Department of Clinical Investigation

Annual Research Progress Report



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Tacoma, Washington

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This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 96. Included in the individual reports are title, investigators, funding objective, technical approach, and progress for FY 96. 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 96.

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30 SEPTEMBER 1996

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

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ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1996

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.

Acknowledgements

I would like to take this opportunity to thank MAJ Curtis Yeager, Nancy Whitten, Barbara Jones, Troy Patience, Genie Hough, and SGT Karen Degraffenreid for their efforts which is obvious in the compilation, preparation, and editing of this publication.

Foreword

In FY 96 the number of new protocols submitted and total protocols managed continued to keep us very busy. During this FY, DCI processed 165 new protocols and managed 524 total protocols. MAMC investigators continued to attract clinical trials at an increasing rate, augmenting their extramural funding through multiple foundations. MAMC nurses were again successful in competing for Tri-service Nursing research funding, bringing in over $913,825 in DOD nursing research funding. Forty investigators were trained in our annual Introduction to Clinical Investigation course, and the department continued its strong thrust in molecular biology, training 24 fellows and staff in MAMC's Short Course in Molecular Biology for Physicians. Individual investigators continued the department's thrust in the area of molecular biology. Dr. Kathy Moore's paper characterizing wild-type and alternate sex hormone binding globulin (SHBG) mRNA transcripts in breast cancer was accepted for publication and she continues work on the control of SHBG production as well as the role of SHBG in programmed cell death in breast cancer cells; CPT Wade Aldous partnered with investigators in urology and general surgery to evaluate the presence of telomerase activity in bladder and colon cancers, and with MAJ Keith Martin was the first to describe telomerase activity in malaria cells. CPT Aziz Qabar replaced MAJ Martin, bringing his expertise to the department in the molecular study of the thrombospondins in wound healing and inflammatory response. As Assistant chief and Director of Surgical Research, LTC Rich Sherman has energized research productivity in the Department of Surgery, and especially the Orthopedic service as well as producing new findings in the use of pulsed electromagnetic field generation in the areas of wound healing, musculoskeletal injuries and migraine headaches. MAJ Curtis Yeager also joined the department as C, Immunology, contributing to an important study on cryptosporidium, and was assigned as director of the newly created Research Support Service. He, with Protocol Specialists Nancy Whitten and Barbara Jones, made great improvements in the efficiency of our protocol approval process and production of the Annual Report. They also brought the department successfully through an FDA audit and two Oncology Group audits. MAJ Ron Nielsen, C, Laboratory Animal and Surgery Service, has ably supervised the increased laboratory animal research activity of the surgical services. The support of MG James Peake and BG George Brown, Commanders, COL Darrell Porr, DCCS, COL William Cahill, DCA and COL Patrick Kelly, Director of Medical Education are gratefully acknowledged for their role in the department fulfilling its mission.

Unit Summary

1. Objective

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

2. Technical Approach

Personnel

Description	Rank	MOS
Chief, Clinical Investigation MOORE, Dan C., M.D., COL, MC	06	60P9A
Chief, Clinical Studies Service VACANT		
Director, Surgical Research Service SHERMAN, Richard A., Ph.D., LTC, MS	O5	71F67
Director, Radiological Research Service HO, Vincent B., M.D., MAJ, MC (ETS Aug 96)	O4	61R9C
Chief, Lab Animal & Surgery Service NEILSEN, Ronald E., D.V.M., MAJ, VC	O4	75C64
Chief, Immunology Service YEAGER, Curtis L., Ph.D., MAJ, MS	O4	71A67
Chief, Bioresearch Service MARTIN, Rodger K., Ph.D., MAJ, MS (PCS Jun 96)	O4	71B9C
Chief, Microbiology Service ALDOUS, Wade K., Ph.D., CPT, MS	O3	71A67
Chief, Biochemistry Service QABAR, Aziz N., Ph.D., CPT, MS (Arrived Apr 96)	O3	71B67
NCOIC HERNANDEZ, Carlos I., SFC	E7	91K4R
Senior Animal Care Sgt. BARRETT, Vickie R., SFC	E7	91T4R
Senior Animal Care Sgt. BROWN, Bruce A., SGT	E5	91T2R
Senior Animal Care Sgt. HEATH, George, SGT (EOD Sep 96)	E5	91T2R

Manpower (continued)

