique to the study of human placental tissue. Once established, placental tissue obtained from the Maternal Fetal Medicine IRB approved Placenta protocol or other disposable placental tissue will be examined. It will then be determined if the frequency and or location of apoptotic nuclei, and possibly other markers of activated cellular activity, can be correlated with normal and pathological fetal-maternal states.

Technical Approach: Tissue samples from 5 normal pregnancies and from 5 each maternal-fetal pathological states will be obtained. Each sample will be embedded in paraffin and then stained using the TUNEL method to determine the relative number of apoptotic nuclei. Results from controls and pathological samples will then be compared to determine if the relative amount of apoptosis has predicitve value for placental pathology and placental tissue viability. Other markers of apoptosis may also be examined to determine if they too can be used as predictors of apoptosis and placental health.

Progress: Placental tissue was anonymously collected from normal control, preeclampsia and complicated pregnancies. Coded tissue blocks were submitted for fixation and thin section. The PI blinded to clinical status used the methods modified from Gavrieli for Terminal Deoxynucleotidyl Transferase (TdT)-mediated dUTP nick end labeling (TUNEL) to label apoptotic placenta nuclei. Apoptotic indices were compared among cohorts.

Results: Complicated preeclampsia with oligohydramnios demonstrated significantly increased apoptotic index (19.7 +/- 9.8, p=.0004) than either preeclampsia (8.8 +/- 4.9) or normal control (5.5 +/- 3.0). Conclusion: The apoptotic index predicts severity of maternal disease. Previous work from our lab has shown differential gene expression for cell cycle regulators in pregnancies complicated by oligohydramnios. The apoptotic index may be an effective predictor of perinatal neurologic susceptibility (cerebral palsy) measuring the phenotypic expression of accelerated placental senescence related to severity of maternal disease.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/134	**Status**: Ongoing

Title: Establishment of a Primary Myocyte Cell Culture Line from Dystrophin-deficient (mdx) Mouse Embryonic Fibroblasts (Mus musculus).

Principal Investigator: CPT Robert J. Organ, MC

Department: Pediatrics	**Facility**: MAMC

Associate Investigator(s): Steven X. Skapek, MD

Start Date:	**Est. Completion Date:**	**Periodic Review:**
9/19/2001	Sep 04	N/A

Study Objective: Establish primary myocyte cell cultures from mdx mouse embryonic fibroblasts (MEFs) with the DNA construct pBABEpuroMyoD, and wild type mdx MEFs. ii. Demonstrate a dependent relationship in dystrophin- deficient myocytes between the activation of NF-kB, the aberrant expression of cyclin D1, and the presence of apoptosis.

Technical Approach: This study proposes establishing primary myocyte cell cultures from mdx and wild type Mouse Embryonic Fibroblasts (MEF). It has already been established that it is extremely difficult to obtain a pure population of mdx myoblasts in culture; others have demonstrated that cultures of mdx myoblasts from neonatal to adult mice don't grow properly51,52,53,54. To overcome this problem we propose establishing mdx mouse embryonic fibroblasts in culture, a procedure already well established (see attached methodology). 6 mice will be purchased; 3 mdx and 3 controls. The 2 females of each group will be impregnated, and then at the appropriate time the females will be euthanized and the embryos will be harvested for embryonic fibroblasts. We will then transduce these cells with a gene that will cause them to start differentiating into myoblasts. The transduction of the embryonic fibroblsats will produce a cell line of primary myoblasts from both the wild type mouse and the dystrophin-deficient (mdx) mouse.

Progress: This study recently received final IACUC approval. Work on this protocol has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/104 **Status**: Ongoing

Title: Newborn Infant Speech Perception

Principal Investigator: MAJ Randall C. Zernzach, MC, USAF

Department: Pediatrics **Facility**: MAMC

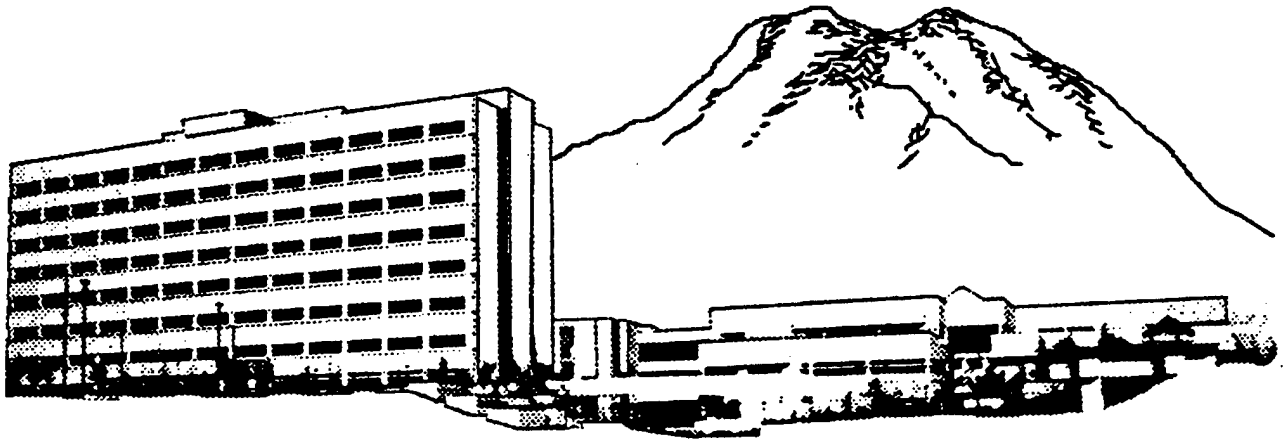
Associate Investigator(s): Lori A. Loan, PhD; Christine Moon, PhD

Start Date:	Est. Completion Date:	Periodic Review:
6/13/2001	May 03	N/A

Study Objective: Characterize the effect of experience on typically developing newborn infants' perception of speech and language.

Technical Approach: The current proposal for research is for a 2-year study of newborn infant discrimination of familiar and unfamiliar speech sounds. Three experiments will comprise the study. The first will test newborns' ability to discriminate mother's voice from a stranger voice when the speech samples are brief. The second experiment will examine whether infants respond preferentially to their mother's native language when the samples are brief. In the third experiment, infants will be tested for their ability to discriminate brief vowel sounds from among well- and poorly-formed exemplars in English. Each of the three experiments will require data from 80 participants for a total of 240 infants. Because the attrition rate for completion of the 10-minute session is likely to be about 35%, it is expected that approximately 360 infants will be recruited and that 120 will not complete the experiment. Prospective participants will be 1-5 days old and will be identified from hospital records. Eligibility will be based upon criteria that indicate typical, uncomplicated newborn development. Parents will be contacted in their hospital rooms by the experimenters who will present the study and obtain signed, informed consent. Infants will be transported to a quiet area near the newborn unit for a 20-minute session. A pacifier that is connected to a pressure transducer will be placed in the infant's mouth. If the pacifier is accepted, headphones will be placed over the infant's ears. After a 1-minute baseline period to measure sucking pressure, computer-controlled sounds at conversational levels of intensity will be presented for 9 minutes, contingent upon infant sucking pressure. Frequency of sucks during particular stimuli will be the dependent measure. Data analysis will be based upon a comparison of sucking frequency during different sounds. Results of the experiments will be presented at professional conferences and submitted as articles for publication in professional journals.

Progress: In the four months since approval, instrumentation of the infant speech perception apparatus has been completed and the equipment was moved into the hospital. Instrumentation took longer than anticipated due to the need for specialized computer programs and difficulty finding a programmer skilled in both the particular computer language and electronics. Approval of the process for cleaning the pacifiers was obtained. The nursing staff on the Mother Baby Unit was informed of details of the study in two in-service presentations. Space in which to conduct study sessions and store equipment was identified and the study is now ready to begin recruiting participants and collecting data.



Detail Summary Sheets

Physical Therapy, Physical Medicine & Rehabilitation Service

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/030 **Status**: Completed

Title: Physical Therapy Treatment Effectiveness for Osteoarthritis of the Knee: A Prospective, Randomized, Controlled Comparison of Supervised Clinical Exercise and Manual Therapy Procedures versus A Home Exercise Program

Principal Investigator: COL Nancy E. Henderson, SP

Department: PMRS/Physical Therapy **Facility**: MAMC

Associate Investigator(s): COL Gail Deyle, SP; MAJ Robert L. Matekel, SP; Skyeann Allison; MAJ Jeremy Hutton, SP; CPT John Stang, SP; CPT David Gohdes, SP; CPT Mike Ryder, SP; CPT Matt Garber, SP

Start Date:	Est. Completion Date:	Periodic Review:
12/18/1997	Oct 98	3/28/2000

Study Objective: To evaluate the effectiveness of manual physical therapy treatment for osteoarthritis of the knee compared to a home exercise program.

Technical Approach: Subjects will be randomly assigned to one of two treatment groups. Subjects will undergo a thorough clinical examination by the treating physical therapists and then turned over to a trained research assistant (tester) blinded to the group assignment. The tester will obtain measurements of the dependent variables using the Wester Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and a six-minute walk test. The subjects will be returned to the treating therapist and treatment will begin as per group assignment. Group 1 will perform an in-clinic series of closely supervised exercises. Subjects will also receive manual physical therapy as indicated by examination and do home based exercise on the days when they are not in clinic. At the end of eight sessions the subject will be retested with the tester 2 days after the last exercise session and at the same time of day as the pretest. Group 2 will receive a home based exercise program, instructed to the subject by the treating physical therapist, and a detailed supporting handout and compliance log. Subjects will return to the clinic 2 weeks later to ensure proper execution of the exercises and compliance with the program. After completing 4 weeks the subject will be retested with the tester 2 days after the last exercise session and at the same time of day as the pretest.

Progress: A total of 37 subjects enrolled in this study at MAMC. Of these, seven were unable to perform the 1 year follow-up testing due to reasons not related to the investigation. Testing consisted of performance on the WOMAC tests and the distance walked in six minutes at the initial visit, at 4 weeks, 8 weeks and one year after participation in the study. This is a multicenter study. Data from MAMC has been fully collected. Data analysis is pending completion of data entry at the other sites. No data analysis or conclusions are available at this time. Forthcoming information on publications (to include abstract) and presentations will be forwarded to DCI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/027 **Status**: Terminated

Title: Mandatory Physical Training and Physical Readiness in Postpartum Soldiers

Principal Investigator: COL Nancy E. Henderson, SP

Department: PMRS/Physical Therapy **Facility**: MAMC

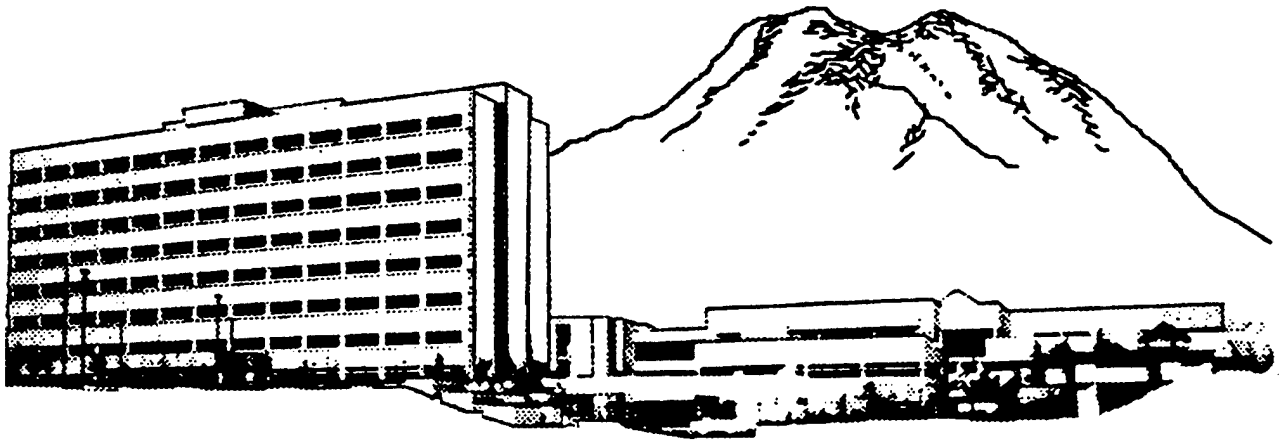
Associate Investigator(s): COL Roderick F. Hume, MC; CPT Mary C. Adams, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/26/1999	Jan 02	3/28/2000

Study Objective: (1) To compare the proportion of MPPPT trained soldiers who pass the Army Physical Fitness and body-fat standards at 6 and 12 months postpartum to the proportion of non-pregnant controls who pass during the same time interval, (2) to compare injury rates in MPPPT trained soldiers during the postpartum period to the injury rates in non-pregnant controls during the same time intervals, (3) to compare postpartum fitness, body-fat and injury rates in MPPPT trained soldiers to postpartum soldiers exempt from MPPPT and (4) to compare postpartum fitness, body-fat and injury rates in MPPPT trained soldiers to non-MPPPT trained postpartum soldiers (an historical control).

Technical Approach: Subjects will be scheduled for 3 appointments during this one year study; day 1, 6 months and one year. At each appointment body composition will be measured and subjects will be asked to complete a questionnaire, to include questions about age, ethnic background and exercise patterns. Medical records will be reviewed for injuries or illness. PT scores from the last PT test taken and from the next 2 PT tests will be recorded.

Progress: This study has been terminated due to lack of funding without having been initiated at MAMC.



Detail Summary Sheets

Preventive Medicine Service

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/037	**Status**: Completed

Title: Analysis of a Tuberculosis Epidemic on Kenyan Tea Estates

Principal Investigator: CPT Steven E. Battle, MC

Department: Preventive Medicine	**Facility**: MAMC

Associate Investigator(s): COL Jeffrey D. Gunzenhauser, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
1/23/2001	Feb 01	N/A

Study Objective: Document the presence of a tuberculosis epidemic on Kenyan tea estates and identify major causative factors using statistical analysis and descriptive techniques.

Technical Approach: This analysis provides a description of the prevalence, responses and factors behind the region's TB epidemic. In western Kenya, data from the referral hospital of 27 tea estates, with a total population of 45,850, was retrospectively surveyed for the period between January 1990 to December 1998. Co-morbidities and demographic information was obtained and analyzed. Individual estate prevalences, and medical standards, infrastructure and perceptions regarding disease burdens were assessed and matched to possible prevention strategies and technologies. Statistical methods will determine the association between TB admissions and malaria admissions.

Progress: The tuberculosis epidemic on western Kenyan tea estates correlates temporarily and causitively with the emergence of AIDS as an important etiology of mortality in the early 1990's. Worsening malarial burdens are likely another factor contributing to this ongoing TB epidemic. These results are consistent with previously described analyses of TB epidemiology and associations between TB, HIV/AIDS and malarial rates.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/012 **Status**: Terminated

Title: Noninvasive Measurement of the Surface Radiation Dose of Nuclear Medicine Patients Utilizing Thermal Luminescent Dosimeters (TLD)

Principal Investigator: LTC Mark W. Bower, MS

Department: Preventive Medicine **Facility**: MAMC

Associate Investigator(s): Scott Hudson; MAJ Stacia L. Spridgen, MS

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Apr 00	8/28/2001

Study Objective: Determine the response of thermoluminescent dosimeters (TLD) on the surface of personnel undergoing typical Nuclear Medicine procedures at positions where occupational radiation dose measuring TLD are normally worn.

Technical Approach: Patients referred to Nuclear Medicine as part of their normal medical care will be given one to two small thermoluminescent dosimeters (TLD) at the time of their injection and will be asked to wear them in designated locations; at the hip, collar or breast pocket. The amount of time the TLD is worn will be recorded. The TLD response from patients undergoing similar nuclear medicine procedures will be correlated to determine an average response for that procedure and then compared to the calculated TEDE. Correlation will also be made between the symptomatic and non-symptomatic patients.

Progress: This study was terminated due to the PCS of its principal investigator and the inability to enroll enough subjects during FY 01 to be able to perform data analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/090 **Status**: Ongoing

Title: Development of an ADS-based Syndromic Surveillance System Using Sexually Transmitted Diseases as a Prototypic Sentinel Condition

Principal Investigator: COL James E. Cook, MC

Department: Preventive Medicine **Facility**: MAMC

Associate Investigator(s): COL Jeffrey D. Gunzenhauser, MC; COL Kelly T. McKee, Jr., MC; CDR Randy Culpepper, MC (Navy); MAJ Andrew R. Wiesen, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	July 01	5/22/2001

Study Objective: (1) To build an interface between the Ambulatory Data System (ADS) and a Geographic Information System (GIS) by linking these systems to extract information on outpatient Sexually Transmitted Diseases from 2 geographically distinct Army installations: Fort Bragg, NC, and Fort Lewis, WA, and (2) To verify ADS diagnoses reported through CEIS by linkage with laboratory data on tests performed to diagnose syphilis, gonorrhea, and chlamydia contained in CHCS at Madigan Army Medical Center.

Technical Approach: The study population is any Madigan beneficiary who had a lab test performed for an acute STD syndrome (syphilis, gonorrhea, or chlamydia), who had an ICD-9 diagnosis for an acute STD syndrome (same) recorded in CEIS via ADS, or both. The study period is 1 Jan 97 through 31 Dec 99. To ensure that lab tests or clinic visits occurring on the margins of the study period are identified and included, data will actually be collected for the period Dec 1996 through January 2000, but will eventually be truncated to delete information on any beneficiaries for whom BOTH the lab test and the clinic visit occurred outside of the study period. Beneficiaries for whom at least one of these events occurred within the study period will be included in the analysis.

Patients with ADS-based diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be identified in central CEIS data files by one of the research collaborators. Information extracted from CEIS will include FMP, SSN, date of birth, clinic visit location, date of clinic visit, and ICD-9 coded diagnosis. Patients with diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be extracted from the Madigan CHCS system by the principal investigator using the ad hoc query. Information extracted from CHCS will include FMP, SSN, gender, date of birth, address of beneficiary (street address, city, state, and ZIP code), date of lab test, lab test result, and MEPRS code of the clinic (medical resource center) at which the test was ordered.

These two data acquisition efforts will identify all persons with a positive laboratory diagnosis for an acute STD syndrome, a positive ICD-9 diagnosis for the same acute STD syndromes, or both. However, because the primary analytic technique of the study will be McNemar's 2x2 table, information will also be needed on beneficiaries who had both a negative lab test and an ADS-based ICD-9 diagnosis for a condition other than an acute STD syndrome. To complete this cell of the 2x2 table, patients at Madigan who had a negative test for syphilis (RPR/VDRL), gonorrhea (culture or GenProbe), or chlamydia (Chlamydiazyme or GenProbe) during the study period will be identified. Their SSNs and FMPs will be collected in a data set and sent to associate investigator to batch merge with CEIS to identify ICD-9 codes resulting from clinic visits during which these diagnostic tests were performed. The merging of these two data sources will in this way identify persons for whom both a CHCS-recorded test was performed and an ICD-9 code was entered in ADS from the related clinic visit, both of which are NEGATIVE for a diagnosis of an acute STD. This approach is exhaustive in identifying all persons who fit these criteria during the study period.

The study method described will require that personally identifying information must be shared between investigators on the East Coast and at Madigan. Specifically, information on patients with positive diagnosis for acute STD syndromes will need to be sent from the CEIS extraction origin to the investigator at Madigan to validate whether or not a lab test was performed and what the result was. Similarly, personal identifiers on all Madigan patients for whom a diagnostic test for an acute STD syndrome is recorded in CHCS will need to be sent to the CEIS POC to ascertain whether an encounter was documented in ADS (CEIS) and whether a diagnosis of an acute STD syndrome was recorded.

To protect privacy, efforts will be made to safeguard data. Names of beneficiaries will not be abstracted from either source. Family Member Prefix (FMP) coupled with the sponsor Social Security Number (SSN) will serve as the means of record linkage. Once all data has been collected, data from the two sources (CEIS and CHCS) will be merged (by FMP and SSN). Dates of birth will be converted to ages. After merging and age conversion, FMPS, SSNs, and DOBs will be eliminated from the data set. Address information will be maintained, however, to allow for precise mapping of beneficiary residence. If the GIS program purchased for this study is unable to use specific street address information, this field will be deleted, and only city, state and zip code information will be maintained in the final data set used for analysis. Geographic information data usable in a GIS system (ArcView or comparable software) will be purchased or downloaded from the Internet. Clinical data will be merged into the GIS to plot frequencies of specific diagnoses by Zip Code, SMSA, or county of residence, as the GIS software will allow.

Progress: Work has not yet been initiated on this study at MAMC. This collaborative study, involving researchers at USAMRIID and their contractors, continues to negotiate a number of non-science related administrative requirements.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/092	**Status**: Completed

Title: Outpatient Morbidity Study of ROTC Cadets During Advanced Camp

Principal Investigator: COL Jeffrey D. Gunzenhauser, MC

Department: Preventive Medicine	**Facility**: MAMC

Associate Investigator(s): LTC Gregory A. McKee, MS

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/27/2000	Oct 00	5/22/2001

Study Objective: To estimate incidence rates of outpatient morbidity experienced by Cadets participating in Advanced ROTC Camp at Ft. Lewis, WA and to associate the occurrence of various medical conditions with various phases of the Advanced ROTC Camp.

Technical Approach: This observational study will look at medical records and personnel rosters compared to training schedules for cadets in ROTC Advanced Camp. Medically reported incidents will be divided up according to how many "person-days" are spent at each part of camp. This study will analyze what sort of injuries and illnesses are associated with various stages of the ROTC Advanced Camp.

Progress: Data collection and analysis for this study have been completed; however an abstract for this study is not available at this time due to PCS of PI.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/033 **Status**: Completed

Title: Breast Cancer Risk Assessment Among Women Beneficiaries Eligible for Medical Care in the Pacific Northwest, Region 11

Principal Investigator: COL Jeffrey D. Gunzenhauser, MC

Department: Preventive Medicine **Facility**: MAMC

Associate Investigator(s): MAJ Heidi P. Terrio, MC; Troy H. Patience, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Dec 99	1/23/2001

Study Objective: To measure the prevalence of major breast cancer risk factors among female DOD beneficiaries in TRICARE Region 11, to estimate mammography usage rates among female beneficiaries in TRICARE Region 11 and to advise female beneficiaries that there is a genetics screening program available to all through the Breast Cancer Initiative in Region 11.

Technical Approach: 16,000 women beneficiaries will be mailed a one-page anonymous questionnaire on risk factors for breast cancer, and preventive screening prevalence with regard to self-breast exam, clinical breast exam and mammogram. Three mailings will be sent out in an effort to try and get a better than 70% response rate. All recipients of this questionnaire will be offered genetic counseling.

Progress: 7163 surveys were returned and data was entered. Overall mammography screening rates in the past two years for female beneficiaries in the prime screening age-group (50-70) approached 90%, which is excellent and far above the hypothesized level. Several aspects of the study are still under analysis, including specific analyses MTF and a Geographic Information System Analysis.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/036 **Status**: Completed

Title: Rates of Health Care Utilization by Smokers, Smokeless Tobacco Users, and Non-tobacco Users in a Population of Young, Active Duty Soldiers

Principal Investigator: CPT Michael E. Parker, MC

Department: Preventive Medicine **Facility**: MAMC

Associate Investigator(s): COL Jeffrey D. Gunzenhauser, MC; COL James E. Cook, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Feb 01	N/A

Study Objective: To compare rates of health care utilization between tobacco users and non-users in a young, adult population.

Technical Approach: This retrospective cohort study will asses the utilization of health care as measured by provider visits in young tobacco users versus young non-tobacco users. The approximately 440 soldiers of the 864th ENG BN as of January 1999 will be the subjects of this study. Health Risk Appraisal (HRA) survey data as of January 1999 will serve as the basis for assessment of tobacco use status. Members of the 864th ENG BN will then be followed using ADS data to calculate the number of provider visits and the overall out-patient visit rates over the next 12-18 months. ICD-9 codes captured in the ADS system will allow the study investigators to sub-analyze provider visits for respiratory and musculoskeletal problems. The study will report overall visits in person-time and visits and visit rates for musculoskeletal and respiratory complaints in person-time. The statistical significance will be analyzed using the Mann-Whitney-U test. Privacy of subjects will be protected by removing SSNs and assigning unique study identification numbers before the investigators have access to the data for analysis.

Progress: In total, 375 soldiers met inclusion criteria for the study. The overall rate ratios demonstrate increased use of outpatient visits among smokers and confirm what many clinicians suspect. The increased use of health care resources was also seen with visits specifically for orthopedic complaints but, surprisingly, not for respiratory visits. These findings are tempered by non-significant p-values. Despite the statistical insignificance, the magnitude of the rate ratio (1.47) of the total number of visits between smokers and non-smokers invites thought. Had a normal distribution been assumed for this data and the p values computed from a t test, the results would have been significant with a p=0.03. However, the abnormal distribution of this data demands a nonparametric test. Inherently, the Mann Whitney U is limited in the statistical inferences it presents, because it depends soley on the ranking of the number of visits in each individual soldier; the magnitude of the difference in number of visits between ranks is not considered; important aspect of the data are ignored by the Mann Whitney U analysis. Another puzzling result in our analysis implied a protective effect from smokeless tobacco use. Again, the p-values were not significant, and at n=19, the sample size of smokeless tobacco users was small. Our interpretation is that this finding is spurious, and due to chance variation, but deserves confirmation in another study.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/053 **Status**: Ongoing

Title: Using Readily Available Data to Monitor and Surveil Active Duty Injury Occurrence

Principal Investigator: MAJ James S. Wadding, MC

Department: Preventive Medicine **Facility**: MAMC

Associate Investigator(s): LTC James D. Wells, MC; CPT Ryung Suh, MC; COL Jeffrey D. Gunzenhauser, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/28/2000	May 00	2/27/2001

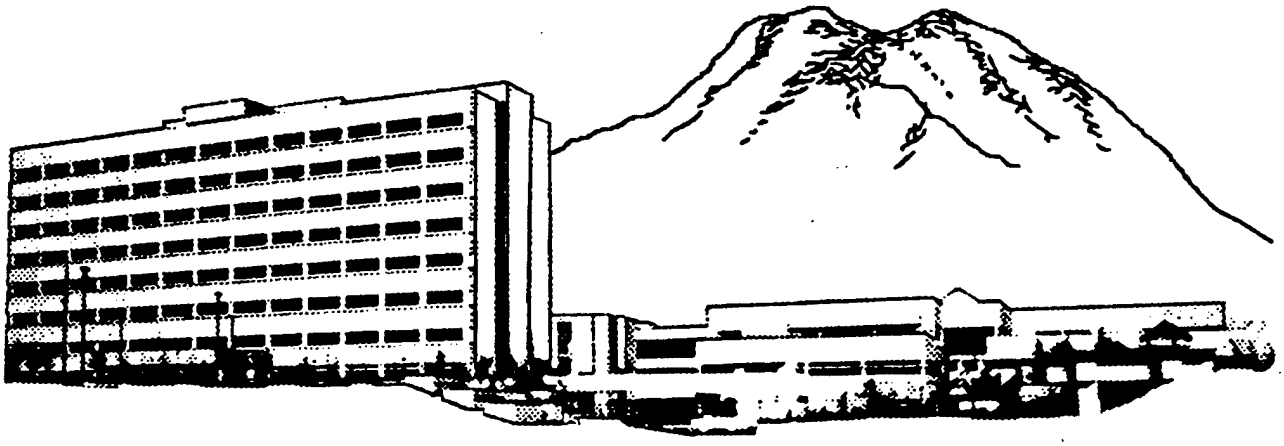
Study Objective: To determined if CHCS data can be used to predict loss of readiness due to injury and musculoskeletal illness (in the form of temporary profiles) and to aid in identifying problem areas and possible prevention opportunities on a recurring and real-time basis.

Technical Approach: This study is a pilot retrospective cohort study of the frequency and rates of key medical events related to injury occurrence in soldiers. A descriptive analysis of these events will provide thoughtful insight into the magnitude of morbidity typically severe enough to warrant lost-duty time. By looking at records of "sentinel" medications and clinic visits (entries in CHCS which predict the presence of injury or musculoskeletal illness) in CHCS) this study will evaluate the approximate lost time in a military population due to injury. Incidence of injury and illness will be verified by looking at the Standard Installation/Division Personnel Database (SIDPERS). Compiled data from random record selection will provide a profile of military readiness with regard to musculoskeletal injury and lost time due to injury.

Progress: 10.5% (n = 4363) of the 41,592 soldiers assigned to Fort Lewis during the 40-month study period met the case definition, and the accumulation of cases appeared to be uniform over time. This is beneficial because as we progress to developing a metric for surveillance, we will be able to look at shorter time periods, eg, 3- or 6- months, and still obtain a reliable estimate of the true population rate. While our case definition includes substantial variation in possible clinic-drug combinations (36), some common themes emerge: 1) Physical Therapy and Orthopedics were the most frequently used clinics among both cases and the population as a whole, and 2) Ibuprofen and other non-steroidal anti-inflammatory drugs accounted for the majority of drug prescribing in both groups.

Compared to other Fort Lewis soldiers, cases were more likely to be: female; older, especially in the 30-39 y/o age group; African-American; less-educated, with a considerable proportion having less than a high school degree at study entry; enlisted, especially higher ranking enlisted personnel E5-E9 (Sergeant to Command Sergeant Major); and to be assigned to Combat Support or Combat Service Support trains. Our finding that females were more common among cases compared to the overall population is consistent with prior military and civilian studies that indicate injury rates in women are higher than men after controlling for exposure13 (given that the Army is representative of one conglomerate working population). Bell et al.14 has suggested that this may not be purely a function of gender; rather, it may instead be related to underlying current physical fitness, particularly cardiovascular fitness. The finding that higher-ranking enlisted soldiers are over-represented among cases compared to the overall population is not unusual in itself; this is typically considered an age-related effect. Interestingly, there does not appear to be a similar effect among higher-ranking officers, which would be expected if age were the only explanation. Multivariate analysis will be carried out in ongoing studies to further investigate this relationship. After this descriptive part of our study, we believe that the data sources used in this study have the potential to monitor injury 'outbreak' information of importance to commanders and to measure the impact of injury on health care cost and utilization of interest to medical planners. A major strength of our study is the use of a large cohort over a long period of observation. While it did take a substantial amount of work to assemble the data

sets for this 40-month period, especially the SIDPERS information, we would like to remind the reader that we intend for this to be used routinely on a monthly or, at most, quarterly basis. We feel confident at this point that Preventive Medicine Officers should be able to capture, in near real-time, injuries with a significant impact on soldier readiness and health care utilization. Potential limitations of our study include: 1) missing data - the presence of any missing data has the potential to introduce bias. We were uncertain at the beginning about the quality of demographic information we would obtain from SIDPERS. However, missing data really did not appear to be a substantial problem for this portion of our study, with most demographic breakdowns resulting in less than one percent missing or unknown information; 2) proxy measures for injury - The primary underlying assumption of our study is that some temporal sequence of clinic visits and drug prescriptions correlates with an injury substantial enough to restrict work. We hope that the next part of our study which will correlate clinical information with profiles (actual lost-duty time) will help alleviate our concerns with respect to both; and 3) conceptual abstraction - though easy to use and adaptable to changes within CHCS, the proxy measures used for surveillance are difficult to grasp conceptually. This may make it a "difficult sell" to unit commanders who typically yearn for hard numbers and may limit its usefulness on a routine basis. However, commanders are likely to be receptive to timely information if we are able to detect trends early and provide useful feedback and recommendations.



Detail Summary Sheets

Department of Psychology

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/105	**Status**: Ongoing

Title: Telemental Health / Electronic Neuropsychology (e-NP)

Principal Investigator: LTC Gregory A. Gahm, MS

Department: Department of Psychology	**Facility**: MAMC

Associate Investigator(s): CPT Rhonda Koch, MS; LTC Bruce E Crow, MS; Dennis Kelly; Jack T Norris

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/27/2000	Jul 01	6/26/2001

Study Objective: (1) Evaluate ability of the ANAM2001, a computerized battery of cognitive assessment measures, to serve as a screening instrument for neuropsychological evaluations, (2) Establish infrastructure, procedures, and policies at MAMC to support an Army electronic neuropsychology service (e-NP), (3) Implement a secure server delivery platform for the ANAM2001 and demonstrate its functionality and (4) Explore the modification of ANAM2001 for true internet enabling.

Technical Approach: Patients who consent to participate in this study will, following their signing of the consent form, be assigned a case number. The case number will be input in place of the patient's name and SSN for all subsequent information gathering. Case system code will be consistent with the system under development at WRAMC for computerized neuropsychological reporting. This system identifies the test location, in this case MAMC, along with a new sequential 7 digit number. Thus the first subject would be MAMC0000001. Study subjects will complete a computerized history questionnaire containing pertinent questions regarding their background. Following completion of the questionnaire, a psychometrist (test administrator) will set the patient up with a series of automated neurocognitive measures (ANAM2001). Data from the automated measures will be transmitted to a secure server physically located within MAMC. Subjects will then be evaluated using the traditional neuropsychological evaluation measures utilized within the neuropsychological clinic.

Progress: No work on this study was initiated during FY01 as the protocol is awaiting MRMC approval.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/109 **Status**: Ongoing

Title: Virtual Primary Care Clinic

Principal Investigator: LTC Gregory A. Gahm, MS

Department: Department of Psychology **Facility**: MAMC

Associate Investigator(s): MAJ Jerald W. Rumph, MC; MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Mar 01	8/28/2001

Study Objective: (1) Develop an internet based primary care related service for implementation into the APCC, (2) Determine costs/feasibility of implementing functions as outlined in the original proposal and subsequent Statement of Work, and (3) Develop sub-protocol(s) for IRB approval for patient utilization study using the internet services with complete impact statements.

Technical Approach: This study will establish a prototype Virtual Clinic (VC) which will be designed to handle many of the administrative aspects of the APCC. Specific functional options for the VC will be documented and costs for development will be determined. The cost for the various options will be documented and decisions regarding function implementation will be made. A functional model will be operational by 01 January 2001, with data being gathered from January to March 2001. Information about subject interactions with the VC will be ready on the final reporting date of 05 March 2001.

Progress: This study received review and approval by MAMC IRB, CIRO and USAMRMC during FY00. Virtual Clinic development experienced several technical road blocks. Start date is expected to be January 2002.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/071 **Status**: Ongoing

Title: Virtual Primary Care Clinic - Applied Research

Principal Investigator: LTC Gregory A. Gahm, MS

Department: Department of Psychology **Facility**: MAMC

Associate Investigator(s): MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; CPT Patricia A. McKay, MC; LTC Fujio McPherson, AN; Deland Peterson, Ph.D.; CPT Richard Reed, MC; MAJ Jerald W. Rumph, MC; LTC Mary A. Schwenka, AN; LTC Gary A. Wheeler, MC; COL Nancy A. Woolnough, AN

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Aug 01	N/A

Study Objective: (1) Implement a "virtual" primary care clinic (VPCC) e-health service within the APCC, (2) Determine full range of costs for implementing this program and document usage, (3) Evaluate the impact of these services on patient and provider satisfaction, clinic productivity and workload and (4) Support clinical implementation studies utilizing this clinic, measure impact upon clinical outcome, and project component impact.

Technical Approach: This project will implement an e-health VPCC within the APCC at MAMC, which will support a range of patient and provider support that can augment the present access and nature of patient care. Evaluation within this project includes the technical and functional components associated with the VPCC development, impact on patient and provider satisfaction and health system interactions. This VPCC protocol serves as the basic protocol upon which subsequent protocols are linked and describes the basic functionality of the VPCC which is necessary for the other studies implementation.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/138 **Status**: Ongoing

Title: Evaluation of the Field Deployable Record - Behavioral Health

Principal Investigator: LTC Gregory A. Gahm, MS

Department: Department of Psychology **Facility**: MAMC

Associate Investigator(s): 1LT Richard Barton, MS; LTC David W. Hough, MC; LTC Reginald Howard, MS; Jessica C. Oehlrich, RA; Deland Peterson, Ph.D.;

Start Date:	Est. Completion Date:	Periodic Review:
10/23/2001	Dec 01	N/A

Study Objective: Implement the Field Deployable Record-Behavioral Health electronic record system in garrison and deployment environments, evaluate the FDR-BH on completeness, usefulness, functionality, and user-friendliness, and support clinical implementation studies utilizing this information system.

Technical Approach: Twenty providers from Madigan Army Medical Center's Psychology and Psychiatry departments will use this system to record their patients' behavioral health record data. Using a survey design, subjects' demographic data, computer use, and documentation and workload history will be assessed. Every two weeks, providers will rate the overall system on completeness, usefulness, ease of use and functionality as well as specific ratings of the history and encounter documentation sections. After the six-week study period, total documentation time, workload accounting, and accurate session documentation will be measured by documentation time as calculated by the FDR-BH, ADS/KGADS completion, and ratings by independent reviewers respectively. Successful implementation and execution of this FDR-BH protocol, in combination with its Internet and PDA capabilites will support future research initiatives.

Progress: This study recently received final IRB approval.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/079	**Status**: Ongoing

Title: Primary Care Outpatient Management of Depression Using Internet Technology (VPCC Substudy)

Principal Investigator: Deland Peterson, Ph.D.

Department: Department of Psychology	**Facility**: MAMC

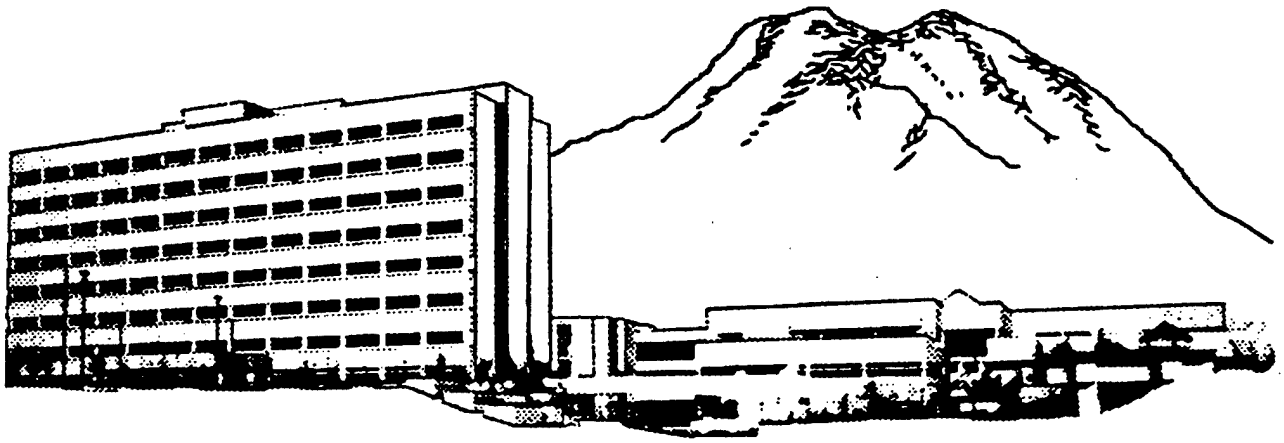
Associate Investigator(s): LTC Gregory A. Gahm, MS; LTC Fujio McPherson, AN; John Allison, M.D.

Start Date:	**Est. Completion Date:**	**Periodic Review:**
3/27/2001	Jan 02	N/A

Study Objective: (1) Implement an e-health based primary care depression treatment protocol, (2) Evaluate the treatment effectiveness of e-health augmentation of primary care provider's treatment of depression, (3) Evaluate the workload requirements and appropriateness of having primary care providers to include nurse practitioners and primary care physicians working in collaboration with a clinical psychologist to implement supportive psychotherapy into this process, (4) Identify the use and potential role of complimentary/non-traditional medical practices among patients with depression, (5) Evaluate patient satisfaction with this system and (6) Evaluate provider satisfaction with this system.

Technical Approach: Patients will be provided with, and asked to sign, an information sheet that describes the study and the requirements on the patient. The will have the opportunity to ask questions of the PI. Patients suffering from depression and eligible for enrollment in VPCC will be assigned to three groups, one with health psychology augmentation of the VPCC primary care team, one being treated by a VPCC primary care team, and one being treated by usual primary care. They will be assessed before initiating treatment and at the conclusion of the VPCC treatment period with the Zung depression scale, a scale measuring their use of alternative treatment methods, and the SF-36v2 health status scale. They will also regularly provide information on sleep quality, use of exercise, and medication usage throughout the treatment period. At the conclusion of this study, information on medical visits and satisfaction with treatment will be collected. Anticipated improvements with treatment progress, resource use and satisfaction with treatment will be evaluated.

Progress: Initiation of this study at MAMC is pending final approval by USAMRMC.



Detail Summary Sheets

Department of Radiology

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/088 **Status**: Ongoing

Title: Comparison of Computed Tomography Angiography and Digital Subtraction Angiography for the Pre-Operative Evaluation of Carotid Artery Disease

Principal Investigator: CPT David M. Danielson, MC

Department: Radiology **Facility**: MAMC

Associate Investigator(s): CPT David M. Keadle, MC; CPT Christopher R. Spence, MC; MAJ Sean P. Murray, MC; LTC Stephen M. Yoest, MC; James H. Timmons, MD; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Troy H. Patience, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Jul 00	01/22/2002

Study Objective: To evaluate the accuracy of Computed Tomography Angiography (CTA) in the evaluation of patients with atherosclerotic carotid artery disease. Comparison will be made with the with the accepted gold standard evaluation, digital subtraction angiography.

Technical Approach: The study sample will be obtained from consecutive patients who have had clinical evaluation and a duplex ultrasound examination in the vascular surgery clinic and who were referred for conventional angiographic examination of the carotid arteries. The plan is to evaluate 40 patients, although a preliminary statistical analysis will be performed after the first 20 patients to assure adequate sample size. Patients who agree to participate in the study will have CTA performed at least 72 hours prior the conventional angiography. These studies will be read by two radiologists. Conventional angiography will then be performed and will be read by two different radiologists. The physicians performing and reading the angiogram will be blinded to the results of the CTA study. Percent stenosis of the carotid artery will be computed using the North American Symptomatic Carotid Endarterectomy Trial method. The results of the CTA will be compared with the conventional angiogram using paired T-test analysis. The CAT scan protocol used for the CTA exams is as follows: a non-contrast scan will be done first from the skull base to the aortic arch. These will be true axial images at 5 mm slice thickness and intervals using settings of 120 kV and 200 niA. Next, a contrast-enhanced study will be performed. 125 ml of non-ionic contrast material will be injected at a rate of 4ml per second. During the dynamic administration of this contrast material, a scan will be performed from the skull base to the aortic arch. These images will be acquired helically with a pitch of 2 and a slice thickness of 3 mm, and will use settings of 120 kV and 250 mA. These images will be reconstructed at 1 mm thickness, and will be reformatted in sagittal and coronal planes. In addition, 3 dimensional and maximum intensity projection (MIP) images will be obtained. The projected CT weighted dose (weighted 2/3 peripherally and 1/3 centrally) is 9.78 mGy for the contrast scan and 14.76 mGy for the non-contrast scan. If the ultrasound and the CTA show only unilateral disease, the angiogram on the contralateral side will be abbreviated and will consist of only one contrast run as opposed to three. This will decrease the catheter time in that artery, which is suspected to decrease the chance of stroke. In addition, the decrease in radiation from excluding the two runs will likely exceed the extra radiation from the CTA.

Progress: To date, 28 subjects have enrolled in this study at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/034 **Status**: Ongoing

Title: Computed Tomography Guided Percutaneous Placement of Injection Coils Ligated to Suture and Thoracoscopic Pulmonary Resection

Principal Investigator: CPT Carl Decker, MC

Department: Radiology **Facility**: MAMC

Associate Investigator(s): CPT John P. Reinschmidt, MC; MAJ Lawrence M. Casha, MC; MAJ Sean P. Murray, MC; MAJ David P. Tracy, MC; James H. Timmons, MD; MAJ Scott C. Williams, MC; LTC Maceo Braxton Jr, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/18/1997	Indef	11/28/2000

Study Objective: The primary objective is to reduce the number of displaced localization devices by the use of a Cook helical coil tied to a suture line as an alternative to the hookwire for VATS. A secondary objective is to reduce damage that occurs with displacement of wires.

Technical Approach: Twenty patients already slotted for needle localization with Hawkins III wires will have either coils attached to suture or hookwires placed. They will then be taken to the OR and thoracic surgery will remove the coils or hookwires with VATS. The degree of displacement and associated complications will be compared to our current 90% Hawkins III wire displacement rate.

Progress: One subject enrolled in FY01, for a total of 17 subjects (10 microcoil, 7 hookwire) at MAMC. This protocol continues to enroll subjects with an ultimate enrollment goal of 20. There have been no adverse events associated with this study.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/085 **Status**: Completed

Title: Radiographic and Clinical Correlation of the Outcome of Calcaneal Osteotomy for Talocalcaneal Valgus

Principal Investigator: MAJ Gina J. Kim-Ahn, MC

Department: Radiology **Facility**: MAMC

Associate Investigator(s): Rush A. Youngberg, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Dec 99	8/22/2000

Study Objective: Review the literature regarding radiographic determination of talocalcaneal valgus and assess the three standard radiographic measurements of talocalcaneal alignment from the Cobey view. Introduce the Cobey view to the radiology community. Correlate the clinical outcome of patients undergoing calcaneal osteotomy for talocalcaneal valgus with each of the three measurements.

Technical Approach: Review of charts of patients who have had the Cobey view will be performed. For each patient's Cobey view, three measurements for the talocalcaneal valgus will be made independently by two radiologists. These measurements will be compared to each other and correlated with clinical assessment and selection for surgery. The readers will be blinded to patients' subsequent clinical management. Both initial and follow-up Cobey views will be assessed. Charts of post-operative patients will also be reviewed to assess outcome.

Progress: 64 patient records were analyzed in this retrospective study. Radiographic measurements of calcaneovalgus deformity correlated well with clinical presentation. Of the four techniques studied, the Kim-Ahn measurement was the most obtainable and it provided a high predictive value for surgical interventions. No further work was accomplished on this study in FY01, and the study was reported as completed, 12 Jun 01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/093 **Status**: Terminated

Title: Magnetic Resonance Imaging of the Sternum

Principal Investigator: CPT Andrea R. Manzo, MC

Department: Radiology **Facility**: MAMC

Associate Investigator(s): Rush A. Youngberg, M.D.; LTC John D. Pitcher Jr., MC

Start Date:	Est. Completion Date:	Periodic Review:
07/17/1998	May 99	3/27/2001

Study Objective: To determine the magnetic resonance imaging characteristics of the normal sternum and anatomical variations.

Technical Approach: We propose to study 25 adults with no prior history of trauma using a torso array coil. MR images will be obtained in T1-weighted sequences in the sagittal and coronal planes. The patients we propose to study will be patients scheduled for MR imaging for other indications.

Progress: This study was terminated, 27 Mar 01, due to the PCS of the principal investigator and a failure to identify a new PI to take over this study.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/099 **Status**: Terminated

Title: Comparison of MRI with Bone Scintigraphy in the Evaluation of Suspected Hip Stress Fractures

Principal Investigator: CPT Paula J. Shepherd, MC

Department: Radiology **Facility**: MAMC

Associate Investigator(s): Jerome Billingsley, M.D.; Rush A. Youngberg, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Dec 99	8/28/2001

Study Objective: To determine whether MRI is at least as sensitive, and possibly more specific than bone scintigraphy in the detection of hip stress (fatigue) fractures.

Technical Approach: The first 50 consecutive patients who present for an initial bone scan or MRI to evaluate for hip stress (fatigue) fracture as ordered by their health care providers, will be consented for both studies (bone scan and MRI) if they agree to participate in the study and meet the URI screening criteria. Results are available to clinicians upon completion of the interpretation of each study, Patients will undergo the alternate study within 5 days of completion of the study for which the patient initially presented. Plain films are not required prior to either study, however are often already obtained before presenting for further imaging. If obtained, these films are available for review by both the nuclear medicine physicians and MRI radiologists interpreting the studies; however the diagnosticians are blinded to the results of the alternate study (bone scan or MRI). The appropriate statistical test is the McNemar test, as the subjects are paired. There is no gold standard for diagnosing hip stress fractures.

Progress: This study was reported as terminated, 28 Aug 01. No work was initiated on this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/166 **Status**: Terminated

Title: Cost Effectiveness of Early MRI in Traumatic Wrist Injury

Principal Investigator: Rush A. Youngberg, M.D.

Department: Radiology **Facility**: MAMC

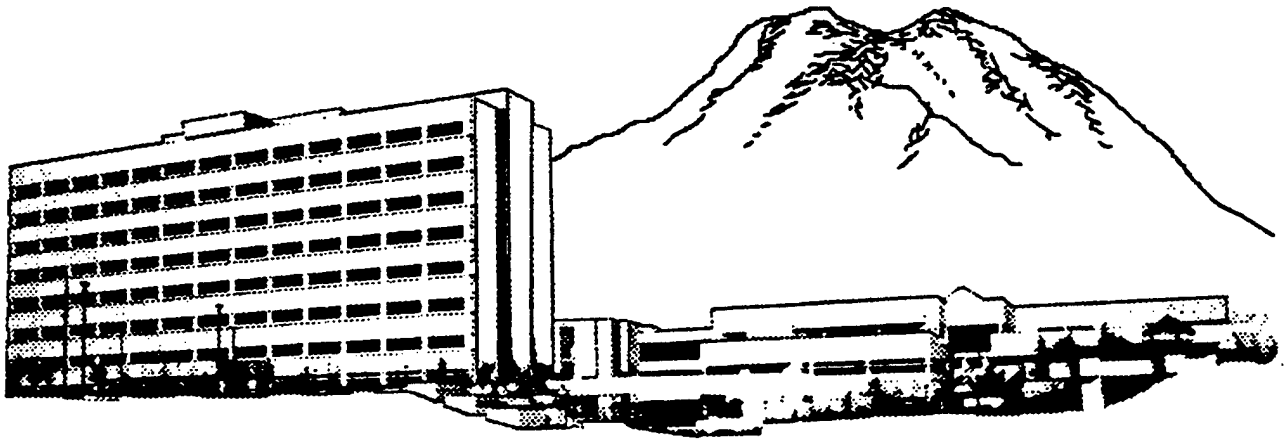
Associate Investigator(s): MAJ Richard S. Makuch, MC; COL John M. Bauman, MC; CPT John D. Crocker, MC; S. P. Scheer, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
08/18/1995	Feb 96	8/20/1998

Study Objective: To determine the cost effectiveness and utility of scintigraphy in the management of patients with traumatic wrist injury whose initial radiographs are negative, yet who clinically are felt to have scaphoid fractures.

Technical Approach: This is a prospective blinded study to determine the cost effectiveness of a more accurate, slightly more expensive imaging modality in the management of patients with traumatic wrist injury. All patients over 18 years of age with a fall on the outstretched hand (a "FOOSH" injury) will be included. One hundred patients will be enrolled. Those enrolled in the study will undergo a limited high resolution bone scan of each wrist (the uninjured wrist will serve as a comparison to the injured wrist) within 48-96 hours of the time of injury. When the clinician has determined that management is complete, the clinician will have access to the bone scan results, prior to the patients' discharge from care. The radiographs will be reviewed by the chief of musculoskeletal radiology, the bone scans by a staff nuclear medicine physician, and the clinical evaluation and follow-up will be performed per usual orthopedic clinic practice at MAMC. Costs will be calculated based on the CHAMPUS allowable reimbursement for the services rendered as defined by the 1995 CPT codes of the American Medical Association. Data analysis will include determining if there is statistical significance between the costs of caring for clinically "false positive" fractures and the costs of early bone scintigraphy.

Progress: This study was terminated, 21 Aug 01, by the Department of Clinical Investigation. The principal investigator left his position at Madigan and the Chief, Department of Radiology reported no staff member claimed knowledge of this protocol.



Detail Summary Sheets

Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/088 **Status**: Ongoing

Title: A Prospective, Randomized Study Comparing the Outcome of Carotid Endarterectomy Using New Generation Dacron or Expanded Polytetrafluoroethylene (e-PTFE) Carotid Patching

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): LTC Stephen B. Olsen, MC; COL David F. J. Tollefson, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Jun 02	6/26/2001

Study Objective: The primary objective of this study is to compare the performance of the newest generation Dacron and e-PTFE patches with respect to: (1) postoperative stroke/thrombosis, (2) recurrent carotid stenosis and (3) intraoperative handling/blood loss.

Technical Approach: After informed consent, patients will be randomized to patch angioplasty with either a Hemashield Finesse patch or a Gore-Tex Acuseal patch. Surgeons will rank the handling of the patch on an analog scale. Time to cessation of bleeding will be monitored. Patients will have an intraoperative duplex , and follow-up duplex examinations at 3, 6, 9, 12, 18 and 24 months after the operation. Rates for carotid restenosis will be determined. Perioperative and late neurologic morbidity will be identified and determined.