Description	Rank	MOS
Animal Care Specialist DELUCIA, Julie A., SPC (ETS Jun 96)	E4	91T10
Animal Care Specialist DUDLEY, Derric A., SPC (PCS Sep 96)	E4	91T10
Animal Care Specialist LONG, Brett W., SPC (Arrived Jan 96)	E4	91T10
Lab Tech KEENE, Corey A., SGT	E4	91K2R
Lab Tech SOLA, Milagros, SPC (Arrived Apr 96)	E4	91K10
Lab Tech POOL, Rosemary, PFC (ETS Sep 96)	E4	91K1R
Lab Tech BOUMA, Cheri Ann, PFC (PCS Mar 96)	E3	91K10
Research Admin Scientist MOORE, Katherine H., Ph.D.	GS13	0601
Med Tech MATEJ, Louis A., B.S., M.T.	GS11	0644
Med Tech WRIGHT, James R., B.A., M.T.	GS11	0644
Med Tech STYNER, M. J., B.S., M.T.	GS11	0644
Med Tech BULLOCK, Jeff M., B.S., M.S., M.T.	GS11	0644
Statistician (Medicine) PATIENCE, Troy H., B.S.	GS09	1530
Research Protocol Specialist WHITTEN, Nancy J., B.A.	GS09	1087
Clinical Research Associate JONES, Barbara A. (Arrived Oct 95)	GS05	0303
Sec/Steno HOUGH, Eugenia R.	GS06	0318
Maintenance Worker KAEO, Curtis	WG7	4749

Funding FY 96

INTRAMURAL FUNDING

Civilian Salaries	$448,400
Military Salaries	$641,636
Consumable Supplies	$95,900
Contractual Services	$7,500
BLIC "C" MEDCASE Equipment	$0
Capital Equipment	$194,092
TDY - departmental	$4,000
TDY - Research presentations	$36,800
SUBTOTAL	$1,428,328

EXTRAMURAL FUNDING

Federal sources:	
Tri-service Nursing	$913,825
USAMRDC	$259,890
Others	$127,020
Non-federal sources:	
FACT	$17,407
PC3	$126,639
HMJ	$138,350
Others	$373,517
SUBTOTAL	$1,956,648

GRAND TOTAL **$3,384,976**

3. Progress

During FY 96, there were 524 active protocols that received administrative and/or technical support during the year. Of these, 350 are presently ongoing, 11 are in a suspended status, 120 were completed, and 46 were terminated. The principal investigator distribution was as follows: 411 staff protocols (includes 188 group oncology protocols), 38 resident protocols, 69 fellow protocols, 2 intern protocols, and 1 active duty student protocol. There were 165 new protocols and 4 protocols were reactivated.

There were 107 publications in nationally recognized journals and 81 presentations at regional or national medical association meetings.

4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI:
133 protocols involving 131 residents
135 protocols involving 37 fellows

5. Other training programs supported by DCI:

Training protocols:	Department of Surgery: 3
	Department of Emergency Medicine: 2
	Department of OB/GYN: 1
	Department of Clinical Investigation: 1
	I Corps: 2

6. Other protocols supported:

1 USDA protocol
1 Active duty student protocol
1 Bassett Army Community Hospital, Ft. Wainwright protocol

Committee Members

Commander
Madigan Army Medical Center
BG GEORGE J. BROWN, M.D., MC

Clinical Investigation Committee

Chairman
Chief, Clinical Investigation
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Pediatrics
Department of OB/GYN
Department of Family Practice
Department of Emergency Medicine
Department of Nursing
Department of Medicine
Department of Surgery
Department of Pathology
Department of Radiology
Pharmacy Service
Physical Medicine & Rehabilitation Service
Surgical Research Service, DCI
Clinical Studies Service, DCI
Microbiology Service, DCI
Biochemistry Service, DCI
Bioresearch Service, DCI
Immunology Service, DCI
Lab Animal and Surgery Service, DCI
Medical Statistician, DCI

Committee Members (cont'd)

Human Use Committee

Chairman
Chief, Clinical Investigation
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Nursing
Department of Radiology
Department of Ministry and Pastoral Care
Pharmacy Service
Social Work Service
Center Judge Advocate
Non-institutional Member
Surgical Research Service, DCI

Animal Use Committee

Chairman
Chief, Surigical Research Service, DCI
LTC Richard Sherman, MS

Chief or delegated representative of:

Department of Clinical Investigation
Lab Animal & Surgery Service
Department of Nursing
Veterinary Services
Non-institutional Member
NCOIC, Lab Animal & Surgery Service, DCI

Bryon L. Steger Research Award

This award is given to residents, 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 1996:

MAJ Liem T. Bui-Mansfield, Department of Radiology for his research project entitled *Cost Effectiveness of Screening Knee MRI: A Prospective Evaluation of 50 Consecutive Patients*

Other nominees were:

CPT Bradley F. Schwartz, Department of Surgery, Urology Service, for his research project entitled *A Randomized Prospective Comparison of Antibiotic Tissue Levels in the Corpora Cavernosa of Patients Undergoing Penile Prosthesis Implantation Using Gentamicin Plus Cefazolin versus an Oral Fluoroquinolone for Prophylaxis.*

CPT Stephen M. Salerno, Department of Medicine, Internal Medicine Service, for his research project entitled *The Effect of Antibiotics on Morbidity and Mortality in Ischemic Colitis.*

Fellow's Research Award

This award is given to fellows, 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 1996:

MAJ Michael D. Eisenhauer, Department of Medicine, Cardiology Service for his research project entitled *Beneficial Impact of Aorto-coronary Graft Markers on Post-Operative Angiography.*

Other nominees were:

MAJ Richard F. Williams, Department of Medicine, Hematology/Oncology Service, for his research project entitled *The Effect of Tamoxifen on Cell Growth, Bcl-2 and Bax in MCF-7 Breast Cancer Cells In Vitro: A Preliminary Report.*

MAJ John R. Caton, Department of Medicine, Hematology/Oncology Service, for his research project entitled *Male Breast Cancer: The Department of Defense Experience.*

CPT Kurt W. A. Grathwohl, Department of Medicine, Internal Medicine Service, for his research project entitled *Bedside Videoscopic Placement of Feeding Tubes: Development of Fiberoptics through the Tube.*

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 1996:

COL Thomas H. Mader, Department of Surgery, Ophthalmology Service, for his research project entitled *Refractive Changes During 72 Hour Exposure to Altitude Following Refractive Surgery.*

Other nominees were:

MAJ Rodger K. Martin, Department of Clinical Investigation, for his research project entitled *The Polymerase Chain Reaction as a Diagnostic Tool for Preterm Labor and Delivery.*

COL Robert E. Jones, Department of Medicine, Endocrinology Service, for his research project entitled *Synthesis of Ether Lipids and Phosphatidylethanolamine by Ejaculated Human Spermatozoa.*

COL Gary D. Davis, Department of Obstetrics/Gynecology, for his research project entitled *Behavioral Treatment of Exercise Induced Urinary Incontinence Among Female Soldiers.*

CPT Wade K. Aldous, Department of Clinical Investigation, for his research project entitled *A Fluorescent Method for Detection of Telomerase Activity.*

MAJ Thomas F. Burke, Department of Emergency Medicine, for his research project entitled *The Use of Intravenous Morphine for Early Pain Relief in Patients with Acute Abdominal Pain.*

MAJ J. Brantley Thrasher, Department of Department of Surgery, Urology Service, for his research project entitled *Immunohistochemical Localization of Insulin-like Growth Factor Binding Proteins -2 and -3 in Prostate Tissue: Clinical Correlations.*

LTC Edward R. Carter, Department of Pediatrics, for his research project entitled *Evaluation of Heliox in Children with Acute, Severe Asthma: A Randomized Crossover Trial.*

LTC Gregory N. Bender, Department of Radiology, for his research project entitled *Small Bowel Biopsy through an Enteroclysis Catheter to Augment Findings at Enteroclysis and Hypotonic Duodenography.*

LTC Gregory N. Bender, Department of Radiology, for his research project entitled *Double Contrast Upper Gastrointestinal Barium Examination with Biopsy Versus Endoscopy with Biopsy in Dyspeptic Patients.*

MAJ Curtis J. Hobbs, Department of Medicine, Endocrinology Service, for his research project entitled *Nandrolone, a 19-Nortestosterone, Enhances Insulin-Independent Glucose Uptake in Normal Men.*

LTC Gregory N. Bender, Department of Radiology, for his research project entitled *Nonendoscopic Gastric Mucosal Biopsy to Augment Double-Contrast Upper Gastrointestinal Barium Examination.*