Progress: 23 subjects enrolled in this study at MAMC in FY01 with no SAE's reported. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/098 **Status**: Completed

Title: A Multicenter, Double-blind, Randomized, Parallel Placebo-Controlled Study of the Safety and Efficacy of Chronic Oral Beraprost Sodium in Patients with Intermittent Claudication (Fontaine Stage II Peripheral Arterial Occlusive Disease)

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 02	6/26/2001

Study Objective: Primary objective of this study is evaluation of Beraprost Sodium (BPS) on exercise capacity as assessed by a defined treadmill walk test in patients with intermittent claudication (Fontaine Stage II peripheral arterial occlusive disease, (PAOD). Absolute claudication distance (ACD) will be the primary efficacy endpoint. Secondary objectives: (1) Evaluation of the effect of Beraprost Sodium on Initial Claudication Distance, (2) Evaluation of the safety of BPS in these patients, assessed by adverse events and clinical laboratory parameters, (3) Evaluation of the effect of BPS on the quality of life assessments, and (4) Evaluation of the effect of BPS on the percentage of responders to drug treatment.

Technical Approach: This study will evaluate up to 12 subjects at MAMC for intermittent claudication. After an initial screening exam including physical, neurological, cardiovascular, and cutaneous exams, the subjects will be started on a single-blind (patient blinded) placebo run-in period. During this time, the patient will be monitored to see if they improve significantly without the use of actual medication. Additionally, they will be checked to make sure that they are taking their medication in a timely manner. Subjects who take their medication regularly and who do not exhibit too much improvement in the first 3-week period will then be started on a double-blind, placebo controlled study period of 48 weeks. Subjects will periodically be seen for physical exams and administered treadmill tests. Results of subject treadmill tests and QOL questionnaires will be used to assess objective outcomes.

Progress: Eleven subjects consented in this study at MAMC in FY01, for a total of 30 subjects consented. Twenty subjects were randomized, and 10 successfully completed the study and rolled over in the open label extension protocol. Five SAE's have been reported, including one MAMC SAE (event unrelated to study participation). This study closed to enrollment in FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/046 **Status**: Ongoing

Title: A Pivotal Study to Evaluate the Safety and Efficacy of Cryopreserved Bilayered Cellular Matrix (Cryo-OrCel) for the Treatment of Venous Ulcers Protocol #100-VLU-01-CLN

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): COL David F. J. Tollefson, MC; LTC Dennis Febinger, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Sep 01	N/A

Study Objective: This is a pivotal study to determine the safety and efficacy of Crypreserved Composite Cultured Skin (Cryo-CCS) plus standard care compared to standard care alone in the treatment of venous ulcers. This study will be conducted using Crypreserved Composite Cultured Skin and will begin with an Initial Phase to evaluate any risk of an immune response.

Technical Approach: The study is divided into two phases. The initial phase will enroll approximately 12 patients at three centers. This phase will be open label and all patients will receive CCS. After those patients have received up to four applications of CCS, Investigators will select and enroll a sufficient number of patients to yield 176 evaluable subjects (8-10 at MAMC) into the randomized phase, which will be an open label, parallel group, randomized study of at least 176 patients enrolled among 35 centers in the United States. The 26-week study consists of four periods: a two-week screening period, a four-week Active period, an eight week Maintenance period, and a three month Follow-up period. All patients will be enrolled for a maximum of 26 weeks. The Initial phase will be an open label phase-in period to further assess the potential for an immune reaction. After meeting the inclusion/exclusion criteria, including a two week trial of standard care, these twelve patients will receive up to four weekly applications of CCS (Active period, Visits 1 to 5). If no safety issues emerge, enrollment may continue in the Initial phase until all 12 patients have been enrolled and treated. Patients in the Initial phase will continue through the Active and Maintenance (Visits 6 to 13) periods. Patients whose ulcers are not healed by visit 13 are considered completed subjects and their study participation is ended. Subjects with complete healing at any point during the study will enter the follow-up period. They will be followed on a monthly basis (every 25 -35 days) for three months from the date of 100% re-epithelialization. Subjects who achieve healing are considered completed subjects if they finish all the required follow-up visits.

The Randomized phase (evaluation of 176 patients) will begin if no device-related adverse events have occurred in the Initial phase which would increase the risk to patients and prevent the discontinuation of the study. Patients are initially evaluated at a screening visit. After meeting the enrollment criteria, (two trial of standard care) patients will be randomized to a treatment group. Patients randomized to the CCS treatment group will receive weekly applications of CCS along with standard care. Patients randomized to the standard care treatment group will receive up to four weeks of standard care alone. Patients in either treatment group who do not achieve healing during the Active period will enter the Maintenance period, which consists of up to eight additional weeks of standard care alone. Patients whose ulcers are not healed by visit 13 are considered completed subjects and their study participation ends. Patients whose ulcers heal completely at any point during the study will enter the follow-up period. They will be followed monthly (every 25-35 days) for three months from the date of 100% re-epithelialization. Patients who achieve healing are considered completed patients if they finish all required follow-up visits.

Progress: No subjects enrolled in this study at MAMC in FY01 due to an FDA hold. Currently a revised protocol and consent form are being submitted incorporating FDA changes.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/082 **Status**: Completed

Title: A Multicenter Open-Label Evaluation of the Safety and Efficacy of Chronic Beraprost Sodium in Patients with Intermittent Claudication (Fontaine Stage III Peripheral Arterial Occlusive Disease): A Continuation Study

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): COL David F. J. Tollefson, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Apr 03	N/A

Study Objective: The primary objectives of this study are to collect additional safety information about the long-term administration of BPS, as assessed by adverse experiences and clinical laboratory parameters and collect additional efficacy information, as assessed by absolute claudication distance and initial claudication distance on exercise treadmill tests.

Technical Approach: This trial is a multicenter, open-label, continuation study. Patients who completed all Week 48 assessments in the BIR 02:01 study, regardless of treatment assignment, will be eligible to immediately enter this trial. Screening assessments for this study will be conducted at the BIR 02:01 Week 48 Visit. This study will last for at least one year, and may be extended beyond one year, until one or more of the following occurs: BPS becomes commercially available or the sponsor terminates the study.

Progress: Ten subjects were rolled over into this extension study of the original randomized protocol (MAMC #200098). One non-MAMC SAE was reported by study sponsor. Enrollment in this study has been closed by the study sponsor.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/122 **Status**: Ongoing

Title: A Double-Blind, Randomized, Placebo-Controlled Study to Assess the Efficacy and Safety of Circulase for the Treatment of Critical Leg Ischemia Protocol WFI 01-01

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): LTC Dennis Febinger, MC; CPT Philip Mullenix, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Oct 02	N/A

Study Objective: To test the hypothesis that Circulase treatment improves clinical outcome by reducing the risk of major amputation in subjects with critical leg ischemia who have undergone a recent peripheral revascularization procedure.

Technical Approach: Patients will be randomized to one of two double-blinded treatment groups-Circulase 40 mg or Placebo The total goal for enrollment is 6-10 patients here at MAMC. Informed consent will be obtained by one of the investigators or by one of the study coordinators. They will verbally explain the study purpose and requirements. After all questions have been answered, the patient will be instructed to read, sign and date the consent in the presence of a non-study related witness The patient will then enter the screening phase, which will last 10 days. The following assessments will be performed: Medical history, Physical examination, Electrocardiogram, Peripheral vascular intervention history, Assessment of critical leg ischemia (presence of ulcers or gangrene, ischemic rest pain, hemodynamic status assessment, ABI's, wound tracings and photographs), Neuropathy assessment, QOL measurements (SF-36, Pain VAS), Concomitant medication assessment, Urine and Laboratory measurements. After verification of patient eligibility based on inclusion/exclusion criteria the patient is eligible to be randomized. Within a 24 hours of the planned revascularization procedure the study coordinator will contact the ClinPhone Interactive Voice Response system (IVRS) to assign the next available subject number. Test administration procedures should begin within 24 hours the revascularization procedure, unless contraindicated by the Investigator. Test material may be delayed, up to 3 days from the date of randomization if a clinically significant condition is present, which in the investigators opinion poses a safety risk. The test material should be initiated as soon as the patient is stabilized. If the patient is unable to initiate the test material within 3 days they will be withdrawn from the study. After dosing the patient will be monitored for all adverse events and the administrator will assess the severity and risk to the patient and will administer medical treatment to alleviate symptoms for hemodynamic stability. Before releasing the patient from the hospital the investigator will provide a detailed post -operative description of the revascularization procedure. All Test material procedures are performed identically at each treatment visit. A total of 40 test material administrations are to be performed over the 56 day dosing period. The patient will receive study infusion in the vascular clinic 5 days a week (Monday-Friday). In the event that home healthcare is accessible, the patient may receive home infusions at the discretion of the investigator. The investigator will instruct the home health care provider on the protocol, drug administration, and drug pharmacokinetics. The investigator will be accessible by phone during home infusion should the home health care provider need to contact him. All patients will be required to return to the clinic for physical exams and outcome evaluations at week 8, EOT, or if they have an SAE. At each dose the patient will be monitored for all adverse events, concomitant medications, and hemodynamic stability prior to being released from the study site.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/123 **Status**: Ongoing

Title: A Double-Blind, Randomized, Placebo-Controlled Study to Assess the Efficacy and Safety of Circulase in Conjunction with Peripheral Revascularization for the Treatment of Critical Leg Ischemia Protocol WFI-01-02

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): LTC Dennis Febinger, MC; CPT Philip Mullenix, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Sep 02	N/A

Study Objective: To test the hypothesis that Circulase treatment improves clinical outcome by reducing the risk of major amputation in subjects with critical leg ischemia who have undergone a recent peripheral revascularization procedure.

Technical Approach: This protocol will be studying male or female patients 40 years or older, with critical leg ischemia after undergoing a distal revascularization procedure. Patients will be randomized to one of two double-blinded treatment groups-Circulase 40 mg or Placebo The total goal for enrollment is 6-10 patients here at MAMC. Upon obtaining informed consent, the patient will enter a 10 day screening phase and the following assessments will be performed: medical history, physical exam, electrocardiogram, peripheral vascular intervention history, assessment of critical leg ischemia (presence of ulcers or gangrene, ischemic rest pain, hemodynamic status assessment, ABI's, wound tracings and photographs), neuropathy assessment, QOL measurements (SF-36, Pain VAS), concomitant medication assessment, urine and laboratory measurements. Patient will already be scheduled to receive a distal revascularization procedure involving an artery beyond the popliteal as part of their normal standard of care. Patients requiring treatment of proximal lesions in conjunction with a described distal procedure are acceptable. After verification of patient eligibility based on inclusion/exclusion criteria the patient is eligible to be randomized. Within 24 hours of the planned revascularization procedure the study coordinator will contact the ClinPhone Interactive Voice Response system (IVRS) to assign the next available subject number. Test administration procedures should begin within 24 hours the revascularization procedure, unless contraindicated by the Investigator. Test material may be delayed, up to 3 days from the date of randomization if a clinically significant condition is present, which in the investigators opinion poses a safety risk. The test material should be initiated as soon as the patient is stabilized. If the patient is unable to initiate the test material within 3 days they will be withdrawn from the study. After dosing the patient will be monitored for all adverse events and the administrator will assess the severity and risk to the patient and will administer medical treatment to alleviate symptoms for hemodynamic stability. Before releasing the patient from the hospitial the investigator will provide a detailed post -operative description of the revascularization procedure. Including: Arteriogram showing the patency of the Index Operation in communication with the run-off, Magnetic resonance angiography (MRA) showing the patency of the Index operation, Color duplex scanning showing patency of the Index Operation, and Increase in distal ABI by at least 0.15 over pre-operative ABI. All Test material procedures are performed identically at each treatment visit. A total of 40 test material administrations are to be performed over the 56 day dosing period. At each dose the patient will be monitored for all adverse events, concomitant medications, and hemodynamic stability prior to being released from the study site. At Week 1,the patient will receive a study infusion in the vascular clinic given by a nurse or a CRC-RN. Prior to the dose being given the patient's blood pressure will be recorded. The patient will be placed in the supine position using an appropriate indwelling catheter, syringe pump and infusion line. The dose will last approximately 10 minutes. Also at this visit an ECG will be done, at least 45 minutes after the start of test material.

The Week 8 visit will occur the last week of treatment (days 50-56) and the following procedures will be performed: Test material procedures (if patient is still receiving treatments), Physical exam, Assessment of critical leg ischemia, Index operation patency surveillance (Arteriogram, Magnetic resonance angiography, Color duplex scanning, and/or Increase in distal ABI by at least 0.15 over pre-operative ABI), Laboratory measurements, QOL measurements (SF-36, VAS), ECG (post drug administration), Neuropathy assessment, Drug Reconcillation (after final dose), Monitoring for all adverse events, concom med's and vascular interventions, Hemodynamic status assessment (ABI's). Following the eight week treatment period and visit the patient will enter the follow-up period.The patient will be contacted by telephone, once a month for the full one year period, to assess AE's and Concom med's. After the 30 day period only serious adverse events will be assessed and reported. Patients will return at months 6 and 12 month. An Exit Visit for those patients that discontinue participation in the study the following procedures will be done. The data collected will be the reduction in the event rate which is defined as the proportion of patients who undergo a major amputation or die within 6 months from the initial treatment. This will be analyzed by logistic regression testing for the drug effect on the event rate while adjusting form the following baseline characteristics: diabetic status, ischemic ulcer/gangrene presence and anti-platelet therapy.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/163 **Status**: Ongoing

Title: Clinical Evaluation of the Handling and Performance of the HEMASHIELD Knitted Double Velour Fabric and Polytetrafluoroethylene (PTFE) Patched for Carotid Endarterectomy Patch Procedures in Patients

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Edmund A. Kanar; George J. Collins, Jr.

Start Date:	Est. Completion Date:	Periodic Review:
09/20/1996	Nov 98	8/28/2001

Study Objective: The objective of this randomized, parallel group, multi-center study is to evaluate the performance of the test product, the HEMASHIELD Knitted Double Velour patch in comparison to the control product, the Gore-Tex patch, for use as a carotid artery patch following carotid endarterectomy in patients.

Technical Approach: This is a prospectively randomized, multi-center clinical trial in which a maximum of 40 patients will be enrolled, with approximately equal numbers of patients in each of the 2 treatment groups, Hemashield patch vs. the Gore-Tex patch. Anticipated MAMC enrollment is approximately 20 patients. Patients included in this study will be evaluated preoperatively, intraoperatively, at discharge from the hospital, and at 3 months, 6 months, 12 months and up to a total of 24 months postoperatively. Follow-up evaluations will include a medical history and physical exam at 3, 6, 12 and 24 months and duplex ultrasound testing at 6 and 12 months (with optional duplex scan at 24 months) for assessment of patch repair. Completion of follow-up assessment and final report is anticipated about one and one half years after the first patient enrollment.

Progress: 40 subjects enrolled in this study at MAMC and continued to be followed during FY01. There have been no SAE's reported. This study is closed to further enrollment, but remains ongoing to continued subject follow-up.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/081 **Status**: Completed

Title: A Double-Blind, Randomized, Parallel Group, Placebo-Controlled Study to Evaluate the Safety and Efficacy of NM-702 in Subjects with Intermittent Claudication

Principal Investigator: COL Charles A. Andersen, MC

Department: Surgery **Facility**: MAMC

Associate Investigator(s): COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; CPT Chatt A. Johnson

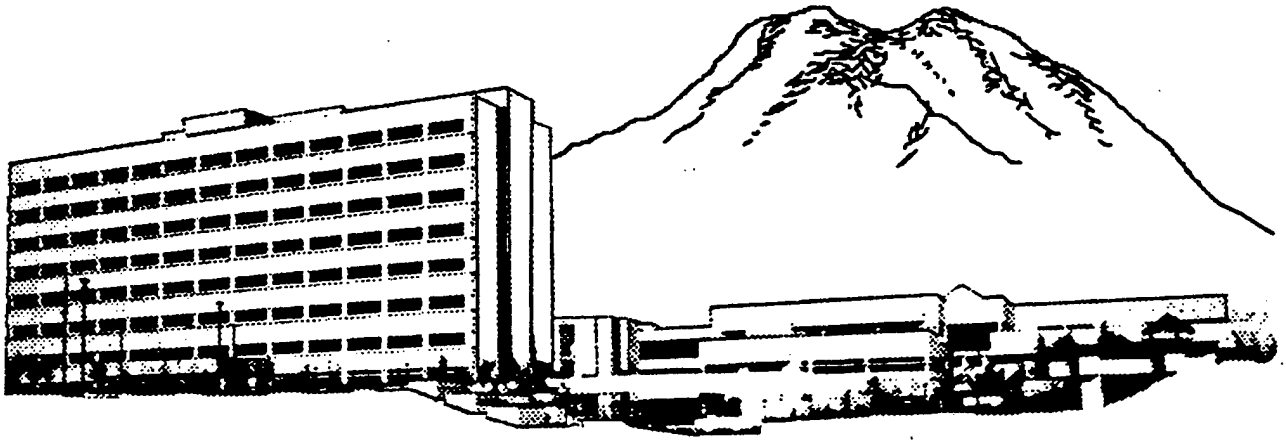
Start Date:	Est. Completion Date:	Periodic Review:
07/27/1999	Aug 00	7/24/2001

Study Objective: (1) Demonstrate the efficacy of NM-702 at three different doses compared to placebo in the treatment of patients with intermittent claudication. The following assessments will be used to determine efficacy: improvement in peak walking time, improvement in claudication onset time, and change in functional status as measured by the Health Status Survey Questionnaire and Walking Impairment Questionnaire, (2) Assess the safety of NM-702 treatment in subject population as determined by physical examination, blood and urine analysis, Holter monitoring, 12-lead. ECG, blood pressure measurements and by evaluation of adverse events and concomitant medication usage.

Technical Approach: This will be a double-blind, parallel-group, dose- response study in which subjects will be randomized to receive either 1, 2, or 4 mg of NM-702, or placebo, twice a day for 12 consecutive weeks. A total of 200 evaluable subjects (50 per group) will be studied. A minimum of 10 study sites will participate in this trial. Total study time per subject, including follow-up, is one year.

Subjects will be seen in clinic 2-3 times during the screening period to obtain two consecutive treadmill results (peak walking time) that are within 25% of each other on separate days. Also, ail baseline information will be collected on the first screen attempt. Upon enrollment into the study, subjects will be required to walk on the treadmill until claudication onset, administered two assessment questionnaires and given drug. Subjects will return to clinic for three visits over the ensuing 12 week treatment period. At that time, EKGS, treadmill test for claudication onset time, and assessment questionnaires will be performed. Subjects will be seen twice in clinic during follow-up period. Adverse events, including significant laboratory abnormalities, will be recorded on the Case Report Forms.

Progress: 16 patients enrolled in this study in FY 00 at MAMC, with 4 patients screen failures. 12 patients have been randomized to study drug and will be followed until September 2002. All adverse events have been reported to the IRB. Patient enrollment continues.



Detail Summary Sheets

General Surgery Service, Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/142 **Status**: Ongoing

Title: A Prospective, Randomized, Double-blind, Multicenter Trial Assessing the Safety and Efficacy of Sequential (intravenous/oral) BAY 12-8039 (moxifloxacin) 400 mg every 24 hr Compared to Intravenous Piperacillin/Tazobactam 3.375 gm every 6 hr Followed by Oral Amoxicillin/Clavulanic Acid Suspension 800 mg every 12 hr for the Treatment of Patients with Complicated Intra-abdominal Infections

Principal Investigator: LTC Kenneth S. Azarow, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC Ronald J. Place, MC; CPT Leroy J. Trombetta, MC; CPT James A. Sebesta, MC; CPT Christopher K. Sanborn, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Feb 02	9/25/2001

Study Objective: To compare the safety and efficacy of sequential (intravenous/oral) moxifloxacin every 24 hours with the combination of intravenous piperacillin/tazobactam (Zosyn*) every 6 hr followed by oral amoxicillin/clavulanic acid (Augmentin*) suspension every 12 hours for the treatment of adult patients with complicated intra-abdominal infections.

Technical Approach: The primary diagnosis of each patient in this study will be complicated intra-abdominal infection defined as an intra-abdominal infection in which an operative procedure or percutaneous drainage is required for diagnosis and management. Findings at operation must confirm the presence of an intra-abdominal infection (e.g., presence of purulent exudate and inflamed or necrotic tissue).

Patients will be randomized to one of two treatment groups. Treatment Group 1: Experimental treatment arm of Moxifloxacin 400 mg, administered by intravenous infusion over 60-minutes every 24 hours plus a piperacillin/tazobactam placebo infusion every 6 hours. If the patient is switched from intravenous to oral moxifloxacin 400 mg tablet every 24 hours, they will also receive amoxicillin/clavulanic acid placebo suspension every 12 hours.

Treatment Group 2: Standard treatment arm of Piperacillin/Tazobactam 3.375 gm, administered by intravenous infusion over 60-minutes every 6 hours plus a moxifloxacin placebo infusion every 24 hours. If the patient is switched from intravenous piperacillin/tazobactam to oral amoxicillin/clavulanic acid suspension 800 mg every 12 hours, they will also receive a moxifloxacin placebo tablet every 24 hours.

For both treatment groups, at the investigator's discretion, a switch to oral therapy could be made if the following criteria are met; (1) patient is clinically improving on intravenous therapy, (2) gastrointestinal motor activity has returned as indicated by passage of gas or feces per rectum or ostomy or (3) gastrointestinal function is present as indicated by tolerance of enteral feedings, either by mouth or by tube (including jejunostomy). Patients will be evaluated for complete recovery.

Progress: Between 1 October 00 and 1 October 01, 5 subjects were screened for possible enrollment to the multicenter Complicated Intra-Abdominal Infection study. One subject met all eligibility criteria and was enrolled to the study in August 01. This individual completed study treatment and follow up according to the protocol without complication. All study data has been reported to central study personnel for the subject enrolled. Final CIRO approval was received and CRDA with the Henry M. Jackson Foundation for the Advancement of Military Medicine completed in February 01. The study was opened at MAMC in April 01, and in May 01, a nurse data coordinator was hired under contract to assist with inter-departmental coordination, (laboratory, pharmacy, ward, clinic), patient screening, enrollment, assessments, and follow up. The Principal Investigator attended a project Investigator's Meeting in New Orleans, LA in May 01. 3 Sub-investigators were added to the project in July from surgical resident staff. Protocol

Amendments 1 and 2, updated consent form, and revised Investigator Brochure submissions to MAMC IRB were approved. Protocol Amendment 3, revised consent form, and an updated Investigator Brochure were submitted to the IRB in FY 01, and will be considered in early FY 02. All regulatory requirements are up to date. In September 01, the protocol was approved for continuation by MAMC IRB.

Serious Adverse Events: None at MAMC. Non-MAMC IND Safety Reports FY 01: The study drug continues clinical trials in many and international centers for the indications of complicated intra-abdominal infection and complicated infections of skin and skin structures. IND Safety Letters from 1 Oct. 00 to 1 Oct. 01 reported 9 Serious Adverse Events (SAE) plus 4 follow-up reports to investigators in all BAY 12-8039 clinical trials. MAMC IRB has been notified of these events. 4 additional FY 01 IND Safety Letters dated late August and September 01 are expected to be received and are expected to be reported to MAMC IRB in the near future. The Principal Investigator assessments based on review of SAE reports received were that no changes were required in the MAMC protocol or Informed Consent Document.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/021 **Status**: Terminated

Title: A Multicenter Trial of Adjuvant Interferon Alpha-2b for Melanoma Patients with Early Lymph Node Metastasis Detected by Lymphatic Mapping and Sentinel Lymph Node Biopsy

Principal Investigator: LTC Alan L. Beitler, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): COL William C. Williard, III, MC; MAJ David E. McCune, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Jan 12	10/24/2000

Study Objective: (1) Determine whether regional lymphadenectomy plus adjuvant high dose interferon alpha-2b therapy improves disease-free and overall survival for melanoma patients with early (sentinel lymph node-only) nodal metastasis detected by histology or immunohistochemistry, compared to lymphadenectomy alone, (2) Determine whether regional lymphadenectomy plus adjuvant high dose interferon alpha-2b improves disease-free and overall survival for melanoma patient with lymphadenectomy alone, (3) Determine whether lymphadenectomy alone improves disease-free and overall survival for patients with submicroscopic (detected by PCR only) sentinel node metastasis, compared to observation, (4) Determine the natural history (recurrences and survival) of patients with submicroscopic (detected by PCR only) sentinel lymph node metastasis, (5) Determine the positive and negative predictive value of RT-PCR analysis of sentinel lymph nodes to identify patients at risk for recurrence and death, and (6) Determine the positive and negative predictive value of RT-PCR analysis of peripheral blood to identify patients at risk for recurrence and death.

Technical Approach: All patients 18 to 70 years old with melanoma > or = to 1.0 mm Breslow thickness, no evidence of distant metastasis by history and physical examination, chest x-ray and liver function tests, and no palpable regional lymph nodes will be eligible, provided that the other entry criteria have been met. The Sunbelt Melanoma Trial is divided into 2 separate protocols, plus a preliminary trial. Protocol A includes patients with histologically or immunohistochemically positive sentinel nodes. Protocol B includes patients with histologically and immunohistochemically negative nodes, and PCR positive sentinel nodes. Patients with negative sentinel nodes (PCR, histologically and immunohistochemically) will be observed. After consenting into the preliminary trial, patients will be registered into the study. Lymphatic mapping and sentinel lymph node biopsy will be performed. A portion of each sentinel node will be frozen and stored for PCR analysis at a later time. The remaining lymph nodes will be sent for routine histology &/or serial sectioning and immunohistochemical staining. Patients eligible for Protocol A will sign a new informed consent form. A peripheral blood specimen for PCR analysis will be obtained. All Patients will undergo regional lymph node dissection. Patients with 1 positive sentinel node will be randomized to receive either observation or high dose adjuvant interferon alpha-2b therapy, with stratification by Breslow thickness and the presence of absence of tumor ulceration. If the patient has more than one positive sentinel node, any evidence of extracapsular extension of tumor or any non-sentinel node that is positive for metastatic melanoma will not be randomized, but will be treated with standard therapy. These patients will be followed to determine the predictive value of prospective peripheral blood PCR analysis for survival and recurrence. This group of patients also wills be eligible to go off study and participate in other protocols if desired. Patient eligible for Protocol B will sign a new informed consent form. A blood sample will be collected for eventual PCR testing, and will be randomized into 1 of 3 treatment arms: observation, lymph node dissection, or lymph node dissection plus one month high dose interferon treatment. These groups will be stratified by Breslow thickness and the presence/absence of ulceration. All patients will be followed, per standard of care, for up to 10 years, including, but not limited to, a visit every 3 months for years one and two, every 4 months

for year three, every 6 months for years four and five, and yearly thereafter. Peripheral blood will be obtained for PCR analysis upon entry into Protocols A or B, at the 3 and 12 month postoperative visits, and yearly thereafter. Chest x-ray and liver function tests will be obtained annually per standard of care. Lymph node tissue is to be sent to the National Genetic Institute for immediate PCR testing of submicroscopic sentinel node metastasis to determine protocol A or B eligibility. The peripheral blood samples will be stored at the NGI until PCR testing can be conducted; as these tests are tangential to the study and can be completed as time permits. All tissue and blood samples will be destroyed upon closure of the study and not stored for future genetic research.

Progress: Since receiving initial IRB approval, only two subjects have been screened for enrollment. Both subjects were screen failures. This study has been terminated at MAMC at the request of study investigators due to poor accrual.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/005 **Status**: Completed

Title: Surgical Skills Practicum - Advanced Trauma Life Support for Doctors (ATLS) Using the Goat (Capra hircus)

Principal Investigator: COL William E. Eggebroten, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/20/1998	Oct 01	10/11/2000

Study Objective: The objective of this training exercise is to teach physicians one safe method of performing six lifesaving procedures for trauma patients.

Technical Approach: This training protocol will instruct MAMC residents in the initial management of trauma patients. The students will practice the safe methods of performing the following lifesaving procedures in the order listed: venous cutdown, peritoneal lavage, chest tube placement, pericardiocentesis, thoracotomy and vessel cross clamp, cricothyroidotomy. The procedures will be performed after the animals are properly prepared and adequately anesthetized for surgery. The endpoint of this training will be completion of all procedures or evidence of excessive duress or anesthetic instability. Students will be evaluated by instructors on the basis of direct observation of psychomotor skills and verbalization of the indications, contraindications and potential complications of each procedure.

Progress: This study reached trienniel expiration, 18 Oct 01. The protocol has been terminated and replaced by MAMC protocol #201091.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/083 **Status**: Completed

Title: Porcine Iliac Artery Injury Model for Testing of Absorbable Vascular Templates

Principal Investigator: CPT Mohamad I. Haque, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Scott R. Steele, MC; LTC Kenneth S. Azarow, MC; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; COL William C. Williard, III, MC; MAJ David P. Tracy, MC; MAJ Sean P. Murray, MC; COL Charles A. Andersen, MC; CPT Alec C. Beekley, MC; MAJ Ronald E. Nielsen, VC

Start Date:	Est. Completion Date:	Periodic Review:
06/19/1998	Jun 01	8/24/1999

Study Objective: (1) To determine if pigs can serve as an adequate living tissue model for testing the in vivo absorption of polyphosphasene vascular templates and (2) if the absorbable vascular templates or stents will effectively treat deliberate, non-transecting iliac artery injuries in a porcine model in a reproducible fashion.

Technical Approach: An absorbable template will be unilaterally placed in each pig's normal iliac artery using manual and angiographic techniques via an arteriotomy in the opposite iliac artery. Impact of the stent will be assessed immediately through intraoperative arteriographic measurement of luminal diameters. Impact of the templates over time will be assessed by repeat angiography with subsequent sacrificing of the animals and tensile strength testing, routine histopathologic evaluation, and electron microscopic evaluation of the arterial segment containing the experimental stent at one, two, three, four, and five weeks after stent placement. Bilateral, non-transecting iliac arteriotomies will be created in a standard fashion in each pig, placing an experimental absorbable vascular template across one lesion using manual, endovascular and/or angiographic techniques, and primarily repairing the opposite lesion with standard vascular suture techniques. Resulting artery and stent patency and integrity will be assessed by intraoperative arteriography. Impact over time will be assessed via repeat arteriography with subsequent sacrifice of the animals and tensile strength testing, routine histopathologic evaluation, and electron microscopic evaluation of the segments of artery containing the experimental stent at one, two, three, four, and five weeks following stent implantation. These results will be compared with the results of the same tests done on the arteriotomies that were repaired primarily with suture.

Progress: This protocol reached triennial expiration, 19 Jun 01, and was closed prior to production of a viable absorbable vascular template. No work was completed on this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/074 **Status**: Ongoing

Title: Introduction of Telomerase into Type II Pneumocytes: Effect on Life span and Surfactant Production

Principal Investigator: MAJ Matthew J. Martin, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Scott R. Steele, MC; CPT Todd M. Rossignol, MS; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Nov 00	7/24/2001

Study Objective: (1) Determine whether cells purchased from ACT will not have any significant telomerase activity or surfactant production prior to transfection with hTERT, (2) If ACT cells exhibit telomerase activity then they will not be used and we will attempt to culture and sustain a population of normal rat type II pneumocytes, (3) Transfect normal rat type II pneumocytes with a vector including the human telomerase catalytic subunit, (4) Assess telomerase activity in transfected cell population and control group, (5) Assess telomere length in transfected cell population and control group, (6) Assess pulmonary surfactant production in transfected cell population and control group, and (7) Stain transfected cell population and control group for B-galactosidase, a biological marker for cellular aging.

Technical Approach: Type II pneumocytes (CCL-149) will be purchased from ACT and grown to confluence. The cells will be extracted and telomerase activity will be assayed. If the cells exhibit a negative telomerase activity, then they will be used for the remainder of the study, if not, then a population of normal rat type II pneumocytes will be cultured from a rat lung. The appropriate cells will then be transfected with the nTERT cDNA gene. This will be accomplished using one of the procedures of transfection, either the bombardment techniques, Lipofectin or other. After transfection and growth of the cells to confluence, the cells will be assays again for Telomerase activity as above. Non transfected cells will be used as a control group. Telomere length will be determined. Pulmonary Surfactant production will be measured using either Western Analysis or another method as well as B-Galactosidase activity as a biological marker of cell aging.

Progress: Dr. Martin continues to try to introduce telomerase into the pneumocytes. This bench study remains ongoing.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/118 **Status**: Ongoing

Title: Total Colonic Manometry in the Evaluation and Management of Pediatric Functional Colonic Obstruction.

Principal Investigator: MAJ Matthew J. Martin, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Scott R. Steele, MC; COL James M. Noel, Jr., MC; LTC David Wiechmann, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Indef.	N/A

Study Objective: 1) Characterize basic patterns of normal and pathologic colonic motility on colonic manometry 2) Use total colonic manometry to diagnose the etiology of functional colonic obstruction 3) Establish a prospective clinical database of all patients referred for refractory functional obstruction that includes demographic data, colonic manometry results and interpretation, medical and surgical management, short and long term patient outcomes, and quality of life before and after intervention 4) Analyze manometry results, patient data, and treatment outcomes to increase the knowledge base of pediatric functional obstruction and design treatment strategies to maximize patient outcomes and quality of life.

Technical Approach: This will be a prospective study to collect and analyze a clinical database on all patients referred for refractory functional obstruction who undergo total colonic manometry. Any patient who is thought to be a candidate for surgery will have a surgeon's review of all data except manometry data. A written surgical opinion will be documented - the surgeon will be blinded to the patient's identification data at this point. A follow up surgical opinion will be obtained following manometric evaluation. Any change in the decision to proceed with surgery or any change in the planned procedure will be considered a positive impact. Chi-Square analysis will be used to determine if manometric data yields a change in surgical opinion. The surgeon will become unblinded when he meets the family after all data have been collected and opinions have been given.

It should be noted that this study will not change the way these patients are dealt with or evaluated in any fashion. Presently patients are evaluated with manometry and after a joint surgical and gastroenterologic evaluation a combined opinion on how to proceed is offered to the family. This will not change and will take place once the surgeon is unblinded. Thus this study evaluates the surgeon rather than the patient.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/078 **Status**: Completed

Title: Inflammatory Response Related to Tracheobronchial Distention in Pigs (Sus scrofa) Using Absorbable Tracheal Stents

Principal Investigator: MAJ Matthew J. Martin, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Ronald A. Gagliano, MC; CPT Alec C. Beekley, MC; CPT Leroy J. Trombetta, MC; MAJ Andrew B. Silva; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	May 01	9/13/2000

Study Objective: To characterize the inflammatory reaction and granulation tissue formation following absorbable stent placement in the pig airway. To achieve this long term objective, our pilot should demonstrate any differences between in vivo and in vitro absorption of the stents.

Technical Approach: A total of 10 pigs will be utilized in this study, two pigs per group during a 5 week period of time. Group 1 will have stent insertion with sacrifice of the animals at day 7; Group 2 will be sacrificed at day 14; Group 3 will be sacrificed at day 21; Group 4 will be sacrificed at day 28 and Group 5 will be sacrificed at day 35. All animals will undergo histologic examination of Thier airways to include videoscopic recordings in order to more accurately measure airway lumen diameters and tissue condition and reactivity.

Progress: This protocol reached triennial expiration, 22 May 01. No work was accomplished on this study in FY 01, awaiting production of a viable absorbable tracheal stent from the study sponsor.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/133 **Status**: Completed

Title: Development of an In-vivo Model of Free Radical Production Utilizing Dihydroethidine in the Rat (Rattus Norvegicus)

Principal Investigator: CPT Rebecca E. McGuigan, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Jerome M. McDonald, MC; CPT Todd M. Rossignol, MS; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/13/2000	Sep 03	7/13/2001

Study Objective: To determine a reproducible and inexpensive method of quantitatively measuring free radical production in the rat.

Technical Approach: This study will utilize 10 "control" rats and 10 "test" rats that have been anesthetized and then subjected to ischemia/reperfusion by clamping and then unclamping the aorta above the celiac trunk. A fluorescent label for the presence of free radicals (specifically superoxide) will be injected during the experiment. The animals will be sacrificed and specified organs analyzed using a spectrophotometer for quantitation of the production of superoxide. In addition, a well-known marker of lipid peroxidation, malondialdehyde (MDA) will be measured to verify that the free radical superoxide has indeed been produced. This study was amended.

Progress: Forty-two animals were used. Experimental animals underwent general anesthesia, midline laparotomy, HE injection, cross clamping of the supramesenteric or supraceliac aorta, and subsequent reperfusion. Ischemia and reperfusion times were initially adjusted. Ultimately, HE injection occurred at time 0, cross clamping at time 15 minutes, reperfusion from time 60 to 150 minutes. Control animals underwent only laparotomy and HE injection. The animals were euthanized and their small intestine, liver, and lungs taken for study. The tissue was homogenized and ethidium bromide fluorescence and malondialdehyde measured.

There were five experimental and five control animals that had supraceliac clamping and nearly identical operative conditions. The average amount of ethidium produced in the small intestine of the experimental animals in this group was 0.6207 AFU/mg protein and in the control animals was 0.3643 AFU/mg protein. Significance was tested with a Student's T test and achieved with a p value of 0.02. There was not a significant difference in the ethidium produced in the lung or liver (as expected, due to short reperfusion time and immediate euthanasia). In addition, there was not a significant difference in the malondialdehyde produced in the small intestine of these animals. Hydroethidine likely acted as a scavenger of superoxide and prevented lipid peroxidation to some extent, thus explaining why malondialdehyde results did not differ between the two groups. All work on this protocol was completed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/120 **Status**: Ongoing

Title: Steroidogenic Factor 1 (SF-1) in Human Breast Cancer Tissue

Principal Investigator: CPT Rebecca E. McGuigan, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC Kenneth S. Azarow, MC; Meera Ramayya, MD; Helmut Zarble, MD; CPT David Ward, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Sep 01	N/A

Study Objective: This study will try to demonstrate the presence of mRNA and protein expression of Steroidogenic factor-1 (SF-1) and aromatase in estrogen receptor positive breast cancer cell lines and breast cancer tissue.

Technical Approach: This study will try to measure the presence of SF-1 and aromatase in breast cancer cell lines, normal breast tissue and breast cancer tissue. The following methods will be used: 1. RNA extraction and real time PCR; 2. Protein extraction and western blot; 3. Immunohistochemistry. In addition, cDNA microarrays will be used to determine if the expression of SF-1 alters the pattern of gene expression in breast tissue. Chi square test will be performed on the presence or absence of SF-1 with significance being a p value of less than 0.05.

Progress: Thus far preliminary work has been done on several breast cancer cell lines and positive/negative control tissues. Cell lines have been grown in culture and protein and RNA extraction has been performed. Western blot analysis has been performed using anti-SF-1 and aromatase antibodies, but conditions for Western blot have not yet been optimized. Four patients have been enrolled to date. Their tissue has been frozen for protein and RNA extraction to be performed once conditions for the Western blot are optimized.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/004 **Status**: Completed

Title: Forward Surgical Team (FST) Sustainment Training Using the Goat Model (Capra hircus)

Principal Investigator: LTC Clifford A. Porter, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC David C. Elliott, MC; MAJ Ann Everett, AN, CRNA; CPT Michael S. Murphy, AN; LTC Craig M. Ono, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/20/1998	Oct 01	8/11/2000

Study Objective: FST personnel will be exposed, gain experience and demonstrate proficiency in invasive resuscitation procedures.

Technical Approach: FST personnel must achieve a score of 70% on the written exam at the end of the didactic instruction before proceeding to the hands on portion of the exercise. Anesthetized adult goats will be used to train medical personnel basic surgical and emergency resuscitation skills they are expected to perform in combat. These tasks include: cricothyroidotomy (needle and surgical), endotracheal intubation, needle thoracentesis, chest tube placement, open thoracotomy, peritoneal lavage, exploratory laparotomies (FST surgeons), pericardiocentesis, intravenous catheterization, venous cutdown and techniques of suture placement (abdominal fascial closure). This protocol doesn't vary from previously accepted regimens for this purpose.

Progress: This protocol held 3 sessions during FY01 for a total of 6 sessions since protocol approval. This protocol is completed. Further training of this nature will be done under MAMC protocol #201091.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/087 **Status**: Ongoing

Title: Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)

Principal Investigator: LTC Clifford A. Porter, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): COL William E. Eggebroten, MC; COL William C. Williard, III, MC; LTC Kenneth S. Azarow, MC; LTC Alan L. Beitler, MC; LTC David C. Elliott, MC; LTC David M. Watts, MC; Preston L. Carter, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Aug 02	10/11/2000

Study Objective: To familiarize General Surgery residents, staff and invited surgeons from our community with techniques in the performance of advanced laparoscopic techniques. This training will include esophagus, stomach, biliary, small and large intestine, spleen, liver and retroperitoneal procedures. The training benefit will accrue to General Surgery residents, staff and invited surgeons by introducing these techniques or reinforcing earlier acquired skills in a controlled environment. Familiarity with these techniques will allow an increased margin of safety for patients decreased operative time, and minimizing of potential complications.

Technical Approach: Pigs will be maintained in an NPO status for 12 hours prior to the scheduled training procedures. An intramuscular tranquilizer will be used to aid in animal handling and preoperative management. General anesthesia will be induced with injectable agent and maintained by inhalational agent. Following anesthesia induction, pigs will be intubated endotracheally, will have an indwelling intravenous catheter placed in an ear vein for intraoperative fluid support, will have an orogastric tube inserted and connected to central suction for as-needed gastric decompression, and will be clipped and scrubbed as per aseptic surgery technique for the body regions of interest (e.g. abdomen, chest, etc.). Preoperative preparations will be conducted in the DCI animal surgery preparation and recovery room immediately adjacent to the DCI surgery. Following preoperative preparation, anesthetized animals will be transferred to either DCI surgery suite.

Five training sessions are scheduled for this training, they are: Advanced Laparoscopic Esophageal and Gastric Surgery, Advanced Laparoscopic Biliary Surgery, Advanced Laparoscopic Small and Large Intestinal and Rectal Surgery, Advanced Laparoscopic Splenectomy and Liver Surgery, and Advanced Laparoscopic Retroperitoneal Dissection and Lymph Node Dissection. Each session will be formalized into one day continuing medical education programs consisting of 1 hour of didactic lecture, 4 hours of hands-on procedural and/or instrumentation orientation using inanimate training models and non-living human or animal tissues, and 3 hours of live (anesthetized) animal laboratory for definitive procedural training. Each animal will be used for a single training session only, and will be euthanized at the end of the session without recovery from general anesthesia. Non-survival/training surgical procedures will be performed using clean (simulated aseptic) technique. Each training session will utilize up to four pigs.

Progress: Two training sessions were held in FY01, utilizing a total of 6 animals. Both staff and residents participated with excellent skills learned. These sessions have significantly improved medical readiness and direct patient care through enhanced skills learned.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/115 **Status**: Completed

Title: Relationship Among Differentiation, Apoptosis, and Telomerase Activity in Neuroblastoma Cell Lines

Principal Investigator: CPT Christopher K. Sanborn, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC Kenneth S. Azarow, MC; CPT Craig See, MC; Robert S. Sawin, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Nov 00	10/23/2001

Study Objective: Determine the level of telomerase activity in human neuroblastoma cell lines via PCR-ELISA assays before and after induced differentiation by retinoic acid. Relate telomerase activity to apoptosis using the CDDE+ technique before and after differentiation for assay.

Technical Approach: This study will synchronize the SK-N-DZ neuroblastoma cell line in culture by utilizing the isopyknic centrifugation technique. Baseline TRAP, CDDEplus, and pp60c-src assays on the SK-N-DZ cells will be performed to establish baseline values of telomerase activity, apoptotic activity and level of c-src expression respectively. Subculture of the cells will then be subjected to either normal culture medium or culture medium enhanced with retinoic acid. After 3, 6, and 10 days of treatment, the above assays will be performed again to analyze differences between each cell group as compared to its untreated control group.

Progress: Methods: SK-N-DZ human neuroblastoma cells were synchronized by nutritional deprivation. They were then differentiated using 0.01mM, 0.1mM, and 1.0mM retinoic acid. Differentiation was verified by pp60c-src ELISA, which identifies the protein product of c-src proto-oncogene, a marker of differentiation. At days 0, 3, 6, and 10 telomerase activity was assayed by telomerase repeat amplification protocol (TRAP). The Cell Death Detection ELISA (CDDEplus) was used to quantify apoptosis. Telomerase activity per 105 cells was calculated for each retinoic acid treatment group, at each interval. A comparison was then made between treated and untreated cells using a 2-tailed student's T-test.

Results: Cells treated with retinoic acid appeared to have an increased c-src protein level, correlating with differentiation. There was no statistically significant difference in telomerase activity/cell count between controls and differentiated cells ($p > 0.4$). Conclusions: In support of our prior experiment, telomase activity does not appear to be significantly different in differentiated neuroblastoma cells controlled for cell cycle phase and apoptosis. This supports the theory that differentiation does not require decreased telomerase activity in this solid tumor model.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/001 **Status**: Ongoing

Title: Glycosylated Hemoglobin in Diabetics Undergoing General Surgery Procedures

Principal Investigator: CPT Christopher K. Sanborn, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Philip Mullenix, MC; LTC Kenneth S. Azarow, MC; LTC Ronald J. Place, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Apr 01	N/A

Study Objective: To determine if elevation of glycosylated hemoglobin is a predictor of post-operative complications in patients with diabetes mellitus.

Technical Approach: Subjects identified by the general surgery service and meeting inclusion criteria will have preoperative labs to include glycosylated hemoglobin, blood glucose, serum blood urea nitrogen, serum creatinine, and urinalysis. Oral hypoglycemics will be stopped the day prior to the scheduled procedure and not restarted until the patient restarts oral intake. For insulin dependent diabetics, the usual morning insulin dose will be given. On arrival, subjects will have their blood sugar checked and will be started on a solution of 5% dextrose. Demographics, the date of operation, use of prophylactic antibiotics, operative complications, postoperative complications, and other factors will be followed. The primary investigator will be blinded to the HbAIc data. At the end of the collection period, statistical analysis will be performed using chi-square. Wounds will be examined on postoperative day five and described as uncomplicated, seroma, or frankly infected. The seromas will be further subclassified as (1) gram stain negative, culture negative, (2) gram stain positive, culture negative, or (3) gram stain and culture positive.

Progress: Three subjects enrolled in this study at MAMC during FY01. The study has undergone a hiatus while investigators try to work out an enrollment/data collection system that would work more efficiently within their clinic.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/124 **Status**: Terminated

Title: Clinical Pathway for Resectional Gastric Bypass for Morbid Obesity Focusing on Postoperative Diet

Principal Investigator: CPT James A. Sebesta, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT Craig See, MC; LTC David M. Watts, MC; LTC Kenneth S. Azarow, MC; Preston L. Carter, M.D.; LTC Ronald J. Place, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Oct 02	7/24/2001

Study Objective: To determine if an aggressive management of the postoperative diet can safely decrease the length of stay for the morbidly obese patients who undergo resectional gastric bypass.

Technical Approach: Patients will be randomized into one of two groups, the standard diet or the study diet. The patient's demographic information will be collected and recorded on the clinical pathway form. Operative and postoperative data points will be collected. All patients will receive the same anesthetic and have their postoperative pain controlled with a patient controlled anesthesia device and will be given Ketorolac 30mg IV on the evening of surgery and 15mg IV every 8 hours for 72 hours. Every patient will receive the same antibiotic, DVT prophylaxis and anti-emetics including: Cefotetan 2gm IV every 12 hours for 24 hours, Heparin 5000 mg SQ twice a day, and Inapsine 1.25 mg IV every 6 hours as needed.

All patient activity will be controlled. This will consist of out-of-bed to chair at least three times a day starting on postop day number 1; ambulate within the room at least three times per day on postop day number 2; and ambulate in the halls at least three times a day on each subsequent day. A nasogastric tube will be placed intraoperatively and will be removed on the morning of postoperative day one. Anti-emetic use is authorized and will be documented.

Subjects randomized to the standard diet will receive nothing by mouth until demonstration of full intestinal activity by the passage of flatus. The patient will then be given gastric bypass clear liquids for 24 hours. If the patient has no more than one episode of nausea requiring anti-emetics and no emesis, they will be transitioned to a post-gastric bypass diet and discharged after receiving nutritional instructions and tolerating two solid meals without nausea or emesis.

Subjects randomized to the study diet will receive nothing by mouth until the morning of postop day number two. Patients will then be started on a 30cc per hour gastric bypass clear liquid diet until 2200 hours. This will be self administered and documented by the patient. If the patient has no more than one episode of nausea requiring anti-emetics and no emesis, they will be transitioned to ad lib gastric bypass clear liquid diet for postoperative day number three. When the patient has no more nausea requiring anti-emetics of emesis for 24 hours, they will receive nutritional instructions for gastric bypass soft diet and discharged. All patients will receive a phone call daily for three days after discharge by surgeons who are blinded to the study to monitor progress and screen for complications. Postop wound evaluations will also be performed by the same surgeons.

Progress: This study was reported as terminated, 11 Oct 01, due to difficulty with subject enrollment. No subjects enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/083 **Status**: Ongoing

Title: Does the Concentration of Gastrin Releasing Peptide Receptors on the Surface of Human Neuroblastoma Specimens Predict the Aggressiveness of the Tumor?

Principal Investigator: CPT James A. Sebesta, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): LTC Kenneth S. Azarow, MC; Robert S. Sawin, M.D.

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Nov 01	N/A

Study Objective: To evaluate the concentration of Gastrin Releasing Peptide Receptors on the surface of neuroblastoma tissues and correlate this to the aggressiveness of the individual tumor. This potentially could be used as a prognostic tool during the initial evaluation of neuroblastomas.

Technical Approach: This study will evaluate 50 tumor specimens using a radioligand to mark each receptor and a gamma counter to determine the number of bound radioligands based on the known activity of the radioactive label. The clinical nature of the tumors will compared to the receptor density to determine if an increased number of receptors indicates a more aggressive tumor requiring aggressive early therapy.

Progress: This study has not yet been intiated at MAMC pending funding and availability of tumor tissue.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/089 **Status**: Ongoing

Title: Comparison of Harmonic Scalpel vs. Electrocautery Following Hemorrhoidectomy

Principal Investigator: CPT Scott R. Steele, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Matthew J. Martin, MC; LTC Ronald J. Place, MC; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Apr 02	N/A

Study Objective: 1) Prospectively evaluate the post-operative pain and oral narcotic requirement after performing hemorrhoidectomy with a harmonic scalpel vs. electrocautery. 2) Evaluate the time to return to duty following hemorrhoidectomy using each procedure; 3) Determine differences in complication rates following hemorrhoidectomy after each procedure; 4) Evaluate the differences in blood loss and operative time following hemorrhoidectomy after each procedure.

Technical Approach: In this study we will compare the post-operative pain and narcotic use in 118 consecutive patients with symptomatic grade III or IV hemorrhoids when using the harmonic scalpel versus standard electrocautery while using maximal NSAID therapy. We will use a visual analogue scale for patients to quantify their pain pre-operatively and then on postoperative days 2 and 7. Post-operative narcotic requirements per 24 hours will similarly be recorded on post-operative days 2 and 7. We will call patients on postoperative day 28 to ensure no further complications. Data will be analyzed using a t-test.

Progress: Thirty-four subjects enrolled in this study at MAMC during FY01. One subject had to be withdrawn when more than one procedure was required to be done. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/110 **Status**: Ongoing

Title: Intra-operative Drain Use in Gynecomastia Patients Undergoing Subcutaneous Mastectomy

Principal Investigator: CPT Scott R. Steele, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Matthew J. Martin, MC; LTC Kenneth S. Azarow, MC; LTC Ronald J. Place, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/26/2001	May 02	N/A

Study Objective: Prospectively evaluate the complication rate associated with gynecomastia patients undergoing a subcutaneous mastectomy with and without intra-operative drain placement.

Technical Approach: Patients will be identified by the General Surgery Service. Any patient meeting the inclusion criteria for the study (as listed above) will be randomized prospectively to drain placement or no drain placement. Randomization will be performed by placing sealed envelopes in random order containing slips of paper with either "drain" or "no drain" inside in a three-ring binder. Randomization will occur in four consecutive groups of 8, with 4 "drains" and 4 "no drains" in each group. The General Surgery staff (RP) will have the binder. Envelopes will be taken consecutively with each new patient entered into the study and brought into the operating room at the time of operation sealed. Demographic data will be collected pre-operatively. A General Surgery resident and staff will then perform a standard subcutaneous mastectomy. Randomization will occur prior to skin closure. Additionally, patients will record post-operative narcotic use per 24 hours for the first ten days (see Appendix B). Any patient requiring narcotic use past 10 days will be identified as having prolonged pain. All patients with a drain will follow-up in a standard clinic appointment on post-operative day 3, where the drain will be removed. Additionally all patients will follow-up in a standard clinic appointment on post-operative day 14. At the follow-up visits, we will assess the patient for possible complications via physical exam and by patient's history. The General Surgery staff will then keep the form, and a blinded investigator (KA) will make a follow-up phone call on post-operative day 28 to ensure no other complications occurred. Results will be analyzed using Chi-Square Analysis with significance level at $p<0.05$.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/058 **Status**: Completed

Title: Telomerase Activity in Metastatic Nueroblastoma: A Nude Mouse Model (mus musculus, nu/nu)

Principal Investigator: CPT Leroy J. Trombetta, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT James A. Sebesta, MC; LTC Kenneth S. Azarow, MC; CPT Jeffrey A. Vos, MC; CPT James Nunley, MC; M. J. DeHart, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
10/11/2000	Nov 03	N/A

Study Objective: The objective is to evaluate the difference in telomerase activity between a primary neuroblastoma tumor and the subsequent foci of metastasis with the following objectives: 1) Telomerase activity in a metastatic foci of tumor is higher than that of the primary tumor. 2) Xenograft primary tumor will express morphologic differentiation as compared to the in vitro culture, and will therefore express a lower telomerase activity.

Technical Approach: Nueroblastoma tumor cells will be injected into immunocompromised mice. Once sufficient tumor growth has occurred, tumor tissue will be harvested and examined by DCI lab for telomerase activity.

Progress: All work on this study has been completed at MAMC; however, the final abstract is not yet available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/086 **Status**: Terminated

Title: Telomerase Enzyme Activity in a Metastatic Neuroblastoma Nude Mouse Model

Principal Investigator: CPT Leroy J. Trombetta, MC

Department: Surgery/General Surgery **Facility**: MAMC

Associate Investigator(s): CPT James A. Sebesta, MC; M. J. DeHart, B.S.; Robert S. Sawin, M.D.; CPT Jeffrey A. Vos, MC; Cynthia Pekow, Ph.D.; LTC Kenneth S. Azarow, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/28/1999	Apr 00	9/14/2001

Study Objective: To evaluate tolemerase activity in human neuroblastoma tumors grown in nude mice, with attention to the difference in telomerase activity between primary tumor and metastases.

Technical Approach: All foci of gross metastatic disease and the primary tumor will be assayed for telomerase activity via the TRAP-ELIZA as follows: Telomerase activity will be determined using the telomere repeat amplification protocol (TRAP assay). First, a sample of each tumor is cut and weighed. The sample is then manually pulverized, and 200-400 ul of lysis reagent added, depending on the size of the sample. Samples are then placed on ice for 30 minutes to ensure maximum cell lysis. Samples are then centrifuged at 4 degrees centigrade and 15,300 rpm for 30 minutes, after which the supernant is removed and the precipitate discarded. Protein content of each sample is determined using the Pierce BCA Protein Assay Reagent microliter plate protocol. Stock BSA protein solution is serially diluted and used as standards. Protein concentration of each sample is determined by plotting spectrophotometer absorbance against the standard controls. The TRAP assay is performed with the 21 samples. Serial dilutions of each sample using 6, 0.6, and 0.06 ug of protein are run simultaneously along with a positive and negative control at each dilution for a total of 69 samples. The positive control will be a thyroid carcinoma specimen proven to have telomerase activity. Sterile water is added to each sample to bring the total volume to 25 ul. The reaction mixture is added to each sample. This mixture is run through a PCR protocol. During this process, telomerase already present in the sample adds TTAGGG repeats to the biotin labeled primer. Then, the DNA polymerase amplifies the product. Thus, amount of product is dependent upon telomerase activity present in the sample. ELISA is then done to quantify the amount of telomerase product in each sample according to kit instructions. The DNA products is denatured and hybridized to a Digoxigenin labeled probe. Hybridized samples are then placed into a streptavidin impregnated microliter plate. The sample is immobilized to the microliter plate via a streptavidin-biotin bond. The microliter plate is incubated then washed with buffer solution. Anti-Digoxigenin antibody conjugated to a peroxidase is then added, and the solution incubated and rinsed. TME substrate is added, and the peroxidase reacts with the substrate resulting in a purple product. After incubation, a stop reagent is added, which results in a final product that is variable intensity of yellow. The microliter plate is read in a spectrophotometer at 450 nm with background of 655 nm. The absorbance value thus represents telomerase activity in the neuroblastoma specimen. Data to be collected and analyzed includes: 1) Telomerase enzyme activity level represented by the absorbance values obtained from the TRAP-ELISA. Telomerase activity of the in vitro cell line, primary subcutaneous tumor, and metastatic foci will be compared; 2) Histologic analysis of neuroblastoma cell line, primary tumor and metastatic foci will be compared.

Progress: This study was terminated and a rewritten version resubmitted for review/approval. No work had been initiated on this study at MAMC during the approval period.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/020 **Status**: Ongoing

Title: Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis

Principal Investigator: CPT Amy L. Young, DO

Department: Surgery/General Surgery **Facility**: MAMC

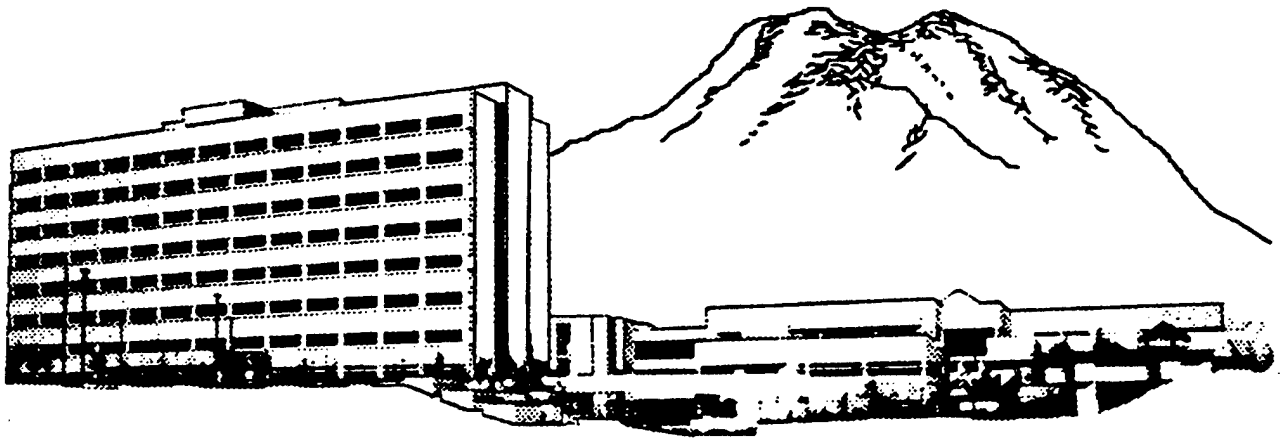
Associate Investigator(s): LTC Alan L. Beitler, MC; MAJ Jospeh P. Miller, MC; LTC Kenneth S. Azarow, MC; LTC Ronald J. Place, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Jul 02	N/A

Study Objective: (1) To evaluate individual and institutional learning curves for airway assessment by analyzing diagnostic accuracy as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, (2) To develop individual and institutional learning curves for the skill of endotracheal intubation as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, and (3) To evaluate a model (Cumulative sum analysis) for assessing the technical proficiency of surgical interns in the skills of airway assessment and endotracheal intubation.

Technical Approach: Surgical interns will receive standardized training on airway anatomy and assessment coupled with a practical session on intubation in ATLS models. These house officers will then perform airway assessments and endotracheal intubations on surgical patients who are 18 years or older, ASA class I or II, and who do not require rapid sequence intubation. Each attempt will be supervised and scored by a staff anesthesiologist or CRNA using a standardized data sheet. A successful assessment will be one where the airway classification matches the supervising staff's determination. A successful intubation will be insertion of an endotracheal tube within 30 seconds of laryngoscopy initiation, documented by end tidal CO2. If an attempt is unsuccessful, the process may be repeated. Each consecutive attempt will be recorded separately. A data sheet will be filled out and a new score assigned for each attempt, even when there are multiple attempts on a single patient. Supervising staff will determine if and when they need to step in and intubate the patients themselves. Data sheets will be turned in to the principal investigator, who will calculate CUSUM values and plot learning curves. Data will be monitored during the rotation. At the completion of the 4-week experience, these results will be shared with the interns and staff. After an entire class of interns has completed the rotation, the results will be submitted for publication and presentation.

Progress: 150 subjects participated in this study. Conclusion: It appears the average MAMC General Surgery Intern requires 10 attempts at Airway Assessment and 18 attempts at Endotracheal Intubation to plateau off the learning curve. From this the study concludes that the month-long rotation on Anesthesia for these Interns should provide at least this many task attempts to ensure proficiency. An Intern that approximates these learning curves will have an objective demonstration of expected performance accuracy. An Intern that continues to display a steep learning curve beyond these averages, should alert staff to the need for extra training needs.



Detail Summary Sheets

Ophthalmology Service, Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/034 **Status**: Terminated

Title: Refractive Changes in a Low-tension Oxygen Setting Following Placement of Intracorneal Ring Segments

Principal Investigator: MAJ Steven M. Brady, MC

Department: Surgery/Ophthalmology Surgery **Facility**: MAMC

Associate Investigator(s): Larry White, M.D.; COL Vernon C. Parmley, MC; COL Thomas H. Mader, MC; MAJ Mark L. Nelson, MC; Troy H. Patience, B.S.

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Apr 00	12/19/2001

Study Objective: To observe changes in corneal shape and visual acuity that may take place in subjects exposed to low oxygen tension environments more than one month following the placement of intracorneal ring segments.

Technical Approach: This protocol will evaluate 20 subjects with intracorneal ring segments (ICRS) in a low tension oxygen setting. Refractive changes and corneal topography in subjects who have undergone ICRS implantation and who have been exposed to a controlled low-tension oxygen setting (via airflow restrictive goggles) for 2 hours will be compared to myopic controls who have experienced the same low-tension oxygen goggle system. Results will be compared to others who are exposed to altitudinal changes known to affect corneas who have undergone various keratorefractive procedures.

Progress: This study was terminated due to low enrollment during FY01. Four subjects enrolled in this study at MAMC with no significant data analysis available. In addition, the company providing the intracorneal ring segments went bankrupt.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/050 **Status**: Completed

Title: A Phase III Study of MDX-RA Compared with Placebo Administered in Patients Undergoing Phacoemulsification or Planned Extracapsular Extraction for Cataract

Principal Investigator: MAJ Keith F. Dahlhauser, MC

Department: Surgery/Ophthalmology Surgery **Facility**: MAMC

Associate Investigator(s): COL Vernon C. Parmley, MC; COL Thomas H. Mader, MC; MAJ Mark F. Torres, MC; CPT Benjamin B. Chun, MC; MAJ Mark L. Nelson, MC; CPT Keith J. Wroblewski, MC; MAJ Roger K. George, MC; COL Kevin J. Chismire, MC; COL Dennis R. Beaudoin, MS

Start Date:	Est. Completion Date:	Periodic Review:
01/16/1998	Apr 99	1/23/2001

Study Objective: Describe and compare the safety of a single dose of the murine immunotoxin MDX-RA to placebo over a six-month period post-randomization, and to test the efficacy of MDX-RA by comparing the proportion of patients in the treated group to the proportion of patients in the placebo group who have had a visual acuity explainable YAG laser capsulotomy by 24 months of follow-up.

Technical Approach: In Phase I, subjects will undergo a pre-operative screening evaluation period prior to eye surgery for inclusion into the study; within four weeks for ophthalmic evaluations and within 2 weeks for physical evaluation. In Phase II, subjects will undergo phacoemulsification or planned extracapsular cataract surgery and receive 100 units of MDX-RA or placebo. In Phase III, during the 24 month follow-up period, ophthalmic examination, concomitant medication use, and occurrence of adverse experiences will assess safety. Subjects will be monitored for the need of visual acuity explainable YAG laser capsulotomies as the primary efficacy variable.

Progress: Six patients enrolled in this study at MAMC and continue to be followed. One patient was hospitalized with respiratory distress; however this event was considered unrelated to study participation. This study is currently closed to patient enrollment. Amendment #4 was IRB approved, which extended the study period from 24 to 36 months for those patients enrolled.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/017	**Status**: Ongoing

Title: The Effect of Latanoprost on Basic Tear Secretion

Principal Investigator: CPT Clifton S. Otto, MC

Department: Surgery/Ophthalmology Surgery **Facility**: MAMC

Associate Investigator(s): LTC Robert A. Mazzoli, MC; COL Kevin J. Chismire, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
11/19/1999	Jun 00	11/26/2000

Study Objective: To measure the difference in basic tear production before and after administration of topical latanoprost.

Technical Approach: After measuring the normal amount of tears secreted by subjects, each subject will have 0.005% latanoprost put into the conjunctival sac of the left eye. Tear secretion will again be measured. The subject will be sent home with instructions to put latanoprost into their left eye once a day for seven days. After seven days they will return and have their tear secretion rates measured as before. Patients will also return for a one-month follow up evaluation to detect any side effects from one week use of latanoprost.

Progress: One subject entered this study in FY00 at MAMC; however, no subjects enrolled in FY01. This study has been terminated by the PI due to difficulty with subject enrollment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/117 **Status**: Ongoing

Title: A Pilot Study on the Use of Laser Assisted In-Situ Keratomileusis (LASIK) versus Photorefractive Keratectomy (PRK) in Active Duty U.S. Army Personnel for the Correction of Myopia and Astigmatism

Principal Investigator: COL Vernon C. Parmley, MC

Department: Surgery/Ophthalmology Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Keith F. Dahlhauser, MC; MAJ Steven M. Brady, MC; MAJ Robert B. Carroll, MC; CPT Clifton S. Otto, MC; CPT WIlliam Lim, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
8/22/2000	Dec 03	7/24/2001

Study Objective: The purpose of this study is to compare laser assisted in-situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) using the Summit autonomous excimer laser system and the Bausch and Lomb Hansatome keratome as surgical methods for treating myopia and astigmatism in active duty soldiers.

Technical Approach: Approximately five hundred subjects who meet the inclusion criteria and who are active duty Army personnel between the ages of 21-55 with non-flying duties will be invited to participate in this study. The Argon fluoride excimer laser (193nm wave length) will be used to reduce the myopia and astigmatism of spectacle or contact lens dependent soldiers according to standard nomograms build into the laser controlling software of the excimer. Central ablation diameter will be 6.5 mm. Preoperative Assessments: Clinical examination will include past ocular and medical history, eye surgery or trauma, current medications, possible allergies, and a review of previous examinations and refractions. Hard contact lenses must be removed four weeks prior to the examination, and soft contact lenses must be removed one week prior to evaluation. Pupil size, uncorrected and best corrected visual acuity, manifest and cycloplegic refraction, keratometry and corneal topography, intraocular pressure, slit lamp biomicroscopy, central pachymetry, dilated ophthalmoscopy, and glare contrast sensitivity will be completed during the preoperative assessment and at the third month and one year examination. Subjects must be available for one year follow-up. If the volunteer states his/her desire to participate in the study, the consent process will be completed and a surgical date scheduled. On the day of surgery, each subject will be randomized (computer generated randomization) to undergo either bilateral sequential LASIK or PRK. All postoperative examinations will be performed at Madigan Army Medical Center. The subject will be examined on day 1, day 3, day 7, 1 month, 3 months, 6 months and 1 year.

At the one-month, three-month and one year evaluations, subjects will complete a questionnaire that subjectively assesses quality of vision and satisfaction with the procedure, as well as their subjective assessment of their ability to perform in their MOS. At the one-week evaluation, subjects will also indicate number of days after the procedure before they could return to full duty. If they have not returned to full duty by the one-week evaluation, this will be noted with a comment to ask again at the one-month evaluation if the patient has returned to full duty. The questionnaire used in this study is patterned after the functional vision test used in prospective evaluation of radial keratotomy study and the VF-14 visual function test developed for assessing visual performance in patients with cataracts.

Progress: This study has not yet been initiated at MAMC, awaiting possible funding through USAMRMC.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 99/052	**Status**: Terminated

Title: Correction of Low Myopia (-1.00 to -3.50 diopters) in Active Duty Personnel

Principal Investigator: COL Vernon C. Parmley, MC

Department: Surgery/Ophthalmology Surgery	**Facility**: MAMC

Associate Investigator(s): COL Thomas H. Mader, MC; CPT David M. Bushley, MC; CPT Michael A. McMann, MC

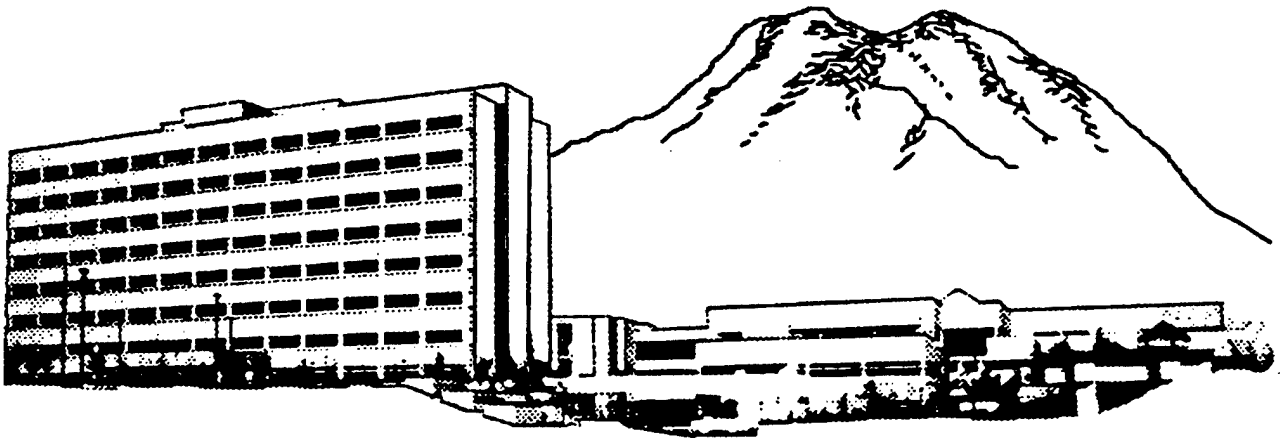
Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Jun 02	3/27/2001

Study Objective: To determine the feasibility of correcting low myopia in active duty U.S. Army soldiers with the intrastromal corneal ring segment system (ICRS) developed by Keravision(r).

Technical Approach: We plan to recruit 100 patients into the study (200 eyes). Prior to performing the procedure, a baseline complete eye examination will be performed, including several tests of visual acuity. Pre and postoperative tests will also be conducted to determine the effect of the procedure on military performance. These tests will include M-16 weapons fire with and without protective mask, day and night navigation in good and inclement weather, and a subjective questionnaire on satisfaction with the procedure and symptoms associated with the procedure. The questionnaire will also address the effect on performance in the field after insertion of corneal rings.

The procedure involves inserting two small curved pieces of plastic into the stroma of the cornea, using a special trephine to create the stromal tunnel. The procedure can be done under topical anesthesia in the operating room (for sterility). The procedure takes approximately 15 to 20 minutes to perform. Evaluations will occur on postoperative day (POD) 1 and 6, and again at 1 month, 3 months, 6 months, and 1 year. If the patient consents, the second eye will be done 1 week following the first eye. The same postoperative follow-ups will occur for the second eye. Key data to be analyzed include: Post-operative visual acuity compared with pre-operative visual acuity; : Post-operative refraction compared with pre-operative refraction, post-operative need for glasses; post-operative ability to perform specifically tested functions (weapons firing, ability to function in field without correction).

Progress: This study was reported as terminated, 12 Oct 01, due to inability to secure funding.



Detail Summary Sheets

Orthopedics Service, Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/086 **Status**: Ongoing

Title: A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough

Principal Investigator: LTC Edward D Arrington, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): Hollis Potter, M.D.; CPT Roger W. Dougherty, SP; LTC Patrick St Pierre, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/15/1996	Apr 99	10/23/2001

Study Objective: To determine if tendon repair to a cancellous trough is necessary for rotator cuff repair in humans.

Technical Approach: Forty patients with proven rotator cuff tears will be randomized to two surgical groups. Group A will have their rotator cuff tendon repaired to the greater tuberosity after a trough is made in the greater tuberosity of the humerus. Group B will have their rotator cuff repaired to the cortical bone of the greater tuberosity of the humerus without the creation of a trough. A thorough debridement of soft tissue to include bursa and scar will be performed in both groups. Postoperative treatment will be the same for each group. Clinical evaluations and physical exams to include range-of-motion, shoulder impingement signs and tenderness will be performed at one, six, twelve and twenty-four month follow-ups by the physical therapist department. The modified Hospital for Special Surgery (HSS) Score as well as an analog pain, function, and satisfaction score will be used for clinical evaluation. A significant difference in the assessment of strength scores would indicate superiority of one method over the other. MRI evaluations will be performed at six, twelve and twenty-four months. The MRI will be evaluated by an MRI radiologist at the HSS in New York City, New York, who will be blinded to the method of treatment for each patient. Criteria for success by MRI has been established by a recent study performed at the HSS by the radiologist and the principle investigator.

Progress: A total of 22 patients enrolled in this study at MAMC. Patient enrollment is complete and follow-up continued on enrolled patients during FY01. LTC Arrington assumed the role of PI following the PCS of LTC St. Pierre. There was no patient activity during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/014 **Status**: Terminated

Title: Quantification of Thermal Shrinkage of the Shoulder Capsule

Principal Investigator: CPT Brendon R. Connolly, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): LTC Patrick St Pierre, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Sep 00	N/A

Study Objective: To objectively measure thermal shrinkage upon the shoulder and compare these values with those from standard open shoulder capsular shift procedures.

Technical Approach: Thirty intact shoulder specimens will be harvested from fresh-frozen human cadavers. They will be thawed for 24 hours prior to use. We will use the previously described direct measurement technique of Lubowitz et al (8) for all capsular maesurements. Sixty cc of saline will be injected directly into the shoulder joint using an 18 gauge needle via an anterior approach over a 60 second period. The moment the syringe is emptied of all 60cc of saline, the direction of the plunger will be reversed and the joint will be aspirated fully. The amount of aspirated fluid will be a direct measure of the capsular volume. his will be repeated three times for each specimen and the results will be averaged. Standard anterior and posterior arthroscopic portals will then be established. A thorough arthroscopic evaluation will be performed on each specimen to assess for any lesions that would fulfill exclusion criteria. A Mitek VAPR probe will be introduced through the anterior portal. Tightening will proceed across the inferior glenohumeral ligament and up the anterior capsule to include the middle and superior glenohumeral ligaments. Each pass of the probe will be a single radial pass from the glenoid side to the humeral side of the capsule. Portals will then be switched and, with the VAPR in the posterior portal, the posterior capsule will be treated in a similar manner. After thermal shrinkage is complete, all instruments will be removed and arthroscopic cannulae of known volumes and one-way valves will be inserted in both portals to seal the capsule. The previously described direct measurement technique will then be used to measure the new capsular volume. Data will be obtained from the direct measurement of capsular volume both before and after thermal capsular shrinkage. The amount and percentage of capsular shift will be calculated and compared to known values for the standard open procedure. Data will be evaluated using a one-way ANOVA to determine differences between groups. Also, the Student's paired t-test will be used to determine the significance of the differences between the types of capsular shift.

Progress: This study has been terminated at MAMC, as the study methods were found not to be technically feasible for use with cadavers.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/016	**Status**: Ongoing

Title: Biomechanical Comparison of a New Modified Mason-Allen Suture Anchor Technique with Traditional Methods in Rotator Cuff Repair

Principal Investigator: CPT Brendon R. Connolly, MC

Department: Surgery/Orthopedic Surgery	**Facility**: MAMC

Associate Investigator(s): LTC Patrick St Pierre, MC; CPT Kurtis L. Kowalski, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
10/24/2000	Sep 00	N/A

Study Objective: Collect information regarding the strength and biomechanical characteristics of new absorbable suture anchors combined with a modification of a previously described suture technique for use in repairs of the rotator cuff. Compare these results with traditional methods of suturing and rotator cuff reattachment as well as currently available non-absorbable suture anchors.

Technical Approach: Thirty rotator cuff/proximal humerus specimens will be harvested from fresh-frozen human cadavers. The rotator cuff will be divided at its insertion on the humeral head. The rotator cuff will be repaired using 6 methods - new modified Mason-Allen suture anchor technique with either the Mitek Panalok RC, the Arthrex Biocorkscrew, or the Fastin RC; the arthroscopic double-mattress technique using the Fastin RC and the Arthrex Biocorkscrew; and the traditional transosseous technique with a horizontal mattress suture. Five examples of each method will be tested and the results averaged within each group. Number 2 Ethibond suture will be used for every repair. The rotator cuff and humerus will then be attached in an identical and reproducible manner to specialized bone and tendon clamps. Biomechanical testing will be performed with the Instron device. A cyclic pre-load of five newtons will be applied for five cycles (7). Each specimen will then be tested to tensile failure at a uniform rate of displacement. The resulting load-deformation curve will then be used to calculate the energy to failure, maximum load to failure, and peak stiffness. The mode of failure (anchor pullout, eyelet breakage, suture breakage, knot failure, or tendon failure) will also be documented. Data will be evaluated using a one-way ANOVA to determine differences between groups. Also, the Student's paired t-test will be used to determine the significance of the differences between the types of repair with respect to all the matched outcome variables.

Progress: All work on the Instron has been completed. Data is currently being analyzed by the statistician. Results are unavailable at this time.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/047 **Status**: Terminated

Title: An Open Label, Multicenter Study to Evaluate the Use of Dermagraft in Patients with Diabetic Foot Ulcers (Protocol DG-04-08-0998)

Principal Investigator: Vickie R. Driver, DPM

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): COL Charles A. Andersen, MC; April McKenna, MD

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Mar 01	N/A

Study Objective: The objectives of this study are to gain experience on the use of DERMAGRAFT in a broader patient population than is presently being studied in the ongoing pivotal trial and to expand health care provider access to DERMAGRAFT while a pivotal trial for this device is being conducted.

Technical Approach: This study will be conducted under a Treatment Investigational Device Exemption (IDE) as specified in 21 CFR 812.36. This is an open label, multicenter study to evaluate the use of DERMAGRAFT in patients 18 years or older with foot ulcers deemed to be of diabetic etiology on the basis of a medical history and physical exam. Subjects will have a current diagnosis of Type I or Type II diabetes mellitus. The 20-week study is designed as follows: Patients will undergo a pre-study screening to determine eligibility for study entry. Enrollment (Day 0) will occur two weeks after the screening visit if all inclusion/exclusion criteria have been met. Sharp debridement will be performed to remove any necrotic or hyperkeratinized tissue from the wound and wound margins. After debridement, if minimal bleeding is observed, and in the opinion of the investigator the bleeding would not affect the take of the implant, the patient can be enrolled immediately in the study. If extensive bleeding is observed so that the wound cannot support the take of the implant, the bleeding must be stopped by elevating the leg and applying pressure to the wound. If bleeding subsides enough to support the implant, DERMAGRAFT can be implanted in the wound. If not, the wound must be treated as clinically indicated, appropriately dressed, and the patient instructed to return within the next 48 hours to be re-evaluated for enrollment in the study. The size of the ulcer will be measured using a ruler. If a patient's ulcer has increased in size by 50% or more during the screening period, the patient can be re-screened for the study after 30 days from the time the increase was determined (Day 0). All patients will be fitted with an off-weight bearing device that redistributes weight away from the ulcer. Patients will be evaluated at weekly intervals after the first treatment for a total of up to 20 visits, or until the foot ulcer heals completely. Throughout the treatment period, patients will have up to 8 applications of Dermagraft. At Follow-Up Visit Week 20, or at the visit when the ulcer is completely healed, the ulcer will be evaluated for healing and infection. If the ulcer has not healed, the investigator will debride the ulcer and determine ulcer dressing. At this point, the patient's participation in the study will be complete and he/she will be followed in the clinic as determined by the investigator.

Progress: No subjects enrolled in this study at MAMC in FY01. The study was terminated, 24 Sep 01, as Dr. Driver chose not to continue Madigan's participation in this study.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/081 **Status**: Ongoing

Title: A Prospective, Randomized, Comparative, Parallel Study of Hyalofill Wound Dressing in the Management of Indolent Diabetic Foot Ulcers

Principal Investigator: Vickie R. Driver, DPM

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): COL Charles A. Andersen, MC; LTC Jeffrey P. Zimmerman, MS; CPT Troy N. Morton, MC; Mary Anne Landowski, RN

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Apr 03	N/A

Study Objective: The primary objectives is to compare the proportion of ulcers completely healed by the Hyalofill protocol of care to the standard protocol of care to the management of indolent diabetic ulcers. Secondary objective is to compare the mean time to healing, and the cost effectiveness of the two protocols of care.

Technical Approach: This is a prospective, stratified, randomized, comparative, parallel group, multi-center clinical trial comparing the number of ulcers completely healed by the Hyalofill protocol of wound care to the standard protocol of wound care in diabetic patients with an indolent (defined as not healing as anticipated with at least 6 weeks of wound care) diabetic foot ulcer with adequate arterial perfusion, for wound healing to the affected limb. A total of 200 patients will be enrolled with about 10 patients enrolled at MAMC. Patients will be stratified by Wagner Grade and location prior to randomization and will be assigned to either a wound care protocol of Hyalofill or the standard protocol of wound care. Individual study participation is 20 weeks or to complete healing (100% re-epitheliazed), whichever occurs first. Standard of care for the purposes of this protocol is: (1) Sharp debridement to remove necrotic tissue, (2) If the wound is dry, DuoDERM Gel will be used. If the wound requires exudate management, Kaltostat wound dressings will be used, (3) Either of these two products will receive Allevyn Non-Adherent as a cover dressing, (4) The foot ulcer will then be appropriately supported with either Aircast (plantar) or accomodative footwear (non-plantar), depending upon the ulcer location. The Hyalofill protocol care group is defined as: (1) Sharp debridement to remove necrotic tissue, (2) If the wound is dry, Hyalofill will be pre-moistened with normal saline and placed directly on the wound, (3) If deemed necessary by the Investigator, DuoDERM Gel may be used and placed directly on top of the Hyalofill dressing, (4) If the wound requires exudate management, Hyalofill (non-moistened) will be placed directly on the wound, (5) If deemed necessary by the Investigator, Kalostat dressings may be used and placed directly on top of the Hyalofill dressing. Patients will be seen weekly until 20 weeks or wound healing whichever occurs first. At each weekly assessment, the wound will be debrided (if necessary), the investigator will assess the ulcer (location, characteristics, absence/presence of pain, evidence of extrinsic mechanical trauma, and percentage of granulation tissue slough present), and a peri-ulcer description will be performed. At Weeks 4, 8, 12 and 16, an acetate tracing and photograph of the ulcer will be obtained. At week 20 or healing, a blood sample will be obtained to assess metabolic control, an acetate tracing and photograph of the ulcer will be performed and both the ulcer and pre-ulcer descriptions will be done. The mean time to healing will be done by wound tracings. Cost Effectiveness will be calculated using Mean time to healing, Percentage of ulcers completely healed in 20 weeks, Cost associated with dressing changes (e.g., labor, dressing supplies), and Complications (e.g., infection, in-patient hospital stay and procedures related to the study ulcer).

Progress: Thirteen patients consented in this study at MAMC in FY01. Three MAMC SAE's have been reported to the IRB; 3 patient hospitalizations with one death (unrelated to study participation). Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/098 **Status**: Ongoing

Title: Linezolid IV or PO Compared to Unasyn IV or Augmentin□ PO for the Treatment of Patients with Diabetic Foot Infections-A Randomized, Open-label Phase IV Clinical Trial

Principal Investigator: Vickie R. Driver, DPM

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): COL Charles A. Andersen, MC; LTC Jeffrey P. Zimmerman, MS; Mary Anne Landowski, RN; CPT Troy N. Morton, MC; CPT Alec C. Beekley, MC; Eric J. Heit, DPM; Hsing-His James Lee, DPM

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	May 03	N/A

Study Objective: Primary Objective: To assess the clinical effectiveness, safety, and tolerance of intravenously and orally administered Linezolid when compared with Unasyn IV and Augmentin PO in treating diabetic foot infections. Selected Additional antibiotic agents may be added to each treatment arm for specific indications. Secondary Objectives:To assess the microbiological efficacy (i.e. bacteriological eradication rate) of each treatment arm, to compare the clinical outcome of selected subsets of enrolled subjects, e.g., those initially treated as outpatients vs. inpatients; those treated with oral vs. intravenous agents; those with or without osteomyelitis, and to assess predictive value of the probe to bone test in the diagnosis of osteomyelitis.

Technical Approach: This randomized, open label, comparator-controlled study will compare the clinical efficacy, microbiological efficacy, safety, and tolerability of the two regimes in the treatment of diabetic foot infections: Linezolid IV or PO (600 mg every 12 hours). All enrolled patients can start therapy with either IV or PO Linezolid. The investigator can switch from IV to PO Linezolid at anytime during the course of Patient therapy. Outpatients will start with PO Linezolid only. Unasyn IV (3g every 6 hours) or Augmentin PO (500 mg every 8 hours) for hospitalized patients. Patients receiving Unasyn can switch to Augmentin PO at the investigators' discretion. For outpatient settings, patients can be randomized to Augmentin PO (500 mg every 8 hours). If the patient is assigned to the Unasyn/Augmentin treatment group and they are MRSA positive, they will receive an IV treatment with Vancomycin.

Patients enrolled will be randomized to one of these two treatment arms. The intended treatment duration is 14 days for both treatment arms to include a screening visit, Day 7, Day 14, Day 21 and End of Treatment visit to evaluate response. If osteomylitis, infection in the bone, is present the investigator may treat the patient with the study regimen up to 28 days. Upon switching to oral medication a clinical observation will be made (including wound description and vital signs). A final Follow-up Visit will occur after the End of Treatment Visit between day 21-28 to assess the woundand evaluate clinical response.

Progress: Four subjects enrolled in this study at MAMC in FY01. No SAE's have been reported by the study sponsor or at MAMC. All four subjects continue to receive treatment with some noted improvement in their wounds. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/128 **Status**: Ongoing

Title: A Prospective, Multicenter, Open-Label Study to Evaluate the Safety and Efficacy of Apligraf in the Treatment of Diabetic (Primarily Neuropathic) Foot Ulcers That Have Not Adequately Responded to Standard Therapy (Protocol #CGSO769B US08)

Principal Investigator: Vickie R. Driver, DPM

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): COL Charles A. Andersen, MC; CPT Troy N. Morton, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/28/2001	Jan 03	N/A

Study Objective: Primary: Evaluate the safety and efficacy of Apligraf in patients with diabetic (primarily neuropathic) foot ulcers that have not adequately responded to standard therapy and to determine the time (in days) to complete healing of the target wound. Complete wound healing is defined as full epithelization of the wound with the absence of drainage. Secondary: Determine the rate of sustained healing, defined as complete wound healing documented for two consecutive weeks after the wound is declared to be completely healed, determine the reoccurrence rate in a three-month period following the healing of ulcers, determine changes from baseline in Quality of Life (QOL)/Medical Resource Utilization, and document, via weekly photography, the healing characteristics of diabetic (primarily neuropathic) foot ulcers treated with Apligraf.

Technical Approach: This will be an open-label, study in approximately 100 patients with diabetic (primarily neuropathic) foot ulcers at up to 20 centers. Study duration is 12 weeks with 3 months follow-up. Patients with ulcers that appear to be healing spontaneously during the screening period (>30% reduction in area within 7 days prior to application of Apligraf) will not proceed to the treatment period. The remaining patients with ulcers that are thus defined as being hard to heal may enter the treatment period; however, patients with clinically infected ulcers must not be allowed in the study.

The screening period will occur within 1 week prior to the Treatment Period. The wound will be surgically debrided and dressed. The dressing will stay in place for 1 week. Patients will be instructed on off-loading. The Investigator will order Apligraf and patients will return the following week for the initial application of Apligraf. During the treatment period, Day 0 up to Week 12, the wound will be evaluated prior to the application of Apligraf. Patients who still satisfy the inclusion/exclusion criteria will have Apligraf applied at Day 0. A second application is permitted. Safety and efficacy evaluations will be performed weekly. Efficacy will be assessed by clinical observations at weekly visits. Photographs will be obtained at baseline and at each visit thereafter for the duration of the study. Wound tracings will be performed at selected timepoints. Safety will be assessed by clinical observation including signs and symptoms of infection. The study completion will be defined as the time of complete wound healing or 12 weeks after initial application of Apligraf. If healing is achieved prior to Week 12, the patient will proceed immediately to the week 12 evaluations and enter the follow-up period. All patients will have three monthly follow-up visits after Week 12 (or documented healing). In addition, patients who have target ulcers that have healed by or at 12 weeks will be evaluated weekly for two weeks following documented healing. The primary efficacy variable will be time to complete wound healing, defined as full epithelialization of the wound with the absence of drainage. Secondary efficacy variables are the incidence of 100% wound healing at Week 12 and for patients whose ulcer healed, the next two weekly assessments will evaluate whether the healing was sustained for two consecutive visits. The follow-up period starts at the visit the physician indicates the target ulcer is 100% healed.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/093 **Status**: Completed

Title: A Prospective Outcome Study of Posterior Lumbar Interbody Fusion in Soldiers

Principal Investigator: MAJ Tad L. Gerlinger, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Robert W. Molinari, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Aug 00	5/22/2001

Study Objective: To determine the functional outcome and patient satisfaction of Posterior Lumbar Interbody Fusion (PLIF) in a military patient population.

Technical Approach: This prospective outcome study evaluates general health, pain, function and satisfaction in a consented patient population with degenerative disc disease. Patients will either elect to have posterior lumbar interbody fusion or not. Both groups will be given a validated outcome questionnaire at 3, 6, 12, and 24 months from when they elected to have the surgery or not. At 6, 12, and 24 months, patients will submit data from their PT tests. Results from both groups will be compared.

Progress: A total of 15 patients enrolled in this study. Instrumented PLIF surgery performed in active duty U.S. servicemen with chronic low back pain and single level lumbar disk degeneration results in high rate of return to full military duty. Servicemen treated with this technique are less likely to receive a back pain disability discharge or a permanent physical limitation profile when compared to servicemen treated nonoperatively. Outcomes with respect to pain, function and satisfaction are excellent in those servicemen who are able to return to unrestricted duty. The protocol was reported as completed, May 2001.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/081 **Status**: Terminated

Title: A Prospective Randomized, Blinded Study, Comparing Treatment of Fifth Metacarpal Neck Fractures

Principal Investigator: MAJ Tad L. Gerlinger, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): COL Frederic L. Johnstone, MC; Mary Miklos-Essenberg

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Jun 00	06/22/1999

Study Objective: To determine the effectiveness of treating fifth metacarpal neck fractures with closed reduction and casting with the metacarpal phalangeal joint in neutral and utilizing a three point mold.

Technical Approach: Patients with fifth metacarpal neck fractures will be randomized to undergo non-operative treatment, comparing closed reduction and casting with the metacarpal phalangeal joint in neutral and utilizing a three point mold, to closed reduction and casting with the metacarpal phalangeal joint approximating 90 degrees (the current standard technique). Outcome will be measured by the amount of residual angulation, grip strength compared to the contralateral hand, rotatory malalignment and range of motion at three weeks and again at three months after the injury.

Progress: Study has been terminated by PI, May 2001, due to lack of available time for study completion.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/066 **Status**: Ongoing

Title: Healing of Tibial Stress Fractures Using Pulsed Electromagnetic Field (PEMF) Therapy

Principal Investigator: CPT Karin A . Johnson, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): LTC (Ret) Richard A. Sherman, MS; COL Nancy E. Henderson, SP; 1LT Kristine A. Youngstom, SP; Jerome Billingsley, M.D.; MAJ Susan Ishikawa, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	Dec 01	5/22/2001

Study Objective: To determine whether application of non-thermal, pulsed high peak power, high frequency, electromagnetic energy (PEMF) over the tibial stress fracture site used in conjunction with standard therapeutic approaches, reduces the amount of shin pain and increases endurance on the treadmill in relation to those receiving standard treatments with sham PEMF's.

Technical Approach: This study is a double-blind, placebo controlled study of active duty soldiers but with tightly controlled outcome measures. All subjects will receive the standard treatment in addition to PEMF or sham and will begin participation within 30 days of initial complaint after confirmation of stress fracture diagnosis by both physical findings and bone scan. Prior to initial exposure, each subject will fill out a standardized questionnaire which assesses ability to function in the work and home environment in relation to lower limb pain and disability. Each will also be evaluated for duration of walking on a treadmill until discomfort to standardize assessment of pain and endurance, and will have their bone density measured. Subjects will be randomly assigned to be exposed to either a PEMF generator putting out actual fields or an inactive (sham) generator. This will be an entirely double-blind study as the subjects will not be able to tell which group they are in because the devices sound the same and because the patients cannot feel the machine operating. The physical therapy technician who operates the device will know which generator each subject is exposed to but will not know which generator is putting out actual fields and which is the sham. The physical therapists and physician doing the evaluations will have no idea which group the patients are in. The function questionnaire and the treadmill test will be repeated at the end of the two week exposure period and then four weeks and six months after. A power analysis shows that 33 subjects will be needed in each group assuming that the actual exposure group will do better than the placebo group (one-tailed test) and that an 80% chance of finding a difference between the two groups at a 0.05 level of significance is sufficient to perform the study. Eighty subjects will be recruited to begin the study to permit a reasonable 15% dropout rate.

Progress: 27 subjects enrolled at MAMC during FY01 for a total enrollment of 35. Preliminary evaluation of results to date show trend toward benefit from treatment. It is not statistically significant after the first 20 patients. Additionally, bone density from the first 30 patients is abnormal (-0.5 standard deviations). A new protocol is being developed to address bone density of Ft. Lewis soldiers.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/095 **Status**: Ongoing

Title: Delayed versus Immediate Open Repair of Achilles Tendon Rupture; A Randomized Prospective Trial

Principal Investigator: CPT Glenn J. Kerr, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): MAJ John G. DeVine, MC; CPT George K. Bal, MC; LTC John D. Pitcher Jr., MC; MAJ Robert V. Williamson, MC; COL Frederic L. Johnstone, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/16/1997	Jun 01	5/22/2001

Study Objective: To evaluate the differences in surgically repairing Achilles tendon ruptures immediately, or waiting 10-14 days to perform the repair.

Technical Approach: All patients identified with acute Achilles tendon ruptures, who are being considered for surgical repair, will be presented the option of enrolling in this study. The subjects will be randomized to one of two Groups: Group I - Immediate surgical repair (within 72 hours) of the Achilles tendon, or Group II - delayed (between 10 and 14 days) surgical repair of the tendon rupture. The patients will be randomized using a computer generated randomization table. We will initially randomize the first ten patients, and a subsequent power analysis will be performed at 6 month follow-up to insure that enough patients are enrolled to make our results significant. The next 20 patients will be randomized using a second computer generated table. The post-operative course for both Groups will be the same. The patients will be followed up at 2 week, 6 week, 9 week, 6 month, 12 month, and 24 month intervals. They will be evaluated for post-operative complications and functional outcome.

Progress: Three subjects enrolled in this study at MAMC during FY01, for a total enrollment of 32 patients overall. Subject enrollment is complete, however data collection continues in order to obtain patient data from their 6th and 12th month follow-up visits.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/015 **Status**: Ongoing

Title: Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques

Principal Investigator: CPT Kurtis L. Kowalski, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): LTC Patrick St Pierre, MC; CPT Brendon R. Connolly, MC; LTC Edward D Arrington, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Sep 00	9/26/2001

Study Objective: Test the strength and biomechanical characteristics of native and intact coracoclavicular ligament complexes as well as various reconstructive techniques for treating high-grade acromioclavicular joint separations.

Technical Approach: Thirty coracoclavicular bone-ligament-bone specimens will be harvested from fresh-frozen human cadavers. Unidirectional tensile loading will be performed with the Instron device. Tensile loading will be applied to the clavicle at a uniform rate until failure of the coracoclavicular ligament complex occurs. The coracoclavicular ligament will then be reconstructed using either gracilis tendon, palmaris longus tendon, or SIS graft. The grafts will be looped multiple times under the coracoid process and over the top of the clavicle. It will be secured to itself with a #2 Ethibond suture. They will then be tested to failure as previously described. Data will be obtained from the Instron device regarding tensile strength, load to failure, stiffness, and elongation to failure. Statistical analysis will be performed using a one-way ANOVA to determine differences between groups as well as Duncan's multiple range test to determine specific differences.

Progress: Instron work with native/intact shoulders was completed during FY01. The study remains ongoing while awaiting cadaver grafts to be able to complete Instron work on reconstructed shoulders.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/111 **Status**: Terminated

Title: Capsular Shrinkage with Bipolar Radiofrequency in Functional Ankle Instability

Principal Investigator: CPT Kurtis L. Kowalski, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Susan Ishikawa, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Dec 02	N/A

Study Objective: To assess prospectively the effectiveness of radiofrequency capsular shrinkage in patients with functional ankle instability compared to a group of patients with functional ankle instability who did not have this procedure performed.

Technical Approach: This is a prospective randomized pilot study in patients with ankle impingement and functional instability that will compare arthroscopy and debridement alone to arthroscopy, debridement, and thermal capsular shrinkage. The subjects involved will be blinded as to which group they randomize to. Preoperative evaluation will include history and physical, stress radiographs, and completion of a modified AOFAS Ankle-Hindfoot Scale. Postoperatively, the control group will undergo the standard rehabilitation protocol for arthroscopic debridement. The experimental group will undergo a longer period of immobilization necessitated by the nature of their procedure. Both groups will undergo standard postoperative follow-up with the treating surgeon. The patients will be evaluated again with stress radiographs and a modified AOFAS Ankle-Hindfoot Scale at 6 months and 1 year postoperatively to assess their response to surgical intervention. A power test will be performed at 6 months to determine the number of patients required to make a significant difference between the two groups and more patients will be added to the study as needed.

Progress: This protocol has been terminated. No work had been accomplished on the study and the original investigators have left MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/057 **Status**: Completed

Title: The Effect of Tapped, Untapped and Undertapped Pilot Holes on the Pull-out Strength of Lumbar, Thoracic, and Sacral Pedicle Screws

Principal Investigator: MAJ Robert W. Molinari, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): MAJ Tad L. Gerlinger, MC; CPT Brendon R. Connolly, MC; MAJ John G. DeVine, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Jun 01	N/A

Study Objective: To compare the pullout strength of lumbar, thoracic, and sacral pedicle screws inserted with tapped, undertapped and untapped pilot holes.

Technical Approach: This study will be the first to compare the pullout strengths of pedicle screws inserted into tapped, undertapped, and untapped pilot holes in the thoracic, lumbar and sacral spine. Five human cadaveric spines, stripped of soft tissue, will be obtained en bloc, fresh frozen in saline, and stored at -20C as per previously validated techniques (2-6, 8). Visual inspection will exclude specimens with fractures, anatomic anomalies, or any other bony pathology. DEXA scans will be performed to quantify bone mineral density(BMD) of each spine. The specimens will then be thawed and the pedicle screws will be inserted into pilot holes made according to one of three methods: 3/8 inch drill preparation to inch depth(untapped), pedicle probe followed by the tap recommended by the manufacturer for the specific screw size(tapped), or pedicle probe followed by tapping with one size smaller tap than prescribed for the specific size screw(undertapped). The entire side of each spine will have screws inserted with only one technique, the other side will be entirely prepared with one of the other two techniques, allowing for direct side to side comparison of each of the three techniques. All screws will be inserted to 40mm and the image intensifier will be used to obtain a measurement of pedicle width and ensure accurate screw placement. 5mm screws will be placed in the thoracic spine and 6mm screws in the lumbar and sacral spine. Insertional torque will be measured with a digital torque wrench. The intact spines will then be potted in cement after being wrapped in cellophane to prevent cement intrusion into the bodies. The cement will extend up to the pedicles, as to not interfere with fixation of the screw to the Instron. Biomechanical testing will then be performed with the Instron device. The potted spine will be rigidly secured to the base of the Instron and the screwheads held with a drill chuck to the axial load cell. Each screw will then be subjected to axial tension until failure at a uniform rate of displacement. The resulting load-displacement curve will then be used to calculate screw pullout strength, screw displacement before failure, and energy absorption before failure. The mode of failure (screw pullout or screw breakage) will also be documented. Data will be evaluated using ANOVA to determine differences in pullout strength between the three types of pilot hole preparation. Furthermore, the BMD for each group will be compared, as well as the pedicle width and insertional torque.

Progress: All cadaveric use has been completed. 144 data point collected, 4 spines used, 144 screws set. Data analysis is in progress.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/009 **Status**: Ongoing

Title: Positional Assessment of the Maxwell-Brancheau Arthroeresis Implant on the Subtalar Joint Using Three-Dimensional Surface Computed Tomography

Principal Investigator: CPT Troy Morton, SP

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): Brent A. Clark, DPM; Richard O. Jones, DPM; LTC Doug A. Vermillion, MC; LTC Morgan P. Williamson, MC; MAJ Jay F. Wigboldy, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Jan 01	N/A

Study Objective: To provide evidence that will help answer the following question: what position, relative to the articular facets of the subtalar joint, does the MBA arthroeresis device assume when placed according to manufacturer's guidelines.

Technical Approach: Six patients will be enrolled in this study. Patient's surgeries have all been performed by the same surgeon and he will evaluate records individually and identify each patient for inclusion in the study. Scans will be performed and the results will be reported individually for each subject foot as well as collectively for the group. At the time of the CT, each patient will complete a post-operative questionnaire. The primary investigator will complete the AOFAS hindfoot score for each patient at this time.

Progress: Seven patients enrolled in this study at MAMC during FY01. No adverse events have been reported.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/065 **Status**: Ongoing

Title: Study of the Treatment of Articular Repair (STAR): A Prospective, Longitudinal Within Patient Evaluation of the Effectiveness (Durability) of Carticel (autologous cultured chondrocytes) Compared to Non-Carticel Surgical Treatment for Articular Cartilage Defects of the Knee

Principal Investigator: LTC Doug A. Vermillion, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): LTC Patrick St Pierre, MC; MAJ James A. Hall, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/25/2000	Jun 06	4/24/2001

Study Objective: To compare the effectiveness (durability) of Carticel autologous chondrocyte implantation in patients who have had an inadequate response to a prior non-Carticel surgical cartilage repair procedure (including debridement, microfracture, drilling, abrasion arthroplasty or other surgical treatment) within the previous 3 years for significant articular cartilage defects of the femoral condyle.

Technical Approach: This study will be a longitudinal, prospective, multicenter, within patient evaluation of 100 patients with articular cartilage defects of the knee who have had inadequate response to a prior non-Carticel surgical treatment. Patients who had an inadequate response to a prior non-Carticel surgical treatment will be implanted with Carticel (autologous cultured chondrocytes). the overall condition of the knee will be evaluated Using Modified Cincinnati Knee Rating System at baseline and every 6 months postoperatively. The SF-36 health survey will be used to assess global health status at baseline and follow-up visits. The primary endpoint of the study will be time to treatment failure, and will be compared via chart review of consented patients to the durability of past treatments.

Progress: From 1 Oct 00 to 1 Oct 01, a total of 6 subjects were consented and screened for possible enrollment to the study through the stage of arthroscopic assessment of the affected knee and collection of cartilage samples for future repair of damaged articular surface(s). 4 of these subjects were eligible to proceed to enrollment in the STAR study. Autologous chondrocyte culture was authorized for these individuals at the central study laboratory, and the cultured cells were replaced after a period of healing in repair of one to three previously identified osteochondral defect(s) in the affected knee joint. Repair procedures required arthrotomy. In several subjects, concomitant surgical repairs of alignment or structure of the affected knee were performed as allowed by the protocol. All subjects are currently in postoperative follow up, completing progress questionnaires at 6-month intervals, and progressing through study rehabilitation guidelines and physical therapy, with periodic orthopedic evaluations in the MAMC clinic. All data was collected and returned to the central data managers and all queries answered through the 31 August 01 end of study enrollment. No adverse events have been reported in MAMC or Non-MAMC subjects participating in this clinical trial. The Principal Investigator attended the meeting, "Current Concepts: Articular Cartilage Injuries of the Knee" offered by University of California, Sports Medicine Department, San Francisco in June 2001.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/112	**Status**: Ongoing

Title: Post-operative Shoulder Pain: A Prospective Randomized Trial Comparing the Pain Infusion Pump to the Pre-induction Interscalene Block

Principal Investigator: MAJ Daniel W. White, MC

Department: Surgery/Orthopedic Surgery	**Facility**: MAMC

Associate Investigator(s): LTC Edward D Arrington, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
6/26/2001	Feb 02	N/A

Study Objective: Determine the efficacy of the pain control infusion pump (PCIP) in controlling post-operative pain in patients undergoing shoulder surgery.