PUBLICATIONS

FISCAL YEAR 96

DEPARTMENT OF ANESTHESIOLOGY AND OPERATIVE SERVICES	
Polaner DM	The Use of Heliox and the Laryngeal Mask Airway in a Child with an Anterior Mediastinal Mass. Anesth Analg 82(1): 208-210, 1996.
DEPARTMENT OF CLINICAL INVESTIGATION	
Moore DC	Natural Course of Subclinical Hypothyroidism in Childhood and Adolescence. Arch Pediatr Adolesc Med 150(3): 293-297, 1996.
Sherman RA, Camfield MR, Arena JG	The Effect of Presence or Absence of Low Back Pain on the MMPI's Conversion V. Military Psychology 7(1): 29-38, 1996.
Sherman RA, Karstetter KW, May H, Woerman AL	Prevention of Lower Limb Pain in Soldiers Using Shock-Absorbing Orthotic Inserts. J Amer Podiatric Med Assoc 86(3): 117-122, 1996.
Sherman RA, Woerman AL, Karstetter KW, May H	Prediction and Portrayal of Repetitive Stress-Induced Lower Limb Pain Disorders Among Soldiers in Basic Training Using Videothermography. Clinical Journal of Pain 11(3): 236-241, 1995.
Sherman RA, Woerman AL, Karstetter KW	Comparative Effectiveness of Videothermography, Contact Thermography, and Infrared Beam Thermography for Scanning Relative Skin Temperature. J Rehab Research Development 33(4), 1996.
DEPARTMENT OF DENTISTRY	
Bandrowsky T, Vorono AA, Fiaschetti DK	Mandible Fracture in a Child With Menkes' Kinky Hair Syndrome. J Oral Maxillofac Surg 54(1): 105-107, 1996.
Vorono AA	The Oral and Maxillofacial Surgeon: Roles in the Deployed Hospital. Army Medical Dept Journal 95(8): 12-14, 1995.
DEPARTMENT OF EMERGENCY MEDICINE	
Schmidt TA, Iserson KV, Freas GC, Adam JG, Burke TF, Derse AR, Goldfrank L, Kalbfleisch ND	Ethics of Emergency Department Triage: SAEM Position Statement (Special Contributions). Academic Emergency Medicine 2(11): 990-995, 1995.
Vandenberg JT, Rudman NT, Ramos DE	Large-diameter Suction Tubing Significantly Improves Simulated Vomitus Evacuation Times. Academic Emergency Medicine 3(5): 480, 1996.
Wilson LA, Cummins RO	Moonlighting Revisited. Ann Emerg Med 27(1): 102, 1996.
DEPARTMENT OF FAMILY PRACTICE	
Blount BW, LeClair BM, Miser WF	Army Family Physician Satisfaction. Military Medicine 160(10): 501-505, 1995.
Bradshaw DM, Miser WF, Collins RN	Non-clinical Roles of Army Family Physicians in Their First Post-residency Assignment and Their Level of Preparedness for These Roles. Military Medicine 161(9): 547-551, 1996.