Technical Approach: The next 50 consecutive patients who are scheduled to undergo elective shoulder surgery to address subacromial impingement syndrome with or without a rotator cuff tear; or, acromio-clavicular degenerative disease, who meet induction criteria will be advised of the nature of the study and, upon agreement, will be entered in the study. Once consent is obtained, a randomization table will be utilized to assign the patients to Group A (pain control infusion pump) or Group B (pre-induction interscalene block). The time of determination of randomization will be in the preoperative evaluation. Patients in Group A will undergo surgery and then have a BREG MP 130 Multiport Catheter placed in the subacromial space. The catheter will be attached to the BREG 3000 Pain Control Infusion Pump with a standardized dose of 0.5% Marcaine. Patients in Group B will undergo a standardized pre-induction interscalene block utilizing the current standard technique by the anesthesia provider with 0.5% Marcaine. All patients will receive standardized anesthesia during the procedure and will spend the night of surgery in the overnight observation unit, as is our current standard of care.

All patients will be given a PCA with intravenous narcotics overnight, which is the current Madigan Orthopedics standard procedure. There will be "on demand" dosage with no continuous dosing settings on the PCA device. The dose of narcotic used overnight will be recorded. During the hospital stay, the computerized inpatient record will serve as a record of use of pain medications, nausea medications, and difficulties overnight. On the day after surgery, the surgeon who performed the surgery will administer the first questionnaire. This questionnaire will consist of a 10-centimeter visual analog scale for pain, nausea, and pain control satisfaction as well as narcotic and non-narcotic analgesic use tabulation. The visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time of surgery to the present. This form will be collected by the surgeon and placed in the study file located in the orthopedic clinic research data collection office. The patient will be instructed to return for a follow-up appointment at seventy-two to ninety-six hours for operative site evaluation. They will be asked to keep a running total of all narcotic and non-narcotic pain medications used from the time of discharge until the follow-up appointment for wound evaluation.

All patients will follow-up in the clinic at seventy-two to ninety-six hours for operative site evaluation. At this time, the patients in Group A will have the pain control infusion pump catheter removed from the shoulder. At this time, the number of narcotic and non-narcotic pain medications utilized will be totaled. The patient will be administered the same questionnaire used previously. Again, the visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time discharge to the present. The questionnaire will again be collected and added to the file in the orthopedic clinic. The patients will be asked to keep a running total of all narcotic and non-narcotic pain medications used from the time of the first follow-up appointment until the follow-up appointment seven to eight days after surgery. All patients will subsequently follow-up at seven to eight days after surgery for completion of the

surgery data and to evaluate the operative site. Again, the same questionnaire will be administered. Again, the visual analog scales will be used to record their most intense pain, worst nausea, and overall pain control satisfaction from the time discharge to the present. The questionnaire will again be collected and added to the file in the orthopedic clinic.

After ten patients have completed the three questionnaires, a power analysis will be performed on the data collected. The data analyzed will include comparison of visual analog scores for pain, nausea, and overall pain control satisfaction. A direct comparison of amount of narcotic and non-narcotic pain medications will also be conducted. Based on the statistical analysis and the power analysis, the study population size will be determined based on the number of patients that will be required to achieve statistically significant results. The study will then be continued until the appropriate number of patients has been enrolled. Any patient that develops a complication during the study period will be evaluated at the time of the onset of the complication. The complication will be evaluated and treated in according with the current standard of care. All data regarding the complication will be collected and maintained as part of the study data. Complications will be continuously followed and data collected until the condition has been resolved, stabilizes, or the study is concluded.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/125 **Status**: Ongoing

Title: Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome

Principal Investigator: MAJ Christopher J. Wilson, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

Associate Investigator(s): LTC Patrick St Pierre, MC; CPT Brian K. Konowalchuk, MC; LTC Edward D Arrington, MC; CPT Neil C. Vining, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Jun 01	2/27/2001

Study Objective: To evaluate the difference in pain relief and functional outcome for subacromial impingement syndrome for patients who are treated with either a subacromial injection of corticosteroids or a subacromial injection of Ketorolac.

Technical Approach: This double-blind, randomized study will enroll approximately 40 patients with uncomplicated impingement syndrome for treatment with either subacromial corticosteroids or Ketorolac. Subjects with subacromial impingement will be given either 6cc 1% lidocaine with epinephrine and 40 mg Triamcinolone (Control) or 6cc 1% lidocaine with epinephrine and 60mg injectable Toradol (Test). Patient evaluation will be done at the time of injection and at 4 weeks post-injection.

Progress: 21 subjects enrolled in this study at MAMC during FY01. Both steroid and ketorolac have been effective in reducing symptoms and improving function; however, it is too early to tell which medication may prove to be more effective. The eventual finding may be that they are equally effective. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/125 **Status**: Completed

Title: External Fixation of Displaced Clavicle Fractures

Principal Investigator: MAJ Christopher J. Wilson, MC

Department: Surgery/Orthopedic Surgery **Facility**: MAMC

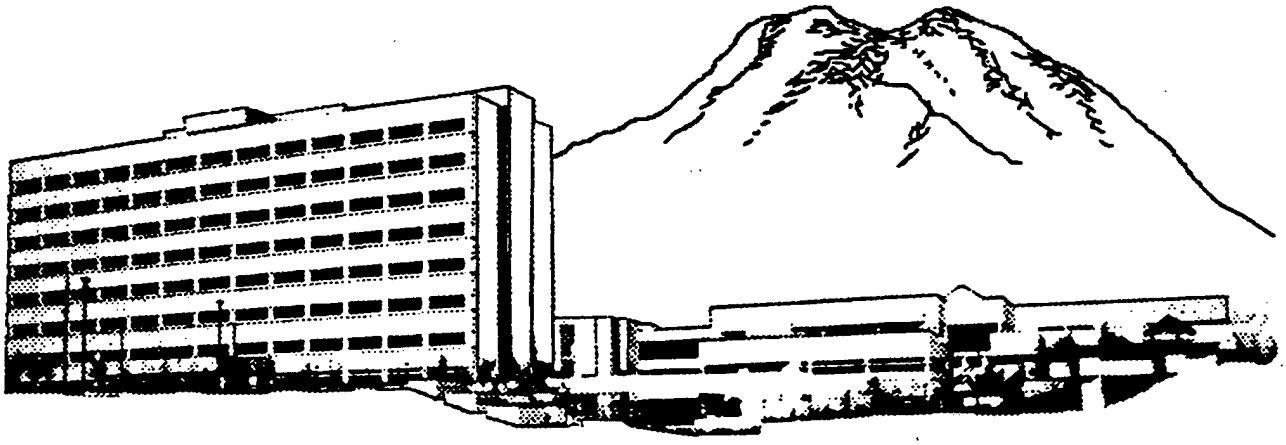
Associate Investigator(s): MAJ Greer E. Noonburg, MC; LTC Patrick St Pierre, MC; LCDR Clayton G. Turner, MC, USNR; COL Frederic L. Johnstone, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/18/1997	Aug 99	6/26/2001

Study Objective: Determine the efficacy of external fixation in the treatment of clavicle fractures with greater than 100% displacement.

Technical Approach: Patients will be drawn from males and nonpregnant females over age 18, with acute traumatic clavicle fractures having greater than 100% displacement on radiographs. The study population will range from 10 to 20 subjects. After inclusion in the study, and a pre-operative examination, the subjects will be taken to the operating room for placement of threaded pins through four 1-cm incision sites over the clavicle. An Orthofix Pennig II External Fixator will be attached to the pins and the fracture reduced to as close as possible to anatomic alignment. After surgery, the patient will be given pain medications, instructed in pin site care, and sent home. The patient will be evaluated weekly by an orthopaedic surgeon (4-8 weeks) and usually will receive clavicle x-rays with each appointment. The external fixator will be removed in the clinic in four to eight weeks, depending upon healing of the fracture as evident on x-ray. Subsequent post-operative exams at 3, 6, and 12 months will be conducted. Outcome variables will be evaluated for functional outcomes (motor strength, range of motion, tenderness at the fracture site, residual displacement/deformity, time of healing, ability to perform occupation and activities of daily living).

Progress: Eighteen subjects enrolled in this study at MAMC. All patient visits and data collection has been completed; however, an abstract of findings is not yet available.



Detail Summary Sheets

Otolaryngology Service, Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/139 **Status**: Ongoing

Title: Use of Elastin Patch for Repair of Traumatic Tympanic Membrane Perforations in the Chinchilla (Chinchilla laniger)

Principal Investigator: CPT James V. Crawford, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

Associate Investigator(s): MAJ Paulino E. Goco, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/19/2001	May 04	N/A

Study Objective: (1) Laser soldering of liquid albumin coupled with elastin can provide an immediate functional repair of tympanic membrane perforations (2) that elastin biomaterial can facilitate tympanic membrane repair in acute tympanic membrane perforations (3) that elastin biomaterial compares favorably with traditional paper patch techniques In non-technical terms state the objective of this protocol, or the hypothesis to be accepted or rejected.

Technical Approach: This study will utilize an elastin biomaterial (Oregon Medical Laser Center, Portland, OR) to repair acute TM perforations in an animal model (Chinchilla langier). TM perforations will be created with a thermal loop under general anesthesia and then repaired immediately utilizing elastin biomaterial with or without laser-activated tissue adhesive. A comparison study with the standard paper patching technique will also be conducted in parallel. We anticipate that the elastin biomaterial will prove to be a functional patch material for TM perforations, as confirmed by tympanometry, and will promote rapid healing. If this is true, there is potential for application to the acute repair of traumatic TM perforations in humans, which can result in decreased morbidity and accelerated return to full-functioning capacity.

Progress: This study recently received final IACUC approval. Work on this protocol has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/068 **Status**: Terminated

Title: Pharmacotherapy of Meniere's Disease. Project 1: Effects of General Anesthesia on the Vestibular System

Principal Investigator: CPT James V. Crawford, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

Associate Investigator(s): LTC Vincent D. Eusterman, MC; George A. Gates, M.D.; JO Phillips

Start Date:	Est. Completion Date:	Periodic Review:
04/27/1999	Dec 00	9/26/2000

Study Objective: Document and quantify the extent of vestibular suppression after general anesthesia.

Technical Approach: The subjects will have an otologic history and then undergo an abbreviated rotating chair test. This non-invasive procedure is a standard clinical test and can be completed in 20 minutes. The rotating chair is done using the Neuro-Kinetics equipment. The subjects is seated on a chair that rotates gently from the left to the right and back again in a sinusoidal manner at frequencies of from 0.01 to 0.64 Hz at a velocity of 60 degrees/sec. For the purposes of this research the test procedure will be limited to the 0.4 and 0.8 Hz frequencies, where the test-retest results are best. The test is done in the dark with the subject's eyes open after calibrating the system with standard gaze shifts. The resultant eye movements are recorded by skin surface electrodes and digitized, filtered, and the slow phase eye velocity is computed and stored. The average gain, phase, and asymmetry of the vestibulo-ocular reflex eye movements are computed for each test frequency and compared against age normals. A change in gain of 0.5 standard deviations averaged across the 0.04-0.08 Hz frequencies will be the key outcome parameter. Finally, the vestibular time constant will be determined from the time it takes the VOR to stop after a step deceleration of the chair. To obtain 103 evaluable subjects, we estimate 130 people will need to be test preoperatively, expecting 10% to have abnormal vestibular tests and anticipating that 15 % will not complete the postoperative testing. About 95 % of the subjects are expected to be tested at MAMC, leaving an estimated 5 % to be tested at UWMC. An additional 10 control subjects will be tested at MAMC to ensure the test-retest reliability of our facilities.

Progress: Only one patient enrolled in this study in FY00 at MAMC. There has been no further study enrollment. The investigator elected to terminate the protocol.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/104 **Status**: Completed

Title: Measurement of Nasal Patency. Project 1: Measurement of Nasal Flow using Full-body Plethysmograph and Comparison with Visual Analog Scale

Principal Investigator: CPT John W. Hariadi, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

Associate Investigator(s): MAJ Paulino E. Goco, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jul 01	8/28/2001

Study Objective: Document nasal flow and resistance before and after application of Oxymetazoline Hydrochloride 0.05% and comparison with visual analog scale.

Technical Approach: Measure nasal flow volume loop using Sensormedics V6Z Autobox Full-body Plethysmograph. Data will be obtained by having subjects breathe through each nares individually, then through mouth as control. Subjects will have 2 cotton pledgettes soaked in oxymetazoline 0.05% placed in each nares for 15 minutes and the measurements repeated thereafter. Subjects also record a Visual Analog Scale before and after decongestion with oxymetazoline. This consists of a 100mm line marked with "extremely clear" at zero and "extremely blocked" at 100mm. The subjects are asked to indicate their subjective sensation of nasal congestion by marking the line for each nasal cavity, before and after application of the topical decongestant. Subjects use a 2x2 gauze to obstruct the contralateral nasal passage during assessment.

Progress: 6 subjects enrolled in this study at MAMC during FY01. There appears to be a correlation between nasal flow/airway resistance changes as measured by the full-body plethysmograph and the subjects' visual analog scores. Conclusion: The full-body plethysmograph is an objective measurement of nasal patency, correlates with the patient's subjective assessment as indicated by the visual analog scale, and can be used as outcome measurements.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/079 **Status**: Completed

Title: Determining Optimal Nonsurgical Treatment for Auricular Cartilage Contouring in a Rabbit Model

Principal Investigator: CPT Phillip L. Massengill, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

Associate Investigator(s): MAJ Paulino E. Goco, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/18/2000	May 03	8/30/2001

Study Objective: To evaluate a potential nonsurgical technique for auricular contouring and to compare the results of auricular contouring with various proteolytic enzyme preparations (hyaluronidase, elastase, and relaxin) in combination with auricular splinting.

Technical Approach: Phase I (pilot phase) will utilize fresh slaughter house-derived (ex-vivo) rabbit ears randomly assigned to one of three treatment groups, Group I - hyaluronidase; Group 2 - elastase and Group 3 - relaxin. The ex-vivo ears will have varying concentrations or volumes of the specified enzyme injected into the auricular cartilage and will be mounted and weighted so as to allow gravity to bend the ears at the injected region if the cartilage is softened. Three ears each will be injected with each of three enzyme concentrations/volumes in each treatment group. Evaluation for cartilage softening will be performed at 24, 48 and 72 hours postinjection and the solution concentration that allows the cartilage to maximally soften, without cartilage destruction, will be determined for each of the enzymes. Phase II will involve five rabbits for each selected enzyme volume/concentration. Rabbits will be placed under general anesthesia, with one ear injected with the test compound and the other ear injected with a volume of sterile, physiologic saline that is equal to the injected test compound volume. Following injection, both ears will be contoured manually, and molded with lightweight, Aquaplast splinting material. Rabbit ears will remain splinted for four weeks.

Progress: The study consisted of ten animals where one ear was the test compound ear and the other ear acted as a control. Five ears were injected with hyaluronidase and five with elastase. After injection, the ears were contoured and splinted for a period of four weeks. Considering just the test compound ears at 4 weeks, 60% showed complete response, 40% showed partial response, and 0% showed no response. At six weeks (2 weeks post splint removal) 30% of the ears had maintained contour demonstrating a complete response. The study certainly suggests that nonsurgical management can be effective in correcting ear deformities with bioactive enzymes in a rabbit model. Long term results as well as other test compounds would require further study to determine their effectiveness.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/050 **Status**: Ongoing

Title: Pediatric Bronchoesophagology Laboratory Using Swine (Sus scrofa)

Principal Investigator: MAJ Douglas Sorensen, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

Associate Investigator(s): Andrew Inglis, M.D.; MAJ Andrew B. Silva

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Mar 02	5/18/2000

Study Objective: To familiarize the junior otolaryngology residents at MAMC and the UW and the Pediatric Surgery fellows at CHMC, with the endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children. This would include familiarization with esophageal and tracheal foreign body removal, rigid and flexible endoscopic techniques and endobronchial laser use. Familiarity with these techniques would allow an increased margin of safety for children undergoing these procedures and better prepare the endoscopist to assist and then perform these procedures when necessary. Increased endoscopic training experiences will increase operative efficiency and minimize the potential operative risks involved in these procedures.

Technical Approach: This is a 4-hour afternoon laboratory session. The LARS, under the supervision of an attending veterinarian, will administer the anesthesia. During this time, 3 pigs will be anesthetized under general anesthesia using IM Rompun/ketamine (2.2mg/kg 20mg/kg). LARS will then obtain intravenous access. Once an adequate plan of anesthesia has been reached, the course participants will perform rigid and flexible bronchoscopy with extraction of a foreign body and esophagoscopy under the supervision of an attending endoscopist. In order to maximize the number of procedures that can be performed within the shortest amount of anesthetic exposure, three live animal stations will be used. The first and second station will be used to teach rigid endoscopy and foreign body removal. The third station will be used to teach flexible endoscopy and foreign body removal. There will also be two additional teaching stations. One will involve instrument set up and use, while the other will involve a teaching station for removal of a safety pin.

Approximately 20 endoscopic procedures will be performed on each animal. Foreign bodies will be used that reproduce those encountered in clinical practices (peanuts, beans, Lego). The foreign bodies will be endoscopically placed and extracted from the bronchus and trachea, under direct vision of the participants and instructors. At the end of the laboratory session, the pigs will be euthanized while they are still under general anesthesia in accordance with the IAW LARS SOP for euthanasia.

All course participants will perform bronchoscopies and foreign body removal on models prior to operating on the swine. The course participants will also participate in a half-day didactic component prior to the laboratory session and will be required to undergo a post course quiz. Completion of the training will be determined by the participant's ability to successfully, and atraumatically perform a bronchoscopy and esophagoscopy with airway foreign body removal.

Progress: There were no training sessions held under this protocol in FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/093 **Status**: Ongoing

Title: A Double Blind Placebo Controlled Trial of Montelukast for the Treatment and Prevention of Recurrence of Chronic Nasal/Sinus Polyposis and Chronic Hyperplastic Sinusitis

Principal Investigator: CPT Jamie R. Steger, MC

Department: Surgery/Otolaryngology **Facility**: MAMC

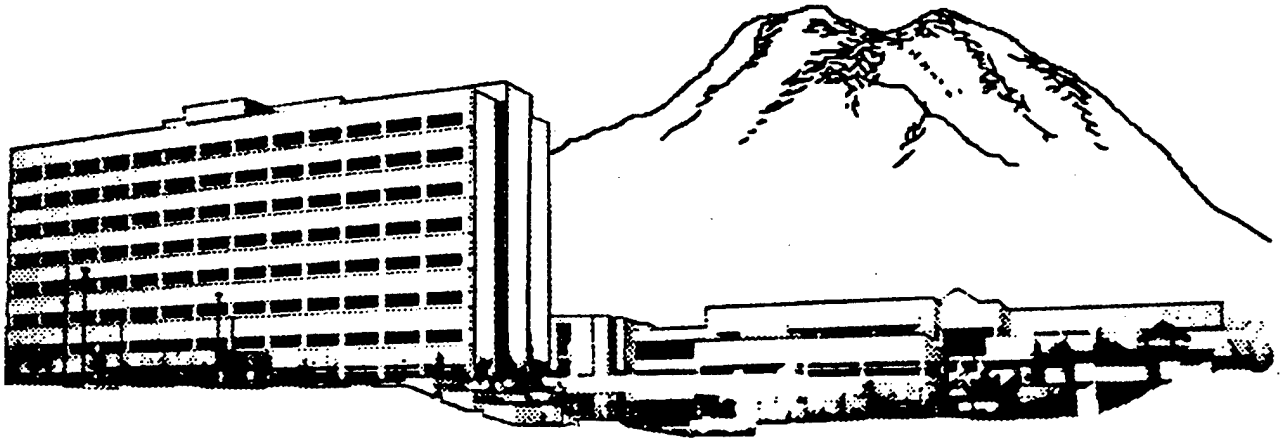
Associate Investigator(s): MAJ Douglas M. Sorensen, MC; LTC John C. Walker, MC

Start Date:	Est. Completion Date:	Periodic Review:
4/24/2001	Dec 01	N/A

Study Objective: To ascertain if combining montelukast with topical nasal steroids results in more rapid resolution of nasal polyposis and chronic hyperplastic sinusitis.

Technical Approach: This is a prospective, randomized, double blinded, placebo controlled trial to ascertain if adjunctive therapy of a LTRA, montelukast, will lead to more rapid and complete resolution of chronic hyperplastic sinusitis with nasal or sinus polyposis. Sixty patients will be recruited from Family Practice, Adult Primary Care, Pulmonary medicine, Allergy, and ENT with clinical chronic hyperplastic sinusitis and nasal/sinus polyps. Baseline evaluation will include history, physical examination with rhinoscopy, symptom scores, sinus CT, nasal acoustic rhinometry, skin testing to a standardized panel of aeroallergens, IgE, chem 10 panel, CBC, quantitative immunoglobulins, and tetanus titer. All subjects will have therapy initiated with nasal lavage and nasal fluticasone proprionate 50 ucg/puff, 2 puff each nostril bid. They will then be randomized to receive either placebo or montelukast 10 mg/day in double-blinded controlled fashion. Follow up with evaluations with symptom scores, acoustic rhinometry, and rhinoscopy and sinus CT will be performed at 12 weeks. Comparison will be made to their baseline data and between the active and placebo groups. Acoustic rhinometry, symptom scores, standardized rhinoscopy scores and standardized grading of sinus CT were chosen to facilitate gathering of objective data that would be comparable.

Progress: Three subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.



Detail Summary Sheets

Urology Service, Department of Surgery

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/090 **Status**: Ongoing

Title: A Two-Phase, Double-Blind, Randomized, Parallel-Group Design, Multicenter Study of FLOMAX Capsules, 0.4 mg versus Placebo in Male Patients with Acute Urinary Retention Related to Benign Prostatic Hyperplasia

Principal Investigator: MAJ Sunil K. Ahuja, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Raymond A. Costabile, MC; LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC; LTC Henry E. Ruiz, MC; CPT Andrew C. Peterson, MC

Start Date:	Est. Completion Date:	Periodic Review:
3/27/2001	Apr 02	N/A

Study Objective: To establish whether the administration of FLOMAX improves the outcome of a trial without catheter (TWOC) after an episode of acute urinary retention, and to determine whether spontaneous voiding is maintained over the course of six months of active treatment.

Technical Approach: This double-blind, placebo-controlled, randomized trial, is designed in two phases to examine whether FLOMAX capsules, 0.4 mg as compared to placebo, can increase the success rate of TWOC in patients with acute urinary retention due to BPH (Phase I). The trial is powered to detect significant differences between FLOMAX and placebo in Phase I. Phase II of the trial is designed to examine whether patients who successfully voided spontaneously in Phase I, can be maintained catheter free on treatment with FLOMAX compared to placebo over a six-month period. The overall design of Phase II will examine whether FLOMAX can prevent or delay reoccurrence of acute urinary retention due to BPH. Visit 1 may be performed after diagnosis of AUR and catheterization occur. If refered from the ER, Visit 1 must be performed within 72 hours of catheterization in order to be eligible for the study. Following obtaining of informed consent the study coordinator will review and record any relevant medical history for the last two years and review the inclusion/exclusion criteria for Phase I. Upon determining patient eligibility, the rest of Visit 1 procedures will be performed, sitting vital signs, physical examination, digital rectal examination, prostate volume, laboratory testing, concomitant therapy, and adverse events. The patient will then be randomized and a medication number will be assigned. The patient will be on study medication for 72-96 hours (3-4 days). The catheter must be in place during this treatment time. Patients will take the first dose of medication in the office the same day as Visit 1 and then 7 days of drug dispensed with instructions to take one capsule orally, one half-hour after breakfast for the next 3-4 days. If the dose is not taken one half-hour after breakfast, the patient will have up to three hours to take their dose. If the patients does not then take their medication within this three hour window the dose is considered missed. The patient should not double up doses at the next dosing time, instead only the next regular dose should be taken at the instructed time. Patients will be instructed to return to the clinic within 3-4 days (72-96 hours) after Visit 1. Visit 2 (day 3 or 4): At this visit, the patient's bladder will be filled with normal saline solution through the catheter to promote voiding. When the patient feels the sensation to urinate, the catheter will be removed and the patient instructed to spontaneously void. A successful spontaneous void is defined as a voided amount of at least 100ml and a post-void residual volume of equal to or greater than 300ml. Post-void residual volume will be measured, using ultrasound, for those patients that void spontaneously. These patients will be given the option of continuing in the Phase II portion of the study. Visit 2 is the final visit for patients who are unable to void spontaneously. These patients will not be allowed to continue to Phase II of the study and must be withdrawn. These patients will be re-catheterized and all Visit 2 procedures, as checked in the flow chart including laboratory tests will be completed and all study medication will be returned. These patients will consult their own physicians for further treatment. Any patient who has removed his catheter or had it removed at another institution, should be discontinued and all end of study procedures performed. If the patients blood work from Visit 1 has clinically significant abnormal lab values,

the patient should be withdrawn and all end of study procedures completed. Visit 2 procedures consist of physical examination, sitting vital signs, removing urethral catheter, laboratory tests (this test will only be completed for those patients not continuing on to the Phase II portion of the study), voided urine volume, post-residual volume (by pelvic ultrasound), medication compliance, adverse events, concomitant therapy, termination of trial medication for Phase I, study medication for the Phase II portion will be dispensed only if the patient is continuing on to the Phase II portion and meets all the inclusion/exclusion criteria.

Phase II inclusion criteria: Patients who have voided spontaneously at Visit 2, at least 100ml and a post-void residual volume of more than or equal to 300ml, at Visit 2. Patients will be re-randomized and a new medication number will be assigned. Patients will be dispensed a 90 day supply of medication and instructions to take their medication one half hour after breakfast. If the dose is not taken one half hour after breakfast, the patients will have up to three hours to take their dose. If the dose is missed the patient must not double up at the next dosing time. Instead only the next regular dose may be taken. These patients will be asked to return to the clinic 90 days from Visit 1. Visit 3 (90 days): This visit will collect the following information: sitting vital signs, medication compliance, adverse event and concomitant therapy. The patient will be ask to spontaneously void and voided urine will be collected and measured. A post-void residual measurement using pelvic ultrasound will also be done. A 90 day supply of medication will be dispensed and instructions to take their medication one half hour after breakfast. If the dose is not taken one half hour after breakfast, the patient will have up to three hours to take their dose. If the dose is missed the patient must not double up at the next dosing time. Instead only the next regular dose may be taken. These patients will be ask to return to the clinic 180 days after Visit 1. Visit 4 PEOT/EOT (180 days): This visit will collect the following information: physical examination, digital rectal exam, sitting vital signs, laboratory testing, voided urine volume, post-void residual volume (by pelvic ultrasound), prostate volume (by transrectal ultrasound), medication compliance, adverse events, concomitant therapy. The patient will also be ask to return all unused trial medication at this visit.

Progress: Four subjects enrolled in this study at MAMC in FY01; however all have been withdrawn, one due to an adverse events and three were screen failures for Phase 2. All four subjects completed Phase 1 of the trial with one MAMC SAE, hospitalization with MI, felt to be unrelated to study participation. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 200/019	**Status**: Ongoing

Title: A Pilot Study of Radiofrequency Induced Coagulation Necrosis of Solid Renal Masses

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology	**Facility**: MAMC

Associate Investigator(s): MAJ David G. Omdal, MC

Start Date:	**Est. Completion Date:**	**Periodic Review:**
11/19/1999	Dec 04	10/24/2000

Study Objective: (1)To assess the capability of radiofrequency (RF) energy to induce a predictable zone of necrosis within renal tissue / tumor, (2) to determine the viability of cells within the zone of necrosis via pathological evaluation and (3) to evaluate the response and follow up in patients who are not candidates for surgical resection of their solid renal masses.

Technical Approach: This prospective, nonrandomized study will treat various stages of renal cell cancer using radiofrequency (RF) induced necrosis of tumor tissue. The investigator will use ultrasound imaging to place an electrode into the affected tissue. The appropriate dose of RF energy will be released into the tissue in the immediate area. If the patient is a candidate for resection nephrectomy, the treated tissue will then be resected and assessed by pathological evaluation. After treatment, both groups will be followed and monitored to assess changes in the tumor and surrounding tissue.

Progress: 13 subjects have been enrolled. Pathological specimens in the ablate and resect arm of the study (7 enrolled) show a zone of necrosis that is at least 2mm larger than the volume of the needle electrode. Patients in the ablate only arm of the study (6 enrolled) all tolerated the procedure without morbidity. follow-up imaging demonstrated tissue destruction without evidence of tumor progression or recurrence. Study remains ongoing.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/045 **Status**: Completed

Title: A Pilot Phase II, Placebo-controlled, Double-blind Study of KMD-3213 in patients with the Signs and Symptoms of Benign Prostatic Hyperplasia (BPH) Protocol #KMD-3213-US021-99

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; LTC Henry E. Ruiz, MC; CPT Cecily K. Peterson, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Mar 01	1/23/2001

Study Objective: To test various aspects of KMD-3213 in patients with benign prostatic hyperplasia, including: (1) the most effective doses, (2) if the efficacy of KMD-3213 is maintained over time or if tolerance develops, (3) effects of KMD-3213 on vital signs in the target population, and (4) effects on electrocardiogram parameters, heart rate, and clinical lab tests in the target population.

Technical Approach: This multicenter, double-blind study will treat patients on one of three different treatment arms. After a 4-week placebo lead-in period, patients will be given either 0 mg, 4 mg, or 8 mg KMD-3213 to take daily for 8 weeks. At the end of the 8-week treatment period, efficacy of the drug will be assessed through uroflowmetry and questionnaires.

Progress: A total of 3 subjects enrolled and completed study treatment at MAMC. Final closure of this study at MAMC was reported to the 28 Aug 01 IRB. Data analysis is not yet available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/087 **Status**: Terminated

Title: Phase II Dose-ranging Study of HuKS-IL2 in Patients with Hormone Refractory Prostate Carcinoma

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Karen C. Evans, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Jun 02	

Study Objective: (1)To evaluate the clinical activity of different dosing regimens of HuKS-IL2 by prostate-specific antigens (PSA) response, (2) To evaluate clinical activity by objective anti-tumor response, if applicable, (3) to determine the safety and tolerability of HuKS-IL2 administered at various drug levels and dosing schedules, (4) to evaluate the pharmacokinetics and immunogenicity of HuKS-IL2, (5) to evaluate the feasibility of different dosing regimens of HuKS-IL2, and (6) to compare the immunologic activity of different dosing regimens of HUKS-IL2 based on total lymphocyte counts, CD3+, CD4+, CD8+, CD19+, CD16+, and CD56+ cell counts.

Technical Approach: This open-label, dose-ranging study treats patients for 4 months and follows them for 4 weeks afterward. Patients will be treated with either 4mg/m2 or 6mg/m2 IV infusion on dosing days for 3, 4, or 5 consecutive days according to the assigned treatment cohort. Clinical activity will be determined by change in PSA, improvement in measurable disease sites, pain, and quality of life assessments.

Progress: This study was terminated per the study sponsor; effective 16 Feb 01, when it was decided not to initiate protocol at any study sites.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/103 **Status**: Completed

Title: A Six-month, Open-label, Fixed-dose Study to Evaluate the Safety, Tolerance, Pharmacokinetics and Endocrine Efficacy of Two Doses of LA-2550 22.5 mg in Patients with Advanced Prostate Cancer

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jul 01	8/28/2001

Study Objective: (1) To evaluate the safety and tolerance of two doses of LA-2550 22.5mg in patients with advanced prostate cancer, (2) To evaluate serum testosterone and LH levels following two doses of LA 2550 22.5mg in patients with advanced prostate cancer, and (3) To determine the pharmacokinetic (PK) profile of serum leuprolide acetate following two subcutaneous injections with LA 2550 22.5mg in a subset of patients with advanced prostate cancer.

Technical Approach: This open-label study will administer 2 subcutaneous injections of LA-2550 22.5 mg to patients with Jewett Stage C1, C2, D1, or D2 prostate cancer. The injections will be given at Day 0 and Month 3, with the patient returning daily and/or weekly for health assessment and blood sampling. Final assessments and evaluation will take place at Month 6. During participation in this study, patients will be monitored for safety through physical examination, vital signs, clinical laboratory values and adverse events.

Progress: This study was reported as completed at MAMC, 18 Jul 01. Two subjects enrolled and completed study participation. While the study was ongoing at MAMC, two adverse events were reported to the IRB; one a MAMC subject hospitalized with asthma. This event was felt to be unrelated to study participation.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/111 **Status**: Terminated

Title: A Phase III Crossover Study Evaluating the Efficacy and Safety of Uprima (Apomorphine HCl Tablets) Sublingual (2, 3, 4 mg) in Combination with Sildenafil Citrate (25 or 50 mg) in the Treatment of Male Erectile Dysfunction (#M00-181)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Sep 01	10/23/2001

Study Objective: The primary objective of this study is to determine the safety and efficacy of Uprima (2, 3, 4, and 5mg) in combination with sildenafil citrate (25 or 50mg) compared with Uprima (2, 3, 4, and 5mg) alone and sildenafil citrate (25 or 50mg) alone in the treatment of patients with male erectile dysfunction.

Technical Approach: Subjects with erectile dysfunction will be randomized to receive medications on one of two arms of this study. Patients will be randomized to either arm and receive the following dosing combinations in any order: Arm One: 2mg Uprima and placebo, 25mg sildenafil and placebo, or 2mg Uprima and 25mg sildenafil. Arm Two: 2mg Uprima and placebo, 50mg sildenafil and placebo, or 2mg Uprima and 50mg sildenafil. Patients and their wives/partners will both be required to sign consent forms. Diaries will be completed after each attempt at sexual intercourse. At office visits during the various periods of either arm of the study, both the patient and his partner will fill out questionnaires regarding erectile/sexual function. At the end of each treatment period, the subject will undergo a complete physical exam, ECG, and clinical lab test. The patient will wait between 48 and 96 hours to start the next period of the study. At the end of each period, both the patient and the partner/wife will fill out questionnaires (International Index of Erectile Function and Treatment Satisfaction Questionnaire for the patient, Brief Sexual Function Inventory and the Treatment Satisfaction Questionnaire for the partner.)

Progress: This study was terminated by the study sponsor in response to FDA concerns about the study methods prior to its intitation at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/112 **Status**: Ongoing

Title: A Phase III, Randomized, Multicenter, Placebo-controlled, Double-blind, Clinical Trial to Study the Efficacy and Safety of CyPat (Cyproterone Acetate [CA]) for the Treatment of Hot Flashes Following Surgical or Chemical Castration of Prostate Cancer Patients and Its Impact on the Quality of Life in these Patients

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Raymond S. Lance, MC; CPT Andrew C. Peterson, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Sep 01	7/24/2001

Study Objective: 1) To determine the efficacy of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or "medical castration" (LHRH agonist treatment); 2) To compare the effectiveness of the two doses (50 and 100mg) of CyPat for control of hot flashes; 3) To deterermine safety (based on adverse events and laboratory parameters) of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or "medical castration" (LHRH agonist treatment); 4) To determine the impact of CyPat treatment on the quality of life in surgically or chemically treated cancer patients.

Technical Approach: After a one-week screening observation period, subjects will be randomized to receive either placebo, 50mg, or 100 mg of CyPat to control hot flashes. For 12 weeks, subjects will record incidence of hot flashes, and will periodically have checkups to ensure patient safety. Patients will complete quality of life questionnaires on a monthly basis during the treatment phase of this study. After the 12-week double-blind randomized part, eligible patients will have the option of continuing to take CyPat (100mg) for 6-9 months in an open label tolerability study.

Progress: Fourteen patients enrolled in this study at MAMC during FY01. Two SAE's have been reported to date; one MAMC patient hospitalization with acute onset memory loss (recovered), which was reported as unrelated to study participation. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/140 **Status**: Terminated

Title: A Randomized, Multicenter, Phase III Trial Evaluating the Efficacy and Safety of BCI-ImmuneActivator (KLH) versus Adriamycin in BCG Refractory or Intolerant Patients with Carcinoma in situ with or without Resected Superficial Papillary Bladder Cancer

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Jan 04	

Study Objective: To demonstrate the superior efficacy of BCI-ImmuneActivator versus Adriamycin (Doxorubicin Hydrochloride) in patients with carcinoma in situ (CIS) with or without resected superficial papillary bladder cancer who are refractory or intolerant to Bacillus Calmette Guerin (BCG) intravesical therapy and to evaluate the toxicity and safety of BCI-ImmuneActivator when administered intradermally and intravesically as compared to Adriamycin administered intravesically.

Technical Approach: This is a multicenter, prospectively randomized trial in patients diagnosed with CIS of the bladder with or without resected superficial papillary tumor, confirmed by biopsy within 3 months of study entry who have failed at least 1 course of BCG treatment or are intolerant of BCG therapy. Subjects randomized to the BCI-ImmuneActivator Arm will receive a sensitizing intradermal injection of BCI-ImmuneActivator about 2 weeks prior to receiving the study medication intravesically into the bladder. Subjects will then receive weekly instillations of study medication for 6 weeks. If they are complete responders at week 12, they will receive monthly therapy for 3 months. Partial or non-responders will receive weekly instillations for another 6 weeks, then if they become complete responders, will begin monthly treatments as above. Subjects randomized to the Adriamycin Arm will receive weekly Adriamycin intravesically into the bladder for 6 weeks. If complete response they will begin monthly installations for 3 months beginning at week 13. Partial or non-responders to Adriamycin will be withdrawn from the study.

All subjects will have cystoscopy every 3 months to evaluate response. At week 24, if complete response is noted, subjects will continue to receive monthly maintenance instillations of study drug or Adriamycin for another 6 months. Partial or non-responders will be withdrawn from the study.

Progress: This protocol was terminated, 22 May 01, per the study sponsor. No subjects enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/141 **Status**: Ongoing

Title: A Study Evaluating the Efficacy, Safety, and Tolerability of L-377202 in Bidimensionally Measurable, Androgen-Independent Prostate Cancer (Protocol No. 004-00)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; LTC Henry E. Ruiz, MC; MAJ Nancy Shaffer, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Dec 02	9/25/2001

Study Objective: The primary objectives of this study are to determine bidimensionally measurable disease radiologic response rates after treatment with L-377202 and to evaluate the general safety and tolerability of L-377202. The secondary objectives are (1) to determine bidimensionally measurable disease response rates (tumor burden, bone scan), (2) to evaluate PSA response rates obtained, (3) to evaluate pain and analgesic response rates, (4) to evaluate health-related quality-of-life responses, (5) to determine time to response, time to progression and response duration, (6) to determine duration of time during which patients maintain an ECOG performance status <= 1, (7) evaluate 1 year cancer-specific and overall survival following treatment with L-333202, and (8) assess the effect of L-277202 treatment on biochemical markers of bone turnover.

Technical Approach: This is an open, nonrandomized study of male patients at least 30 years old with androgen-independent prostate cancer and bidimensionally measurable disease. After screening, eligible patients will be treated with a 30 minute infusion of L-377202, 225 mg/m2 every 21 days. Each patient will be treated with at least 2 cycles, though additional cycles may be administered for stable or responding disease. Doses will be adjusted according to degree of myelosuppression experienced by each patient.

If a response or stabilization of disease is demonstrated, patients may continue to be treated for an indefinite number of cycles until either evidence of disease progression is documented, inclusion criteria can not be satisfied (except for PSA), or exclusion criteria are met. Assessments for disease progression must be performed every 2 treatment cycles. Pain will be assessed with the present pain intensity (PPI) scale of the McGill-Melzack Pain Questionnaire. Analgesic use will be assessed with the analgesic diary. Health-related quality-of-life will be assessed with the EORTC QLQ-C30 and the Osoba Quality-of-Life Module Prostate-14. The health economic impact of L-377202 will be assessed by collecting health resource utilization with the Health Economic Assessment case report form, which will be completed by the investigator or his designee. Duration of Time with an ECOG performance status <= 1 is defined as the number of days during which a performance status of <= 1 is reported.

Progress: This protocol closed to patient entry, 14 Jun 01, per the study sponsor. One patient enrolled in this study at MAMC in FY 01 and continues to receive treatment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/044 **Status**: Completed

Title: In-Clinic Evaluation of the Safety and Efficacy of Topical Alprostadil (PGE1) for the Treatment of Female Sexual Arousal Disorder (Vivus Protocol: FSD-02)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Henry E. Ruiz, MC; COL Gary D. Davis, MC; CPT Sandra L. Hernandez, MC; MAJ Raymond S. Lance, MC; CPT Leah P. McMann, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Nov 01	N/A

Study Objective: To evaluate the safety of and genital response to topical Alprostadil for the treatment of Female Sexual Disorder.

Technical Approach: This is a double-blind, randomized, placebo-controlled study that will evaluate approximately 80 post-menopausal or surgically sterilized women at approximately 5 study sites. Women enrolled into this study will have a diagnosis of Sexual Arousal Disorder based on medical history, physical examination, and a baseline psychological questionnaire. Following a screening evaluation (visit 1) women will be sequentially enrolled in groups of 8 patients per site to treatment with 100mcg (group 1) or 400mcg (group 2) doses of Alprostadil. Treatment will consist of 2 doses (visits 2 and 3) administered in clinic, one of Alprostadil at the dose level specified for each group and the other of a matching placebo. Doses will be randomized with an equal probability of active drug and placebo doses being administered first. Active drug and placebo solutions that are identical in appearance will be applied topically to the periurethral area and the outer vagina. Following application of the study medication, patient responses in conjunction with visual sexual stimulation and neutral (non-sexual) video stimulation will be followed for a period of one hour, and for an additional hour without visual stimulation. Assessments will include patient ratings of genital wetness/lubrication, pelvic fullness, genital warmth/tingling, pain, emotional excitement, satisfaction with level of arousal, and level of sexual satisfaction. A washout period of at least 72 hours will separate each treatment. The final visit (visit 4) will be an exit visit.

Progress: Eighteen subjects consented and 11 randomized. Seven not randomized included 4 subjects who withdrew their consent and 3 subjects who did not meet inclusion/exclusion criteria. The last enrolled patient's end of study visit was completed 24 Aug 01. No SAE's had been reported. This study has been completed at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/048 **Status**: Terminated

Title: An Eight-Month, Open-Label, Fixed-Dose Study to Evaluate the Safety Tolerance, Pharmacokinetics, and Endocrine Efficacy of Two Doses of LA-2575 30 mg in Patients with Advanced Prostate Cancer

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Dec 02	N/A

Study Objective: (1) To evaluate the safety and tolerance of two subcutaneous (SC) doses of LA-2575 30mg in patients with advanced prostate cancer, (2) To evaluate serum testosterone and LH levels following two doses of LA-2575 30mg in patients with advanced prostate cancer and (3) To determine the pharmacokinetic (PK) profile of leuprolide acetate following two subcutaneous injections with LA-2575 30mg in a subset of patients with advanced prostate cancer.

Technical Approach: This is a multicenter, open-label, fixed-dose investigation of (2) doses of LA-2575 30mg administered to patients with Jewett Stage A2,B, C, or D adenocarcinoma of the prostate and/or a rising PSA after failed local therapy for prostate cancer. Approximately 70-85 patients (2-3 per site) will receive a single, SC injection of LA-2575 30mg at baseline and month 4 (for a total of two injections); the patients will be followed for eight months. Male patients between the ages of 40 and 85 years with Jewett Stage A2, B, C, or D adenocarcinoma of the prostate and/or a rising PSA after failed local therapy will be evaluated for eligibility to enter the protocol. The screening visit will take place within 3-16 days prior to initial LA-2575 30mg administration. Patients who meet all eligibility criteria will be given a patient number on Day 0 (Baseline) and entered into the study. On Day 0, patients will receive a single dose of LA-2575 30mg SC between 0600 and 1000 hours. The first 24 patients (Group A) will have additional analyses performed at specific timepoints throughout the study for measurement of serum leuprolide acetate. At Month 4, patients will be given another SC injection of LA-2575 30mg. Blood samples for various hormone determinations will be collected at specific timepoints. Patients will return to the investigational center at daily and weekly intervals for assessment and blood sampling. During participation in the study patients will be monitored by, physical examinations, vital signs, clinical laboratory values, and adverse events. Final assessment and evaluation will take place at Month 8.

Progress: This trial was reported as completed by the study sponsor. Enrollment had been met prior to MAMC obtaining final approval.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/049 **Status**: Terminated

Title: A Non-randomized, Multicenter Phase III Trial Evaluating the Efficacy and Safety of BCI-Immune Activator (KLH) in Patients who have Failed Adriamycin in Protocol BCI-9804 for the Treatment of Carcinoma in situ With or Without Resected Superficial Papillary Bladder Cancer (Protocol BCI-2001)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Feb 05	N/A

Study Objective: (1) To Demonstrate responsiveness and efficacy of BCI-ImmuneActivator in Adriamycin (Doxorubicin Hydrochloride) treatment failure patients with carcinoma in situ (CIS) with or without resected superficial papillary bladder cancer who are refractory or intolerant to Bacillus Calmette Guerin (BCG) intravesical therapy, (2) To Evaluate the responsiveness, toxicity and safety of BCI-ImmuneActivator, when administered intradermally and intravesically to patients who have failed the Adriamycin (Doxorubicin Hydrochloride) previously administered intravesically, and (3) The endpoint is complete response at the 15-month evaluation. All other patients who enter the study will be considered non-responders for analysis of the endpoint.

Technical Approach: This multicenter study will be conducted at approximately fifteen centers across the United States. The number of patients who enter this study will be determined by the percentage of the anticipated 75 patients in the Protocol BCI-9804 that receive Adriamycin and that do not have a complete response to Adriamycin. (The sponsor estimates this to be about 60% of patients, based on SWOG experience and published response/failure rates). Patients who met the inclusion criteria for the BCI-9804 protocol, were successfully enrolled into that study, and failed the clinical response evaluation at the 12 week visit may be considered for enrollment into the BCI-2001 trial, and will be followed up to 15 months following enrollment. Male and female patients who are at least 18 years of age will need to have had a cystoscopic exam and cytology within six weeks of study entry. Patients must have opted against or have had a medical contraindication to cystectomy.

Patients who are enrolled into the BCI-2001 study will receive a sensitizing dose of 0.2cc (1.0mg) BCI-ImmuneActivator (KLH) injection intradermally in the upper thigh. Patients will also receive an intravesical administration, which consists of 1.0cc (5.0mg) BCI-ImmuneActivator in 49cc of sterile, preservative free saline solution; the final volume is 50cc, administered intravesically into the bladder. The sensitizing dose will be administered only at week -2. They will then receive the BCI-ImmuneActivator weekly from week one through week six. A clinical response evaluation will be performed at week 12, and Partial Responders and Non-Responders will begin receiving BCI-ImmuneActivator weekly from week 13 through week 18. Complete Responders will receive BCI-ImmuneActivator Monthly Maintenance Therapy at weeks 13, 17, and 21. All patients will have a Clinical Response Evaluation at week 24.

Starting at six months, Complete Responders will continue on the BCI-ImmuneActivator Monthly Maintenance Therapy and will have a Clinical Response Evaluation every three months, at month 9 and month 12. At nine months, all patients will have a Clinical Response Evaluation, and subjects determined to have disease progression will be taken off the study and offered standard therapy. At month 15, a Post-Treatment Follow-Up will be conducted, and study participation will be terminated.

Progress: This study was terminated at MAMC, 22 May 01, per study sponsor. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/050 **Status**: Ongoing

Title: A Multicenter, Randomized Phase III Study of Adjuvant Oncophage Versus Observation in Patients with High Risk of Recurrence After Surgical Treatment for Renal Cell Carcinoma

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Raymond S. Lance, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Feb 03	N/A

Study Objective: The primary objective of the study is to ascertain whether patients randomized to receive Oncophage treatment for surgically resected, locally advanced renal cell carcinoma have a statistically longer survival than patients with no adjuvant treatment. The secondary objectives of the study are (1) To ascertain whether patients randomized to Oncophage have a statistically longer progression-free survival than patients with no adjuvant treatment and (2) To further characterize the safety of treatment with Oncophage.

Technical Approach: This is an international, multi-center, randomized, open-label Phase III study in which patients with surgically resected, locally advanced renal cell carcinoma at high risk of recurrence will be randomized post-operatively to receive adjuvant treatment with Oncophage or no adjuvant treatment (observation, standard of care). Approximately 850 patients will be enrolled internationally over a period of two years to obtain 712 evaluable patients for overall survival and progression free survival in this trial. At least 12 patients will be enrolled at Madigan Army Medical Center.

Prior to surgery and after informed consent is obtained, patients will be screened for study and inclusion/exclusion criteria will be reviewed. Vital signs, performance status, and laboratory tests will be performed including proof of non-pregnancy. Other appropriate studies to fully define the extent of existing or suspected malignant and non-malignant disease will be done including CT-chest, CT or MRI of abdomen/pelvis, and CT or MRI of the brain. A bone scan will be performed if clinically indicated. All patients will undergo complete surgical resection of their tumors, and will be randomized to receive adjuvant treatment with Oncophage or to receive no adjuvant treatment. Patients will be stratified for histological grade, nodal status, and performance status. The major part of the patient's tumor will be sent to Antigenics for preparation of Oncophage, which is an autologous tumor-derived vaccine. Patients randomized to Oncophage treatment will receive the first four injections at weekly intervals and thereafter at two-week intervals, until possible disease progression, excessive toxicity, or the patient's available supply of Oncophage is depleted. Patients will receive a ruler and diary and asked to record possible reactions to the vaccine which may occur at home. Patients on both arms will be assessed for adverse events, vital signs, performance status, lab tests, x-rays, safety and efficacy at 1-3 month intervals for the first year. All patients will undergo x-rays every 3 months for first year. Thereafter, they will be evaluated every 6 months for possible progressive disease until death. Auto-antibodies will be monitored every 6 months for the first year for patients receiving Oncophage and once every year for patients on the observation arm.

Progress: No subjects have been enrolled at MAMC during FY01 and no SAE's reported. This study remains ongoing to subject enrollment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/097 **Status**: Ongoing

Title: A Multicenter, Phase IIb, Four Arm, Dose Finding, Randomized, Placebo-Controlled Study to Determine the Long Term Prostate Cancer Chemoprevention Efficacy and Safety of 20 mg, 40 mg, & 60 mg Daily of GTx-006 in Men with High Grade Prostate Intraepithelial Neoplasia (PIN)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; COL Kevin J. Chismire, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	Oct 02	N/A

Study Objective: Primary: 1) To determine whether GTx-006 is able to reduce the incidence of prostate cancer in men with high grade PIN; 2) To evaluate the safety of GTx-006 (general, ocular, hormonal, semen profile and liver toxicities); 3) To determine the effective dose of GTx-006. Secondary: 1) To determine whether GTx-006 is able to eliminate or reduce high grade PIN lesions; 2) To test the effects of GTx-006 on serum total and % free PSA levels; 3) To assess the population; 4) pharmacokinetics of GTx-006; 5) To investigate whether GTx-006 affects prostate volume; 6) To assess the effects off GTx-006 on low grade PIN; 7) To assess quality of life issues.

Technical Approach: This phase IIb, multicenter, double-blind, placebo-controlled study will be looking at the efficacy and safety of GTx-006 in men with high grade prostate intraepithelial neoplasia (PIN). Eligible subjects will receive GTx-006 or identical appearing placebo for maximum treatment duration of 12 months. A total of 500 subjects will be enrolled across the United States (125 in each arm), with 120 subjects being enrolled into a semen sub-set (30 in each arm) that will look at sperm count. Inclusion criteria includes: diagnosis of high grade PIN (grade II or III) on prostate biopsy, PSA of 12 ng/ml, and adequate bone marrow, liver and renal function. Exclusion criteria includes: prior chemoprevention therapy, diagnosis of prostate cancer on initial evaluation or history of other cancer, visual acuity of 6/12 or worse, active eye disease or intraocular surgery, any infection requiring treatment, severe concurrent illness judged by the investigator as causing difficulty with adequate follow-up/compliance, thromboembolic disease, chromic hepatitis/cirrhosis, or subject taking any of the following medications: finasteride or testosterone-like supplements, such as DHEA (Dehydroepiandrosterone), herbal medications or dietary supplements for prostate health such as PC-SPES and Saw Palmetto. Subject may wash-out of excluded medications for 30 days and then be eligible for study as long as he agrees not to re-start medication while on study. Before performing any study related procedures, the study coordinator or investigator will explain the purpose of the study to the patient, the study procedures and the study schedule. After giving the patient a chance to ask questions, the coordinator will have the patient read and sign the informed consent. Then a member of the study staff will obtain a medical history, history of prior medications within 30 days, & vital signs. Blood and urine specimens will be sent to a central laboratory. An investigator will give a complete physical examination, including Digital Rectal Examination (DRE). A Transrectal Ultrasound (TRUS) and prostate biopsy will be done if none done within 6 months. A pathologist from a central laboratory will confirm the results of the biopsy prior to randomization. In addition, an ophthalmic examination will be done. Upon determining that the patient qualifies after review of all tests, inclusion/exclusion criteria and examinations, then the patient will be randomized within 30 days of the screening visit. He will be given a subject number and randomized to one of 4 treatment arms - 20 mg, 40 mg, 60 mg or placebo. To randomize the patient, the coordinator will use the next sequential randomization number from the block of study drug supplied by the study sponsor. Also, at the randomization visit the following procedures/assessments will occur: check for concomitant medications and symptoms of illness/injury, obtain vital signs, do semen analysis -

sperm count (subset of subjects from selected sites), administer Quality of Life Questionnaire (QOL), obtain lab specimens, and dispense daily diary instructing patient how to complete drug intake information. The study drug will be started in the clinic during this visit. The study staff will then contact the patient by telephone within seven (7) days to assess study drug compliance and tolerance. The patient will return at 3 months, 6 months, 9 months, and 12 months after randomization. The procedures/assessments will be the same as at the randomization visit with the addition of the following: drug accountability at each visit, physical examination at each visit including DRE, urinalysis at each visit, Semen analysis at Months 6 & 12, TRUS for volumetric measurement of prostate at months 6 & 12, prostate biopsy at Months 6 & 12, and ophthalmic examination at Month 12. In the event that the patient discontinues prematurely from the study, he will be asked to return to the site as soon as possible to have the 12-Month assessments/procedures performed, regardless of the study day.