Emerine RW	A Health Risk Appraisal and Needs Assessment of the Active Duty Population on Naval Air Station Whidbey Island, 1996.
Miser WF, Blount W, Leclair BM, Schirner WA, Weightman GW, Maness DL, Jones R	The Practice of Obstetrics by Army Family Physicians. J Amer Board Family Practice 9(3): 174-181, 1996.
Miser WF, Evans P, MacDonald DC	Teaching the Professional Boundaries in the Physician-Patient Relationship, Letter to the Editor. JAMA 1996.
Murray MJ, Evans P	Sudden Exertional Death in a Soldier with Sickle Cell Trait. Military Medicine 161(5): 303-305, 1996.
Whittaker P, Hassett V, Hassett W	Hypothermia in an Apparently Alert Woman. US Army Medical Dept Journal: 23-24, 1995.
MADIGAN CANCER INSTITUTE	
Kao CC, Rand RP, Holt CP, Pierece R, Timmons JH, Wood DE	Internal Mammary Silicone Lymphadenopathy Mimicking Recurrent Breast Cancer: A Case Report. Plastic & Reconstr Surg, 1996.
Kao CC, Rand RP, Holt CP, Pierece R, Timmons JH, Wood DE	Internal Mammary Silicone Lymphadenopathy Mimicking Recurrent Breast Cancer: A Case Report. Plastic & Reconstructive Surg, 1996.
DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE	
Moore JW, Cambier PA	Transcatheter Occlusion of Patent Ductus Arteriosus. J of Interventional Cardiology 8(5): 517-531, 1995.
DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE	
Hobbs CJ, Jones RE, Plymate SR	Nandrolone, A 19-Nortestosterone, Enhances Insulin-independent Glucose Uptake in Normal Men. J Clin Endocrin Metab 81(4): 1582-1585, 1996.
Jones RE	Synthesis of Ether Lipids and Phosphatidylethanolamine by Ejaculated Human Sperm, 1996.
DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE	
Brilliant SE, Lester PA, Ohno AK, Carlon MJ, Davis BJ, Cushner HM	Hemolytic-uremic Syndrome Without Evidence of Microangiopathic Hemolytic Anemia on Peripheral Blood Smear. South Med J 89(3): 342-345, 1996.
DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE	
Morris JT, Beckius M, Jeffery BS, McAllister CK	Cavitary Lung Disease Caused by Mycobacterium Simiae and Nocardia Asteroides. Infections in Medicine 13(3): 216-217, 1996.
DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE	
Do NV, Lemar HJ, Reed HL	Thyroid Hormone Responses to Environment Cold Exposure and Seasonal Change: A Proposed Model. Endocrin and Metabol 3(1): 7-16, 1996.
Landry FJ, Horwhat JD, Tomich D, Pinski L	Felodipine as an Alternative to More Expensive Calcium Antagonists in Mild to Moderate Hypertension. South Med J 89(6): 573-577, 1996.

Leclerc KM, Landry FJ	Benign Nocturnal Leg Cramps, Current Controversies Over Use of Quinine. Postgrad Med 99(2): 177-178, 1996.
Lesho EP	Can Tuning Forks Replace Bone Scans For Identification of Tibial Stress Fractures?. JAMA 0(0): , 1996.
Lesho EP, LeBrun C, Landry FJ, Tsuchida AM, Cooper RH	Fatal Duodenovacal Fistula Caused By Peptic Ulcer. Southern Medical Journal 89(9): 925-926, 1996.
Salerno SM, Landry FJ, Schick JD, Schoomaker EB	The Effect of Multiple Neuroimaging Studies on Classification, Treatment, and Outcome of Acute Ischemic Stroke. Ann Intern Med 124(1): 21-26, 1996.
DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE	
Elliott MA, Peroutka SJ, Welch S, May EF	Familial Hemiplegic Migraine, Nystagmus, and Cerebellar Atrophy. Ann Neurol 39(1): 100-106, 1996.
Newmark J	Thoracic Outlet Syndromes: A Non-surgeon's Perspective for Those Caring for Musicians. Work 7(2): 95-107, 1996.
Newmark J, Halliday AW	Field Neurology: The Role of the U.S. Army Neurologist Under MedForce 2000. Military Medicine 161(7): 367-368, 1996.
DEPARTMENT OF MEDICINE, PULMONARY SERVICE	
Dillard TA, Knutson SW, Berg BW, Mehm WJ, Phillips YY	Accuracy of Formulae for Predicting Hypoxemia During Air Travel. American J Resp Crit Care Med, 1996.
Grathwohl KWA	Videoscopic Placement of Feeding Tubes: Development of a Through the Tube Technique, 1996.
Grathwohl KWA, Bruns BJ, LeBrun CJ, Ohno AK, Dillard TA, Cushner HM	Does Hemodilution Exist? Effects of Saline Infusion on Hematologic Parameters in Euvolemic Subjects. South Med J 89(1): 51-55, 1996.
Grathwohl KWA, Thompson JW, Riordan KK, Roth BJ, Dillard TA	Digital Clubbing Associated with Polymyositis and Interstitial Lung Disease. Chest 108: 1751-1752, 1996.
Pina JS, Meyer CA, Billingsley JL, Matlock JP, Horan MP, Knodel DH	Inflammatory Diseases of the Lung Causing False-positive 131iodine Whole Body Scans in the Evaluation of Papillary Thyroid Carcinoma: Two Case Reports. Chest 110(2): 565-567, 1996.
Roth BJ	Evaluating Pleural Fluid. Chest 110(1): 7-8, 1996.
Salerno SM, Ormseth EJ, Roth BJ, Meyer CA, Christensen ED, Dillard TA	Sulfasalazine Pulmonary Toxicity in Ulcerative Colitis Mimicking Clinical Features of Wegener's Granulomatosis. Chest 110(2): 556-559, 1996.
Salerno SM, Strong JS, Roth BJ, Sakata V	Eosinophilic Pneumonia and Respiratory Failure Associated with a Trazodone Overdose. Am J Respir Crit Care Med: 2170-2172, 1995.

DEPARTMENT OF NURSING	
Acselrod BJ	A Descriptive Study of the Development of Critical Pathways in the Perioperative Nursing Department in Two Northwest Hospitals, 1996.
Hopkins DL	The Diagnosis of Ineffective Communication in Acutely Ill, Intubated, & Ventilated Adults: Frequency and Factors Related to the Identification of This Nursing Diagnosis. 1996.
Metcalf MD	Descriptive Study of Military Families with Children Who are Medically Fragile, A Needs Assessment. 1996.
Rovira LB	Intensive Care Unit Nurse Perceptions of the Graphical User-Interface to Support Medication Record Retrieval Tasks, 1996.
Young-McCaughan SB	Sexual Functioning in Women With Breast Cancer After Treatment With Adjuvant Therapy. Cancer Nurs 19(4): 308-319, 1996.
DEPARTMENT OF OBSTETRICS/GYNECOLOGY	
Davis GD	Uterine Prolapse After Laparoscopic Uterosacral Transection in Nulliparous Airborne Trainees: A Report of Three Cases. J Reprod Med Obstretr Gynecol 41(4): 279-282, 1996.
Macedonia CR, Calhoun BC, Hume RF, Patience TH, Kopelman JN, Maslow AS, Littlefield R, Collins D	Volumetric Display of Three-Dimensional Ultrasound Data for Telemedicine Applications in Perinatology. Amer J Obstet & Gynecol 174(1), 1996.
Markenson GR, Foley KS, Maslow AS, Kopelman JN	The Effects of Atrial Natriuretic Factor and Angiotensin II on Fetal-Placental Perfusion Pressure in the Ex Vivo Cotyledon Model. Amer J Obstet & Gyneco 173(4): 1143-1147, 1995.
PREVENTIVE MEDICINE SERVICE	
Goldman DP	The Seroprevalence of Cryptosporidium Infection Among Active Duty Soldiers. UW Thesis, 1996.
Jones RO, DeBorja J, Baer MS	Symmetrical Peripheral Gangrene Requiring Digital Amputation in Meningococcal Infection. 1996.
DEPARTMENT OF PEDIATRICS	
Carter ER	Teaching: Has the Time Come and Gone?. Chest 110(2): 308, 1996.
Carter ER, Guevara JP, Moffitt DR	Pulmonary Hemorrhage in an Adolescent with Henoch-Schonlein Purpura. West J Med 164(2): 171-173, 1996.
Carter ER, Webb CR, Moffitt DR	Evaluation of Heliox in Children Hospitalized with Acute Severe Asthma, a Randomized Crossover Trial. Chest 109(5): 1256-1261, 1996.