Progress: This study recently received final approval. Start date for subject enrollment is pending sponsor approval to begin the study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/107 **Status**: Ongoing

Title: A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Jul 02	N/A

Study Objective: Primary: To evaluate the safety and efficacy as measured by time-to-disease progression. Secondary: To evaluate the effect of 10 mg Astrasentan on: PSA progression, Biochemical bone markers, Bone scan index, Survival and to evaluate the effect of the study drug on quality of life and performance status and to perform population pharmacokinetic analysis.

Technical Approach: This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. The patient will be randomized in a 1:1 ratio to receive either atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Neither the investigator nor the patient will know which arm the patient is on. Participants will be assigned a 4-digit study number and will be given study drug prior to leaving the clinic. Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. Participants will visit the clinic on Day 14, Weeks 4, 8, & 12, and every 6 weeks thereafter. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. In addition, at each visit the patient will receive a physical examination, & will have vital signs taken. Atrasentan trough plasma concentrations will be measured at Week 4 & Week 12 only. Laboratory analyses (chemistry, hematology, etc.) will be performed at a central laboratory. Quality of Life (QOL) assessment questionnaires will be completed at Day 1, Week 4, Week 12 and every 12 weeks thereafter. The QOL questionnaire will also be completed at final visit and 30 days later. A diary will be given to the patient to collect a record of medication taken for pain. The diary will be reviewed at each visit. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends (as defined by when 650 subjects have experienced confirmed events of disease progression). The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who

did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC. One non-MAMC SAE has been reported but did not cause a revision to the MAMC protocol or consent.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/113 **Status**: Ongoing

Title: A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer, M00-258

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Jul 02	N/A

Study Objective: To evaluate the safety of 10 mg Atrasentan for the treatment of prostate cancer. In addition, the pharmacokinetic parameters of Atrasentan will be defined in a sub-population of subjects.

Technical Approach: This is a phase III, open label study evaluating the safety of 10 mg Atrasentan in men with hormone refractory prostate cancer. All men enrolled in this protocol must have successfully met all of the eligibility criteria for this trial and have completed one of the following Phase III trials:

M00-211: A Phase III, Randomized, Double-Blind, Placebo controlled Study Evaluating the Safety and Efficacy on 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer

M00-244: A Phase III, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic Hormone Refractory Prostate Cancer

Eligible men will receive a single, oral dose (soft gelatin capsule) of 10 mg atrasentan before leaving the clinic (Day 1). They will then continue taking the same dose of study drug once a day at approximately the same time each day. The study participants will be asked to return to the clinic on study days 14 & 28, at Week 12, and then every 12 weeks thereafter. Upon study completion the participants will be asked to come into the clinic for a final assessment, and will return again for a safety evaluation 30 days after the last dose of study drug. Blood will be drawn at every visit. Urine samples will be obtained at visit Day 1, Day 28, every 12 weeks and at final visit.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC. One non-MAMC SAE has been reported to date with no change to the MAMC protocol or consent.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/121 **Status**: Ongoing

Title: A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Andrew C. Peterson, MC; CPT Leah P. McMann, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/24/2001	Sep 02	N/A

Study Objective: 1) To evaluate the safety and efficacy as measured by time-to-disease progression; 2) To evaluate the effect of 10 mg Astrasentan on: PSA progression, Biochemical bone markers, Bone scan index; 3) Survival; 4) To evaluate the effect of the study drug on quality of life and performance status; and 5) To perform population pharmacokinetic analysis.

Technical Approach: This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last less than or equal to 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. After the patient has met eligibility criteria, the patient will be randomized in a 1:1 ratio to receive either atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. In addition, at each visit the patient will receive a physical examination, & will have vital signs taken. Atrasentan trough plasma concentrations will be measured at Week 4 & Week 12 only. Laboratory analyses (chemistry, hematology, etc.) will be performed at a central laboratory. Quality of Life (QOL) assessment questionnaires will be completed at Day 1, Week 4, Week 12 and every 12 weeks thereafter. The QOL questionnaire will also be completed at final visit and 30 days later. A diary will be given to the patient to collect a record of medication taken for pain. The diary will be reviewed at each visit. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends. The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC. One SAE has been reported to date but did not cause a revision to the MAMC protocol or consent.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/089 **Status**: Ongoing

Title: Phase III Randomized, Double-Blind Study of DFMO vs. Placebo in Low Grade Superficial Bladder Cancer

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Robert C. Allen, Jr., MC; MAJ Bryon D. Joyner, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC; LTC Henry E. Ruiz, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Mar 03	8/28/2001

Study Objective: To compare DFMO to placebo in patients with low grade superficial bladder cancers according to a) time to first reccurrence of tumor, and b) toxicities.

Technical Approach: This will be a phase III randomized, double blind study of DFMO (an inhibitor of ornithine decarboxylase) versus placebo in low-grade superficial bladder cancers. Patients who meet the eligibility criteria will be stratified according to 1) history of newly diagnosed vs. recurrent; 2) stage Ta vs. T1; 3) grade 1 vs. grade 2; and 4) multifocal vs unifocal tumors. Then patients will be centrally randomized to receive either DFMO 1 gm/day or placebo, orally for 12 months in a double-blind fashion. Treatment will be discontinued in the presence of biopsy-proven recurrent disease, unacceptable toxicity, or patient refusal; however, every effort will be made to continue follow-up on these patients until the end of study. Patients will be followed with cystoscopy every three months for 2 years (every 6 months the 3rd year and annually for the 4th year). Based on 1.5 year enrollment and 3 year follow-up, study duration will be 5.5 years. CBC, including platelet count will be required within 12 weeks of randomization and at 6 months. An audiogram will be required at baseline and when indicated during the study. An independent pathologist will centrally review tumor specimens.

Progress: Since initial approval, nine patients consented, 6 during FY01. Seven patients have been randomized and one is in screening. There have been no SAE's at MAMC but 4 reported by the sponsor to include one with hearing loss and 3 hospitalizations. To date there are four active patients plus the one in screening and 1 patient withdrew consent prior to randomizing, 1 withdrew after starting drug, 1 patient the sponsor terminated and 1 patient had an AE that caused him to be withdrawn from the trial. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/090 **Status**: Ongoing

Title: A Randomized Double-Blind Placebo-Controlled Phase III Trial Evaluating Zoledronate Plus Standard Therapy versus Placebo Plus Standard Therapy in Patients with Recurrent Carcinoma of the Prostate Who Are Asymptomatic with Castrate Levels of Testosterone and Have Rising PSA Levels Without Radiologically-evident Metastatic Disease

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Bryon D. Joyner, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, Jr., MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC; LTC Henry E. Ruiz, MC; MAJ David E. McCune, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/24/1999	Oct 05	8/28/2001

Study Objective: To determine if intravenous infusions with 8mg zoledronate is superior to placebo in the prevention of bone metastases.

Technical Approach: This is a prospective, stratified, randomized, double blind, placebo-controlled multicenter study in parallel groups. Five hundred prostate cancer patients with castrate levels of testosterone who are progressing biochemically by PSA only and have no radiologically evident metastases will be enrolled. Patients will be stratified according to the prior local treatment and the time interval between surgical castration or initiation of LHRH agonist and trial entry. Patients will receive double-blind study treatment until the development of bone metastases. After the development of bone metastases, all patients will receive open-label 8 mg zoledronate until the end of the study. Both the double-blind treatment phase and the open-label treatment phase have a fixed assessment schedule that must be followed. Once patients have completed the 48th month of the fixed assessment schedule, all patients will be followed for survival until LPLV (Last Patient Last Visit). LPLV for this study is defined as the time when the last patient completes the 4th month of study visit or has died. Assuming a placebo bone metastases-free survival rate of 20% at 2 years, this study is powered to determine if sequential infusion with 8 mg zoledronate administered every 4 weeks is superior to placebo in increasing the bone metastases- survival rate at 2 years to 32% (reduction of the hazard rate of bone metastatic disease in patients with prostate cancer by 29%). It is planned that the data from all centers that participate in this protocol will be combined, so that an adequate number of patients will be available for analysis. The Biostatistics department of Novartis will analyze the data from this study.

Progress: Since initial approval, 11 subjects have been consented and 4 randomized. There have been no patients enrolled since October 2000 and 17 SAE's reported to date. This study has been on FDA hold from subject enrollment while it looks at the safety data.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/095 **Status**: Terminated

Title: The Evaluation of Seminal Leucocytes and Cytokine Function of Infertile Males

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): None.

Start Date:	Est. Completion Date:	Periodic Review:
8/24/1999	Sep 01	7/24/2001

Study Objective: To evaluate leucocyte function in infertile males and fertile controls.

Technical Approach: Patients seen in infertility clinic have a semen analysis as part of their routine evaluation. An aliquot of this semen analysis (approximately 10 microliters) will be cryopreserved in liquid nitrogen for immunohistochemical and microscopic (H&E) analysis for leucocyte, cytokine and germ cell composition and cataloging. Cell types will be counted on a hemocytometer to determine leucocyte composition after preferential staining with immunoreagents. Measurement of ROS by luminol florescence will be performed on fresh aliquots of semen specimens. Semen aliquots will also be obtained from patients undergoing vasectomy and vasectomy reversal. These aliquots will serve as controls (healthy, fertile males) and changes in leucocyte/cytokine composition before and after sterilization/reversal can also be documented. Semen analysis from vasectomy patients (known fertile controls) will be analyzed before and after vasectomy to establish mean populations of seminal leucocytes in healthy "normal" males. By measuring these populations before and after vasectomy, the testicular WBC contribution will be established. These "norms" of seminal WBC population can then be compared to infertility patients to evaluate any deviation in seminal leucocyte population. Immunoassays will be performed to measure levels of Interferon alpha, beta, gamma, as well ass IL-2, IL-6 and TNFalpha. Additional cytokines may be measured as immunoassays are developed. Total seminal leucocyte count and differential seminal leucocyte count will be compared in infertile males and fertile male controls using the Student's two-sample t test to evaluate statistical significance. Seminal cytokine levels in fertile and subfertile males will also be analyzed using the Student's two-sample t test.

Progress: This study was terminated, 25 Jul 01, per the PI. Work on this study had not been initiated.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/096 **Status**: Terminated

Title: Macroscopic and Microscopic Anatomy of the Arterial Supply to the Human Vas Deferens

Principal Investigator: LTC Raymond A. Costabile, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): None.

Start Date:	Est. Completion Date:	Periodic Review:
8/24/1999	Sep 01	7/24/2001

Study Objective: (1) Describe the gross and microscopic blood supply to the vas deferens, (2) Assess the variability of the arterial and venous structures, (3) Assess collateral blood supply to the vas deferens, and (4) Utilize the new understanding of the vascular supply to improve operations on the spermatic cord, scrotal adnexa and vas deferens.

Technical Approach: Gross dissection of the, deferential blood supply: a) Gross dissection of cadaveric and specimens; b) Dissection of en bloc spermatic cord specimens from fresh and frozen cadavers; c) Microdissections on cadaveric specimens and autopsy specimens and recording of findings using photos and drawings. Microscopic description of deferential blood supply: a) Injection studies will be performed using India ink injections of the deferential artery, internal iliac artery and internal spermatic artery; b) Histologic sections will be performed using a dissecting microscope in the straight and convoluted portions of the vas deferens sagitally and transversely. These sections will be recorded using photomicrographs and drawings from medical illustrators.

The microscopic penetration of blood supply to human tissue does not lend itself to variability. The means by which arteries penetrate the wall of the vas deferens will likewise have minimal variability in normal vas deferens and deferential arteries. For this reason microdissection of 10 cadavers will give 20 examples of the method of penetration, providing more than 'adequate numbers for our purposes. The cadavers will be supplied from the Anatomical Teaching Lab at USUHS. They will either be fresh or frozen cadavers. A total of 10 cadavers will be required for this study.

Documentation of the blood supply to the vas deferens will be performed using photographs. Medical illustrations will be required since this is an anatomical study, pictures will be needed to present and/or publish data from this study. Medical illustrations will be done at the Graphics Department at USUHS or through the Graphics Department at HMJF.

Progress: This study was terminated, 25 Jul 01, per the PI. Work on this study had not been initiated.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/044 **Status**: Completed

Title: Detection of Occult Metastasis in the Peripheral Blood of Prostate Cancer Patients

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Oct 01	1/23/2001

Study Objective: To investigate the utility of several biomarkers for the detection of micrometastasis in the peripheral blood of patients with and without metastatic prostate cancer. Telomerase activity, human telomerase reverse transcriptase catalytic subunit (hTERT) mRNA expression, and cytokeratin 19 (CK19) mRNA expression will be examined in circulating cancer cells.

Technical Approach: Subjects will be selected through the prostate cancer patient database existing in Urology Service, Department of Surgery, MAMC. Subjects will be divided into 5 groups of 25 patients each. Blood samples will be collected in tubes containing EDTA, subject identifiers will be removed and the sample assigned a number. A total of 23 ml of blood will be collected per subject; 4 x 5 ml tubes will be used for immunomagnetic enrichment with subsequent RT-PCR and telomerase activity assays and 1 x 3 ml tube will be used to separate serum for VEGF quantitation.Those samples undergoing immunomagnetic enrichment (4 tubes of 5 ml blood per patient), mononuclear cells (MNCs) will first be isolated from the anticoagulated blood. Each 5 ml blood sample will be layered over 5 ml of Histopaque-1077 solution in 15 ml tubes and centrifuge at 400 x g for 30 min at room temperature to separate the MNC layer from the red cells and plasma. These MNCs will be washed twice in RPMI 1640/5% FBS according to manufacturer's instructions and then will be resuspended in 1 ml phosphate buffer saline/1% FBS/0.;6% NaCitrate. The epithelial cells will be harvested from these MNCs using 1 x 107 immunomagnetic beads coated with the epithelial-specific monoclonal antibody BerEP4. Bead-coated cells will be washed 3x in PBS/1% FBS/0.6% NaCitrate and then 1x PBS. Harvested epithelial cells then will be processed for hTERT, CK19 and B2-microglobulin mRNA expressions.

Progress: CK19 transcripts were detected in a higher proportion of metastatic prostate cancer patients than non-cancer controls ($p<0.05$; Fisher's exact test). CK19 was detected in 6 of 8 (75%) patients with known metastatic disease, 2 of 7 (29%) cancer patients having 3 successively rising serum prostate specific antigen (PSA) levels following radical prostatectomy or external beam radiation therapy, and 3 of 31 (10%) non-cancer controls. Telomerase activity was not detected in any subject with metastatic disease and in 2 of 7 (29%) prostate cancer patients with rising PSA levels. Serum VEGF levels did not correlate with disease status. Conclusions: CK19 mRNA expression may be a useful biomarker to detect micrometastatic tumor cells in prostate cancer patients. Further investigation with greater numbers of cancer patients and controls is warranted. Telomerase activity and serum VEGF levels do not appear to be reliable biomarkers of occult metastasis in patients with prostate cancer.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/140 **Status**: Ongoing

Title: Intratumoral Treatment of Human Prostate Cancer Xenografts by Polymeric Gel Delivery of Yttrium-90 with and without Taxol

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ John B. Halligan, MC; LTC William B. Reece, MC; CPT Jack R. Walter, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/24/2001	Sep 04	N/A

Study Objective: We hypothesize that intratumoral injection with polymeric gel containing cytotoxic chemo- and/or radiotherapeutic agent(s) will result in tumoricidal activity against human prostate xenografts without significant migration to other body tissues or fluids..

Technical Approach: 6-8 week old male nude mice will be injected, subcutaneously, in the upper back with 2 x 106 LnCap cells (the only human prostate cancer cell line that is androgen sensitive, thus better reflecting clinically localized prostate cancer) in 0.1-0.2 cc suspensions. Mice will be randomly assigned to specific control/treatment groups at the time of cancer cell injection. Tumors will grow to 6-10 mm in diameter over approximately 4-6 weeks, at which time control or treatment intervention will be applied as described below. A control group of 5 mice will have no therapy applied. 5 other control mice will receive intratumoral injections with the polymeric compound alone. Treatment group Ia will consist of 15 mice receiving intratumoral injection of polymeric gel plus Yttrium-90. Treatment group Ib will include 15 mice receiving intratumoral injections of Yttrium-90 alone (no polymeric gel). Treatment group IIa will include 10 mice subjected to intratumoral injection of polymeric gel combined with Yttrium-90 and Taxol. Treatment group IIb will include 10 mice receiving intratumoral injection with yttrium-90 plus Taxol alone (no gel). Treatment group IIIa will have 10 mice getting intratumoral injection with Taxol in the polymeric gel. Finally, treatment group IIIb will receive intratumoral injection with taxol alone (no polymeric gel). The treatment injection volume will be standardized between and within treatment groups, and will not exceed 0.1 cc. Five animals each, in treatment groups Ia and Ib will euthanized 5 days following intratumoral injections of yttrium-90 in order to measure for systemic radiation (bioavailability/ biodistribution). Lungs, liver, kidneys, blood, urine and colonic feces will be harvested and tested with a beta counter.

Progress: This study recently received final IACUC approval. Work on this protocol has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/104 **Status**: Terminated

Title: Telomere Length and Telomerase Activity in Human Testicular Cancer

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): CPT Wade K. Aldous, MS; MAJ J. Brantley Thrasher, MC; MAJ Kenneth W. Westphal, MC; CPT Keith J. O'Reilly, MC; Troy H. Patience, B.S.; Lisa M. Pierce, D.Sc.

Start Date:	Est. Completion Date:	Periodic Review:
06/16/1995	Jul 97	6/26/2001

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous testicular tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of testicular cancer.

Technical Approach: Tissue samples will be taken from 40 male patients undergoing surgical resection for testicular cancer. All malignant and benign tumor types resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to Rsa1 and Hinf1 restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into the telomere repeats on a known DNA primer. These will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

Progress: During annual review of this study, the IRB noted only four patients enrolled since initial approval was granted, 16 Jun 95, and suggested the study be terminated due to insufficient patient accrual to warrant continuation. Dr. Lance felt poor accrual was due to the rarity of the tumor being studied but agreed to terminate this project, 26 Jun 01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/147 **Status**: Completed

Title: Comparison of Quality of Life (QOL) Differences Between Radical Retropubic (RRP) and Radical Perineal Prostatectomy (RPP) for Clinically Localized Prostate Cancer

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ J. Brantley Thrasher, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/17/1997	Sep 99	9/25/2001

Study Objective: To determine QOL differences between patients undergoing RRP and those undergoing RPP for clinically localized prostate cancer.

Technical Approach: This study will prospectively evaluate and compare the QOL of male patients 30-80 years of age who undergo RRP and RPP for clinically localized carcinoma of the prostate. The study will utilize a validated questionnaire, the UCLA-RAND Prostate Cancer Index, administered to the patients (alone and without interruption) at least one week prior to the procedure and then at 1 month, 3 months, 6 months and 1 year postoperatively. This instrument will allow us to compare the effects of the 2 procedures on the patients' health-related QOL and eventually aid the urologist in choosing the appropriate approach for each patient.

Progress: This study has been completed with 236 patients enrolled; however data has not yet been compiled or written in abstract form.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/092 **Status**: Ongoing

Title: Multicenter Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analysis

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Raymond A. Costabile, MC; MAJ J. Brantley Thrasher, MC; CPT Jack R. Walter, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/17/1998	Jan 13	7/24/2001

Study Objective: Comprehensive longitudinal collection, maintenance and analysis of prostate cancer-specific and demographic standardized information from a large cohort of military health care beneficiaries from multiple geographically diverse health care centers.

Technical Approach: Standardized data collection instruments will be used at ten military medical centers by clinical research personnel and physicians to collect comprehensive prospective and retrospective information from men with prostate cancer. Patients will be followed proactively at a minimum of every twelve months until death. Data will be entered and maintained securely at USUHS in a relational database designed exclusively for this purpose. Standard statistical analysis will include survival analysis and univariate and multivariate analysis for prognostic factors.

Progress: During FY01, 325 subjects were enrolled into the database, for a MAMC total of 1462 patients. Study enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/114 **Status**: Ongoing

Title: A Uniformed Services Comprehensive Database and Tissue Repository for the Study of Epidemiological, Detection, Natural History, and New Management Strategies for Prostate Cancer

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Stephen C. Groo, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/15/1998	Jun 03	8/28/2001

Study Objective: To establish a prostate cancer serum and tissue repository that will focus on the pathology and contain supportive clinical data for the study of the etiology of prostate cancer and will incorporate a demonstration project to illustrate the utility of the repository by examining interracial differences among men with prostate cancer.

Technical Approach: Subjects will be asked to allow the intraoperative collection of a blood sample, tissue biopsies of the excised organ and use of these specimens, as well as the retrieval and use of their original archival biopsy tissue. The sera and tissue will be tested for new markers in later studies to be conducted by both military and civilian prostate cancer researchers. Some of serum and tissue may be supplied to other research centers in the future.

Progress: Funding was just recently secured for this study. Work will be initiated once a coordinator is hired.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/003 **Status**: Ongoing

Title: A Randomized Double-Blind Comparative Trial of Bicalutamide (CASODEX) 150 mg Monotherapy Versus Placebo in Patients with a Rising PSA After Radical Prostatectomy for Prostate Cancer

Principal Investigator: MAJ Raymond S. Lance, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): Lori A. Loan, PhD

Start Date:	Est. Completion Date:	Periodic Review:
10/20/1998	Jan 01	9/25/2001

Study Objective: (1) To compare bicalutamide 150 mg with placebo for time to treatment failure; (2) Quality of Life.

Technical Approach: Subjects will be randomized to receive either bicalutamide 150 mg daily or placebo until treatment failure, which is defined as an adverse event leading to withdrawal of randomized therapy, objective disease progression, death, initiation of systemic treatment or radiotherapy, or withdrawal from study therapy for any reason. Quality of Life data includes a PSA anxiety questionnaire (MAX-PC) and the FACT-P instrument, time to objective disease progression, PSA response, and time to PSA progression.

Progress: A total of 17 patients enrolled in this study at MAMC, with no patients enrolled during FY01. Thirteen patients received study treatment, three patients withdrew prior to screening or receiving study drug and one patient was a screen failure. One patient died; however this death was considered unrelated to study participation. Patient follow-up continued during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/026 **Status**: Terminated

Title: Retrospective Study of the Loss of Heterozygosity at the p53, RB, DCC, and APC Tumor Suppressor Gene Loci in Patients with Multiple Primary Genitourinary (GU) Malignancies

Principal Investigator: CPT Leah P. McMann, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Raymond S. Lance, MC; Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC; CPT Jeffrey A. Vos, MC; COL Jerome B. Myers, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Nov 00	11/28/2000

Study Objective: To investigate the roles and possible interactions of the tumor suppressor genes p53, RB, DCC, and APC in patients with multiple primary genitourinary (GU) malignancies.

Technical Approach: Using archival formalin-fixed, paraffin-embedded tumor specimens from patients from the MAMC Tumor Registry and from charts of patients identified and treated in the MAMC Urology Clinic, the plan is to look for LOH at the p53, RB, DCC and APC gene loci using restriction fragment length polymorphism (RFLP) analysis based on the polymerase chain reaction (PCR). DNA will be extracted from normal and tumor tissue and from deparaffinized tissue slides using the Puregene DNA Isolation Kit. PCR will be carried out using a DNA thermal cycler using 50 to 300 nG genomic DNA, 20 pMol of each primer, 75 mM of each dNTP, and 2 units of Taq DNA polymerase. PCR products will be digested overnight with 2 to 20 units of the appropriate restriction enzyme and run on an agarose or polyacrylamide gel which will be stained with ethidium bromide or SYBR green I and photographed under UV light.

Progress: 16 samples were analyzed in FY00. This study was terminated by the PI under the direction of Dr. Lisa Pierce due to the poor quality of the specimens in the paraffin blocks (some dating back ten years) and lack of biopsy specimens which hampered the results and their reproducibility.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/066	**Status**: Ongoing

Title: Significance of Soluble Fas in the Serum of Patients with Prostate Cancer

Principal Investigator: CPT Leah P. McMann, MC

Department: Surgery/Urology	**Facility**: MAMC

Associate Investigator(s): Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Mar 02	N/A

Study Objective: To determine the level of soluble Fas (sFas) in serum of patients with and without metastatic prostate.

Technical Approach: Elevated serum sFas levels have been shown in hematopoietic and nonhematopoietic malignancies. However, sFas levels in the serum of prostate cancer patients have not been reported in the literature. Serum sFas level may prove to be a useful prognostic indicator for prostate cancer if it is found to correlate with tumor stage and/or grade as well as disease-specific survival rate and post-treatment disease-free interval. The goal of this study is to investigate the utility of serum sFas levels as a biomarker for malignant potential in human prostate cancer. Specifically, we will compare sFas levels in the serum of 20 patients without prostate cancer and 20 patients with benign prostatic hyperplasia with patients who have locally confined (20 patients) or confirmed metastatic (20 patients) prostate cancer and correlate these levels with tumor stage and grade. In addition, we will compare serum sFas levels in the subgroup of locally confined prostate cancer patients before and after definitive treatment with either radical prostatectomy, external beam radiation, or brachytherapy. Serum sFas levels will be quantified using a Fas-specific enzyme-linked immunosorbent assay.

Progress: This study involves collecting serum from patients with prostate cancer and controls and measuring soluble fas levels (sFas) using an ELISA kit. Mean sFas levels are being compared in patients with prostate cancer both before and 3 months after initiation of treatment, whether the patient undergoes surgery, radiation, or hormonal therapy. The goal is 20 patients who undergo surgery, 20 who undergo radiation, 20 undergoing hormonal therapy, 20 men with BPH, and 20 age matched controls. Thus far serum from 12 patients who underwent surgery and two who have undergone radiation (total 14 enrolled) have been collected. Serum from control and bph patients that was previously collected by Dr. Pierce for her micrometastases project is also available. Serum from about 20 controls and 15 bph patients is available. In February and May 2001, investigators utilized two kits to measure mean serum sFas levels in patients with metastatic and localized prostate cancer, and noncancer controls. Findins: Patients with metastatic prostate cancer had higher mean sFas levels compared to noncancer controls, $p<0.05$. This initial pilot data was presented at Madigan Research Day and will be presented at the upcoming Kimbrough Meeting for the Society of Government Service Urologists. It was supposed to be presented at the American Urologic Association Western Section Meeting in September, but the meeting was cancelled due to recent terrorist events. The abstract was submitted for consideration to the AUA National Meeting in May 02.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/069 **Status**: Ongoing

Title: Outcome After Ureteral Reimplantation: A Comparison of Extravesical Versus Intravesical Techniques, A Retrospective Study

Principal Investigator: CPT Leah P. McMann, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Bryon D. Joyner, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Jun 01	N/A

Study Objective: The purpose of our study is to compare outcomes with respect to obstruction, resolution of reflux, and length of hospital stay after extravesical versus intravesical ureteral reimplantation at this institution.

Technical Approach: This is a retrospective chart review to compare outcomes of the extravesical versus intravesical techniques in surgically treating vesicoureteral reflux. This is an effort to determine if one approach is superior to the other in terms of outcome and complication rate at this institution. The sample size of 48 represents those patients who met the inclusion criteria for entrance into the study, namely documentation of vesicoureteral reflux as a primary diagnosis and underwent ureteral reimplantation between 1996 and 2000. If one method is found clearly superior over the other in terms of fewer complications and shorter hospital stay, it may influence the decision of which technique to use in future reimplantations.

Progress: A chart review has been performed of all ureteral reimplants performed by the GU service from 1996 to 2000 fiscal years. Approximately 60 patients were identified. All available followup ultrasound reports and voiding cystourethrograms results were obtained via chcs and patient outpatient charts. Complete data was only available in 33 (both US and VCUG results). Initial findings are that complication rate following either approach is minimal and that with either approach, resolution of reflux occurs in roughly 90%. However length of stay with the extravesical approach is shorter than with the intravesical approach ($p<0.05$).

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/005 **Status**: Terminated

Title: Postpartum Durabilities of Anti-incontinent Surgery in Women of Childbearing Age

Principal Investigator: CPT Andrew C. Peterson, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, Jr., MC; COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; CPT Vanessa D. Dance, MC; CPT Mark Anderson, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Aug 99	10/25/2001

Study Objective: To determine the rate of incontinence surgeries that are performed on women of childbearing age at Madigan Army Medical Center and the outcomes of bladder suspension/anti-incontinence surgeries in patients of childbearing age after vaginal or Caesarian section delivery.

Technical Approach: Charts will be reviewed on patients who have undergone anti-incontinent surgery at MAMC. Those patients of childbearing age (18-45) will be contacted by telephone and a questionnaire administered by the principal investigator. Results of the outcomes of the anti-incontinent surgery in those patients who have subsequently become pregnant and delivered a child will be analyzed. All patients who had become pregnant will be included in the study regardless of the method of delivery, Caesarian section versus vaginal delivery.

Progress: This study was terminated by the PI, 25 Oct 01, due to an inadequate number of eligible subjects.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/017 **Status**: Completed

Title: A Retrospective Review of the Use of Ketoconazole for the Prevention of Postoperative Penile Erections in Penile Reconstructive Surgery

Principal Investigator: CPT Andrew C. Peterson, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): LTC Henry E. Ruiz, MC; CPT Karen C. Evans, MC; LTC Raymond A. Costabile, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Dec 00	9/25/2001

Study Objective: To determine if ketoconazole adequately prevents penile erections after penile surgery.

Technical Approach: This is a retrospective chart review of all patients who have undergone penile surgery at MAMC from 1990 to present date. Data collected will include frequency of postoperative penile erections and the results of the surgical outcomes which will be analyzed to assess the effectiveness of ketoconazole in prevention of postoperative erections. The incidence of postoperative penile erections in patients who received ketoconazole will be compared to those without ketoconazole to establish its effectiveness.

Progress: 32 records were reviewed during FY01 at MAMC, and data collection completed. However, an abstract of the data analysis is not yet available.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/060 **Status**: Ongoing

Title: The Effect of 1,25-dihydroxyvitamin D3 (vitamin D) on Vascular Endothelial Growth Factor (VEGF) mRNA and Protein Expression in Prostate and Bladder Cancer Cell Lines

Principal Investigator: CPT Thomas L. Poulton, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC

Start Date:	Est. Completion Date:	Periodic Review:
4/25/2000	Apr 01	3/27/2001

Study Objective: To determine the effect of varying concentrations of 1,25-dihydroxyvitaminD3 (Vitamin D) on the expression of vascular endothelian growth factor (VEGF) mRNA and protein in prostate and bladder cancer cell lines in vitro. In addition, we will determine the effect of vitamin D exposure on telomerase activity in these prostate and bladder cancer cell lines.

Technical Approach: Cell Culture: The human prostate cancer cell line LNCaP and M12 and the human bladder cancer cell line T24 will be used for analysis in this study. After the cells reach confluency in their appropriate medias, the media will be replaced with fresh media containing either vehicle (0.1% ethanol) or various concentrations of 1,25-dihydroxyvitamin D3 for various times. The cells then will be processed for RNA extraction/Northern Analysis and for protein extraction/Western Analysis. The cells will also be extracted for telomerase activity. Northern Analysis: After total RNA extraction, the RNA will be resoved on a 0.8% agarose-formaldehyde gel, transferred to a Nytran filter and UV cross-linked to the membrane. After prehybridization, hybridization with probes of complementary DNAs for VEGF and 18S RNA will be carried out. Labeling will involve the use of alpha 32P dCTP and measurement is involve densitometry relative to VEGF mRNA present in the samples. Western Analysis: 30 uG of total protein lysates will be denatured and boiled prior to loading on a 12% polyacrylamide gell with a 5% stacking gel and transferred overnight onto a polyvinylidene difluoride membrane. After blocking, the membrane will be probed using a rabbit polyclonal anti-human VEGF antibody, and probed again with a mouse anti-glyceraldehyde-3phosphate dehydrogenase (GAPDH) antibody. The secondary will be a peroxidase-conjugated anti-mouse IgG antibody. Detection will be determined by densitometry using chemiluminescense. Telomerase Activity: Telomerase acitivey will be measured on prostate and bladder cancer cell lines using a commercially available kit (Telomerase PCR ELISA) following manufactureres (Boehringer Mannheim) instructions.

Progress: Two prostate cancer cell lines (LNCaP, M12) and a bladder cancer cell line (T24) were grown to confluency, serum starved for 48 hours, and exposed to various concentrations of 1,25 dihydroxyvitamin D3 (0, 10, 100 nM). At 2 days and 3 days of vitamin D exposure, supernatants were collected and cells were harvested and counted. VEGF secreted into the media was measured by enzyme linked immunosorbent assay. Telomerase activity was measured in the cells using the Telomerase Repeat Amplification Protocol. Results: All three cell lines secreted VEGF protein into the media, although M12 cells produced less VEGF than LNCaP cells ($p<0.05$; student t test) and T24 cells ($p<0.05$ student t test). In vitro vitamin D exposure did not reduce VEGF production in any of the prostate or bladder cancer cell lines. In addition, vitamin D did not decrease telomerase activity in any cell line. Conclusions: The anticarcinogenic efects of vitamin D do not appear to include downregulation of VEGF protein expression and telomerase activity in prostate and bladder cancer. This bench study remains ongoing pending submission and approval of an amendment to look at dose levels and duration of exposure to Vit D.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/013 **Status**: Terminated

Title: A Prospective, Randomized, Comparative Parallel Group Study of CoapTiteTM and Contigen for Urethral Sphincter Augmentation in the Treatment of Stress Incontinence in a Female Population

Principal Investigator: LTC Henry E. Ruiz, MC

Department: Surgery/Urology **Facility**: MAMC

Associate Investigator(s): MAJ Sunil K. Ahuja, MC; LTC George B. McClure, MC; COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; MAJ Stephen D. Seymour, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Jan 04	N/A

Study Objective: To evaluate the safety and efficacy of Coaptite compared with Contigen Bard Collagen implant in female patients with urinary stress incontinence due to instrinsic sphincteric deficiency (leak point pressure 100 cm H20) and without associated urethral hypermobility (as defined by resting or straining angle of 35 from horizontal of the bladder neck). The efficacy evaluation will be based on improvement on the Stamey6 Urinary Incontinence Scale. The safety evaluation will be based on adverse experiences, physical examination, and laboratory test results.

Technical Approach: This is a prospective, multicenter, randomized, comparative, single-blind, parallel-group study to evaluate the efficacy and safety of Coaptite compared with Contigen in female patients with stress urinary incontinence due to intrinsic sphincter deficiency. A total of approximately 280 female patients at five sites in the United States will be enrolled with up to 60 patients enrolled at Madigan Army Medical Center. Patients enrolled under this protocol will be randomized in a 1:1 ratio to either Coaptite or Contigen.

Evaluations will be performed at one year after the last injection in patients randomized to Contigen and annually for two years after the last injection in patients randomized to Coaptite. The primary efficacy variable is the proportion of patients who experience and maintain at least a one grade improvement via the Stamey Urinary Incontinence Scale at 12 months after the last injection treatment.

Progress: This study was terminated prior to obtaining final approval. No work was initiated on this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/158 **Status**: Ongoing

Title: Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis

Principal Investigator: LTC Henry E. Ruiz, MC

Department: Surgery/Urology **Facility**: MAMC

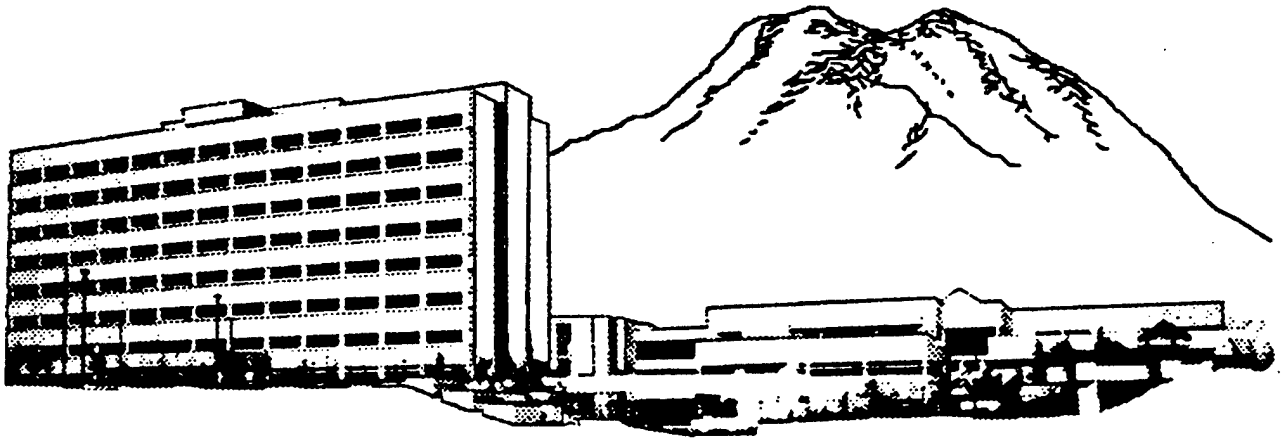
Associate Investigator(s): MAJ J. Brantley Thrasher, MC; CPT Douglas W. Soderdahl, MC; MAJ John B. Ellsworth, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/16/1996	Oct 02	7/25/2001

Study Objective: The primary effectiveness objective is to evaluate the ability of the AMS Ambicor inflatable penile prosthesis to provide an erection suitable for sexual intercourse (device function) as determined by physical examination and patient self-report. Secondary effectiveness objectives include estimating the effects of the prosthesis on patient sexual function and satisfaction, self-esteem, quality of life, and psychological well-being. The study will also evaluate levels of patient satisfaction with various aspects of the prosthesis including rigidity, length, girth and flaccidity. Safety will be evaluated by measuring rates of post implant complications (including device malfunction) and the occurrence of medical conditions.

Technical Approach: This is a multi-center, prospective, cohort study with the pre-implant experience of patients serving as the comparison for the evaluation of effectiveness and safety. The study sample will be derived from patients who present to the clinic with the diagnosis of erectile dysfunction. After an eligible patient makes an informed decision to be implanted with an AMS Ambicor penile prosthesis and signs the surgical consent he will be asked to participate in the study. A total of 250 patients will be recruited nationwide (12-20 being from MAMC) and will be implanted with the Ambicor inflatable penile prosthesis. The primary measure of effectiveness (sexual function, self-esteem, and psychological well-being), will be monitored for 2 years with visits at 6 weeks post-surgery, 6 months, 1 year, 18 months and 2 years. Follow-up for complications, associated medical conditions and other adverse device effects will be followed for 5 years with phone contact at 3 and 4 years, and a visit at 5 years.

Progress: Since initial approval, 38 patients have enrolled, six in FY01, and 29 have received devices. There have been five SAE's reported to include one death (unrelated to study participation) and four hospitalizations (2 of which have been for surgical revisions). Subject enrollment continues.



Detail Summary Sheets

Childrens Oncology Group
(formerly the Pediatric Oncology Group and Children's Cancer Group)

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/072 **Status**: Ongoing

Title: POG 7837: Evaluation of Systemic Therapy for Children with Lymphoblastic Lymphoma Including T-Cell Disease

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): LTC Stephen R. Palmer, MC; MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Pend	6/26/2001

Study Objective: (1) To evaluate a program of intensified CNS therapy for patients with lymphoblastic lymphoma, including T-cell leukemia, treated with the Pediatric Oncology Group's most successful systemic therapy schedule for these patients. This protocol will serve as the control arm for a randomized study, (2) to assess the toxicity and rate of complications encountered by patients receiving POG modified LSA2L2 Therapy in comparison with patient who received therapy using POG 7839 Treatment Arm 1 or POG 7615, (3) to assess the value of cranial radiation therapy plus 3-drug intrathecal chemotherapy in treating occult T-cell leukemia of the central nervous system, using the rate of CNS relapse and the rate of CNS complications for comparison with responses achieved using POG 7837 Treatment Arm 1 and POG 7615 therapy in pediatric patients with T-cell acute lymphocytic leukemia, (4) to assess the therapeutic effectiveness as measured by disease-free survival of POG Modified LSA2L2 Therapy (POG 7837 Treatment Arm 2) compared with responses achieved with POG 7837 Treatment Arm 1 and POG 7615 in pediatric patients with lymphoblastic lymphoma and T-cell leukemia, (5) to provide uniform therapy for patients with lymphoblastic lymphoma, including T-cell leukemia, so as to examine the response of immunologically defined subgroups of T-cell patients to this therapy, and in those patients for who marker studies have been obtained, to correlate response with histopathology and serologic markers, (6) to provide a common protocol for the treatment of patients with widespread T-cell malignancy, offering the opportunity for comparison of response rates among patients who have differing extent of disease.

Technical Approach: This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 1 patient being followed who was consented on an IRB approved 7837 study at Tripler AMC. Follow-up information on this patient will need to be sent to the POG Statistical Office per protocol requirements.

Progress: This protocol has been reactivated, 26 Jun 01, to continue follow-up on one patient enrolled . The protocol had been reported as permanently closed, 22 Jun 99, when Peds Hem/Onc felt the patient lost to further follow-up.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/073 **Status**: Ongoing

Title: POG 8602: Evaluation of Treatment Regimens in Acute Lymphoid Leukemia of Childhood (ALinC #14)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Pend	4/24/2001

Study Objective: (1) To test the concept that intensive asparaginase (ASP) therapy, designed to maintain low asparagine levels for the first six months of maintenance will improve the outcome for patients with standard risk acute lymphocytic leukemia (ALL) when added to pulses of intermediate dose methotrexate (IDM), as compared to intensification with IDM alone, (2) to study the effectiveness in standard risk patients of intensification with a potentially synergistic or additive drug pair, i.e., IDM plus arabinosyl cytosine (AraC), as compared to that of intensification with IDM pulses alone, (3) to determine if administering a pulse of IDM + AraC at three week intervals (early intensification) during the first 4 months of complete remission in children with ALL is superior to administering the same number of IDM + AraC pulses at 12 week intervals (late intensification) during the first two years of complete remission in children with ALL with either "lower" or "higher" risk of relapse, (4) to obtain further information on the immediate and delayed toxicity of the continuation chemotherapy program that incorporates these combinations of methotrexate (MTX) and AraC or MTX and ASP in moderately high doses, (5) to continue to characterize the biological features of acute lymphatic leukemia of childhood, and their independence and interaction (with therapy and each other) as prognostic factors for attaining and maintaining remission, (a) To assess the effectiveness of these regimens for the early pre-B (non-T, non-B, non-pre-B) and pre-B immunophenotypes of All, respectively, (b) To investigate the hypothesis that ploidy and/or the presence of structural chromosome abnormalities predicts prognosis, (6) to learn whether outcome is related to individual patient differences in methotrexate (MTX) availability as measured by sequential determinations of red blood cell (RBC) MTX and folate levels.

Technical Approach: This study has closed to further patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 2 patients being followed who were consented on IRB approved 8602 studies in other POG institutions. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.

Progress: Protocol is closed to patient accrual. Two patients continued to be followed during FY01, 1 patient has been lost to follow-up.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/076 **Status**: Ongoing

Title: POG 8615: A Phase III Study of Large Cell Lymphomas in Children and Adolescents: A Comparison of Two Treatment Regimens - ACOP+ versus APO

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Indef	4/24/2001

Study Objective: (1) To determine the influence of alkylating agent (cyclophosphamide) therapy in advanced-stage large cell lymphomas in children and adolescents, by comparing in a randomized prospective study the efficacy and toxicity of a modified ACOP+ versus a modified APO regimen, (2) to reduce the adverse effects of treatments by elimination of involved field and cranial radiation in the treatment of large cell lymphomas, (3) to evaluate the adequacy of one year of total therapy for advanced large cell Non-Hodgkin's lymphoma (NHL), (4) to study clinical pathologic patterns and biologic characteristics of large cell lymphomas in children and adolescents, (5) to assess the feasibility of the total dose of Adriamycin of 300 mg/M2 on the APO arm (post closure of randomization).

Technical Approach: This study has closed to further patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 1 patient being followed who was consented on an IRB approved 8615 study at Stanford. Follow-up data on this patient will be forwarded to the POG Statistical Office per protocol requirements.

Progress: Protocol closed to patient accrual; however one patient continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/141 **Status**: Ongoing

Title: POG 8650: Intergroup National Wilms' Tumor Study - 4

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/09/1993	Oct 97	5/23/2000

Study Objective: To compare (1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D, (2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy, (3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy, and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

Technical Approach: All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

Progress: This protocol closed to patient entry, 1 Sep 94. One patient enrolled at MAMC in FY93 continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/074 **Status**: Ongoing

Title: POG 8823/34: Recombinant Alpha-Interferon in Childhood Chronic Myelogenous Leukemia

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Pend	4/24/2001

Study Objective: (1) To determine toxicity, response rate and duration of response to therapy with recombinant alpha interferon for newly diagnosed "adult" chronic myelogenous leukemia (ACML) in chronic phase, and for "juvenile" chronic myelogenous leukemia (JCML) occurring within the first two decades. (2) to obtain prospective clinical, laboratory, and genetic data on cases of ACML and JCML treated with recombinant alpha interferon.

Technical Approach: This study closed to patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 3 patients being followed who were consented on IRB approved 8823 studies at Walter Reed Army Medical Center. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.

Progress: Protocol closed to patient accrual; however 3 patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/075 **Status**: Ongoing

Title: POG 9005: ALinC #15 - Dose Intensification of Methotrexate and 6-Mercaptopurine for ALL in Childhood - A Randomized Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/22/1998	Pend	4/25/2001

Study Objective: (1) To determine, in a randomized trial, whether intensification with intermediate-dose methotrexate (ID MTX), and intravenous 6-mercaptopurine (IV 6-MP) is superior or inferior to repeated low-dose, oral methotrexate (LD MTX) and IV 6-MP for prevention of relapse in children with ALL in first remission and at lower risk for relapse, (2) To compare, in a randomized trial, intensification with ID MTX alone versus ID MTX and IV 6-MP for prevention of relapse in children with lower risk ALL in first remission, (3) To determine if RBC MTX/folate levels can be correlated with event free survival.

Technical Approach: This study closed to patient accrual; however HHS guidelines require IRB approval of closed studies when patients are being followed for survival information. Madigan has 6 patients being followed who were consented on IRB approved 9005 studies in other POG institutions. Follow-up data on these patients will be forwarded to the POG Statistical Office per protocol requirements.

Progress: Protocol closed to patient accrual. One patient died in FY97, 5 patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/018 **Status**: Ongoing

Title: POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/18/1994	Nov 94	10/23/2001

Study Objective: (1)To compare the 2-year event-free survival (EFS) of children with newly-diagnosed high-risk medulloblastoma who are treated with cisplatin and VP-16 pre-irradiation vs post-irradiation, (2) To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, (3) To determine whether achievement of a measurable tumor response (PR and CR) to pre-irradiation cisplatin/VP-16 has prognostic significance for children with high-risk medulloblastoma, compared with failure to achieve a measurable response (SD or PD), (4) To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, and (5) To determine if c-myc amplification in medulloblastoma is associated with an adverse prognosis.

Technical Approach: Studies in children and adults have demonstrated the ability to deliver pre-radiotherapy chemotherapy for patients with newly-diagnosed brain tumors without increasing neurotoxicity in association with the subsequent radiotherapy. This approach creates a phase II "window" allowing evaluation of response in these patients who are previously untreated except for surgery. The theoretical anti-neoplastic advantage of this approach is the potentially enhanced efficacy of the radiotherapy when given to "chemically debulked" patients.Half of the children diagnosed with medulloblastoma are now being successfully treated and are surviving for prolonged periods. Until recently, the survival of this group of patients was limited so that long-term effects of therapy were not a concern. As survival increases, one would expect to observe an increase in frequency of certain treatment-related toxicities. There are now a variety of long-term effects which need to be considered in this cohort of patients. Specific evaluations will be made on all patients entered onto this study, so that treatment-related problems may be detected in their early stages and intervention taken. This approach should ultimately improve the quality of life for children diagnosed and treated for brain tumors.

Progress: This protocol closed to patient entry 26 Mar 96. One patient enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/164 **Status**: Completed

Title: POG 9047: Neuroblastoma Biology Protocol

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; COL Bruce A. Cook, MC; COL Stephen R. Stephenson, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/03/1993	Feb 96	8/22/2000

Study Objective: (1) To obtain tissue for the analysis of DNA content of neuroblastoma cells by flow cytometry, (2) To characterize neuroblastoma tumor DNA from POG patients genetically by analysis of N-myc amplification and LOH for chromosome 1p, (3) To develop a reference bank of genetically characterized tumor tissue and DNA that would be available for other studies.

Technical Approach: This is a non-therapeutic study intended to collect tissue from newly-diagnosed neuroblastoma patients = 21 years. Viable tumor tissue, frozen tumor tissue (or marrow) and serum will be collected and forwarded to a designated study site.

Progress: This study closed to patient entry, 5 Apr 01. No patients were enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/056 **Status**: Ongoing

Title: POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/16/1994	Dec 99	11/27/2001

Study Objective: (1) To confirm the outstanding results in patients with lesser risk not-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (AlinC 14, Arm A), (2) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.

Technical Approach: Patients on this study will be treated with a 3-drug induction regimen (vincristine, prednisone, and L-asparaginase) to bring about remission (a state of no apparent disease) in four weeks. This will be followed by a consolidation phase including (6) six courses of intravenous (into vein) intermediate-dose methotrexate (each will require hospital stay) at 3-week intervals. After week 5, daily 6-mercastosurine will be given by mouth until the end of planned treatment. Methotrexate will be given intramuscularly (into muscle) weekly. Periodic "pulses" (infrequent administration) of vincristine and prednisone will be given throughout the first two years of therapy. Additionally, triple intrathecal (into spinal fluid) therapy (TIT) consisting of methotrexate, hydrocortisone, cytosine arabinoside will be given at the start of treatment and periodically through the first two years of therapy to prevent the spread of leukemia to the central nervous system (CNS). The vitamin Leucovorin will be given to prevent methotrexate toxicity. After week 25, during the continuation phase, all medications will be on an outpatient basis. The total duration of therapy is planned to be 2 1/2 years from initial diagnosis. If tests at that time indicate no evidence of leukemia, then all medications will be stopped and you (your child) will be followed closely to be sure that there is no evidence of return of the disease.

Progress: This study closed to patient accrual 15 Nov 99. One patient enrolled in this study at MAMC in FY 96 and another patient was accepted in transfer. Both continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/033 **Status**: Ongoing

Title: POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; COL Bruce A. Cook, MC; COL Stephen R. Stephenson, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/05/1993	Jun 96	10/23/2001

Study Objective: (1) To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites, and (2) To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

Technical Approach: After staging, subjects that qualify will receive Vincristine 1.5 mg/M2 (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/M2/day in 3 divided doses x 28 days, Adriamycin 40 mg/M2/day IV days 1 & 22, and Cyclophosphamide 750 mg/M2/day IV days 1 & 22. Fluid intake is to be > 3000 ml/M2 on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries.

On day 43, or when blood counts recover, the patient will receive Adriamycin 40 mg/M2 IV, Cyclophosphamide 750 mg/M2 IV, Vincristine 1.5 mg/M2 (max 2 mg) IV, and Prednisone 50 mg/M2 in 3 divided doses x 5 days. On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

Progress: This protocol closed to patient accrual 2 Jul 99. Two patients enrolled in this study at MAMC in FY97 and continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/168 **Status**: Ongoing

Title: POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/21/1995	Jul 99	6/26/2001

Study Objective: (1) To assess the toxicity of the combination of Hydroxyurea (HU) and Ara-C combined sequentially with interferon-alpha 2b (IFN) in children with adult type chronic myelogenous leukemia (ACML), and (2) To determine the frequency and duration of hematologic and cytogenetic response, and the length of time needed to achieve response during two years of such treatment.