Fairchok MP, Ashton WS, Fischer GW	Carriage of Penicillin-Resistant Pneumococci in a Military Population in Washington DC: Risk Factors and Correlation with Clinical Isolates. Clinical Infectious Diseases 22(6): 966-972, 1996.
Gries DM, Fairchok MP	Typhoidal Tularemia in a Human Immunodeficiency Virus-Infected Adolescent. Ped Infectious Disease Journal 15(9): 838-840, 1996.
Hinson RM, Naulty C	Letters to the Editor. Journal of Perinatology 15(6): 518-519, 1995.
Rawlings JS, Scott JS	Postconceptional Age of Surviving Preterm Low-Birth-Weight Infants at Hospital Discharge. Arch Pediatr Adolesc Med 150(3): 260-262, 1996.
Stafford EM, Stewart RS, Teague GR, Gomez RR, Crothers BA, Michel TF, Patience TH, Moore DC	Detection of Human Papillomavirus in Cervical Biopsies of Summer Camp ROTC Cadets with Abnormal Papanicolaou Smears. J Pediatr Adolesc Gynecol 9(3): 119-124, 1996.
PHYSICAL MEDICINE & REHABILITATION SERVICE	
Dettori JR, Bullock SH, Franklin RJ, Sutlive TG, Patience TH	The Effects of Spinal Flexion and Extension Exercises and Their Associated Postures in Patients With Acute Low Back Pain. Spine 20(21): 2303-2312, 1995.
Lauder TD, Dillingham TR	The Cervical Radiculopathy Screen: Optimizing the Number of Muscles Studied. Muscle Nerve 19(5): 662-665, 1996.
DEPARTMENT OF RADIOLOGY	
Bender GN, Timmons JH, Williard WC, Carter J	Computed Tomographic Enteroclysis, One Methodology. Investigative Radiology 31(1): 43-49, 1996.
Do-Dai DD, Youngberg RA, Lanchbury FD, Pitcher JD, Garver TH	Intraligamentous Ganglion Cysts of the Anterior Cruciate Ligament: MR Findings with Clinical and Arthroscopic Correlations. J Comput Assist Tomogr 20(1): 80-84, 1996.
Downs DM, Damiano TR, Rubinstein D	Gasserian Ganglion: Appearance on Contrast-Enhanced MR. Amer Society of Neuroradiology 17: 237-241, 1996.
Ho VB	Posterior Fossa Arachnoid Granulations: MR Features and Incidence. RSNA, 1996.
Ho VB, Kinney JB, Sahn DJ	Contributions of Newer MR Imaging Strategies for Congenital Heart Disease. RadioGraphics 16(1): 43-60, 1996.
Mansfield LT, Youngberg RA, Coughlin WF, Chooljian D	MRI of Giant Cell Tumor of the Tendon Sheath in the Cervical Spine. J Comput Assist Tomogr 20(1): 113-115, 1996.
Williams SC, May CC, Contreras M	A Nuclear Medicine Review Manual on the Internet. Amer J Roentgenol 167(3): 585-586, 1996.

DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE

Pettine SM, Place RJ, Babu SS, Williard WC, Kim DG, Carter PL	Stereotactic Breast Biopsy is Accurate, Minimally Invasive, and Cost Effective. Amer J Surg 171(5): 474-476, 1996.

DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

Ainbinder DJ, Tellado M	VA Case of the Month, Armed Forces Institute of Pathology. Sympathetic Ophthalmia, 1995.
George DP, Zamber RW	Chondrosarcoma Metastatic to the Eye. Arch of Ophthalmology 114(3): 349-351, 1996.
George RK, Walton RC, Whitcup SM, Nussenblatt RB	Primary Retinal Vasculitis: Systemic Associations and Diagnostic Evaluation. Ophthalmology 103(3): 384-389, 1996.
Hadley SC, Mader TH, Shannon SG, Mason KT	Early Cataract Extraction for Military Aviators: The US Army Aviation Epidemiology Data Register. Invest Opthal Visual Science 37(3): 759, 1996.
Kastl PR, Ainbinder DJ	Proptosis as the Initial Presentation of Fungal Sinusitis in Immunocompetent Patients. Pract Revs in Ophthal 12(11): , 1995.
Kastl PR, Ainbinder DJ	Ocular Surface Squamous Neoplasia. Prac Revs in Ophthalmology 12(12), 1995.
Mader TH, Blanton CL, Gilbert BN, Kubis KC, Schallhorn SC, White LJ, Parmley VC, Ng JD	Refractive Changes During 72-hour Exposure to High Altitude After Refractive Surgery. Ophthalmology 103(8): 1188-1195, 1996.
Mader TH, White LJ	High Altitude Mountain Climbing After Radial Keratotomy (Letter to the Editor). Wilderness & Environmental Med 1: 77-78, 1996.
Newmark J, Clayton WL	Persian Gulf Illnesses: Preliminary Neurological Impressions. Military Medicine 160(10): 505-507, 1995.
Ng JD, White LJ, Parmley VC, Hubickey W, Carter J, Mader TH	Effects of Simulated High Altitude on Patients Who Have Had Radial Keratotomy. Ophthalmology 103(3): 452-457, 1996.
Torok PG, Mader TH	Corneal Abrasions: Diagnosis and Management. Amer Fam Physician 53(8): 2521-2529, 1996.
Torres MF, Mazzoli RA, Hansen EA, Ng JD, Raymond WR	Combined Porous Implant and Thin Dermis Fat Graft for Complex Socket Reconstruction. Invest Opthal Visual Science 37(3): , 1996.
Witkop GS, Chismire KJ, George DP	Anatomic Considerations in Implantation of the Ahmed Glaucoma Valve. Archives of Ophthal 114: 223-224, 1996.
Witkop GS, Chismire KJ, George DP	Preoperative Calculation of Safe Glaucoma Implant Sites. Invest Opthal Visual Science 37(3): , 1996.
Wroblewski KJ, Dahlhauser K, Parmley VC, Mader TH	Anterior Capsular Contraction in Phacoemulsification. Invest Ophthal Visual Science 37(3): 764, 1996.