Technical Approach: Therapy will be divided into 2 induction phases and a consolidation phase. Induction 1: Therapy will begin with two, or possibly three, weekly courses of hydroxyurea and Ara-C. Each course will consist of treatment given on three consecutive days as follows: after consuming clear fluids only for breakfast, hydroxyurea will be taken by mouth. Two hours later, Ara-C will be administered intravenously over 15 minutes. This will be repeated on the second and third day of each course. Subjects will receive at least two courses, beginning days 1 and 8. If blood counts are still above certain values on day 15, a third course will be given. Induction 2: Once blood counts have adequately recovered from the above chemotherapy, IFN treatment will begin. Subjects will receive IFN given as a subcutaneous injection daily for 14 days. Consolidation: IFN will then be continued at this dosage every Monday, Wednesday and Friday. IFN therapy will be interrupted for at least one week, approximately every 6 weeks, for a threeday course of hydroxyurea/Ara-C. This six-week cycle (IFN three times weekly for five weeks followed by a course of hydroxyurea/Ara-C), will be repeated for a total treatment time of approximately two years, assuming a good response to treatment. Most therapy will be administered at home (IFN) or in the outpatient clinic (hydroxyurea/Ara-C), with the exception being the first course of hydroxyurea/Ara-C and the first few days of IFN therapy, for which hospitalization is recommended. Every effort will be made to continue treatment for at least 90 days. All patients who have signs of progressive (worsening) disease within the first 90 days will be evaluated for possible discontinuation of this therapy. All other patients will continue on treatment for a total of 24 months. For those patients continuing on therapy past 90 days, the treatment will be discontinued (prior to 24 months) if there are signs of progressive disease at any time; if there is no evidence of any improvement by six months or if side effects develop which cannot be tolerated even with reduction in the drug dosages. Therapy may also be stopped at any time if a suitable marrow donor has been found and the physician decides that bone marrow transplantation would be in the patient's best interest. If the patient is still on therapy and responding well after 24 months, then the physician may offer to continue therapy with IFN alone. This will be offered as further therapy, but it will not be part of this study. It is not known how many years interferon may be safely given. The dosage schedule described above is to be considered a guideline. It is very possible that modification will need to be made depending on the side effects encountered. Routine blood tests will be done during the first four to six weeks of therapy (the "induction" phase), and then every one to two weeks while on therapy. A bone marrow aspirate and biopsy will be done prior to start of induction therapy, then twice more at about three month intervals, and then every six months thereafter unless removed from the study because of no response, progressive disease (increased severity), or bone marrow transplantation. A Chromosomal analysis will be completed

on each bone marrow aspirate to find out if the Philadelphia chromosome is present. Each bone marrow aspirate will be followed by an ultrasound study of the spleen in order to determine the size of the spleen.

Progress: This protocol was closed to patient accrual 27 Jan 99. One patient enrolled in this study at MAMC in FY95, was taken off study July 1997 to pursue bone marrow transplant and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/092 **Status**: Ongoing

Title: POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/01/1994	Jun 99	4/24/2001

Study Objective: (1) To improve the survival of patients with osteogenic sarcoma, (2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma, (3) To compare the results of a combined chemotherapeutic regimen (high-dost methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide, (4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery, (5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs, (6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma, (7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

Technical Approach: This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherpay alone.

Progress: This protocol was closed to patient accrual 25 Nov 97 due to adequate patient enrollment. Two patients entered in this study at MAMC in FY96. One patient chose to discontinue treatment early. The other patient completed therapy. Both patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/087 **Status**: Ongoing

Title: POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/17/1995	Jun 99	2/27/2001

Study Objective: (1) To estimate the complete response rate for HIV related malignancies treated with interferon (aIFN), and (2) The secondary objectives are to estimate the one year disease free survival and to evaluate the toxicity of aIFN alone or in combination with anti-retroviral therapy.

Technical Approach: This study will require all patients to be enrolled in POG 9182 and compliance with all specimen submission requirements of that protocol. The study will minimize additional tissue, CSF or blood sampling except as required for monitoring for toxicity and tumor response. This study will take advantage of the demonstrated antitumor and antiviral activity of aIFN alone or in combination with other antiretroviral agents to treat HIV positive children with refractory or newly diagnosed malignancies. As the duration of response is one of the goals of this study, responders will continue on therapy indefinitely. Patients on this study will be treated using a interferon by subcutaneous injection every day for 14 days; then if your child's/adolescent's evaluation allows further treatment he/she will receive a interferon three times a week. This treatment will need to be monitored by a treating physician and blood tests will be performed in order to insure that the treatment is well tolerated and that the dose is appropriate. For that purpose 10cc of blood will be taken once a week.The physician and/or staff will be checking closely to see if any of these side effects are occurring. Routine physical exams, laboratory tests and tests such as biopsy or bone marrow aspiration may be necessary to monitor the effect of the treatment. Side effects usually disappear after the treatment is stopped. In the meantime, the doctor may prescribe medication to keep these side effects under control.

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/058 **Status**: Ongoing

Title: POG 9400: ALinC 16 Classification (C) Protocol

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/16/1994	Dec 99	11/27/2001

Study Objective: (1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission, (2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis, (3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t (9; 2 2) or t (1; 19) chromosomal abnormalities. (optional), (4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia, (5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional), (6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional), (7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL, and (8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

Technical Approach: A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

Progress: This study closed to patient enrollment 15 Nov 99, with a total enrollment of 10 patients. Six patients continue to be followed in this study in FY01 at MAMC following the transfer of 4 patients to other COG/POG institutions.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/144 **Status**: Completed

Title: POG 9404: T-Cell #4 Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced Stage Lymphoblastic Non-Hodgkin's Lymphoma

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/19/1996	Aug 04	6/26/2001

Study Objective: (1) To determine, in a randomized trial, the effectiveness of high dose methotrexate (HD MTX) when added to a multi-agent chemotherapy backbone (DFCI 87-0001) proven effective in T-Cell acute lymphoblastic leukemias (T-ALL) and advanced stage non-Hodgkin's lymphoma (Lymphoblastic NHL), (2) to determine, in a randomized trial, the role of the cardioprotectant Zinecard (DZR) in preventing cardiotoxicity in children with T-ALL and advanced stage Lymphoblastic NHL receiving an anthracycline based regimen, (3) to study the biology of T-Cell lymphoid malignancies by accumulating data on the concurrent ALL classification study (POG 9400) and analyzing the data relative to outcome, (4) to evaluate the correlation of minimal residual disease with event-free survival utilizing the TAL 1 proto-oncogene, (5) to determine the role of p53 and p16 tumor suppressor genes in T-ALL, and (6) to determine if drug sensitivity profiles of blasts cells to Doxorubicin, methotrexate and cytarabine correlate with initial response and subsequent development of relapse.

Technical Approach: Patients will receive induction therapy (weeks 1-6), vincristine every week for 4 weeks, prednisone for 21 days starting day 1 and doxorubicin on days 1, 2, and 22, with or without ZINECARD. During this phase, the drug methotrexate will be given on day 2. Patients will be randomized to receive high dose methotrexate on day 22. Intrathecal methotrexate, Ara-C and hydrocortisone will be given to prevent central nervous system disease throughout the entire three phases of treatment. Once remission has been achieved, patients will receive consolidation therapy (weeks 7-33). Drugs will be given in three week cycles (6-mercaptopurine for 14 days, vincristine and doxorubicin on day 1 of the cycle, prednisone for 21 days) with or without ZINECARD. Asparaginase will also be given during the consolidation phase once a week during weeks 7-26. Patients who received high dose methotrexate on day 22 of induction will also receive it on weeks 7, 10 and 13 of consolidation. At weeks 22-24, all patients will receive radiation therapy to the brain. During continuation (weeks 34-108), patients will receive vincristine, prednisone (every day for five days) and 6-MP (every day x 14 days) every three weeks. Methotrexate, will be given every week except during those weeks when patients receive intrathecal medications.

Progress: This study closed to patient enrollment, 10 Sep 01. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/059 **Status**: Ongoing

Title: POG 9405: ALinC #16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/16/1994	Dec 99	11/27/2001

Study Objective: (1) To determine in a randomized trial, the efficacy of a higher (2.5 gms/mt) versus standard (1 gm/m2) dose methotrexate (MTX) infusion during consolidation. The major endpoint will be eventfree survival among those achieving a complete remission. Secondary comparisons will include sitespecific events and adverse drug reactions, (2) To determine in a randomized comparison, the efficacy of delivering oral 6-MP on a once versus twice daily schedule during continuation, (3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405 and 9406, and (4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

Technical Approach: In this research study, the subject will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as Prednisone, given orally (by mouth) for 28 days; Vincristine, given by a quick intravenous infusion (IV push) on days 1, 8, 15, and 22; L-asparaginase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, Cytarabine Arabinoside (Ara-C), and hydrocortisone will be administered intrathecally (injected into the spinal fluid) at various intervals throughout both the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. After Induction the subject will be randomized (assigned by chance, such as flipping a coin), to a specific regimen to include either standard or high dose IV Methotrexate and receiving oral 6MP once or twice daily. During the period of consolidation (weeks 5-28), the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP). The Methotrexate will be given at a standard or higher dose. In the first week, methotrexate will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. This 2 week treatment will be repeated for a total of 12 cycles. During the period of continuation (weeks 20-130), 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once each week. Patients randomized onto regimens B & D will receive 6MP orally twice daily. The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fail to achieve a complete remission during the induction phase of the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies. These studies will help the doctor to better understand this form of cancer and how treatment can be improved in the future. Chemotherapy given intrathecally into the spinal fluid may cause pain at infusion site, pain in the back, legs or head, fever, headache, vomiting; rarely stiff neck, convulsions, paralysis. Bone marrow aspiration may cause bruising and soreness over the bone from which the marrow sample is taken.

Progress: This protocol closed to patient accrual 26 Dec 95 due to excessive neuro toxicity. Two patients enrolled at MAMC. One patient enrolled in FY95 was taken off study but continues to be followed, one patient enrolled in FY96 was transferred to Portsmouth Naval Med Center.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/060 **Status**: Ongoing

Title: POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/16/1994	Dec 99	11/27/2001

Study Objective: (1) To determine the efficacy of a 2.5 gm/m2 dose versus 1 gm/m2 does intravenous methotrexate infusions during intensified continuation therapy. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events and adverse drug reactions, (2) To determine whether intensified continuation therapy delivering pulses of Ara-C (3 gm/m2 x 4 doses) with asparaginase rescue is superior to standard intensitified continuation with pulses of VM-26/Ara-C. The major endpoint will be event-free survival among those acheiving a complete remission. Secondary comparison will include site-specific events (including secondary AML) and adverse drug reactions, (3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406, and (4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

Technical Approach: Children will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as prednisone, given orally for 28 days; vincristine, given by a quick intravenous infusion on days 1,8,15, and 22; L-asparaginase, injected IM on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, cytosine, arabinoside (Ara-C), and hyrocortisone will be administered intrathecally at various intervals throughout the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. Daunomycin will be given on days 8,15, and 22 intravenously. After the previous treatment, subjects will be randomized to a specific regimen to include either standard or high does Methotrexate or low or high dose Ara-C. During the period known as consolidation, the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP) during weeks 5-6, 10-11, 15-16, 25-26, and 30-31. In the first week of each of these periods, methotrexate (either the standard or the intensified higher dose) will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. At weeks 7, 17, and 27 the subject will receive Ara-C as a continuous infusion for 72 hours (higher dose) or injected under the skin (lower dose). VM-26 will be given as a 45-minute IV infusion before the start of Ara-C and on day 2 with standard dose Ara-C. If the subjectreceive intensified Ara-C, the subjectwill also receive the drugs PEG and G-CSF. PEG is a drug that may lessen the toxic effects of Ara-C, and G-CSF is used to increase the blood count to decrease the risk of infection. At weeks 12, 22, and 32, Ara-C will be infused over 72 hours as described above. Daunomycin (DNR) will be given as a 30-minute infusion before the start and at the end of the Ara-C. In addition to DNR/Ara-C, vincristine is given IV on days 1 and 8, prednisone by mouth on days 1 and 7, and PEG-L-asparaginase IM on day 1. During the period known as continuation, weeks 35-130, standard dose 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once a week. The total time of planned therapy is 130 weeks (2 1/2 years). The subject will be taken off study in case of relapse in the bone marrow,

or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study. Radiation therapy will be suggested if the subjecthave CNS leukemia at diagnosis. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies.

Progress: This study closed to patient enrollment 15 Nov 99. One patient enrolled in this study in FY96, however due to an adverse event during induction was taken off study and has since completed therapy. Another patient accepted in transfer from SUNY relapsed while on therapy and went on to have a bone marrow transplant. Both patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/089 **Status**: Ongoing

Title: POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/17/1995	Jan 01	4/25/2000

Study Objective: (1) To determine the effect of high dose vs. standard dose Ara-C induction on CR (clinical remission) and EFS (event free survival) in Childhood AML, (2) To compare EFS in Childhood AML after 3 cycles of consolidation with or without the MDR (multidrug resistance) modulator CSA (cyclosporine A), (3) To compare the EFS between patients genetically randomized between allogenic BMT and chemotherapy, (4) To evaluate the impact of EFS of various clinical and laboratory factors such as cytogenetics and MDR expression, and (5) To comfirm the superior response of Down syndrome patients utilizing standard induction and non-CSA containing consolidation, and identify specific biologic and pharmacokinetic characteristics in these patients.

Technical Approach: Phase III evaluation of standard vs. high dose Ara-C induction followed by the randomized use of Cyclosporine A as an MDR (multidrug resistant) reversal agent, compared to allogeneic BMT, in childhood AML. Patients will be randomized (assigned by chance, such as flipping a coin) at the time of diagnosis to receive either standard doses or high doses of ARA-C during the initial course of therapy. The chances of receiving any of the therapies is approximately equal. Later in the course of therapy, patients (according to how they were previously randomized) will or will NOT receive the drug Cyclosporine A in combination with the chemotherapy agents, Mitoxantrone and Etoposide. Patients with Down syndrome will not be randomized, but will receive the standard therapy. Earlier studies have shown the three year event-free survival rate for Down syndrome children significantly superior to children without Down syndrome using standard therapy. Also, for this reason Down syndrome patients will not receive Cyclosporine A. If a sibling who is matched for bone marrow transplantation, will receive bone marrow transplantation, which has been shown to be a more effective treatment in controlling AML compared to chemotherapy, providing that consent from the sibling donor can be obtained. If not a sibling donor, studies have shown chemotherapy is superior to matched unrelated donor BMT. However, should the patient choose to pursue an unrelated matched BMT instead of continuing with consolidation chemotherapy, the subject may discontinue the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may also be used for research studies.

Progress: This study closed to patient accrual,15 Aug 99. Two patients enrolled in this study at MAMC. One patient died and the other patient continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 97/071	**Status**: Completed

Title: POG 9425: Advanced Stage Hodgkin's Disease, A Pog Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group	**Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/21/1997	Jul 03	3/28/2000

Study Objective: (1) To test the efficacy of DBVE-PC, an intensive treatment regimen for advanced stage Hodgkins disease that administers doxorubicin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide with G-CSF at 3 week intervals in a dose intensive manner (using cumulative drug doses that may minimize long term toxicity), followed by consolidative radiotherapy, (2) To tailor therapy based on rapidity of response in order to minimize cumulative drug dosages. Those in CR after 3 cycles of DBVE-PC will receive only low dose RT. Those who are not in CR will receive 2 additional cycles of DBVE-PC (+ low dose RT), (3) To determine, in a randomized trial, whether the addition of Dexrazoxane reduces pulmonary and cardiac toxicity of DBVE-based therapy without compromising response.

Technical Approach: Registered study patients will be randomized to receive or not to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 3 cycles of the drug combination etoposide, vincristine, bleomycin, doxorubicin cyclophosphamide, prednisone combination with G-CSF in 3 week intervals. Patients will be restaged after receiving these three chemotherapy courses. Those showing large tumor response will go on to radiation therapy, while those showing partial response will receive 2 additional cycles of chemotherapy and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis after completion of therapy.

Progress: This study closed to patient entry, 23 Mar 01. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/054 **Status**: Ongoing

Title: POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/21/1997	Jul 03	1/22/2002

Study Objective: (1) To tailor chemotherapy courses based on the patients' initial response to therapy, (2) To examine the activity of variable courses of doxorubicin, bleomycin, vincristine, and etoposide (DBVE) and low-dose involved field irradiation, (3) To monitor safety and feasibility of the response-dependent approach, and morbidity, immediate and long term toxicities of the above regimen, (4) To evaluate if limited therapy is adequate for patients with early response, (5) To examine if addition of Zinecard can reduce pulmonary toxicity while not significantly reducing response rate or event-free survival, and (6) To determine if the frequency and magnitude of myocardial injury during therapy, as measured by an elevation of cardiac Troponin-T in the serum, is reduced by the addition of Zinecard.

Technical Approach: Registered study patients will be randomized to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 2 courses of the four drug combination etoposide, vincristine, bleomycin and doxorubicin at 28 day intervals. Patients will be restaged after receiving these two chemotherapy courses. Those showing remission will go on to radiation therapy, while those showing residual disease will receive 2 more courses of the four drug combination and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis.

Progress: This protocol closed to patient entry, 19 Sep 00. Two patients enrolled in this study at MAMC and continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/097 **Status**: Ongoing

Title: POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/19/1996	Jul 02	3/27/2001

Study Objective: (1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood, (2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis, (5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor, (6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide, (7) to improve survival of patients with malignant rhabdoid tumor of the kidney, (8) to study biology and pathology of patients who present with bilateral Wilms tumor, (9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines, and (10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine.

Technical Approach: This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages 1-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.

Progress: One patient enrolled in this study at MAMC in FY96 and transferred to Portsmouth Naval Hospital. One patient was accepted in transfer from Tripler AMC and continues to be followed. One patient was consented for this study in FY01; however, tumor tissue studies determined the patient was not eligible for study participation.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/090 **Status**: Ongoing

Title: POG 9442: National Wilms Tumor Late Effects Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/17/1998	Jul 03	6/26/2001

Study Objective: To determine (1) the frequency of Wilms tumor and other cancers in family members of Wilms tumor patients in order to estimate the recurrence risk in siblings and offspring; test the plausibility of specific genetic modes of inheritance in homogeneous subgroups; and identify familial cancer syndromes (if any) that may involve Wilms tumor, (2) To determine fertility rates of Wilms tumor patients and rates of perinatal mortality, low birth-weight and adverse pregnancy outcomes in relation to the type and amount of cancer treatment received in childhood, (3) To estimate the rates of selected congenital defects and of specified single gene disorders (sentinel phenotypes) in the offspring of Wilms tumor patients, (4) to estimate the rates of second malignancy neoplasms in relation to the dosage of radiation therapy and the use of specific chemotherapeutic agents (actinomycin D, doxorubicin, cytoxan and etoposide) received in childhood, (5) to compare the incidence rate of congestive heart failure among Wilms tumor survivors in relation to the dose of radiation therapy received to abdomen and/or lungs and to the use of specific chemotherapeutic agents.

Technical Approach: The large number of Wilms tumor survivors ascertained by the NWTS during its first twenty years of operation constitutes an ideal cohort for the study of familial risk and late effects of treatment. Four protocol studies have been conducted; treatment protocols and results for the first three studies have been published. A large fraction of the total national U.S. incidence of Wilms tumor has been registered on these studies, probably as much as 70% of an estimated 450-500 cases occurring nationally since 1980. Over 2,500 children who were followed on NWTS treatment protocols have now survived 5 or more years since their original diagnosis. Many of those treated more than a decade ago have reached sexual maturity, so that their reproductive history and the status of their offspring may be evaluated by entry into this study.

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/035 **Status**: Ongoing

Title: POG 9490: Topotecan Followed by Multimodal, Multiagent Therapy for Children and Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/17/1995	Jun 97	10/23/2001

Study Objective: (1) To evaluate the toxicity of the topoisomerase I inhibitor, topotecan, when given alone at a maximum tolerated dose by bolus injection daily X 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease, (2) To estimate the response rate (complete or partial) of such patients to topotecan, and (3) To evaluate the toxicity of a new chemotherapy combination comprising topotecan, cyclophosphamide, and vincristine (VTC) given in alternating cycles with vincristine, actinomycin D, and cyclophophamide (VAC) to patients who have achieved an objective response partial response (PR) or complete response (CR) to topotecan.

Technical Approach: Patients with rhabdomyosarcoma, clinical stage IV disease will receive Topotecan upfront at 2.0 mg/M2/day X 5 IV. Following evaluation, patients with partial response or complete response will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 in conjunction with vincristine and cyclophosphamide. Continuation therapy begin following evaluation at week 25 with VAC/VTC for patients showing PR and CR.

Progress: This protocol closed to patient accrual 1 Nov 96. One patient enrolled in this study at MAMC in FY96 and continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/120 **Status**: Ongoing

Title: POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/17/1996	Jul 03	5/23/2000

Study Objective: (1) To determine in a randomized trial whether the addition of 6 months of delayed intensification with divided dose oral methotrexate (ddMTX) improves event-free survival (EFS) of children with standard risk acute lymphoblastic leukemia, (2) to determine in a randomized trial the effect on EFS of delivering oral 6-mercaptopurine (6-MP) on a divided (twice daily) vs once a day schedule, during delayed intensification and continuation, (3) to study how laboratory data from POG 9400 correlates with outcome by pooling studies 9201, 9405, 9605, and 9406, (4) to assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy, and (5) to describe the occurrence of elevated transaminases and correlation of these with outcome.

Technical Approach: This treatment protocol involves 130 weeks of chemotherapy beginning with standard induction therapy of generally 4 (but up to 6) weeks of chemotherapy consisting of vincristine, prednisone, and L-asparaginase plus triple intrathecal therapy of combined methotrexate, hydrocortisone and Ara-C. Post induction, the treatment is divided into consolidation, intensification, and maintenance phases of therapy. Registration on study occurs post induction therapy at which time patients are randomized to receive 1 of 4 regimens which vary beginning in the intensification phase of therapy.

Progress: This protocol is closed to patient entry 15 Nov 99. Following the transfer of two patients to other COG/POG institutions, four patients are currently being followed under this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/045 **Status**: Ongoing

Title: POG 9631: A Phase II Feasibility Study of Oral Etoposide Given Concurrently with Radiotherapy Followed with Dose Intensive Adjuvant Chemotherapy for Children with Newly-Diagnosed High Stage Medulloblastoma

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Feb 05	12/18/2001

Study Objective: (1) To estimate the response rate and toxicity of children with newly diagnosed high-stage medulloblastoma who are treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (2) To compare the response rate and toxicity of these patients to historical control patients registered on POG study # 9031 TRT 2 (RT alone followed by adjuvant chemotherapy), (3) To estimate the 2-year event-free survival and overall survival of patients treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (4) To compare the 2-year event-free survival and overall survival of these patients to historical control patients registered on POG study # 9031, and (5) To evaluate the toxicity of dose intensive chemotherapy following craniospinal irradiation using oral etoposide, cisplatin, cyclophosphamide and vincristine.

Technical Approach: The goal of this study is to maximize response to initial therapy using oral etoposide concurrently with radiotherapy in children with newly diagnosed high stage medulloblastoma. Adjuvant therapy will continue after radiation using dose intensive chemotherapy.

Progress: No subjects enrolled in this study in FY01 at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/066 **Status**: Ongoing

Title: POG 9720: Idarubicin and Cladribine in Recurrent and Refractory Acute Myeloid Leukemia: A Pediatric Oncology Group Phase II Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/20/1998	Jul 03	2/27/2001

Study Objective: (1) To determine the CR rate of the combination of Idarubicin (IDA) and Cladribine (CDA) in patients with recurrent AML, (2) To determine the CR rate of the combination of IDA and CDA in patients with primary refractory AML, (3) To determine the CR rate of the combination of IDA and CDA in patients with recurrent or primary refractory secondary AML and myelodysplastic syndromes (not related to Down's Syndrome), (4) To determine the toxicities of the combination of IDA and CDA, and (5) To define the pharmacokinetics of CDA administered as a 2 hour infusion.

Technical Approach: Eligible patients will be stratified and receive a five day treatment consisting of IV Idarubicin daily for 3 days and IV Cladribine, 2 hours daily for 5 days. Twenty-four hours after completion of chemotherapy, patients will begin daily subcutaneous injections of G-CSF until blood counts stabilize. A bone marrow aspirate will be done at 3 weeks to assess response. A second course may be given. If patients have progressive disease they will be taken off study.

Progress: No patients enrolled in this study in at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/053 **Status**: Ongoing

Title: POG 9836: Treatment of Children with Diffuse Intrinsic Brain Stem Glioma with Standard Dose Irradiation and Vincristine Plus Oral VP-16

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC; LTC William B. Reece, MC; LTC Stephen M. Yoest, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Jan 04	N/A

Study Objective: (1) To evaluate the efficacy of oral VP-16, Vincristine, and conventional dose radiation therapy on one year survival in children with newly diagnosed brain stem glioma and (2) monitor the toxicity of this therapy in children with newly diagnosed brain stem glioma.

Technical Approach: The prognosis for children with diffuse intrinsic brain stem glioma is disappointing. The usual treatment of children with diffuse, intrinsic brain stem glioma is radiation therapy to the involved area. Recent reports have shown very encouraging results using oral Etoposide for children with recurrent brain stem glioma. The purpose of this study is to determine the effectiveness of vincristine in combination with VP-16 and irradiation in patients with newly-diagnosed brain stem glioma, and also to determine the type of side effects that occur when vincristine, VP-16 and radiation therapy are given together.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/032 **Status**: Ongoing

Title: POG 9900: ALinC 17 Classification (C) Protocol, A POG Non-therapeutic Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 05	1/22/2002

Study Objective: (1) To provide the clinical and laboratory data necessary for placing each patient with ALL onto proper therapeutic trial, and (2) to provide an administrative base to capture classification data for correlative studies in ALL treatment protocols and series of historical protocols.

Technical Approach: At the time of diagnostic evaluation which includes bone marrow aspiration and/or biopsy, 20 ml of bone marrow and 25 ml of peripheral blood will be collected and processed for local laboratory studies and submission to the following POG reference laboratories: 1. Johns Hopkins University for Immunophenotyping. 2. University of New Mexico (UNM) for DNA Index, FISH, Molecular testing, Cell banking. 3. Medical College of Wisconsin for Glucocorticoid receptors. 4. University of Texas Southwestern Medical Center for Homocysteine Children's Hospital of Michigan for Drug sensitivity profiles. 5. MUSC - Children's Hospital for Drug sensitivity profiles. UCSD Medical Center for Tumor suppressor gene studies. The data captured on this protocol will be used in the therapeutic trials, in cross era analysis, and in international collaborations to further define the prognostic importance of biologic features in ALL.

Progress: One subject enrolled in this study in FY00, three subjects in FY01, for a total of four subjects enrolled at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/077 **Status**: Ongoing

Title: POG 9904: ALinC 17 Protocol for Patients with Newly Diagnosed Low Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/12/2000	May 04	4/24/2001

Study Objective: (1) In conjunction with POG 9905, to compare short MTX infusion (2g/m2 over 4 hours) with a longer infusion (1g/m2 over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity. (2) to determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL, (3) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (4) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

Technical Approach: This protocol will randomize between the 4-hour and 24 hour methotrexate infusion and for patients with TEL/AML1 gene, between standard and delayed intensification. Data from POG 9904 and 9905 will be pooled for statistical analysis of efficacy and toxicity. This study will determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). Induction will include three or four drugs (dependent on initial risk classification POG 9900).

Progress: Two subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/076 **Status**: Ongoing

Title: POG 9905: ALinC 17 Protocol for Patients with Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/12/2000	May 04	4/24/2001

Study Objective: (1) To determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL. This objective will also be assessed as part of POG protocol 9904; (2) In conjunction with POG 9904, to compare short MTX infusion (2g/m2 over 4 hours) with a longer infusion (1g/m2 over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity; (3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): (a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; (b) Marrow morphology on day 8, and; (c) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples on day 29 and after consolidation; (4) Using a case control design, quantitate MRD with flow cytometry and molecular techniques, to determine whether late relapse correlates with a given level of MRD in marrow samples obtained and banked at the completion of therapy. To analyze samples obtained at relapse to ascertain whether markers of MRD remain constant i.e., if a relapse not "predicted" by high levels of MRD in remission samples, is it because of a change in the identified markers; (5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction); (6) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

Technical Approach: This study will utilize a 2 x 2 factorial design to answer two randomized questions. The standard arm will recapitulate regimen A of the current POG protocol for standard risk patients. Induction will include three or four drugs (dependent on initial risk classification POG 9900) and consolidation will include 24-hour MTX infusions, at one gram per square meter, given every three weeks for a total of six doses. The two randomizations will assign patients to receive therapy with or without the delayed intensification and receive the IV MTX as a 2 gm/m2 infusion over four hours versus a one gram per m2 infusion over 24 hours. Intensive continuation will include 4 cycles of therapy with each 12 week cycle including 6 courses of divided dose oral MTX, nightly 6-MP, a dose of intrathecal MTX and a pulse of vincristine and dexamethasone. Standard continuation therapy includes weekly MTX, daily 6-MP and vincristine/dexamethasone pulses every 16 weeks. Dexamethasone replaced prednisone in the 9705 pilot study, and will be utilized here because of better CNS penetration and data suggesting that its use enhance event-free survival. The current POG study for standard risk patients includes a randomization to single versus twice daily dosing of oral 6-MP, based on the concept that duration of exposure is critical to anti-metabolite efficacy. This study includes only the traditional single nightly dose. Should the results of the open trial suggest an advantage to the use of divided dose 6-MP, this protocol will be amended.

Progress: Two subjects enrolled in this study in FY01, one subject enrolled in FY00, for a total of three subjects enrolled at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/075 **Status**: Ongoing

Title: POG 9906: ALinC 17 Protocol for Patients with Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL), Evaluation of the Augmented BFM Regiment, a POG Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/12/2000	May 04	4/24/2001

Study Objective: (1) To determine for patients at high risk for treatment failure if the augmented Berlin-Frankfurt-Munster (A-BFM) therapy is superior to ALinC 14/15 therapy, on the basis of historical controls; (2) To determine if minimal residual disease at the end of induction is predictive of an inferior prognosis; (3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; b) Marrow morphology on days 8, and 29; 4) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples and at the end of induction and therapy, (5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (6) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis, and (7) To give Pediatric Oncology Group (POG) investigators experience with BFM-type regimens as these will likely play a major role in Children's Oncology Group (COG) protocols of the future.

Technical Approach: The regimen as defined by POG 9906 will represent a modified version of CCG augmented BFM for patients at high risk for treatment failure as defined by ALinC 17 clinical and biological criteria. Routine whole brain irradiation will not be used. Instead we will rely on intrathecal chemotherapy, except for those with established CNS disease at diagnosis. However, the augmented BFM results remain unsatisfactory for subsets of patients in the following categories: Philadelphia chromosome positive, hypodiploid (<45) modal chromosome number, and M-3 marrow at day 29. Both CCG and POG analyses concur that these groups, comprising approximately 3-4% of newly diagnosed patients with A.L.L., have an EFS <45%. These cases, henceforth classified as Very High Risk, will be entered on a separate combined POG/CCG (COG) trial evaluating new chemotherapy and marrow transplant strategies. Risk group assignment will be determined otherwise by the method of using age, WBC, CNS status, DNA index, and molecular and cytogenetic criteria as established for POG ALinC 17 classification protocol.

Progress: One subject enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/010 **Status**: Ongoing

Title: POG 9917: A Pilot Study of Dose Intensification of Methotrexate in Patients with Advanced Stage (III/IV) Small Non-cleaved Cell Non-Hodgkin's Lymphoma and B-cell ALL

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/24/2000	Oct 10	N/A

Study Objective: (1) To determine if increasing the Methotrexate dose from 1 gm/m2 to 5 gm/m2 in combination with standard treatment as per the POG 9317 protocol is feasible in a group-wide setting, and to assess the toxicity of this intensified therapy, (2) to assess the feasibility of treating patients with CNS disease at diagnosis with VP16/Ifosfamide plus the intensified chemotherapy, in order to confirm the superior survival of this group of patients when treated in this fashion, (3) to prospectively assess toxicities and late effects of such intensive chemotherapy on the central nervous system, cardiac function, and fertility, (4) to informally estimate the costs of hospitalization for the treatment of therapy-related side effects and (5) to evaluate the biology of Burkitt and Burkitt-like NHL and B-ALL with respect to the REAL classification, and to assess the feasibility of obtaining tissue for important biology studies in a group-wide setting.

Technical Approach: This study will be opened to newly diagnosed patients with Stage III and IV NHL and B-ALL with or without CNS disease. The patient's diagnosis will determine the order and frequency of the treatment. Treatment for Stage III and IV NHL and B-ALL without CNS disease will consist of Induction and Consolidation Therapy (Stage III patients will repeat only cycle A of Consolidation therapy and Stage IV patients will repeat an entire cycle, A & B, of Consolidation therapy). Patients with CNS disease will receive Induction, Intensification and Consolidation therapy also repeating cycles A & B of Consolidation therapy. Chemotherapy drugs utilized in this study are Doxorubicin, Leucovorin Calcium, Cytosine Arabinoside, Cyclophosphamide, Mesna, Methotrexate, G-CSF, Vincristine, Dexamethasone, Ifosfamide, Etoposide.

Progress: No subjects enrolled in this study at MAMC in FY01. COG reported a temporary closure to evaluate the first group of patients for toxicity before accruing additional patients, 1 Jun 01. The study reopened following approval of Amendment 1 therapy changes. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/051 **Status**: Ongoing

Title: POG A2971: Treatment of Children with Down Syndrome and Acute Myeloid Leukemia, Myelodysplastic Syndrome, or Transient Myeloproliferative Disorder, a Phase III Group-Wide Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Jan 07	N/A

Study Objective: (1). To evaluate the efficacy (as compared to DS children enrolled on CCG 2891) of reduced dose chemotherapy for DS patients diagnosed with AML or MDS: (1.1) to maintain or improve the current remission rate (94%) in this population of children with low risk (for relapse) disease, and (1.2) to maintain or improve the current disease-free survival rate (88%), (1.3) to reduce acute morbidity & mortality in this high risk (for toxicity) population and (1.4) to determine whether there is a reduction of sequelae in long term survivors. (2). To define our understanding of the natural history of TMD by: (2.1) Establishing a CCG database for patients with TMD, (2.2) Establishing the use of uniform treatment guidelines for TMD, (2.3) Establishing the incidence of subsequent leukemia, and (2.4) Delineating predictive risk factors for subsequent leukemia. (3). To facilitate biologic investigations of leukemia in DS patients through banking of biologic specimens. (4). To facilitate epidemiologic investigations of leukemia in DS patients.

Technical Approach: This study builds upon CCG-2891 and utilizes a reduced variation of DCTER induction, standard timing, to reduce toxicity and maintain or increase efficacy. The added benefits of etoposide and dexamethasone in the DCTER regimen during induction in the DS population is uncertain. The experience with daunomycin, cytarabine (Ara-C), and 6-thioguanine is extensive and is an effective combination during induction. The use of DCTER's (minus the VP16 & steroid) method of administration (continuous infusion) has several advantages in this population, including reduction of long-term cardiac toxicity risk. It is better tolerated than pulse administration, and it is a similar method to the control group (CCG-2891DS patients). As Capizzi II was very well tolerated in this group in CCG-2891, and its efficacy in maintaining DFS has been well established, this therapy will be maintained and will be identical to that given in CCG 2961. This will avoid the possibility of a reduction in DFS at the end of this study without knowing whether the reduction of therapy during induction or during intensification was the cause. TMD: Patients with TMD will be identified utilizing a common diagnostic criteria, treated with a uniform protocol, and then monitored consistently and prospectively. This methodology will permit a truer description of the natural history of this unusual disease. The eligibility criteria utilized within this study will be broad so as to better define this entity. A subgroup will be identified utilizing diagnostic criteria set forth in the current Pediatric Oncology Group observational study of TMD to permit future collaborative efforts. It will as well, by virtue of its longitudinal design permit biologic studies to investigate and elucidate the mechanisms by which this proliferative disease naturally comes under control. Utilizing the nested case-control methodology we will be able to compare, within the cohort of patients with TMD, those who develop AML versus those who do not, and then identify both clinical and biologic prognostic factors. These two groups will also allow examination to determine what biologic mechanisms are present which suppress or fail to suppress eventual neoplastic development.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/100 **Status**: Ongoing

Title: POG A3961: Treatment for Infants and Children with Intermediate Risk Neuroblastoma: A Pediatric Oncology Group/Children's Cancer Group Phase III Intergroup Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 07	6/26/2001

Study Objective: (1) To determine that Intermediate Risk Neuroblastoma with favorable biology will have a >90% event free survival (EFS) and survival (S) with a short course of chemotherapy (4 cycles) over 84 days without primary radiation therapy, (2) To determine that Intermediate Risk Neuroblastoma with unfavorable biology will have a >90% (EFS) with a longer course of chemotherapy (8 cycles) over 168 days without primary radiation therapy, and (3) To determine the acute and long term morbidity/toxicities associated with treating Intermediate Risk Neuroblastoma with surgery and chemotherapy.

Technical Approach: This study is an intergroup Phase III prospective nonrandomized trial to evaluate reduced therapy for intermediate risk neuroblastoma based on clinical and selected biologic, prognostic variables in order to maintain event free survival and survival, and minimize both acute and long-term morbidity in this group of patients. Either prior to or after study entry, patients will undergo an operation to remove as much of the primary tumor and involved lymph nodes as can be safely accomplished with minimum morbidity. Intermediate risk patients with favorable biology will receive 4 cycles of chemotherapy. Second surgery will be done for all patients not in complete remission following recovery from the 4th cycle of chemotherapy. Intermediate risk patients with unfavorable biology will continue with an additional 4 cycles of chemotherapy for a total of 8 cycles. At the conclusion of 8 cycles, the patient shall undergo second surgery. Radiotherapy will be administered to the site of viable residual disease after completion of 8 weeks of chemotherapy and second look surgery for selected intermediate risk INSS Stage 3 or 4 neuroblastoma patients with unfavorable biology.

Progress: No patients enrolled in this study at MAMC during FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/139 **Status**: Ongoing

Title: COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Sep 07	9/25/2001

Study Objective: (1) To compare the event free survival and survival in patients with disseminated lymphoblastic lymphoma treated on four regimens. (NHL/BFM-95 vs. CCG BFM), (2) To determine if treatment with a regimen without high dose methotrexate will maintain the same excellent disease free survival obtained with NHL/BFM-90, (3) To determine if intensification with anthracycline and cyclophosphamide improves disease free survival, (4) To collect outcome data on uniformly treated patients with localized disease or CNS positive disease, and (5) To determine if rapid reduction in tumor volume as defined by chest radiography and CT is predictive of improved outcome.

Technical Approach: Patients with disseminated (Murphy stage III or IV) lymphoblastic lymphoma without evidence of CNS disease will be randomized to one of four treatment regimens: Standard CCG BFM (regimen Al); CCG BFM intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen A2); Standard NHL/BFM-95 (regimen BI); or NHL/BFM-95 intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen B2). Patients with disseminated lymphoblastic lymphoma positive for CNS disease will be assigned to the intensified NHL/BFM-95 arm (regimen B2) with delayed radiation therapy. Patients with localized lymphoblastic lymphoma (Murphy stage I or II) will be assigned to the standard CCG BFM arm without additional intrathecal methotrexate (regimen AO). The duration of each treatment arm is 2 years and consists of Induction, Consolidation, Interim Maintenance, Delayed Intensification, and Maintenance therapies.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/138 **Status**: Ongoing

Title: POG A9952: Chemotherapy for Progressive Low Grade Astrocytoma in Children Less Than Ten Years Old

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/26/2000	Sep 07	9/25/2001

Study Objective: To compare the event-free survival as a result of treatment with both carboplatin and vincristine (CV) or a combination of thioguanine, procarbazine, CCNU, and vincristine (TPCV).

Technical Approach: After as complete as possible surgical resection, without causing increased neurological deficits, a child will be followed without further intervention until signs of progression are observed. Children with progressive symptoms due to tumor and minimal surgery are also eligible without initial follow-up. Children with NF and definitive progression of optic pathway tumors can be entered without surgery. At registration children will be randomly assigned to either CV or TPCV chemotherapy. All children with NF will be non-randomly assigned to CV. All children will be followed until signs of definite tumor progression. The children will not be taken off chemotherapy for stable disease since this may be a desirable outcome.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/088 **Status**: Completed

Title: POG A9961: A Phase III Prospective Randomized Study of Craniospinal Radiotherapy Followed by One of Two Adjuvant Chemotherapy Regimens (CCNU, CDDP, VCR, or CPM, CDDP, VCR) in Children with Newly-Diagnosed Average Risk Medulloblastoma

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/18/1997	Apr 03	3/27/2001

Study Objective: (1) To determine if a cyclophosphamide arm will increase the rate of progression-free survival compared to a CCNU containing arm for children with average-risk medulloblastoma, (2) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of S580 cGy, and adjuvant vincristine, CCNU and cisplatin chemotherapy, (3) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of 5580 cGy, and adjuvant vincristine, cyclophosphamide and cisplatin chemotherapy, (4) To determine the long-term neurocognitive, endocrinologic and cardiopulmonary sequelae of radiotherapy plus adjuvant chemotherapy in children with average-risk medulloblastoma treated with 2340 cGy of craniospinal radiation therapy, local boost radiotherapy, and either one of two drug regimens and to determine if the replacement of CCNU with cyclophosphamide will alter the incidence and degree of sequelae experienced, (5) To determine if cellular/biologic parameters, including tumor molecular genetic analysis, DNA ploidy, mitotic activity markers and immunohistochemical analysis are correlated with progression-free survival, survival and the pattern of disease relapse in children with average-risk medulloblastoma, and (6) To determine the utility of routine MR surveillance studies of the head and spine to detect subclinical recurrent disease.

Technical Approach: Following surgery, patients will be randomized to receive Regimen A or B of treatment. Both regimens will include 2340 cGy of craniospinal radiation and 3240 cGy of boost radiation directly to the primary tumor with weekly vincristine doses. Six weeks following the completion of radiotherapy, patients will begin 8 cycles of maintenance chemotherapy for Regimen A (CCNU, cisplatin and vincristine) or Regimen B (cyclophosphamide, cisplatin and vincristine).

Progress: This study closed to patient entry, 1 Dec 00, as accrual goals had been met. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/109 **Status**: Ongoing

Title: COG AEWS0031-Trial of Chemotherapy Intensification Through Interval Compression in Ewing Sarcoma and Related Tumors, A Phase III Groupwide Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/26/2001	Jun 07	N/A

Study Objective: (1) To determine the effect of chemotherapy intensification using interval compression on event-free survival and survival in children and young adults with Ewing sarcomas and related tumors (Ewing family of tumors), (2) Through linked biology studies, to prospectively assess the prognostic importance of the rearrangement of the EWS gene on chromosome 22, and the presence of RT-PCR evidence of submicroscopic tumor cells in bone marrow and/or peripheral blood at diagnosis and (3) To generate additional hypotheses relating tumor biological characteristics to clinical features that could be tested in future clinical trials.

Technical Approach: This is a randomized controlled study to determine whether chemotherapy intensification by reduction of the intervals between chemotherapy cycles can improve the effectiveness of treatment for Ewing sarcoma and related tumors in children, adolescents, and adults. All patients receive chemotherapy with alternating cycles of vincristine-doxorubicin-cyclophosphamide and ifosfamide-etoposide, with G-CSF (filgrastim) between cycles. Patients in the control arm (Regimen A) will start chemotherapy cycles every 21 days, while patients in the experimental arm (Regimen B) will start cycles every 14 days, or as soon as blood counts have recovered. Primary tumor treatment by surgery, radiation, or a combination will begin at week 13, after four cycles of chemotherapy in Regimen A and six cycles in Regimen B. This study expects to enroll 528 patients nationwide with localized tumors over 4-5 years. Analyses of the study will include assessments of event-free survival and survival, toxicity, the degree of intensification achieved in Regimen B, and the relationship between intensification achieved and outcome.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01	**Number**: 201/108	**Status**: Ongoing
Title: COG ANBL00B1, Neuroblastoma Biology Studies		
Principal Investigator: LTC Kelly J. Faucette, MC		
Department: Childrens Oncology Group		**Facility**: MAMC
Associate Investigator(s): MAJ Robert G. Irwin, MC		
Start Date: 6/26/2001	**Est. Completion Date:** May 07	**Periodic Review:** N/A

Study Objective: (1) To prospectively analyze the factors that are currently used for risk-group assignment (DNA content by flow cytometry, MYCN copy number by FISH, and tumor histology using the International Neuroblastoma Pathologic Classification System) in neuroblastoma tumors at the time of diagnosis, (2) to maintain a reference bank containing clinically and genetically characterized frozen tumor tissue, tumor DNA and RNA, tumor touch preparations, histology slides and blocks, cell lines, and paired normal DNA obtained at the time of diagnosis (all patients), at the time of second-look surgery (high-risk patients), and relapse (all patients) for future research studies, (3) to prospectively analyze the prevalence of 1p, 11q, 14q LOH and gain of 17q; the expression of nerve growth factor (NGF) and its high affinity (Trk-A) and low affinity (p75 NTR) receptors; and telomerase activity in diagnostic neuroblastoma tumors, and to determine the independent clinical significance of these biologic factors compared to MYCN amplification, INSS stage, age, and histologic variables in predicting either response to treatment or outcome, and (4) to build a database of the known biologic prognostic factors for patients on therapeutic studies. Adjustment for, or stratification by, these prognostic factors will be performed when testing for treatment effect in Phase III trials.

Technical Approach: Clinical and biological factors have been shown to have prognostic value in neuroblastoma. Current therapeutic studies for neuroblastoma patients are tailored according to patient risk. In the Children's Oncology Group (COG), risk-group assignment is currently based on INSS stage, age, MYCN copy number, tumor cell ploidy, and Shimada tumor histopathology. However, additional factors have also been shown to have prognostic value including the level of Trk-A expression, multi-drug resistance associated protein (MRP) expression, telomerase activity, CD44 expression, and genetic abnormalities including LOH of 1p, 11q, 14q and gain of 17q. We hypothesize that analyzing additional genetic and biologic factors will result in a further refinement of the current COG risk-group schema, and will, thereby, impact future risk-based approaches to therapy. We further hypothesize that maintaining tumor and nucleic acid banks with well characterized samples will provide invaluable biologic resources for future research studies that will lead to a further understanding of neuroblastoma biology and the development of new, effective therapy for high-risk patients.

Progress: One subject enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/145 **Status**: Ongoing

Title: POG D9602: Actinomycin D and Vincristine with or without Radiation Therapy for Newly Diagnosed Patients with Low-Risk Rhabdomyosarcoma or Undifferentiated Sarcoma: An IRS-V Protocol

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/19/1997	Jul 03	8/28/2001

Study Objective: (1) Treatment of IRS-V low-risk patients with actinomycin D (AMD) and vincristine (VCR), plus local radiotherapy (XRT) for microscopic or gross residual tumor, will result in a failure-free survival rate of 88% at 2 years and an overall survival rate of about 95% at S years from initial diagnosis, (2) Treatment of IR8-V low-risk patients with alveolar rhabdomyonarcoma or undifferentiated sarcoma with vincristine and actinomycin D plus cyclophosphamide (collectively called VAC) will result in a failure-free survival rata of greater than or egual to 70% at two yeare and an overall survival rate of about 80-90% at 5 years, and (3) Reduction in radiation therapy dose for patients with Clinical Group II disease to 36 Gy (from 41.3 Gy) and for Group III patients with orbital disease to 45 Gy (from 50-S' Gy) will result in local control rates of about 90%.

Technical Approach: Patients in Group I have no residual tumor following surgery and will receive no radiation therapy. Patients in Group II have microscopic residual tumor and will receive radiation therapy at a dose lower than the current standard. Patients in Group III, orbit tumor only, have visible residual tumor after biopsy and will receive radiation therapy. The results will be compared to current intergroup rhabdomyosarcoma study results. All patients will begin chemotherapy with the two-drug combination of vincristine and actinomycin D, given over a 3-week period while their tumor specimen is being classified at the IRS Group Pathology Center in Columbus, Ohio. Patients whose tumor is classified as embryonal or botryoid rhabdomyosarcoma will continue to receive vincristine and actinomycin D, given at weeks 12 through 21, 24 through 33, and 36 through 45. Patients whose tumor is classified as alveolar rhabdomyosarcoma or undifferentiated sarcoma will have the chemotherapy drug cyclophosphamide added to the combination of vincristine and actinomycin D, given at weeks 3, 6, 9, 12, 15, 18, 24, 27, 30, 36, and 42. Cyclophosphamide will be added on Week 0 for these patients who show molecular genetic or cytogenetic evidence of the t(2;13) or t(1;13) translocation, or the PAX 3-FRHR or PAX 7-FRER gene fusion product.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/051 **Status**: Ongoing

Title: POG D9802: A Phase II "Up Front Window Study" of Irinotecan (CPT-11) Followed by Multimodal, Multiagent Therapy for Selected Children and Adolescents with Newly Diagnosed Stage 4/Clinical Group IV Rhabdomyosarcoma, An IRS-V Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 06	12/18/2001

Study Objective: (1) To estimate the response rate associated with two cycles of irinotecan when administered as up-front window therapy, using a low-dose protracted intravenous schedule in high-risk, previously untreated children with metastatic rhabdomyosarcoma, (2) To describe the toxicities associated with irinotecan when administered as described in 1, (3) To describe the toxicities of a new drug pair, vincristine and irinotecan, when given in alternating cycles with vincristine, actinomycin D, and cyclophosphamide (VAC) during continuation therapy in patients who achieve a partial or complete response to the irinotecan window, (4) To estimate the overall and failure-free survival of children with metastatic rhabdomyosarcoma treated with irinotecan followed by VAC alone or VAC alternating with vincristine and irinotecan plus radiotherapy, (5) To study the pharmacokinetics of irinotecan in previously untreated children with rhabdomyosarcoma who are treated on a low-dose, protracted course and who also receive vincristine, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by as positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

Technical Approach: Patients with embryonal histology greater than or equal to 10 years of age or alveolar histology (any age) who have stage 4 tumors and who do not have evidence of intracranial extension, base of skull erosion or cranial nerve palsy will be eligible to receive the two cycles of irinotecan as up-front window therapy prior to receiving the standard therapy, Vincristine, Actinomycin D, Cyclophosphamide (VAC), radiotherapy will begin at week 15. Patients with evidence of base of skull erosion or cranial nerve palsy will receive VAC alone and will begin radiotherapy at week 15. Patients with evidence of intracranial extension will receive VAC alone and begin radiotherapy at day 0.

Progress: No patients enrolled in this study in FY01 at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/052 **Status**: Ongoing

Title: POG D9803: Randomized Study of Vincristine, Actinomycin-D, and Cyclophosphamide (VAC) versus VAC Alternating with Vincristine, Topotecan and Cyclophosphamide for Patients with Intermediate-Risk Rhabdomyosarcoma

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 06	12/18/2001

Study Objective: (1) To compare the early response rates (i.e., CR/PR), failure-free survival (FFS) and survival of patients with intermediate risk rhabdomyosarcoma treated with surgery + RT and Vincristine, Actinomycin-D and cyclophosphamide (VAC) or the same alternating with a new combination which substitutes topotecan for actinomycin D (VAC/VTC/VAC), (2) To compare the acute and late effects of these two treatment regimens, (3) To determine the rate of second-look surgery in selected patients with bulk residual tumor at diagnosis (i.e., Clinical Group III) and the proportion of these that render the patient "tumor free" or with microscopic tumor only, (4) To determine the rate of local failure in selected patients with bulk residual tumors at diagnosis (i.e., Clinical Group III) who, following second-look resection, have response-adjusted radiotherapy dose reduction (36 Gy if in complete response or 41.4 Gy for microscopic residual disease), (5) To determine if preoperative radiotherapy followed by second-look surgery for selected patients with bulk residual disease (i.e., Clinical Group III) who respond poorly to induction chemotherapy is feasible, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by a positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

Technical Approach: This study will introduce topotecan to the standard therapy for intermediate risk rhabdomyosarcoma, surgery + RT and Vincristine, Actinomycin D, and Cyclophosphamide (VAC). This randomized study will compare two chemotherapy regimens, VAC versus VAC alternating with Vincristine/Topotecan/Cyclophosphamide (VTC) cycles.

Progress: No subjects enrolled in this study at MAMC in FY01; however, one subject was accepted as a transfer from Seattle, Washington. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/049 **Status**: Ongoing

Title: POG D9902: A Group Wide Protocol for Collecting and Banking Pediatric Cancer Research Specimens. An Intergroup Rhabdomyosarcoma Study Group Protocol

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 10	12/18/2001

Study Objective: (1) To facilitate the collection of human tissue and other biologic specimens (blood, bone marrow) from Intergroup Rhabdomyosarcoma Study Group (IRSG) investigators, (2) To provide a repository for long-term storage of tissue and other biologic specimens (blood, bone marrow) collected by IRSG investigators (referred to as the Bank), and (3) To make available, through the IRSG/Cooperative Human Tissue Network, these materials for approved projects by laboratory-based investigators.

Technical Approach: At the time of initial diagnosis of rhabdomyosarcoma or undifferentiated sarcoma (or at re-excision of the primary tumor, if it occurs prior to the start of chemotherapy), surgical tissue, bone marrow and blood that are no longer needed for diagnosis will be prepared and shipped to the Pediatric Cooperative Human Tissue Network (CHTN) for Banking and Distribution.

Progress: One subject enrolled in this study in FY01 at MAMC. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/052 **Status**: Ongoing

Title: POG P9462: Randomized Treatment of Refractory Neuroblastoma with Topotecan Regimens, Following Deferoxamine (POG only) in an Investigational Window, A POG/CCG Phase II Intergroup Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Jan 04	N/A

Study Objective: Topotecan regimen: To compare Topotecan alone with the combination of topotecan + cyclophosphamide in terms of response rate, toxicity and time to disease progression. Deferoxamine (DFO) window (POG only): To determine the response rate to and toxicity of DFO and the relationship between serum DFO levels and the biological effects, toxicity and efficacy of DFO.

Technical Approach: This study hypothesizes that there are differences in efficacy among the two regimens utilizing topotecan that are under investigation currently; topotecan IV daily x 5, and topotecan plus cyclophosphamide IV daily x 5. Phase I and II studies have demonstrated that neuroblastoma is sensitive to the topotecan IV daily x 5 and the topotecan plus cyclophosphamide IV daily x 5 regimens. The efficacy of adding topotecan to an aggressive multidrug chemotherapy regimen to treat patients newly diagnosed with neuroblastoma will be tested in future phase III randomized studies. In this study of patients with recurrent neuroblastoma, a randomized trial will be conducted in order to determine which of these two topotecan regimens should be tested in the future phase III studies.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/065 **Status**: Ongoing

Title: POG P9641: Primary Surgical Therapy for Biologically Defined Low-Risk Neuroblastoma; A Pediatric Oncology Group Children's Cancer Group, Phase III, Intergroup Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/20/1998	Jul 03	3/28/2000

Study Objective: (1) To determine if low risk INSS stage 2A/2B asymptomatic neuroblastoma patients treated with surgery alone will have a three year survival (S) rate of 95%, (2) To determine if low risk INSS stage 1 asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (3) To determine if low risk INSS stage 4S asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (4) To estimate the response and 3 year event-free survival (EFS) rates of symptomatic patients with chemotherapy, (5) To estimate the EFS and S rates in patients who relapse or progress after initial treatment with surgery alone, (6) To determine the acute and long-term morbidity/toxicities associated with treating low-risk neuroblastoma with surgery alone or with surgery and chemotherapy, (7) To further define and evaluate the prognostic importance of other biologic factors as determined on studies POG #9047 (or its successor), CCG #B973, and by International Neuroblastoma Risk Group criteria, (8) To collect resource utilization data regarding number of hospital days, the extent of transfusion support, and the use of diagnostic imaging, and to compare these with historical CCG study 3881 data.

Technical Approach: Patients in this study will be stratified by stage and extent of disease to either surgery alone or surgery with chemotherapy. Further studies done on patient's tumor specimens may change their classification to "intermediate" or "high" risk neuroblastoma, in which case they will be taken off study and more intensive chemotherapy will be administered.

Progress: One patient enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/127 **Status**: Ongoing

Title: POG P9749: Pilot Intergroup Study of High-Dose Cisplatin, Etoposide and Bleomycin (HD-PEB) Combined with Amifostine in Children with High-Risk Malignant Germ Cell Tumors

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Kenneth S. Azarow, MC; COL Jerome B. Myers, MC; COL Marc G. Cote, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/28/2001	Jul 03	N/A

Study Objective: Primary: (1) To evaluate the early efficacy and toxicity profile of administering high dose cisplatin, etoposide, and bleomycin (HD-PEB) in combination with amifostine to children with high-risk malignant germ cell tumors (GCT) and (2) whether the use of amifostine can reduce the hematologic and non-hematologic toxicities of HD-PEB in these patients when compared to similar patients treated on POG 9049/CCG 8881 with HD-PEB. Secondary: (3) To estimate the response rate of patients with high-risk malignant GCT to HD-PEB with amifostine, (4) to collect samples and facilitate studies which distinguish alpha-fetoproteins of liver and germ cell tumor origins, (5) to facilitate studies & sample collection of germ cell tumor cytogenetics, molecular genetics, and amplification of c-myc, (6) to facilitate studies & sample collection for studies of DNA repair mechanisms in germ cell tumors, (7) to derive tumor cell lines and xenografts of germ cell tumors for use in studies of biologic agents such as experimental chemotherapeutic agents and differentiation agents and (8) to establish a biologic samples bank for germ cell tumors to include frozen tumor, frozen normal tissue, patient blood and parental blood that will be used in future studies that will impact on the clinical care and prognosis of affected patients.

Technical Approach: Induction therapy will consist of four cycles of HD-PEB with amifostine administered at 21-day intervals. Patients > 12 months of age will be pre-treated with amifostine at a dose of 825 mg/m 2 /dose IV over 15 minutes beginning 30 minutes prior to cisplatin administration. After four cycles of HD-PEB, patients will have complete diagnostic imaging evaluation. Patients in clinical CR will electively stop therapy. Patients in clinical PR will have second-look surgery and if there is residual tumor will be eligible to receive two more cycles of HD-PEB. Patients in clinical CR after six cycles will electively stop therapy. Patients not in CR after six cycles will be off study.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/050 **Status**: Ongoing

Title: POG P9754: Protocol for Patients with Newly-Diagnosed Non-Metastatic Osteosarcoma, A POG/CCG Pilot Intergroup Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 06	12/18/2001

Study Objective: (1) To sequentially perform three pilot studies of dose intensified therapy for osteosarcoma: a) doxorubicin dose intensification, b) doxorubicin dose intensification with ifosfamide, c) alkylator intensification. One of these therapies will be used in a randomized study whose objectives will be: (1.1.) To determine whether postoperative dose intensification can improve outcome for standard responders to preoperative chemotherapy, (1.2.) To determine whether the use of dexrazoxane (DXR) cardioprotection during a standard preoperative induction regimen affects histologic response, (2) To pilot a standard preoperative chemotherapy regimen administered with dexrazoxane (DXR) cardioprotection for all newly diagnosed patients with non-metastatic osteosarcoma, (2.1.) To test whether DXR can be safely used with doxorubicin in combination with cisplatin (pilot 1) or cisplatin/ifosfamide (pilots 2,3), (2.2.) To ascertain that the cytotoxicity as measured by tumor necrosis at definitive surgery is not compromised by the used of DXR compared to historic control, (3) To assess the feasibility of administering 600 mg/m2 of doxorubicin with DXR cardioprotection (pilot 1,2) or high dose ifosfamide the etoposide (pilot 3) to standard risk patients who are also being treated with methotrexate and cisplatin (and ifosfamide in pilots 2,3), (4) To evaluate the feasibility of obtaining tumor tissue for analysis of biologic factors in osteosarcoma in conjunction with P9851, and (5) To evaluate the feasibility of assessing musculoskeletal, cardiac, renal and gonadal status after the completion of therapy.

Technical Approach: Two courses of standard chemotherapy will be given prior to surgery, limiting intensification to the population at greatest risk. The cohort with a good response to therapy will continue with non-intensified chemotherapy. For the purposes of this study, good responders will have greater than or equal to 98% necrosis in the tumor specimen resected at definitive surgery. The companion biology protocol POG P9851 will accompany this study.

Progress: No subjects enrolled in this study at MAMC in FY01. Pilot 3 arm closed to subject enrollment 6 Nov 00. Protocol reported temporarily closed, 27 Apr 01, to look at pilot data analysis. Pilot 1 arm opened for continued subject enrollment, 29 May 01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/018 **Status**: Ongoing

Title: POG P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors: A COG Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/19/1999	Nov 04	10/23/2001

Study Objective: (1) To determine the efficacy of irinotecan in the treatment of children with refractory neuroblastoma, sarcomas of soft tissue or bone, other solid tumors, or brain tumors, (2) to further evaluate the toxicity of irinotecan when given daily for 5 days, repeated every 21 days, and (3) to further evaluate the pharmacokinetics/pharmacodynamics of irinotecan and its metabolites SN-38, SN 38G, and APC, using a limited sampling strategy.

Technical Approach: Irinotecan appears to be one of the most active topoisomerase I inhibitors that is clinically available and therefore deserves further evaluation in children with recurrent CNS or solid tumors. Although the optimal schedule for irinotecan is not yet known, antitumor activity has been observed on all schedules of administration. Pharmacokinetic studies, an integral component of this trial will be done to determine if there are correlates with PK parameters and toxicity or response.

Progress: One patient enrolled in this study in FY00 at MAMC, however, Peds Hem/Onc reported this patient's death, due to Influenza A, 26 Jun 01. An SAE report was filed stating the possibility this death could have been a result of the study drug due to delayed neutropenia. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/048 **Status**: Ongoing

Title: POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/22/2000	Feb 10	12/18/2001

Study Objective: (1) To increase our understanding of the basic biology of these tumors, with a distinct possibility that new therapeutic targets may be uncovered. Examples of this type are ErbB-2 and methotrexate resistance factors, (2) To develop a set of biologic prognostic indicators which can be measured at diagnosis and which will be predictive of response and outcome in osteosarcoma. These could then be used in subsequent treatment programs to determine therapy, avoiding excessive toxicity to good risk patients and reserving alternative, more intensive therapy for those at standard risk. Examples include loss of heterozygosity at Rb and MDR, (3) To determine the feasibility of various assays and to develop a reliable mechanism of distributing osteosarcoma samples to various intergroup investigators, with centralized reporting of laboratory results and adequate quality control.

Technical Approach: At the time of biopsy or surgery (definitive or recurrence), tumor tissue that is not needed for diagnosis will be processed and forwarded to the Cooperative Human Tissue Network (CHTN) for distribution. Specimens will include: tumor tissue (Formalin-fixed or formalin-fixed paraffin embedded block or 30 unstained slides; blood samples (heparinized (10 ml), serum (14 ml)). Assays being performed: MDR Immunohistochemistry (University of Rochester); MDR Functional Assays/MRP (Memorial Sloan-Kettering); Methotrexate Transport & Metab (Memorial Sloan-Kettering);Topoisomerase II (Yale University); Bcl-2/Bax (Yale University); Rb/p53 (Fels Institute); ErbB-2 (Memorial Sloan-Kettering); MDM2 (Memorial Sloan-Kettering); pl6/p2l (Hospital for Sick Children); LOH at 3q,18q (Fels Institute); sis,gli,fos (Yale University); SV40 (University of Colorado); myc,RAS (Memorial Sloan-Kettering); metalloproteinase (Yale University); c-met/HGF (Yale University); IGF-I/IGF-IR (University of Maryland); Telomerase (St. Jude Children's); Ploidy (Dana Farber)

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/054 **Status**: Ongoing

Title: COG P9934: Systemic Chemotherapy, Second Look Surgery and Conformal Radiation Therapy Limited to the Posterior Fossa and Primary Site for Children > 8 Months and < 3 Years with Non-metastatic Medulloblastoma - A Children's Oncology Group Phase III Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Children's Oncology Group **Facility**: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Marc G. Cote, MC; LTC William B. Reece, MC; COL John D. Werschkul, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/23/2001	Jan 06	

Study Objective: (1) To determine if the proposed treatment for children > 8.0 months and < 3 years of age at registration with non-metastatic (M0) medulloblastoma is more effective than the combined treatments given to children of the same age and extent of disease on POG 9233, as measured by event-free survival (EFS) rates, (2) to assess the feasibility and safety of the planned use of second look surgery and focal conformal radiation therapy following chemotherapy, (3) to determine the acute and chronic toxicities associated with the above treatment regimens, (4) to describe the neuropsychological and neuroendocrine effects of this systemic chemotherapy, surgery, and local, conformal radiation, (5) to determine the feasibility and validity of a centralized telephone interview based data collection method for neuropsychological evaluations, and (6) to determine the incidence of atypical teratoid/rhabdoid tumor (AT/RT) in children enrolled on this study.

Technical Approach: In this study for young children with relatively low risk medulloblastoma, we will test a new therapeutic approach which begins with maximal safe tumor resection and a 16-week, 4-drug induction chemotherapy regimen of cyclophosphamide, vincristine, cisplatin, and oral etoposide. In comparison to the chemotherapy regimens of studies 8633 and 9233, cisplatin is introduced earlier, and given concurrently with the other agents. As well, etoposide is given in an oral form. Based upon the compelling data that outcome is clearly linked to a complete surgical resection the proposed therapy includes a 'second look' surgery following induction chemotherapy in an attempt to resect residual disease in those patients who have failed to achieve a complete response to chemotherapy. To improve local control rates this clinical trial will test the use of conformal radiation therapy and will determine if these techniques can reduce radiation-related side effects. Following recovery from the initial phase of treatment, patients will receive a maintenance phase of chemotherapy, using cyclophosphamide, vincristine, and the prolonged administration of oral etoposide, to complete one year of therapy.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/023 **Status**: Ongoing

Title: COG P9963: A Phase II Trial of Rebeccamycin Analogue (NSC #655649) in Children with Solid Tumors, A C.O.G. Phase II Study

Principal Investigator: LTC Kelly J. Faucette, MC

Department: Childrens Oncology Group **Facility**: MAMC

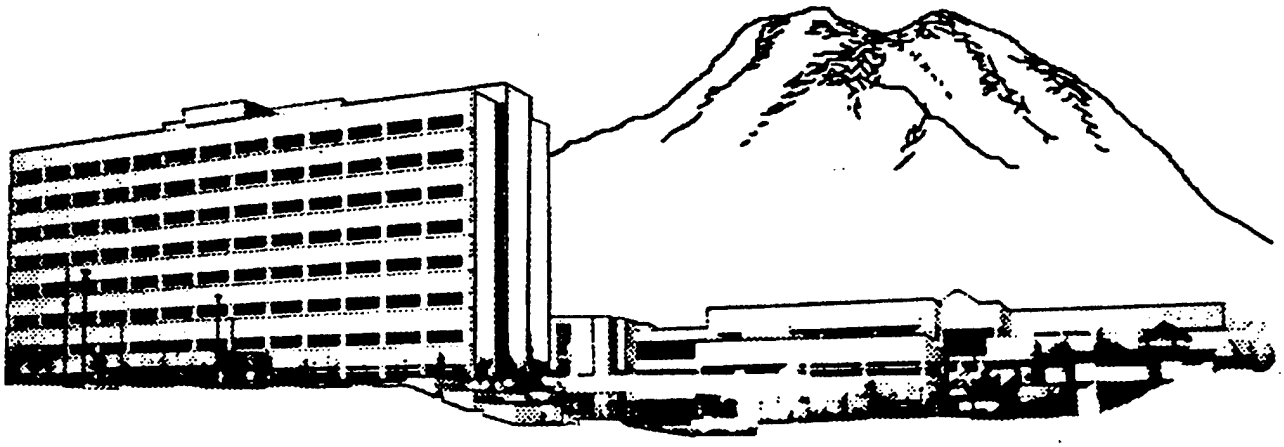
Associate Investigator(s): MAJ Robert G. Irwin, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/28/2000	Nov 03	N/A

Study Objective: Primary Objective: (1) To determine if the proposed treatment for children > 8.0 months and < 3 years of age at registration with non-metastatic (M0) medulloblastoma is more effective than the combined treatments given to children of the same age and extent of disease on POG 9233, as measured by event-free survival (EFS) rates. Secondary Objectives: (2) To assess the feasibility and safety of the planned use of second look surgery and focal conformal radiation therapy following chemotherapy , (3) to determine the acute and chronic toxicities associated with the above treatment regimens, (4) to describe the neuropsychological and neuroendocrine effects of this systemic chemotherapy, surgery, and local, conformal radiation, (5) to determine the feasibility and validity of a centralized telephone interview based data collection method for neuropsychological evaluations and (6) to determine the incidence of atypical teratoid/rhabdoid tumor (AT/RT) in children enrolled on this study.

Technical Approach: This study for young children with relatively low risk medulloblastoma will test a new therapeutic approach. This is designed to (1) increase the disease control rate at 12 months from registration on study by introducing potential surgery and radiation therapy for local disease after four months of systemic chemotherapy, and (2) decrease the early failure rate of chemotherapy utilizing a new schedule of known effective agents. The approach begins with maximal safe tumor resection and a 16-week, 4-drug induction chemotherapy regimen of cyclophosphamide, vincristine, cisplatin, and oral etoposide. In comparison to the chemotherapy regimens of studies 8633 and 9233, cisplatin is introduced earlier, and given concurrently with the other agents. As well, etoposide is given in an oral form. Based upon the compelling data that outcome is clearly linked to a complete surgical resection the proposed therapy includes a 'second look' surgery following induction chemotherapy in an attempt to resect residual disease in those patients who have failed to achieve a complete response to chemotherapy. To improve local control rates this clinical trial will test the use of conformal radiation therapy and will determine if these techniques can reduce radiation-related side effects. Following recovery from the initial phase of treatment, patients will receive a maintenance phase of chemotherapy, using cyclophosphamide, vincristine, and the prolonged administration of oral etoposide, to complete one year of therapy.

Progress: No subjects enrolled in this study at MAMC in FY01. Subject enrollment continues.



Detail Summary Sheets

Gynecology Oncology Group

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 81/035 **Status**: Ongoing

Title: GOG 0041: Surgical Staging of Ovarian Carcinoma

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/16/1981	Jan 86	9/25/2001

Study Objective: To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

Technical Approach: This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a completed and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

Progress: This study closed to patient entry, 12 Feb 87. Thirteen patients were enrolled. Eight patients remain disease free and continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 81/105 **Status**: Ongoing

Title: GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/21/1981	Mar 98	9/25/2001

Study Objective: To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG 0025.

Technical Approach: Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

Progress: This study closed to patient entry, 20 Jul 85. Six patients were enrolled. One patient remains disease free after completing therapy, and continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 84/033 **Status**: Ongoing

Title: GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/17/1984	Dec 88	9/25/2001

Study Objective: To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

Technical Approach: Patients without prior chemotherapy of radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for five years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

Progress: This study closed to patient entry 25 Feb 92. Ten patients were enrolled; of these, 8 patients continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 84/074 **Status**: Ongoing

Title: GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/17/1984	Jul 89	9/25/2001

Study Objective: To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

Technical Approach: Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

Progress: This study closed to patient entry, 10 Feb 92. One patient continued to be followed at MAMC during FY01 and remains disease-free off-therapy.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 86/089 **Status**: Ongoing

Title: GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/15/1986	Feb 94	9/25/2001

Study Objective: To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

Technical Approach: Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

Progress: This study closed to patient entry, 3 Dec 90. Two patients, disease free after completion of therapy, continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 87/104 **Status**: Ongoing

Title: GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Donald H. Kull, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/21/1987	Indef	9/25/2001

Study Objective: To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

Technical Approach: All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

Progress: This study closed to patient entry, 18 Dec 95. One patient, enrolled in FY 88, remains disease free and continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 87/028 **Status**: Ongoing

Title: GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
11/21/1986	Indef	9/25/2001

Study Objective: In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

Technical Approach: The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin in patients with ovarian cancer. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m2 I.V., on day 1 plus cisplatin, 100 mg/m IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

Progress: This study closed to patient entry, 14 Mar 94. Five patients were enrolled. One patient, who remains disease free, continued to be followed at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 87/091 **Status**: Ongoing

Title: GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC; COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/19/1987	Indef	9/25/2001

Study Objective: To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

Technical Approach: Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

Progress: This study closed to patient entry, 3 Jul 95. Three patients were enrolled. All are currently clinically disease free and continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/086 **Status**: Ongoing

Title: GOG 0109 (SWOG 8797): 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 I-A2, I-B, and II-A Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/02/1991	Sep 94	9/25/2001

Study Objective: To determine whether the combination of 5-fluorouracil (5-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 I-A2, I-B, and II-A carcinoma of the cervix and to determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

Technical Approach: Patients must have primary, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, clinical stages I-A2, I-B, or II-A and must have had a radical hysterectomy with total pelvic lymphadenectomy and para-aortic sampling. Patients must have, at surgical evaluation, either histologically confirmed positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins. Patients with confirmed positive para-aortic lymph nodes are not eligible. Patients must not have received prior chemotherapy, immunotherapy (including biologics), hormonal therapy, or pelvic irradiation. Patients will be randomly assigned to receive either 5-FU and cisplatin plus pelvic irradiation or pelvic irradiation alone. Patients with positive high common iliac lymph nodes will receive extended field para-aortic irradiation. Irradiation and chemotherapy will begin simultaneously within six weeks after surgery. Chemotherapy will be given once a week every three weeks for four cycles. Radiation therapy will be given for six weeks. After completion of therapy, patients will be followed every 3 months for two years and every 6 months thereafter. Formal analysis of progression-free and overall survival will be performed at 2 1/2 years after the start of patient accrual to determine if consideration should be given to early termination of either treatment arm.

Progress: This study closed to patient entry, 20 May 94. One patient, enrolled in 1991, remains without evidence of recurrence of disease and continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/074 **Status**: Ongoing

Title: GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, and Unclassified Sex Cord Stromal Tumor)

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Mark E. Potter, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/12/1991	Indef	9/25/2001

Study Objective: To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma as a first-line regimen.

Technical Approach: Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

Progress: This study closed to patient entry, April 1997. One patient had disease detected at second look laparotomy in Sep 98. However, she still has no clinical evidence of disease and continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/063 **Status**: Ongoing

Title: GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: GOG **Facility**: MAMC

Associate Investigator(s): COL Mark E. Potter, MC

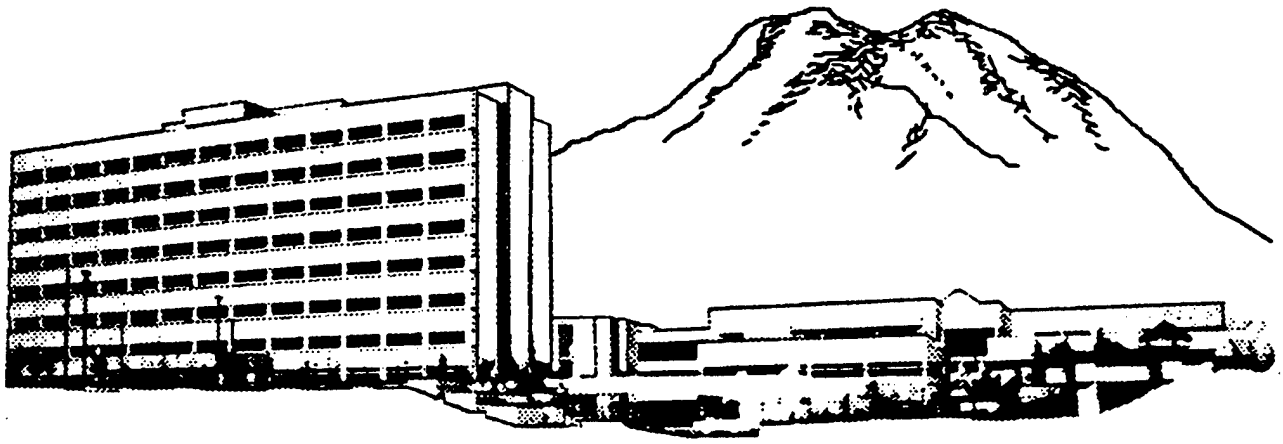
Start Date:	Est. Completion Date:	Periodic Review:
03/05/1993	Oct 97	9/25/2001

Study Objective: To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

Technical Approach: This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m2 not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens.

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered.

Progress: This study closed to patient entry, April 1997. One patient was enrolled who remains without evidence of recurrence of disease and continued to be followed at MAMC during FY01.



Detail Summary Sheets

National Surgical Adjuvant Breast & Bowel Project

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/001 **Status**: Completed

Title: NSABBP C-06: A Clinical Trial Comparing Oral Uracil/Ftorafur (UFT) Plus Leucovorin (LV) with 5-Fluorouracil (5-FU) Plus LV in the Treatment of Patients with Stages II and III Carcinoma of the Colon

Principal Investigator: MAJ Patrick Williams, MC

Department: NSABBP **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/20/1998	Sep 02	10/26/99

Study Objective: (1) To compare the relative efficacy of UFT + LV with that of 5-FU + LV in prolonging DFS and S, (2) to evaluate the prognostic significance of the proposed biomarkers, alone or in combination, in patients treated with 5-FU + LV or UFT + LV, (3) to evaluate relationships of various biomarkers to each other and to evaluate their association with patient and tumor characteristics, (4) to compare QOL in patients with stage II or III carcinoma of the colon treated with either the 5-FU + LV regimen or the UFT + LV regimen.

Technical Approach: Patients will be randomized to one of two chemotherapy regimens following resection of stage II and III carcinoma of the colon. Group 1 will receive 5-Fluorouracil plus high-dose Leucovorin and Group 2 will receive Uracil/Ftorafur plus Leucovorin. Patients will be stratified according to the number of positive nodes.

Progress: This protocol closed to patient accrual 31 Mar 99. One patient enrolled in FY99 at MAMC died of progressive disease. The protocol permanently closed at MAMC, 30 Nov 00.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/147 **Status**: Ongoing

Title: NSABP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum

Principal Investigator: MAJ Patrick Williams, MC

Department: NSABBP **Facility**: MAMC

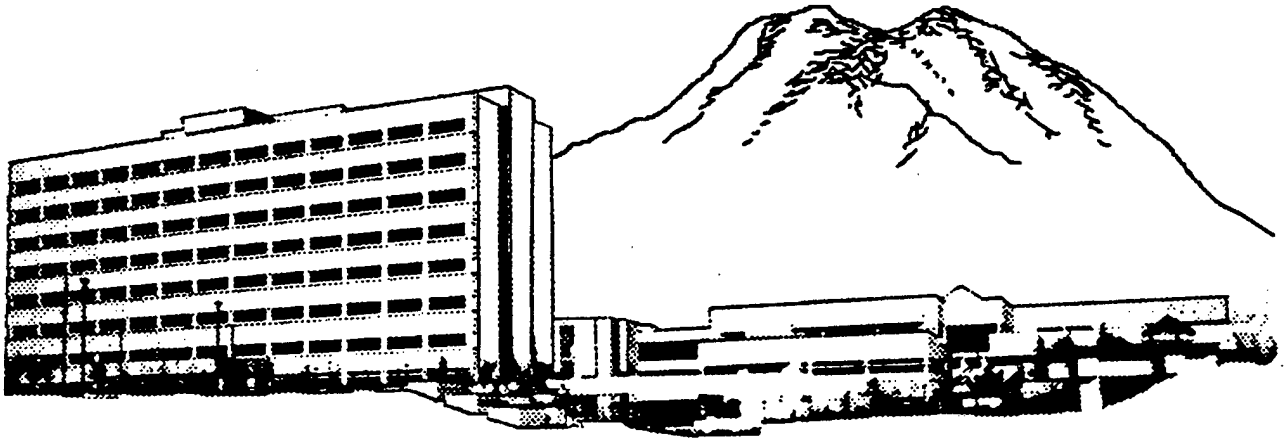
Associate Investigator(s): MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Ines Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/06/1993	Jul 98	7/24/2001

Study Objective: 1). To determine whether the administration of chemotherapy (chemo) with radiotherapy (RTX) preoperatively is more effective than administration of chemo and RTX (C&R) postoperatively in improving disease-free survival and survival in patients with operable carcinoma of the rectum. 2). To determine if the administration of the above C&R preoperatively results in improve-ment local recurrence rates when compared with the regimen administered post-operatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative C&R and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative C&R on the tumor size and pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdomino-perineal resection and local excision alone.

Technical Approach: Patients with operable adenocarcinoma of the rectum wiill receive seven cycles of 5-FU (FU) + leucovorin (LV) and radiotherapy (RTX), where the first three cycles are given preoperatively and the remaining four postoperatively, to seven cycles of FU-LV and RTX given postoperatively. The patients will be randomized into 2 groups. Group 1 patients, in cycle 1, will receive LV 500 mg/m2 by IV infusion and FU 500 mg/m2 will be started 1 hr later. Treatment will be given weekly for 6 weeks followed by a rest period. Treatment will be restarted 21 days after the date of administration of the sixth dose of the previous cycle. RTX will begin after completion of cycle 1. FU 325 mg/m2/day and LV 20 mg/m2/day will be given for 5 days during the first and fifth weeks of RTX (cycles 2 and 3). Surgery will be performed after completion of radiation therapy. After recovery from surgery, four more cycles of FU with LV, as in cycle 1, will be given for a total of seven cycles. Groups 2 patients should have surgery performed no later than 3 weeks after randomization. Chemo will begin after recovery from surgery is complete but no later than 4 weeks postoperatively. LV and FU will be administered as in Group 1. RTX will begin after completion of cycle 1. Cycle 4 should begin after completion of RTX when counts allow, but no later than 5 weeks. Four more cycles of FU with LV will be given for a total of seven cycles.

Progress: This protocol closed to patient accrual, 27 Aug 99. One patient enrolled at MAMC and continues to be followed.



Detail Summary Sheets

Southwest Oncology Group

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 83/056 **Status**: Ongoing

Title: SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC James E. Congdon, MC; COL Friedrich H. Stutz, MC; COL Irwin B. Dabe, MC; MAJ Timothy J. O'Rourke, MC; MAJ Alfred H. Chan, MC; MAJ Thomas M. Baker, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/18/1983	Feb 85	2/22/2000

Study Objective: To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whose pathological size is >3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

Technical Approach: Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

Progress: This study closed to patient entry 15 May 88. Twelve patients enrolled in previous years. Three have died and nine continue to be followed at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/119 **Status**: Ongoing

Title: SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Raymond S. Lance, MC; MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Kurt L. Hansberry, MC; CPT Timothy O. Taylor, MC; CPT Michael D. Bagg, MC; CPT Bradley F. Schwartz, MC; MAJ J. Brantley Thrasher, MC; LTC Luke M. Stapleton, MC; LTC Kenneth A. Bertram, MC; MAJ Patrick L. Gomez, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/03/1994	Jun 98	5/23/2000

Study Objective: 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

Technical Approach: Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

Progress: This study closed to patient entry, 17 Jan 97. One patient enrolled at MAMC and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 88/066 **Status**: Ongoing

Title: SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; COL Irwin B. Dabe, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/15/1988	Jun 91	6/26/2001

Study Objective: To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP-->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

Technical Approach: Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study. MOPP: Nitrogen mustard, 6 mg/m2 IV, days 1 and 8, Vincristine, 1.4 mg/m2 IV, days 1 and 8, Procarbazine, 100 mg/m2 PO per day x 14 days, Prednisone 40 mg/m2 PO per day x 14 days. ABVD: Adriamycin, 25 mg/m2 IV, days 1 and 15, Bleomycin, 10 units/m2 IV, days 1 and 15, Vinblastine, 6 mg/m2 IV days 1 and 15, DTIC, 375 mg/m2 IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m2 IV, day 8; bleomycin, 10 units/m2 IV day 8; and vinblastine, 6 mg/m2 IV, day 8.

Progress: This study closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 89/080 **Status**: Ongoing

Title: SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Nodes and Positive Hormone Receptors

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/15/1989	Sep 99	8/28/2001

Study Objective: To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

Technical Approach: Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

Progress: This study closed to patient entry 1 Aug 95. Seven patients enrolled in this study at MAMC. One patient died in FY96, and 6 patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/087 **Status**: Ongoing

Title: SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; MAJ Paul C. Sowray, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/02/1991	Aug 95	7/25/2000

Study Objective: To acquire fresh snap-frozen lymphoma tissue to establish a central lymphoma tissue repository; to establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group; to use repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status; and to determine if pretreatment phenotype or genotype predict patient outcome with respect to complete response rate, time to progression, and survival using prospective trial designs.

Technical Approach: Patients will be treated according to guidelines outlined in the specific SWOG studies. Treatment decisions will not be based on findings of the Central Lymphoma Laboratory, although clinical variables will be correlated with laboratory findings. The tissue samples will be taken from the pretreatment diagnostic biopsy or rebiopsy based on clinical decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (hematoxylin and eosin) histologic section with accompanying pathology report. The H&E stained slide and report will accommodate morphologic correlation with immunologic findings. Tissue section analysis will be performed at the University of Arizona using three stage immunohistochemistry. Future molecular studies entailing hybridization studies of RNA and DNA fragments using DNA probes will be performed as outlined in future protocols.

Progress: This is a companion study using tissue from other SWOG protocols. Tissue has been collected on three patients. Two patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 90/027 **Status**: Ongoing

Title: SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/19/1990	Dec 99	11/27/2001

Study Objective: To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

Technical Approach: Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

Progress: This study closed to patient entry 15 Feb 94. Six patients enrolled at MAMC in previous years. Two patients have been lost to follow-up, four continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/067 **Status**: Ongoing

Title: SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Howard Davidson, MC; MAJ Paul C. Sowray, MC; MAJ Everardo E. Cobos Jr., MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Patrick L. Gomez, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/14/1991	Jun 94	5/23/2000

Study Objective: To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.

Technical Approach: Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck.

Progress: Four patients enrolled in this study at MAMC in previous years and three continue to be followed. No patients enrolled in this study at MAMC in FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 90/029 **Status**: Ongoing

Title: SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History Follow-up Study in Low-Risk, Node Negative Patients

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Kenneth A. Bertram, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/19/1990	Jan 93	11/27/2001

Study Objective: To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

Technical Approach: Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

Progress: This study closed to patient entry 15 Jan 93. Nine patients enrolled in previous years; however, one patient died in FY97 and another patient was transfered. Seven patients continued to be followed under this study at MAMC during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 89/021 **Status**: Ongoing

Title: SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin + 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in Selected Patients with Duke's B or C Colon Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; COL Irwin B. Dabe, MC; MAJ Mark H. Kozakowski, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; MAJ Everardo E. Cobos Jr., MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/17/1989	Feb 92	12/18/2001

Study Objective: To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

Technical Approach: Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/ mesenteric implants resected enbloc (yes/no); and obstruction (yes/no). RANDOMIZE TO: (1) Observation; (2) Leucovorin 20 mg/m2 + 5-FU 425 mg/m2; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m2 + 5-FU 600 mg/m2; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

Progress: Sixteen patients enrolled at MAMC prior to closure to patient entry, 30 Jul 92. Seven patients have died from their disease and nine continued to be followed during FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/089 **Status**: Ongoing

Title: SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; LTC Luke M. Stapleton, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/02/1991	Aug 95	7/25/2000

Study Objective: To establish a central lymphoma serum repository that will serve as a resource to provide specimens for current and future scientific studies and to utilize the Southwest Oncology Group clinical data base to perform clinicopathologic correlations with the results of those studies.

Technical Approach: No therapy will be utilized in this study and patient treatment will not be based on this study. Patients must meet the eligibility criteria and be registered to one of the following SWOG protocols: 8516, 8809, 8736, or 8816. Ten cc's of blood will be drawn prior to protocol treatment and shipped to the SWOG Lymphoma Serum Repository at Loyola University Medical School.

Progress: This is a companion protocol to other SWOG protocols. Two specimens have been submitted in previous years. Those patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 90/056 **Status**: Ongoing

Title: SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC John A. Vaccaro, MC; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/16/1990	Mar 93	2/22/2000

Study Objective: To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

Technical Approach: Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

Progress: This study closed to patient entry, 1 Apr 92, with two patients enrolled at MAMC. One patient died, FY93, and the other continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/056 **Status**: Terminated

Title: SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/05/1993	Mar 98	12/18/2001

Study Objective: 1) To estimate response rates and survival in patients with Waldenstrom's Macroglobulinemia (WM) receiving fludarabine, with stratification according to whether they have prior therapy. 2) To define prognostic factors that may relate to response, time to progression and overall survival, separately for newly diagnosed and previously treated patients. 3) To estimate the associated hematologic and non-hematologic toxicities.

Technical Approach: Persons with a diagnosis of WM and meeting enrollment criteria can be registered for this study. After the initial workup, to include bone marrow aspiration, those patients without symptoms and with no progression of the disease will be entered in the Observation phase. If they are symptomatic or have progression of the disease or if onset of symptoms and/or progression occurs during the Observation phase immediate Re-registration to the Treatment phase will occur. Fludarabine 30 mg/m2 IV will be administered on days 1 - 5. This schedule will be repeated every 28 days for 4 cycles until the patient's condition is stable without remission, progression occurs, or the disease is stable. If the disease becomes stable without remission or progresses, treatment will be stopped. If there is complete remission, partial remission or improvement the patient will receive an additional 4 cycles of therapy or 2 cycles beyond maximum response, whichever occurs earlier.

Progress: The protocol closed to patient accrual, 1 Sep 98. Two patients enrolled in FY93; however, one patient died of progressive disease and one patient continued to be followed in FY01. This study is now terminated at MAMC and the patient enrolled will continue to be followed under SWOG S9808.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/094 **Status**: Ongoing

Title: SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; LTC Luke M. Stapleton, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/06/1991	Aug 94	8/28/2001

Study Objective: (1) To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on Southwest Oncology Group protocols and at various times in the course of their treatment, (2) To estimate correlations between the presence of cytogenetic features and of clinical, pathophsiological, cellular, or molecular characteristics in these patients and (3) To provide quality control for all Southwest Oncology Group cytogenetic data.

Technical Approach: This is a companion protocol for all Southwest Oncology Group leukemia protocols. Bone marrow or peripheral blood specimens will be forwarded to a SWOG referral cytogenetics laboratory (Oregon Health Sciences University, Portland, Oregon is the nearest to Madigan Army Medical Center). The referral lab will return a cytogenetics report to MAMC. Specimens will be collected as outlined in each individual leukemia protocol.

Progress: No patients enrolled in this study at MAMC in FY01. Five patients enrolled in previous years. Three patients died, two patients continue to be followed. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/033 **Status**: Ongoing

Title: SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for Patients with Local Regional Disease

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Kenneth A. Bertram, MC; LTC Luke M. Stapleton, MC; MAJ Paul C. Sowray, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; COL Joseph F. Homann, MC; COL Daniel G. Cavanaugh, MC; MAJ Everardo E. Cobos Jr., MC

Start Date:	Est. Completion Date:	Periodic Review:
02/01/1991	Jan 94	12/18/2001

Study Objective: To compare, using a prospective controlled randomized study design, the outcomes of therapy of surgery alone versus pre and postoperative chemotherapy and surgery for patients with local regional esophageal cancer (outcome is defined as survival and relapse pattern); to assess the toxicities of a multimodality approach to esophageal carcinoma involving systemic chemotherapy and surgery (the toxicities of surgical resection as initial therapy or following chemotherapy will be assessed as operative morbidity and mortality); to compare the local and distant control rates with the two approaches and to define the pattern of failure; and to compare the impact on overall and disease free survival of multimodality therapy with surgery alone.

Technical Approach: Esophageal cancer is seen in over 10,000 patients a year in the United States and only about 7% of these patients are cured as demonstrated by a five year survival. This study is designed to see whether or not giving chemotherapy will improve that survival. To be eligible patients must have histologic proof of squamous cell carcinoma of the esophagus, disease limited to the total regional area (clinical stage T1-T3, NX,MO), no prior surgery, radiation therapy, or chemotherapy, and adequate bone marrow, liver function, renal function, and pulmonary reserve. Patients must be physiologically fit for proposed chemotherapy and surgery and be greater than 18 years of age. Patients will be randomized to surgery alone, or to receive three cycles of preoperative cisplatinum and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatinum and 5-FU, starting two to six weeks after surgery.

Progress: This study closed to patient entry 31 Dec 95. Two patients enrolled in this study at MAMC. One patient died of progressive disease and one patient continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/062 **Status**: Terminated

Title: SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Richard F. Williams, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/20/1995	Jan 99	1/25/2000

Study Objective: 1) To compare disease-free survival and overall survival between patients with T3NOM0 malignant melanoma who receive adjuvant immunotherapy with an allogeneic melanoma vaccine versus no adjuvant treatment. 2) To evaluate the toxicity of adjuvant immunotherapy with an allogeneic melanoma vaccine in patients with T3NOI10 malignant melanoma. 3) To explore the interaction between the patients' defined HLA types (i.e., whether they are compatible with the HLA phenotypes of the vaccine) and the vaccine treatment effectiveness in terms of disease-free survival and overall survival.

Technical Approach: The study is a randomized study of Interferon Alfa-2b as adjuvant immunotherapy in patients with T3NOM0 malignant melanoma following complete resection. After complete staging, including assessment of any abnormal lymph nodes by biopsy, patients will be randomized either to treatment with four cycles of intramuscular vaccine therapy or observation only and will be followed until death for recurrence.

Progress: This study has been terminated at MAMC. One patient enrolled in this study at MAMC in FY95 and will continue to be followed under SWOG 9808.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 91/069 **Status**: Ongoing

Title: SWOG 9040 (CALGB-9081, INT-0014): Intergroup Rectal Adjuvant Protocol, A Phase III Study

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/14/1991	May 93	5/23/2000

Study Objective: To determine the relative efficacy of: 5-FU; 5-FU plus leucovorin; 5-FU plus levamisole; and 5-FU plus leucovorin and levamisole when combined with pelvic radiation therapy in the treatment of Stages B-2 and C (TNM Stage II and III) rectal cancer. End points used will include local recurrence rates, probability of distant metastases, disease free survival rates, and overall survival.

Technical Approach: This will be a 4-armed study with the same radiation therapy program in all arms, but with varying drug regimens as listed in the objective. 5-FU with radiation therapy will comprise the control arm of the study. Patients will be randomized to treatment arms and they will be stratified by type of operation (abdominal perineal or anterior resection); nodal involvement (none, 1-3, or >3); and invasion through bowel wall or into adjacent organs (none, through muscularis propria, or adherence to or invasion of adjacent organs or structures). Each drug regimen will be given alone on days 1-5 and 29-33, followed by radiation therapy (five weeks) with concomitant chemotherapy on days 57-60 and 85-88. The chemotherapy regimen will then be repeated beginning 28 days after the completion of radiation therapy on days 1-5 and 29-33. If evidence of recurrence is obtained, protocol treatment will be discontinued and the patient followed until death. In the absence of recurrent disease, follow-up observations will be continued for a minimum of 5 years after surgery.

Progress: This study closed to patient entry, 22 Nov 92. Three patients enrolled in previous years and continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/104 **Status**: Ongoing

Title: SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/06/1994	May 98	4/24/2001

Study Objective: This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.

Technical Approach: Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of ademonas or second primary carcinomas.

Progress: This protocol closed to patient accrual 22 Nov 98. Sixteen patients enrolled in this study at MAMC. Two patients are deceased, fourteen continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/096 **Status**: Ongoing

Title: SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/16/1997	Apr 00	4/24/2001

Study Objective: 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.

Technical Approach: Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25' range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatinum alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatinum and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.

Progress: This study closed to patient entry, 29 Nov 99. Two patients enrolled in this study at MAMC and continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/032 **Status**: Ongoing

Title: SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/04/1992	Nov 95	11/27/2001

Study Objective: To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

Technical Approach: Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m2 PO X 14 days, doxorubuicin 30 mg/m2 IV days 1 & 8, and flurouracil 500 mg/m2 IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m2/96 hr and ThioTEPA 800 mg/m2/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m2/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of = 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while therapy is ongoing.

Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death).

At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per

arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about 0.09.

The BCG will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used. Then using the variance information given above, the variance of the difference of means at either time should have a variance of about 0.0099, and the covariance between the two times should be about 0.0079. If there is a constant difference in the scores, then the distribution of the test statistic would be approximately noncentral chi-square with 2 degrees of freedom and concentrality paraments 113*d*d. For a 5% level test, this gives a power of 82% for detecting a difference of d = 0.3.

Progress: This protocol closed to patient accrual 3 Aug 98. One patient enrolled in this study at MAMC and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/097 **Status**: Ongoing

Title: SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/06/1994	Sep 01	4/24/2001

Study Objective: The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA,IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

Technical Approach: Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

Progress: This study closed to patient entry, 24 Apr 00, when accrual goal was reached. Two patients enrolled in this study in FY94. One patient died in FY97 and the other patient continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/097 **Status**: Ongoing

Title: SWOG 9205: Central Prostate Cancer Serum Repository Protocol

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Robert L. Sheffler, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; MAJ Timothy P. Rearden, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/07/1993	Mar 95	5/22/2001

Study Objective: 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

Technical Approach: This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols. All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20C. Samples will be frozen and shipped to the Serum Bank Coordinator.

Progress: No patients enrolled in FY01 at MAMC. Two patients enrolled in this serum study in FY97, and two in previous years, for a total enrollment of four. Three patients have died; one patient continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/010 **Status**: Ongoing

Title: SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup

Principal Investigator: MAJ Raymond S. Lance, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): LTC Raymond A. Costabile, MC; MAJ J. Brantley Thrasher, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/01/1993	Nov 03	9/25/2001

Study Objective: The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

Technical Approach: Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

Progress: This protocol closed to patient entry 1 Jan 97. Total MAMC patients consented 101; patients with incomplete enrollment (i.e., did not receive study drug due to elevated PSA, etc) 18; patients voluntarily withdrawn 23, and patients transferred to another institution 2. Number of patients continuing on active protocol 58.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/136 **Status**: Ongoing

Title: SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; LTC Robert D. Vallion, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; MAJ Timothy P. Rearden, MC

Start Date:	Est. Completion Date:	Periodic Review:
07/02/1993	Jul 98	6/27/2000

Study Objective: To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

Technical Approach: Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

Progress: The protocol closed to patient accrual 9 Apr 97. Ten patients enrolled in this study. One patient was transferred to Keesler, three patients died, 6 patients continue to be followed at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/108 **Status**: Terminated

Title: SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ James S. D. Hu, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; LTC Robert D. Vallion, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/07/1993	May 98	4/24/2001

Study Objective: (1) To evaluate the response rate for refractory myeloma treated with topotecan, (2) to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study and (3) to measure topoisomerase levels in multiple myeloma cells.

Technical Approach: Patients with proven multiple myeloma, with protein criteria present, who have received exactly one prior regimen, and have shown, in the opinion of the investigator, to have disease progression are eligible for this study. All patients will receive topotecen 1.25 mg/m2 q.d. IV over 30 minutes on days 1-5 repeated q 21 days. This schedule will continue as long as patients show complete remission, partial remission or stable disease and toxicity is acceptable. Topotecen dosage can be adjusted on nadir counts of the preceding cycle. It is assumed that topotecen will be of interest if a true response rate of 20% or more is achieved in the treatment of patients with relapsed or refractory multiple myeloma.

Progress: This study closed to patient accrual 15 Feb 95. One patient entered in this study in FY93. This study is now terminated at MAMC and the patient enrolled will continue to be followed under SWOG S9808.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/092 **Status**: Ongoing

Title: SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; CPT Diana S. Willadsen, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/02/1993	May 95	3/28/2000

Study Objective: 1. To acquire fresh snap-frozen lymphoma tissue from patients who relapse or have recurrent disease after being treated on Southwest Oncology Group treatment protocols. 2. To establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group. 3. To use the repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status. 4. To examine the biology of therapy failure in relationship to changes in pretreatment and post-therapy iummunophenotypic data.

Technical Approach: Fresh frozen tissues will be acquired from relapsed patients for basic science protocols, both current and future, designed to better define the biology of relapsed non-Hodgkins's lymphoma. This is not a treatment protocol, nor will results be used to guide treatment decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (Hematoxylin and Eosin) histologic section with accompanying pathology report to The Department of Pathology at the University of Arizona in Tucson.

Progress: No patients have enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 93/166 **Status**: Ongoing

Title: SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ John R. Caton, MC; MAJ Richard F. Williams, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/03/1993	Oct 98	7/24/2001

Study Objective: To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T4BN0-2 colon cancer and selected patients with T3N1-2 colon cancer.

Technical Approach: This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

Progress: This study closed to patient entry, 17 Dec 96. One patient enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/111 **Status**: Ongoing

Title: SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + Levamisole Prior to and Following Combined Pelvic XRT + Bolus 5-FU + Leucovorin in Patients with Rectal Cancer, Phase III Intergroup

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/06/1994	May 98	4/24/2001

Study Objective: 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protacted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatrment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival. 2) To obtain descriptive information regarding relapse patterns and tolerance.

Technical Approach: Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 mg/M2/d) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to and following chemo-radiotherapy as follows: Arm A: bolus IV injection of 5-FU alone b. Arm B: protracted venous infusion of 5-FU alone; Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvid radiotherapy. After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years.

Progress: This study closed to patient entry Sep 00. Four patients enrolled in this study at MAMC. One patient died in FY96. Three patients continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/170 **Status**: Ongoing

Title: SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast Cancer Patients with 0-3 Positive Nodes

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/21/1994	Sep 98	8/28/2001

Study Objective: 1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide. 2) To obtain tumor tissue for biologic studies.

Technical Approach: Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

Progress: The protocol closed to patient entry, 1 May 97. One patient enrolled in this study at MAMC and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/058 **Status**: Terminated

Title: SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ John R. Caton, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/04/1994	Nov 03	3/27/2001

Study Objective: 1) To evaluate the reproducibility of a combined histopathologic grading system of breast cancer. 2) To evaluate the ability of the grading system to predict time to treatment relapse (TTR) and survival. 3) To use multivariate analyses to evaluate the prognostic importance of the grading data relative to the other clinical and biological factors determined as part of SWOG 8294.

Technical Approach: This is a pathology study utilizing the patient set from SWOG 8294. Patients reviewed as part of that study (where cases with adequate specimens for flow cytometry were evaluated and provisionally graded) will be registered to this study. Slides will be reviewed by three investigators and cases will be grouped into 3 prognostic categories. The power calculation for testing the association of this gradfing system with survival will be based on the "2 degree of freedom" logrank test. The Cox proportional hazards model will also be used in the analysis to adjust the comparisons for effects of other factors.

Progress: This study closed to patient accrual 5 Oct 95. Seven patients enrolled in this study in FY94. One patient died, and six patients continue to be followed. This study was terminated and the six patients will continue follow-up under SWOG S9808.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/121 **Status**: Ongoing

Title: SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell Lung Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; COL Walter G. Graves, MC; LTC Maceo Braxton Jr, MC; LTC Blaine R. Heric, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert D. Vallion, MC

Start Date:	Est. Completion Date:	Periodic Review:
06/03/1994	Jun 98	5/23/2000

Study Objective: 1) Access whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year) survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer. 2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases. 3) To obtain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

Technical Approach: Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/M2 IVPB days 1, 8, 29, 36 and VP-16 50 mg/M2 IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II. Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5- year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

Progress: One patient enrolled in this study in FY00 and continues to be followed. Two patients enrolled in FY95; however, both patients are now deceased. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/003 **Status**: Ongoing

Title: SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/21/1994	Oct 98	9/25/2001

Study Objective: To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

Technical Approach: Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

Progress: This study closed to patient accrual, 10 Sep 96. One patient enrolled in FY96 and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/093 **Status**: Ongoing

Title: SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; CPT Diana S. Willadsen, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/17/1995	Feb 99	2/22/2000

Study Objective: 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe (= grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.

Technical Approach: This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizible subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.

Progress: No patients enrolled in this study at MAMC in FY01. One patient enrolled in FY00 and continues to be followed. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 94/163 **Status**: Ongoing

Title: SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/21/1994	Sep 98	8/28/2001

Study Objective: To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

Technical Approach: Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

Progress: This protocol closed to patient accrual, 15 Apr 97. Nine patients enrolled at MAMC. Four patients have died, five continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 95/094 **Status**: Terminated

Title: SWOG 9415: Phase III Randomized Trial of 5-FU/Leucovorin/Levamisole versus 5-FU Continuous Infusion Levamisole as Adjuvant Therapy for High -Risk Resectable Colon Cancer, Intergroup

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/17/1995	Feb 99	2/22/2000

Study Objective: To compare the effectiveness of bolus 5-FU, leucovorin, levamisole versus continuous infusion 5-FU, levamisole as adjuvant therapy for patients with Stage B2, C1 or C2 colon cancer. This will be measured in terms of overall survival. Disease-free survival will be a secondary endpoint.

Technical Approach: This is an intergroup trial involving the Southwest Oncology Group, Eastern Cooperative Oncology Group and the Cancer and Leukemia Group B. Based on previous experience with accrual to INT-0089, and assuming that roughly 1/3 of patients eligible for that study will be entered we anticipate an annual accrual of approximately 600 patients having curative resection of B2, C1, or C2 colon cancer. The primary objective of this study is to compare the survival in patients with high risk resectable colon surgery treated in an adjuvant setting with either 5-FU, leucovorin, levamisole or continuous infusion 5-FU, levamisole. The continuous infusion arm would be judged superior if the true increase in survival is 35%. A secondary endpoint will be disease-free survival. The dose of continuous infusion 5-FU selected for this study of 250 mglm2/d is currently being piloted at an individual institution, and is lower than the common dose of 300 mg/m2/d, which required dose reductions in a previous pilot. In order to verify the appropriateness of this dose in the intergroup setting, we will evaluate toxicity and compliance in the first 40 patients randomized to the continuous infusion arm. Should the frequency of dose reductions or toxicities warrant concem, the study may be amended or temporarily closed while the continuous infusion therapy is reassessed.

Progress: This study closed to patient entry, 15 Dec 99 with one patient enrolled in FY97. This study is now terminated at MAMC and the patient enrolled will continue to be followed under SWOG S9808.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/134 **Status**: Ongoing

Title: SWOG 9419: Tumor Tissue Biopsy for Thymidylate Synthase Expression in Patients with Colorectal Cancer, Ancillary

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
08/15/1997	Apr 01	7/24/2001

Study Objective: 1) To measure thymidylate synthase (TS) expression by polymerase chain reaction in tumor biopsies prior to initiation of fluorinated pyrimidine based therapy in patients with disseminated colorectal cancer and correlate tumor response with level of TS expression; 2) To correlate TS expression in tumor tissue obtained during a potentially curative resection and disease-free survival in patients with Stage II and III large bowel cancer prior to receiving adjuvant therapy with 5-FU based regimen on targeted Southwest Oncology Group trials.

Technical Approach: Tissue samples from patients already on other SWOG protocols will be used. These protocols are: SWOG 9250, SWOG 9303, SWOG 9304, SWOG 9415, and SWOG 9420. Patient treatment will not be affected by registration on this protocol. TS expression will be measured using polymerase chain reaction. The following comparisons will be made: The relationship of TS expression (which may be the most important determinant of whether 5-FU will be effective) with tumor response in the disseminated setting and the relationship of TS expression with recurrence free survival in the post-operative adjuvant patients.

Progress: Five patients enrolled in this study at MAMC in previous years. Two patients have died, three continue to be followed under the treatment protocol. No patients enrolled in FY01, patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/039 **Status**: Ongoing

Title: SWOG 9431: Cytogenetic, Molecular, and Cellular Biology Studies in Metastatic Melanoma Patients, Ancillary

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ Richard F. Williams, MC; MAJ Matthew P. Jones, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
01/16/1998	Jul 01	11/27/2001

Study Objective: (1) To characterize the frequency of non-random cytogenetic abnormalities in regional and distant melanoma metastases (AJCC Stage III or IV) and explore their association with clinical outcome of melanoma patients enrolled onto Southwest Oncology Group trials; (2) to characterize the frequency of specific genetic alterations at either the DNA, mRNA, or protein level and explore the association of these abnormalities with clinical outcome in patients with regional and distant metastases (AJCC Stage III or IV) who are enrolled on Southwest Oncology Group melanoma trials. The specific genes to be studied in this protocol will initially include: p16 (MTS1), nm23; (3) to characterize the host immunologic response to metastatic melanoma by determining whether the in vitro pattern of cytokine expression is consistent with specific subsets of T helper cells (TH1 or TH2) within melanoma deposits. To explore whether host immunologic response varies based on the site of metastatic disease and/or correlates with clinical outcome in patients enrolled on Southwest Oncology Group trials; (4) To obtain peripheral blood, sera and paraffin embedded tumor blocks from patients with metastatic melanoma to create a tissue, cell and sera bank for future studies.

Technical Approach: Following informed consent, tissue and blood samples taken from biopsies will be sent to a special laboratory for storage and scientific testing.

Progress: No patients enrolled in this study in FY01 at MAMC. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/113 **Status**: Ongoing

Title: SWOG 9444: Gastrointestinal Tumor Repository Protocol, Ancillary

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/15/1998	Apr 02	8/28/2001

Study Objective: 1) To establish a central gastrointestinal tumor repository to serve as a tissue resource for current and future scientific studies, 2) to utilize the Southwest Oncology Group clinical database to perform clinicopathologic correlation with the results of those studies, and 3) to test new hypotheses as they emerge.

Technical Approach: Tissue samples obtained during biopsies will be forwarded to a special laboratory for storage and scientific testing.

Progress: One patient enrolled in the study in FY98 and continues to be followed under the treatment protocol. No patients enrolled in this study at MAMC in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/041 **Status**: Completed

Title: SWOG 9510: Evaluation of Topotecan in Hormone Refractory Prostate Cancer, Phase II

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/19/1996	Dec 00	11/28/2000

Study Objective: 1) To evaluate the response (CR and PR only) rate to topotecan in patients with metastatic, hormone-refractory prostate cancer. 2) To assess the qualitative and quantitative toxicities of topotecan administered in a phase II study to patients with metastatic, hormone-refractory prostate cancer.

Technical Approach: Prostate cancer that is refractory to standard first line hormonal manipulations including surgical and chemical orchiectomy has a median survival of about 6 months. The standard of care for hormone refractory prostate cancer is not defined. Response to chemotherapy is poor at about 10 to 15%. This study will assess the response rate and toxicities of Topotecan in hormone refractory prostate cancer patients. The schedule with a 21 day infusion had been tested at New York University and showed only some grade 3 and one grade 4 myelotoxicity. Other side effects are fatigue, nausea, vomiting and diarrhea.

Progress: This protocol closed to patient accrual, 15 Aug 99. Three patients enrolled in this study at MAMC died of progressive disease and the study is now permanently closed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/095 **Status**: Ongoing

Title: SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
04/19/1996	May 99	3/27/2001

Study Objective: 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

Technical Approach: The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

Progress: This study closed to patient entry, 1 Nov 99, due to low patient accrual. Four patients enrolled in this study at MAMC and continued to be followed in FY01.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 96/118 **Status**: Ongoing

Title: SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; CPT Brent L. Kane, MC; LTC Kenneth A. Bertram, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/17/1996	Jun 00	4/24/2001

Study Objective: 1) To determine the efficacy of concurrent cisplatinum and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.

Technical Approach: In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatinum with concurrent radiation therapy may help in local control. This data comes from in vitro as well as in vivo data showing cisplatinum may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatinum and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity.

Progress: The study was reactivated, 24 Apr 01, to continue follow-up on one patient enrolled in this study in FY96 at MAMC. The patient had been reported lost to follow-up, 23 May 00, and the protocol reported as completed at that time.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 98/112 **Status**: Ongoing

Title: SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
09/15/1998	Sep 02	8/28/2001

Study Objective: (1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer, (2) to evaluate a panel of prognostic markers, in order to correlate these measures with survival and recurrence after adjuvant therapy in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer. The specific aims of the companion study will be: (a) to determine whether alterations in the expression of cell cycle related genes (thymidylate synthase, p53, and the cyclin-dependent kinase inhibitors p21 and p27) predict the risk of survival and recurrence in this patient population, (b) to determine whether alterations in markers of metastatic potential-expression of DCC and measures of tumor angiogenesis (microvascular density and vascular endothelial growth factor expression)-predict the risk of survival and recurrence in this patient population, (c) to determine whether a marker of cellular differentiation-sucrase isomaltase-predicts the risk of survival and recurrence in this patient population, and (d) to determine whether interactions among these tumor markers identify subsets of patients with significantly altered outcome.

Technical Approach: Subjects will be randomized and assigned to one of two treatment groups following standard surgical removal of their tumor. Group 1 will receive standard care which is surgery with no additional therapy after the tumor has been removed. Subjects will continue with routine check-ups, doctor visits and test. Group 2 will receive five antibody treatments using MoAb 17-1A. Subjects will receive the drug by as an intravenous infusion over a 2-hour time period once each 28 days. This 2-hour infusion will be repeated every 4 weeks for a total of 5 treatments. During treatment, various blood tests and x-rays will be used to determine whether the disease has returned. With subject's approval, tissue, body fluids, and other specimens obtained during the normal course of treatment will be forwarded to a special research laboratory for storage and scientific testing. Subjects will also be asked to complete a background information form to help define groups of patient being treated.

Progress: One patient enrolled in this study in FY98 at MAMC and continues to be followed. No patients were enrolled in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/037 **Status**: Completed

Title: SWOG C9732: A Randomized Phase III Study Comparing Etoposide and Cisplatin with Etoposide, Cisplatin and Paclitaxel in Patients with Extensive Small Cell Lung Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 02	1/23/2001

Study Objective: To determine whether the addition of paclitaxel to standard chemotherapy treatment (etoposide/cisplatin) improves the survival of patients with extensive SCLC and to compare the tumor response rate and failure-free survival of patients with extensive SCLC who have received etoposide/cisplatin with or without paclitaxel and describe and compare the toxicities associated with etoposide/cisplatin treatment versus etoposide/cisplatin/paclitaxel treatment.

Technical Approach: This study compares two types of chemotherapy to determine the standard of care for extensive small cell lung cancer. Eligible patients will be randomized to receive one of two treatment regimens: Treatment 1 chemotherapy with etoposide and cisplatin or Treatment 2 chemotherapy with etoposide, paclitaxel and cisplatin. Treatment 1, patients will receive etoposide IV each day for 3 days and cisplatin, IV will be given with the first dose of etoposide. This treatment will be repeated every 21 days for a total of 6 treatment courses. Treatment 2, patients will receive paclitaxel and cisplatin, IV on day 1, and etoposide IV days 1-3. G-CSF will be started on days 4-18 to help blood cell counts to recover. This treatment will be repeated every 21 days for a total of 6 treatment courses.

Progress: This study closed to patient enrollment, 1 Jul 01. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/014 **Status**: Ongoing

Title: SWOG C9741: A Randomized Phase III Trail of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
12/15/1998	Dec 01	11/27/2001

Study Objective: (1) To compare sequential chemotherapy with Doxorubicin, Paclitaxel, and Cyclophosphamide to combined Doxorubicin and Cyclophosphamide followed by Paclitaxel for disease-free and overall survival, (2) to determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy courses from 21 to 14 days) will improve disease-free and overall survival, and (3) to compare the toxicity for patients treated with sequential Doxorubicin, Paclitaxel, and Cyclophosphamide with toxicity for patients with concurrent Doxorubicin plus Cyclophosphamide followed by Paclitaxel at 14 and 21 day intervals.

Technical Approach: This is a randomized comparison of several aggressive combination chemotherapy regimens in the treatment of high-risk breast cancer due to positive lymph nodes. It compares the current standard of care for node positive breast cancer with several more aggressive variations. All patients will receive the same number of drugs and the same amount of drugs, but the order in which the drugs are given and the time between treatments (2 weeks versus 3 weeks) will be different. Arm 1, patients will receive Doxorubicin once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses followed by Cyclophosphamide once every 3 weeks x 4 total doses. Arm 2, patient will receive Doxorubicin once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses followed by Cyclophosphamide once every 2 weeks x 4 total doses. Arm 3, patients will receive Doxorubicin and Cyclophosphamide once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses. Arm 4, patients will receive patients will receive Doxorubicin and Cyclophosphamide once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses. G-CSF and Ciprofloxacin will be given concurrent with each arm to help ameliorate side effects of the treatments.

Progress: This study closed to patient accrual, 31 Mar 99. Three patients enrolled at MAMC in FY99 and continue to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/036 **Status**: Ongoing

Title: SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 02	1/23/2001

Study Objective: (1) To determine whether docetaxel improves disease-free survival and overall survival when compared to paclitaxel following 4 cycles of doxorubicin-cyclophosphamide therapy (2) To determine whether weekly administration of taxanes (paclitaxel or docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with the conventional (every 3 weeks) schedule for 4 cycles following 4 cycles of doxorubicin-cyclophosphamide therapy (3) To compare the toxicity of docetaxel given weekly for 12 weeks to that of paclitaxel given every 3 weeks for 4 cycles (4) To compare the toxicity of paclitaxel given weekly for 12 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles (5) To compare the toxicity of paclitaxel given every 3 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles and (6) To compare the toxicity of paclitaxel given weekly for 12 weeks to that of docetaxel given weekly for 12 weeks.

Technical Approach: This study compares aggressive chemotherapy schedules to standard of care for high risk node positive breast cancer. Eligible patients will be randomized into one of four treatment arms: Arm A, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (the standard treatment); Arm B, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (lower dose than standard); Arm C, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (medium dose); and Arm D, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (low dose).

All Arms will receive adriamycin and cyclophosphamide, IV once every 3 weeks for 4 cycles. Then Arm A will receive taxol, IV once every 3 weeks for 4 treatments. Arm B will receive taxol IV once a week for 12 weeks of treatment. Arm C will receive Taxotere IV once every 3 weeks for 4 treatments. Arm D will receive taxotere once a week for 12 weeks of treatment.

Progress: Six patients enrolled in this study at MAMC in FY01 and six enrolled in FY00, for a total enrollment of 12 patients. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/071 **Status**: Ongoing

Title: SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytoxan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/25/1999	Apr 03	5/22/2001

Study Objective: To determine whether Adriamycin/Taxotere will improve disease-free survival and overall survival when compared to Adriamycin/Cytoxan in lymph node positive (1-3 positive nodes) and high risk lymph node negative breast cancer. To compare toxicity of Adriamycin/Taxotere to Adriamycin/Cytoxan.

Technical Approach: This is multi-site study with randomization to one of two arms: Adriamycin/Taxotere (AT) or Adriamycin/Cytoxan (AC). The dosages for the AT group: Adriamycin 60 mg/m2 IV and Taxotere 60 mg/m2 IV over 1 hour infusion every 3 weeks x 4 cycles. Cipro 500 mg PO b.i.d. starting Day 8 and continuing x 10 days. If a patient is allergic to Cipro, an alternative broad spectrum antibiotic may be used. Decadron 8 mg PO b.i.d., beginning one day prior to treatment with Taxotere and continued for two additional days; repeat q 3 weeks x 4 cycles. The dosages for the AC group: Adriamycin 60 mg/m2 IV and Cytoxan 600 mg/ml IV. Every 3 weeks x 4 cycles. In both groups, post-menopausal patients who are ER and/or PR positive will receive Tamoxifen 20 mg PO daily x 5 years at the completion of chemotherapy. G-CSF: Patients who have an episode of febrile neutropenia should be placed on G-CSF according to ASCO Guidelines. Patients who have febrile neutropenia after a subsequent dose of chemotherapy in spite of G-CSF should have the chemotherapy doses lowered by 25%.

Progress: This study closed to patient entry 21 Jan 00. One patient enrolled in this study in FY99 at MAMC and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/102 **Status**: Ongoing

Title: SWOG E2697: Correlation of DNA Damage Index and Clinical Response in the Context of ECOG Trial E3695

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 03	7/24/2001

Study Objective: To determine, using an optimized DNA-PCR assay specific for exon-6 of the glutathione S-transferase (GST-TT, gene, the extent of cisplatin-induced DNA damage in vitro in PBMC obtained from melanoma patients prior to treatment with chemotherapy or biochemotherapy and correlate the extent of DNA damage with clinical response. To determine the optimum cisplatin concentration with which to treat PBMC in vitro that will provide the highest positive and negative predictive value for response to both chemotherapy and biochemotherapy.

Technical Approach: This study is a companion study to SWOG E3695. Patients will have blood drawn prior to receiving chemotherapy. The peripheral blood mononuclear cells will be exposed to different concentrations of cisplatin (one of the chemotherapy drugs in E3695). The amount of cisplatin induced DNA damage will be measured. The amount of damage will be compared to the response of the tumor to chemotherapy to see if there is a correlation.

Progress: This study has not yet received final IRB approval. Answers to the IRB's questions concerning the study laboratory's methodologies have yet to be addressed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/056 **Status**: Ongoing

Title: SWOG E3695: A Randomized Phase III Trial of Concurrent Biochemotherapy with Cisplatin Vinblastine, Dacarbazine, IL-2, and Interferon A-2b versus Cisplatin, Vinblastine, Dacarbazine (CVD) Alone in Patients with Metastatic Malignant Melanoma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Mar 01	2/22/2000

Study Objective: 1) To determine whether this inpatient biochemotherapy is superior to CVD alone based on survival in patients with metastatic malignant melanoma. 2) To determine whether this inpatient biochemotherapy is superior to CVD alone based on response rate, response duration, time to treatment failure, percent CR and percent duration CR in patients with metastatic malignant melanoma. 3) To determine the feasibility of administering this in a biochemotherapy regimen to patients with metastatic malignant melanoma in a Cooperative Group setting. 4) To determine the toxicity of this inpatient biochemotherapy regimen relative to CVD alone in patients with metastatic melanoma treated in a Cooperative Group setting.

Technical Approach: Each subject will be randomized to one of two arms: Arm A (CVD): Treatment will consist of Cisplatin 20 mg/m2 IV over 30 minutes. daily, days 1-4; Vinblastine 1.2 mg/m2 IV daily, days 1-4; Dacarbazine 800 mg/m2 IV over 1 hour, day 1 (only). Treatment can be administered in the outpatient setting. Cycles will be repeated every 3 weeks. Arm B (CVD + IL-2/IFN): Cisplatin 20 mg/m2 IV over 30 minutes daily, days 1-4; Vinblastine 1.2 mg/m2 IV daily, days 1-4; Dacarbazine 800 mg/ml FV over 1 hour, day 1 (only); IL-2 (Chiron) 9 MIU/m2/day by CIV, days 1-4 (96 hours); Interferon alpha 2b (Schering) 5MU/ml sc days 1-5, 8, 10 and 12; G-CSF 5 ug/kg sc qd days 7-16. All patients will be admitted to the hospital on the morning of day 1. Interferon alpha-2b, the IL-2 infusion and the rehydration for cisplatin should be planned to begin around 3 PM. Patients will be discharged ASAP after day 5 with subsequent doses of interferon to be administered in the outpatient setting or at home. Cycles will be repeated at 3 week intervals. Tumor measurements will be obtained prestudy and tumor response will be assessed after every 2 cycles. Patients with stable or responding disease will continue on therapy until disease progression, unacceptable toxicity or until they receive the maximum of 4 cycles. All patients will have renal function tests, blood counts and a thorough physical examination (including neurologic examination) prior to each cycle of chemotherapy. If abnormalities are found, these parameters will be rechecked on a weekly basis and further therapy will be withheld until laboratory values and performance status return to within the eligibility criteria (i.e., ANC > 1500/mm3, Platelets > 100,000/mm3, creatinine < 1.5, bilirubin < 1.5 and Performance Status 0 or 1).

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/040 **Status**: Ongoing

Title: SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 02	12/18/2001

Study Objective: (1) To compare CHOP treatment with or without chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in elderly patients with diffuse mixed, diffuse large cell, and immunoblastic large cell non-Hodgkin's lymphoma of B lineage with respect to response rate, the time to treatment failure, toxicity and survival, (2) To compare IDEC-C2B8 monoclonal antibody as maintenance therapy to observation alone after CHOP chemotherapy with respect to time to treatment failure, duration of response, toxicity and survival after an initial response to induction therapy of CHOP + IDEC-C2B8, and (3) To determine if maintenance therapy with IDEC-C2B8 results in the conversion of any partial responses to a complete response.

Technical Approach: This study adds a new drug, chimeric anti-CD20 monoclonal antibody, to the standard treatment (cyclophosphamide, doxorubicin, vincristine and prednisone, CHOP) of Non-Hodgkin's Lymphoma. Patients eligible for this study will be randomized to receive or not to receive IDEC-C2B8 (anti-CD20) in conjunction with chemotherapy. Treatment Arm A, CHOP plus Anti-CD20 will receive the study drug IV over 6 to 12 hours on Days 7 and 3 before the first treatment cycle of CHOP. Anti-CD20 will also be given 48 hours prior to cycles 3, 5 and 7 of CHOP. Treatment Arm B will receive CHOP for a minimum of 6 or a maximum of 8 cycles. Restaging of disease after 4 cycles and again after 6 cycles will be done to determine response and eligibility to be randomized to Maintenance Treatment Arms C & D. Arm C will continue to receive Anti-CD20 IV, four weekly doses every 6 months for 2 years. Arm D will be the observation group.

Progress: Two patients enrolled in FY00; however, the study closed to patient entry, 18 May 01, at the request of MAMC investigators. Two non-MAMC SAEs were reported, 21 May 01, due to grade 4 and 5 toxicities. The study remains ongoing to continue treatment and follow-up for the two patients enrolled.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 97/070 **Status**: Ongoing

Title: SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour .

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/21/1997	Mar 00	2/22/2000

Study Objective: 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.

Technical Approach: The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation. In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.

Progress: This study closed to patient entry, 30 Apr 01. One patient enrolled in this study at MAMC in FY00 and continues to be followed.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/040 **Status**: Ongoing

Title: SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Jan 03	1/22/2002

Study Objective: Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received >= 5 years of adjuvant tamoxifen, randomized to receive wither Letrozole 2.5 mg daily or placebo daily for 5 years. Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of Letrozole with special attention to: lipid profile as assessed by blood sampling (in a limited number of centers), cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity, the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity, changes in bone density (in a limited number of centers), common toxicities as assessed by reported toxicity. Third: To evaluate overall quality of life.

Technical Approach: This is a multi-centre, double-blind, placebo-controlled parallel randomized trial of the NCIC Clinical Trials Group, supported by Novartis. Patients will be stratified by: receptor status at diagnosis (positive, unknown), lymph node status at diagnosis (negative, positive, unknown), and a prior adjuvant chemotherapy (yes, no). Patients will be centrally randomized to receive one of the following treatments: Arm 1 (letrozole): 2.5 mg po daily x 5 years or Arm 2 (Placebo): po daily x 5 years.

Progress: Five patient enrolled in this study at MAMC in FY01, four patients in FY00, and three patients in FY99, for a total of enrollment of 12 patients. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/121 **Status**: Ongoing

Title: SWOG N9741: A Randomized Phase III Trial of Combinations of Oxaliplatin (OXAL), 5-Fluorouracil (5-FU), and Irinotecan (CPT-11) as Initial Treatment of Patients with Advanced Adenocarcinoma of the Colon and Rectum

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Aug 03	7/24/2001

Study Objective: 1) The primary objective is to compare the time to progression and overall survival in patients with locally advanced or metastatic colorectal cancer who receive one of these treatments: OXAL+5-FU+CF or CPT-11+OXAL or CPT-11+5-FU+CF (control regimen). 2) Secondary objectives include evaluation of toxicity, response rate, time to treatment failure and quality-of-life parameters in patients on the three regimens.

Technical Approach: This trial will compare the current standard of care for metastatic and locally advanced colon cancer to two promising new regiments. The goal is to define the new standard of care for this illness. Subjects will be randomized to receive one of three different treatments using two or three of the following 4 chemotherapy drugs: CPT-11, OXAL, 5-FU, and CF. The 3 different treatment schedules differ in the number of drugs and the amount of the drug you will receive, the amount of time over which the drugs will be given, and the length of cycles (time between doses). A complete physical to include labs, blood tests, scans and X-rays will be given at the beginning of each cycle. The 1st two cycles on the weeks you do not receive treatment, you will be contacted by telephone to talk about how you are feeling and if you are having any side effects. The treatments are as follows: Treatment A: CPT-11 will be given into a vein over 90 minutes followed by CF and 5-FU given into a vein over a few minutes, on day 1 for 4 of 6 weeks, repeated every 6 weeks. (A cycle is 6 weeks); Treatment F: OXAL will be given by vein over 120 minutes followed by CF given over 120 minutes followed by 5-FU (given over a few minutes of time) followed by 5-FU given over 22 hours. The CF and 5-FU are given on two consecutive days. Treatment is repeated every 14 days. This requires placement of an IV tube into a vein under the skin 'of the chest wall. Treatment G: OXAL will be given into a vein followed by CPT-11 over 30 minutes repeated every 3 weeks. Subject will continue same treatment until disease fails to respond to the treatment. If a complete remission is obtained, treatment may be halted and reinitiated if cancer returns. To study the treatment's effect on quality of life, participants will be asked to fill out brief forms with questions about changes in daily routines and health. This will take about 10-15 minutes. The forms will be given to the participants during their visits to the clinic. If the participant is not feeling well enough to fill out the form, a copy will be given to the participant to take home. The participant will be called within the week to go over the questionnaires and get the answers. Family members or friends are not allowed to fill out the questionnaires for the participant. Because quality of life may change over time, the participant will be asked to fill out the same form a number of times during the study (before starting the first cycle of treatment, prior to cycle two, then before every other cycle of treatment, and after the last cycle of treatment).

Progress: No patients enrolled in this study at MAMC in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/120 **Status**: Ongoing

Title: SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel with or without Trastuzumab as Adjuvant Treatment for Women with HER-2 Overexpressing Node Positive Breast Cancer (an Intergroup Study)

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Dec 05	7/24/2001

Study Objective: To see if the addition of Herceptin to standard AC + Taxol is beneficial for women with node positive breast cancer, whose tumors have excess amount of Her-2 gene.

Technical Approach: Subjects will have a full medical history and physical examination taken along with blood tests, chest x-ray, an electrocardiogram (a test that records the electrical activity of your heart), a MUGA or echocardiogram (a test that learns the function of your heart), a mammogram, and other tests that the doctor might feel are needed to fully learn about your disease. Subjects will be randomly assigned to one of three arms: Arm A - Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), Taxol by vein over 1 hour one day every week for a total of 12 treatments. Total length of treatment will be about six months. Arm B - Subjects will be given Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), you will get Taxol by vein over 1 hour one day every week for a total of 12 treatments. After all treatment with Taxol is done (about week 24), Herceptin by vein one day every week for one year. The first dose of Herceptin will be given over about 90 minutes. Subjects will be watched for 1 hour after the first dose of Herceptin. If they do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about 18 months. Arm C - Subjects will be given Adriamycin and Cytoxan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), subjects will be given Taxol, by vein over 1 hour, plus Herceptin, by vein one day every week, for a total of 12 treatments. After all treatment with Taxol plus Herceptin is done (about week 23), subjects will get Herceptin alone one day every week for six months. The first dose of Herceptin will be given over about 90 minutes. You will be watched for 1 hour after the first dose of Herceptin. If subjects do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about one year. Regardless of which treatment, at the end of all chemotherapy, subject may also get tamoxifen, if estrogen or progesterone receptor positive, for five years. If subjects had a lumpectomy, they will also get radiation therapy after chemotherapy has ended. Blood samples will be taken before the start treatment for research use. Subjects will be followed indefinitely.

Progress: One patient enrolled in this study at MAMC in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/010 **Status**: Ongoing

Title: SWOG R9704: A Phase III Study of Pre and Post Chemoradiation 5-FU vs. Pre and Post Chemoradiation Gemcitabine for Postoperative Adjuvant Treatment of Resected Pancreatic Adenocarcinoma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Sep 02	10/24/2000

Study Objective: (1) To determine whether 5-FU based chemoradiation preceded and followed by gemcitabine improves the overall survival, local-regional and distant disease control, and/or disease free survival as compared to 5-FU based chemoradiation preceded and followed by 5-FU in the postoperative adjuvant a treatment of pancreatic carcinoma, (2) To compare the acute and late toxicities between 5-FU based chemoradiation preceded and followed by gemcitabine and 5-FU based chemoradiation preceded and followed by 5-FU and, (3) To prospectively evaluate the ability of post-resectional CA19-9 to predict survival among adjuvantly treated patients who have undergone a potentially curative resection for adenocarcinoma of the pancreas.

Technical Approach: This study compares two different approaches to reducing the risk of relapse after resection of pancreatic carcinoma. 5-FU plus radiation is given to both groups. Pre- and post-radiation chemotherapy is given using either 5-FU or Gemcitabine.

Progress: One patient enrolled in this study in FY00 at MAMC, but died of progressive disease. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/136 **Status**: Ongoing

Title: SWOG S0009: A Phase II Evaluation of Neoadjuvant Chemotherapy, Interval Debulking Followed by Intraperitoneal Chemotherapy in Women with Stage III and IV Epithelial Ovarian Cancer, Fallopian Tube Cancer or Primary Peritoneal Cancer

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/25/2001	Aug 04	N/A

Study Objective: (1) To evaluate the overall survival and progression-free survival in Stage III or IV epithelial ovarian, fallopian tube or primary peritoneal carcinoma patients with bulky disease and/or malignant pleural effusions treated with neoadjuvant intravenous paclitaxel and carboplatin, cytoreductive surgery and intravenous/intraperitoneal paclitaxel and intraperitoneal carboplatin, (2) To estimate the percent of patients successfully cytoreduced to optimal disease (<1 cm residual) following neoadjuvant chemotherapy, (3) To evaluate the toxicities associated with this therapy, and (4) To explore the relationship between tumor p53 expression, cellular proliferation rate as measured by PCNA and apoptotic rate, and human tumor cloning assay results at time of debulking surgery with progression-free survival and overall survival in patients undergoing cytoreductive surgery.

Technical Approach: This protocol evaluates the effectiveness and side effects of a treatment regimen for advanced ovarian, peritoneal, and fallopian tube cancers. The treatment consists of intravenous chemotherapy of paclitaxel and carboplatin (3 treatments), followed by surgery, followed by a combination of intravenous paclitaxel and intra-peritoneal carboplatin and paclitaxel (6 treatments).

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/137 **Status**: Ongoing

Title: SWOG S0012: A Randomized Comparison of Standard Doxorubicin and Cyclophosphamide vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF as Neoadjuvant Therapy for Inflammatory and Estrogen-Receptor Negative Locally Advanced Breast Cancer, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
9/25/2001	Oct 04	N/A

Study Objective: (1) To compare the microscopic pathologic response rates in patients with inflammatory and estrogen-receptor negative locally advanced breast cancer treated with weekly Doxorubicin and daily oral Cyclophosphamide given with G-CSF support to in-patients treated without "standard" Doxorubicin and Cyclophosphamide regimen given every three weeks, (2) To compare the toxicities of these two regimens, (3) To compare the delivered dose intensity of these two regimens, and (4) To assess the association between microscopic pathologic complete response and clinical complete response at the primary tumor site in these patients.

Technical Approach: This trial is designed to compare two different treatment regimens for breast cancer prior to surgery to see if one works better against breast cancer than the other in very poor risk patients who may benefit from up-front chemotherapy. The standard regimen of Adriamycin and Cyclophosphamide given Day 1 every 21 days is compared to a regimen of Adriamycin given once a week for 15 weeks and oral Cyclophosphamide daily for 15 weeks. Filgrastim and trimethoprim sulfa will also be given in this regimen to protect against toxicity of the chemotherapy agents used.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/099 **Status**: Ongoing

Title: SWOG S0019: A Randomized Phase III Trial of ICE Chemotherapy With or Without Rituximab for the Treatment of Relapsed or Refractory CD20 Expressing Aggressive B-Cell Non-Hodgkin's Lymphomas in Patients Not Suitable For High Dose Therapy and PBSCT

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez, MC; MAJ David E. McCune, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/22/2001	Jun 04	N/A

Study Objective: (1) To compare the progression-free and overall survival of patients with relapsed or refractory aggressive large B-cell lymphoma (CD20+) treated with three cycles of ICE (ifosfamide, carboplatin, etoposide) chemotherapy with or without concurrent treatment with four infusions of Rituximab, (2) to evaluate the unconfirmed response rate for patients treated with these regimens, and (3) to evaluate the toxicity of ICE plus four infusions of chimeric monoclonal anti-CD20 antibody Rituximab in these patients.

Technical Approach: This study adds a new drug, (antibody) to the ICE treatment of Non-Hodgkin's Lymphomas in patients who have relapsed or have aggressive large B-cell Non-Hodgkin's and can not be transplanted. The goal is to compare the survival and response rate of those patients treated with ICE vs ICE plus Rituximab in a patient population with poor survival status.

Progress: This study recently received IRB approval and has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/073 **Status**: Completed

Title: SWOG S9700: A Phse II Trail of Infusional 5-Fluorouracil (5-FU), Calcium Leucovorin (LV), Mitomycin-C (Mito-C), and Dipyradamole (D) in Patients with Locally Advanced Unresected Pancreatic Adenocarcinoma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC

Start Date:	Est. Completion Date:	Periodic Review:
05/25/1999	Mar 02	5/22/2001

Study Objective: 1) The primary goal of this study is to assess the one-year overall survival rate in patients with advanced, unresectable pancreatic cancer who are treated with this regimen. 2) To assess the response rate in patients with measurable disease. 3) To evaluate the frequency and severity of toxicities associated with this therapy. 4) To assess the rate of resectability in patients who respond to this regimen.

Technical Approach: Stage II/III (based on AJCC Staging, Version 4) pancreatic adenocarcinoma not amenable to curative resection; PS 0-2; Meas or Eval disease; Histologically or cytologically proven ductal or undifferentiated adenocarcinoma (see protocol for acceptable histological types); No prior systemic CT/RT for pancreatic canc; No other prior malig except adeq treated basal cell or squamous cell skin canc, in situ cervical canc, adeq treated Stage I/II canc from which pt is currently in complete remission, or any other canc from which pt has been dz free for 5 yrs; >= 2 wks beyond any surgical bypass procedure & recovered from all surgical effects. A pancreatic primary canc must be estab by surgical exploration, CT scan or MRI. Pts who have unresec but localized dz are elig (determined by total occlusion or encasement > 75% of main portal vein or superior mesenteric vein, total occlusion of or > 75% circumferential encasement of superior mesenteric artery, celiac axis or common hepatic artery, right or left hepatic arteries, total occlusion of peripheral splenic vein in pts w/o evidence of cirrhosis, tumor size of >= 5 cm involving body or tail of pancreas, or enlargement of celiac axis nodes w/ subsequent biopsy to prove pathologic involvement); Pts must not have lost >15% of actual body wt. (must have an oral intake of greater than 1,200 calories/day at time of regis); Preg/nursing women are ineligible.

Progress: This study permanently closed to enrollment, 15 May 01, with no patients enrolled at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 201/080 **Status**: Ongoing

Title: SWOG S9701: Phase III Randomized Trial of 12 Months vs. 3 Months of Paclitaxel in Patients With Advanced Ovarian, Fallopian Tube or Primary Peritoneal Cancer who Attain a Clinically Defined Complete Response (CR) Following Platinum/Paclitaxel-Based Chemotherapy

Principal Investigator: LCDR John D. O'Boyle, MC, USN

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Patrick Williams, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
2/27/2001	Dec 10	N/A

Study Objective: To assess whether the continuation of paclitaxel, a cycle specific antineoplastic agent, for 12 months following the attainment of a clinically-defined complete response (CR) to initial platinum (carboplatin or cisplatin)/paclitaxel-based chemotherapy can significantly increase progression-free survival and overall survival when compared to a 3-months continuation in women with advanced ovarian cancer and to assess the toxicities associated with prolonged paclitaxel.

Technical Approach: Female patients with histologically confirmed epithelial carcinoma of the ovary, fallopian tube cancer or primary peritoneal cancer. Eligible patients will be randomized to receive paclitaxel (Taxol) once a month for 3 months (3 courses), or once a month for 12 months (12 courses). Patients will be removed from the study if side effects become too severe or in case of disease progression.

Progress: This study closed to patient entry, 13 Nov 01. One patient enrolled in this study at MAMC in FY01, and continues to receive treatment.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/060 **Status**: Completed

Title: SWOG S9806: Randomized Phase II Trial of Carboplatin/Gemcitabine Followed by Paclitaxel or Cisplatin/Vinorelbine Followed by Docetaxel in Advanced Non-Small Cell Lung Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ Ines J. Sanchez-Rivera, MC; MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
03/23/1999	Mar 03	2/22/2000

Study Objective: 1) Assess the survival and failure-free survival of patients with advanced non-small cell lung carcinoma treated with carboplatin and gemcitabine followed by paclitaxel or cisplatin and vinorelbine followed by docetaxel. 2) Evaluate the response (confirmed plus unconfirmed) and toxicities associated with these two regimens in this group of patients with advanced non-small cell lung cancer.

Technical Approach: Pts. must have histologically or cytologically proven new diagnosed selected Stage IIIB or IV advanced primary NSCLC (adenocarcinoma, large cell carcinoma, squamous cell carcinoma or unspecified) or recurrent disease after previous surgery and/or irradiation; pts. with brain mets are ineligible; pts. must have measurable or evaluable disease; pts. with bronchioloalveolar carcinoma or Stage IIIB tumor involving the superior sulcus (Pancoast Tumors) are ineligible; PS 0-1; at least three weeks must have elapsed since the completion of prior RT and surgery and pts. must have recovered from all associated toxicities; measurable or evaluable disease must be present outside the area of surgical resection; pts. must have a serum creatinine <= 2 x IULN and calculated or measured creatinine clearance >= 50 cc/min; pts. must not have recd prior hormonal, systemic or biologic therapy for NSCLC; pts must not receive concurrent hormonal, biologic or RT to measurable or evaluable lesions; pts. may receive concurrent palliative RT to small field non-measurable sites of disease (painful bony mets).

Progress: This study closed to patient entry, 15 Nov 99 and the two patients enrolled in this study in FY99 died of progressive disease. This study is permanently closed at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/019 **Status**: Ongoing

Title: SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/20/1998	Indef	9/25/2001

Study Objective: To relieve the burden on Institutional Review Boards at Southwest Oncology Group Institutions for continuing review of protocols that are closed to patient registration, and on which no patients are currently receiving protocol treatment.

Technical Approach: When a study has been closed to patient accrual and patients have finished treatment, it still requires submission of data to the Southwest Oncology Group to report survival and remission status and occurrence of adverse events. On an annual basis, the Southwest Oncology Group Operations Office will notify the institutions as to which protocols are eligible for transfer to the Long Term Follow-Up protocol by periodically revising the list of applicable protocols. The institutional Principal Investigator or IRB will ultimately decide for the local institution whether the protocol should be included in this protocol or continue to be reviewed on its own. A report will be prepared and submitted for annual IRB review at individual institutions. This report will include title and date closed to patient entry.

Progress: This protocol includes consolidation of the following protocols at MAMC. All of the following protocols are closed to patient entry, the treatment phase is completed, and patients are being followed for survival data only: SWOG #s: 7406, 7433, 7436, 7510, 7713/14, 7808, 7827, 8216/38, 8269, 8313, 8410, 8417/19, 8516, 8600, 8736, 8809, 8892, 8957, 9019, 9125 and 9349. During FY 01, 1 patient enrolled in 9035, 1 patient enrolled on 9003 and 4 patients enrolled in 9514 were included under this follow-up protocol. During FY 00, 2 patients on SWOG 8590 were included under this follow-up protocol. During FY 99, SWOG #s 8854, 9008, 9031 and 9445 were also consolidated.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/009 **Status**: Completed

Title: SWOG S9809: The Effect of Fluoroquinolones on the Disease-Free Interval in Patients with Stage Ta Transitional Cell Carcinoma of the Bladder, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Raymond S. Lance, MC; LTC Raymond A. Costabile, MC

Start Date:	Est. Completion Date:	Periodic Review:
10/26/1999	Sep 02	2/27/2001

Study Objective: To determine if ciprofloxacin improves the recurrence-free survival of patients with superficial transitional cell carcinoma of the bladder treated with a transurethral tumor resection (TURBT), to detect nonrandom cytogenetic changes in recurrent transitional cell carcinoma (TCC) of the bladder (specifically changes involving loss of chromosome 9 and gain of chromosome 7) and to correlate these cytogenetic changes with clinical-pathological indicators of tumor recurrence to cephalexin or Ciprofloxacin.

Technical Approach: Subjects will be randomized into one of two treatment groups; Arm 1, Ciprofloxacin for 3 days starting the night before the TURBT or Arm 2, Cephalexin for 3 days starting the night before the TURBT (if subjects are allergic to penicillin or a cephalosporin then sulfamethoxazole/trimethoprim for 7 days). Follow-up will be conducted for 5 years.

Progress: This protocol closed to patient enrollment due to poor accrual. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 99/038 **Status**: Terminated

Title: SWOG S9832: Enhancing Well-Being During Breast Cancer Recurrence

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
02/23/1999	Feb 03	4/24/2001

Study Objective: To assess the effectiveness of a telephone intervention delivered by breast cancer survivors on well-being of patients experiencing a first recurrence of breast cancer, to examine the impact of sociodemographic, clinical, and psychosocial predictors of well-being in patients experiencing a first recurrence of breast cancer and to examine changes in well-being over time since recurrence.

Technical Approach: This is a randomized study with two arms: 1) standard institutional support or 2) intervention support by Y-ME. Intervention will be delivered by women who are particularly well-qualified to provide support and information: breast cancer survivors who have themselves experienced recurrence. Subjects will be asked to fill out several questionnaires. The questions asked are about how they are feeling and problems theyve experienced related to their cancer. A peer counselor (a women who has also had a recurrence of breast cancer) will be administring 4-8 questionnaires by phone over the course of 4 weeks for those in the invervention group. The subjects will also be asked to fill out a questionnaire 2 and 5 months after their least session. This data will analyzed to determine if the intervention was helpful.

Progress: Per request of the investigators, this protocol was terminated at MAMC, 24 Apr 01, due to lack of interest of the MAMC patient population. The protocol never received final IRB approval.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/038 **Status**: Ongoing

Title: SWOG S9900: A Randomized Phase III Trial Surgery Alone or Surgery plus Preoperative Paclitaxel/Carboplatin in Clinical Stage IB (T2N0), II(T1-2N1, T3N0) and Selected IIIA (T3N1) Non-Small Cell Lung Cancer (NSCLC)

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 00	12/18/2001

Study Objective: (1) To assess whether preoperative chemotherapy with paclitaxel and carboplatin for 3 cycles improves survival compared to surgery alone in previously untreated patients with clinical Stage IB, II and Selected III A non-small cell lung cancer (NSCLC), (2) To compare operative mortality and other toxicities in the two study arms, (3) To evaluate the response rates (confirmed and unconfirmed, complete and partial) and the toxicities associated with the combination of paclitaxel and carboplatin, and (4) To obtain samples for correlation of radiologic, pathologic, molecular and biologic factors with outcome.

Technical Approach: This study compare surgery (the standard therapy) to chemotherapy followed by surgery to determine the standard of care for non-small cell lung cancer (NSCLC). Patients will be randomized to either surgery alone or chemotherapy (paclitaxel, IV, Day 1 every 3 weeks; carboplatin, IV, Day 1 every 3 weeks) for nine weeks prior to surgery. Chest x-rays and CT scans will be repeated to determine response to the chemotherapy and decide when the surgery should be scheduled.

Progress: No patients enrolled in this study at MAMC in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/119 **Status**: Ongoing

Title: SWOG S9901: A Randomized Phase III Trial Comparing Early High Dose Chemotherapy and an Autologous Stem Cell Transplant to Conventional Dose ABVD Chemotherapy for Patients with Advanced Stage Poor Prognosis Hodgkin's Disease as Defined by the International Prognostic Factors Project on Advanced Hodgkin's Disease, Intergroup

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	Aug 03	10/23/2001

Study Objective: 1) To compare in a cooperative group setting the progression-free survival in patients with poor prognosis advanced stage Hodgkin's disease who are treated with induction chemotherapy (ABVD X 5) followed by randomization to ABVD x 3 versus ABVD x 1 plus high dose chemotherapy plus peripheral blood stem cell rescue. 2) To compare the overall survival in this cohort of patients. 3) To compare the toxicities of these treatment regimens.

Technical Approach: This study will attempt to define the role of high dosed chemotherapy with stem cell transplant in the initial treatment of Hodgkin's Lymphoma. The study compares the standard of care (eight cycles of ABVD), to six cycles followed by high dose chemotherapy. Madigan expects to enroll 2 to 3 subjects per year.

Progress: This study has not yet been initiated at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/082 **Status**: Completed

Title: SWOG S9902: Evaluation of the Combination of Docetaxel (Taxotere)/Carboplatin in Patients With Metastatic or Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN), Phase II

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Mar 03	1/23/2001

Study Objective: (1) To assess the survival in patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) when treated with the combination of Docetaxel (Taxotere(r)) and carboplatin plus dexamethasone, (2) To assess time until treatment failure and response rate (unconfirmed and confirmed complete and partial response), and (3) To evaluate the toxicities of this regimen.

Technical Approach: This study will try to determine the response rate of metastatic head and neck cancer to the combination of docetaxel and carboplatin. Subjects will be treated on an outpatient or possible inpatient. Docetaxel will be given IV over a period of 1 hour and carboplatin given IV over a period of 1/2 hour. In addition, subjects may also receive dexamethasone, IV over 30 minutes prior to docetaxel. This treatment will be repeated every 3 weeks as long as their disease stays the same or improves. Subjects will discontinue treatment if their disease progresses.

Progress: This study was reported closed to patient entry, 1 Jan 01, as it had met its accrual goals. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/039 **Status**: Completed

Title: SWOG S9914: Phase II Trial of Paclitaxel, Carboplatin and Topotecan with G-CSF in Untreated Patients with Extensive Small Cell Lung Cancer

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

Start Date:	Est. Completion Date:	Periodic Review:
1/25/2000	Jan 00	2/27/2001

Study Objective: (1) Assess the survival of patients with extensive small cell lung cancer (SCLC) treated with a combination of paclitaxel, carboplatin and topotecan plus G-CSF, (2) Assess response rates of patients with extensive small cell lung cancer (SCLC) treated with a combination of Taxol, carboplatin and topotecan plus G-CSF, and (3) Evaluate the side effects and overall toxicities associated with the combination of paclitaxel, carboplatin and topotecan plus G-CSF.

Technical Approach: Eligible patients will receive the combination of three active chemotherapy drugs, carboplatin, paclitaxel and topotecan for the treatment of extensive small cell lung cancer. Topotecan IV will be given on days 1-4, and carboplatin IV and paclitaxel IV on day 4. Day 5, patients will begin G-CSF as a subcutaneous injection to help blood counts recover. This treatment will be repeated every 3 weeks for a total of 6 cycles.

Progress: This study reached its accrual goals and closed to further patient enrollment, 15 Jun 01. No patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/083 **Status**: Ongoing

Title: SWOG S9916: Docetaxel and Estramustine versus Mitoxantrone and Prednisone for Advanced, Hormone Refractory Prostate Cancer, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Mar 03	5/22/2001

Study Objective: (1) To compare overall survival and progression-free survival in patients with hormone refractory metastatic prostate cancer Stage D1 or D2 (with either measurable or non-measurable disease) randomized between Arm 1 (docetaxel (Taxotere), estramustine (Emcyt)) and Arm 2 (mitoxantrone (Novantrone) and prednisone), (2) To compare qualitative and quantitative toxicity between the two study arms, (3) To evaluate elements of Quality of Life, including: a. Palliation of metastatic bone pain and b. Global Quality of Life, (4) To record PSA values for future correlations with response and survival, and (5) To compare responses between the two treatment groups in patients with BioDimensional measurable disease.

Technical Approach: Subjects will be randomized to received either Treatment Arm 1, Docetaxel and Estramustine or Treatment Arm 2, Mitoxantrone plus Prednisone. Subjects in Arm 1 will receive estramustine as 2 capsules by mouth 3 x every day for 5 days plus a steroid medication by mouth on the 1st and 2nd days to decrease side effects of the docetaxel treatment. Docetaxel will be given IV on the 2nd day of the treatment course. This treatment procedure will be repeated every three weeks. Subjects in Arm 2 will receive mitoxantrone plus prednisone, by mouth twice every day for 3 weeks. The mitoxantrone treatment will be given on the 1st day, IV. This treatment procedure will be repeated every three weeks. All subjects will be asked to complete questionnaires on a regularly scheduled basis to describe the effect on their quality of life while receiving their specific treatments.

Progress: One patient enrolled in this study at MAMC in FY01. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/084 **Status**: Ongoing

Title: SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
5/23/2000	Jan 02	5/22/2001

Study Objective: This study will evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated. Patients will be randomized to one of the following two treatment arms: (A) Casodex, + Zoladex, (B) Novantrone/Prednisone followed by Casodex, + Zoladex. This study will also compare qualitative and quantitative toxicity between the two study arms.

Technical Approach: This study compares standard hormonal therapy after prostate cancer surgery to standard therapy plus chemotherapy to determine the best way to prevent relapse. Subjects will be randomized to receive either Treatment 1, Hormonal Therapy which consists of Zoladex, subcutaneous injection once every 12 weeks for two years or Treatment 2, Hormonal Therapy plus Mitoxantrone plus Prednisone which consists of Zoladex subcutaneous injection once every 12 weeks for two years, Casodex taken orally once a day for two years, Mitoxantrone, IV once every 21 days for 126 days (6 cycles) and Prednisone, taken orally twice a day for 126 days. Following study completion, subjects will be followed every 6 months for two years to assess response.

Progress: One patient enrolled in this study at MAMC in FY01 and continues to receive treatment. Patient enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/101 **Status**: Ongoing

Title: SWOG S9922: A Phase III Trial of Dexamethasone, Cyclophosphamide, Etoposide, Cisplatin (DCEP) and G-CSF with or without Thalidomide (NSC #66847) as Salvage Therapy for Patients with Refractory Multiple Myeloma

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
6/27/2000	Jun 04	10/23/2001

Study Objective: 1) To evaluate and compare the overall and progression-free survival and confirmed remission rates in patients with refractory multiple myeloma treated with the DCEP regimen alone versus DCEP plus thalidomide. 2) To evaluate the qualitative and quantitative toxicities associated with these regimens.

Technical Approach: Most patients with multiple myeloma, even those treated with bone marrow transplant eventually relapse. There is no standard therapy for these patients. Combination chemotherapy and thalidomide have demonstrated actively against relapsed myeloma. This trial tests whether the addition of thalidomide to combination chemotherapy provides additional benefit.

Progress: No patients enrolled in this study at MAMC during FY01. Subject enrollment continues.

Detail Summary Sheet

Date: 28 Sep 01 **Number**: 200/113 **Status**: Ongoing

Title: SWOG S9927: Randomized Trial of Post-mastectomy Radiotherapy in Stage II Breast Cancer in Women with One to Three Positive Axillary Nodes, Phase III

Principal Investigator: MAJ Patrick Williams, MC

Department: SWOG **Facility**: MAMC

Associate Investigator(s): MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ John B. Halligan, MC; MAJ Rajat Bannerji, MC

Start Date:	Est. Completion Date:	Periodic Review:
7/25/2000	Jul 03	7/24/2001

Study Objective: To compare overall and disease-free survival in pre-and post-menopausal women with Stage 11 breast cancer and 1-3 positive nodes treated with or without radiation therapy following mastectomy and adjuvant chemotherapy. 2) To assess local-regional control for this cohort of patients. 3). To assess the potential toxicities of radiotherapy delivered using CT-directed treatment in this cohort of patients.

Technical Approach: Current standard of practice does not include radiation therapy for patients with 1 - 3 positive nodes, but older studies suggest a benefit. This study will determine whether adding radiation therapy to modem chemotherapy will improve overall survival.

Progress: No patients enrolled in this study at MAMC in FY01. Subject enrollment continues.

Index with Investigators, Keywords, and Protocol Numbers

Annual Report Distribution List

Defense Technical Information Center 8725 John J. Kingman Rd. #944 Fort Belvior, VA 22060-6217	2 copies
Clinical Investigation Regulatory Office ATTN: MCCS-GCI CDR AMEDDC&S 1608 Stanley Road Ft Sam Houston, TX 78234-6125	2 copies
Commander USA Medical Research and Materiel Command ATTN: MCMR-RCQ-HR 504 Scott Street Fort Detrick, MD 21702-5012	1 copy
CDR Brooke Army Medical Center ATTN: MCHE-CI Ft Sam Houston, TX 78234-6200	1 copy
CDR Dwight D. Eisenhower AMC ATTN: MCHF-CI Ft Gordon, GA 30905-5650	1 copy
CDR Madigan Army Medical Center ATTN: MCHJ-CI Tacoma, WA 98431-1100	10 copies
CDR Tripler Army Medical Center ATTN: MCHK-CI Honolulu, HI 96859	1 copy
CDR Womack Army Medical Center ATTN: MCXC-FM Box 63H Ft Bragg, NC 28307-5000	1 copy
CDR William Beaumont AMC ATTN: MCHM-DCI El Paso, TX 79920-5005	1 copy
CDR Walter Reed Army Medical Center ATTN: MCHL-CI Washington, DC 20307-5000	1 copy


CARE WITH COMPASSION