DEPARTMENT OF SURGERY, ORTHOPEDIC SURGERY SERVICE	
Arciero RA, StPierre P	Acute Shoulder Dislocation, Indication and Techniques for Operative Management. Clinics in Sports Medicine, 1995.
Carpenter CT, Dietz JW, Leung KYK, Hanscom DA, Wagner TA	Repair of a Pseudarthrosis of the Lumbar Spine, a Functional OutcomeStudy. J Bone Joint Surgery 78(5): 712-720, 1996.
Carpenter CT, Pitcher JD, Davis BJ, Gomez RR, Schofield TD, Youngberg RA	Cystic Hygroma of the Arm: A Case Report and Review of the Literature. Skeletal Radiology 25(2): 201-204, 1996.
Esplin VS, Tencer AF, Hanel DP, Cosio MQ	Restoration of Function of the Thumb Flexor Apparatus Requires Repair of the Oblique and One Adjacent Flexor Tendon Pulley. J Orthop Res 14(1): 152-156, 1996.
Jones RO, Chen JB, Pitcher JD, Gebhart-Mueller EY, Mueller PQ	Rheumatoid Nodules Affecting Both Heels With Surgical Debulking. J Amer Podiatric Med Assoc 86(4): 179-182, 1996.
Rooney RC, Fernicola PJ, Pitcher JD	Arthroscopic Excision of Intra-Articular Ossifications, A Case Report and Review of the Literature. American J of Orthopedics: 437-440, 1996.
StPierre P, Olson EJ, Elliott JJ, O'Hair KC, McKinney LA, Ryan J	Tendon-Healing to Cortical Bone Compared with Healing to a Cancellous Trough, a Biomechanical and Histological Evaluation in Goats. J of Bone and Joint Surgery 77(12): 1858-1866, 1995.
StPierre P, Staheli LT, Green NE, Smith JB	Femoral Neck Stress Fractures in Children and Adolescents. J of Pediatric Orthopaedics 15(4): 470-473, 1995.
DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE	
Edmond C, Billinghurst M, Savage J, Oppenheimer P	The Expert Surgical Assistant: An Intelligent Virtual Environment with Multimodal Input. Health Care in the Information Age, Chapter 65: 590-607, 1996.
Edmond CV, Billinghurst M	Expert Systems in Otolaryngology. Otolaryng Head & Neck Surgery 115(2): 135, 1996.
Edmond CV	Otolaryngology Training and Surgical Simulation. Otolaryng Head & Neck Surgery 115(2): 135, 1996.
Hetherington HE, Hollinger J, Morris MR, Panje WR	Onlay Bone Augmentation With an Osteoinductive Implant. Ann Otol Rhinol Laryngol 105(7): 568-573, 1996.
DEPARTMENT OF SURGERY, UROLOGY SERVICE	
Petroski RA, Thrasher JB, Hansberry KL	New Use of Foley Catheter for Precise Vesicourethral Anastomosis During Radical Retropubic Prostatectomy. J Urol 155(4): 1376-1377, 1996.
Salerno SM	Do Antibiotics Alter the Outcome of Ischemic Colitis?. American J Gastroenterology, 1996.

Schwartz BF, Auman R, Peretsman SJ, Moul JW, Deshon GE, Hernandez J, Rozanski TA, Thrasher JB	Prognostic Value of BHCG and Local Tumor Invasion in Stage 1 Seminoma of the Testis. J Surg Oncol 61(2): 131-133, 1996.
Schwartz BF, Norbeck JC, Hansberry KL, Wettlaufer JN, Thrasher JB	The Role of Cystoscopy Before Radical Prostatectomy. British J of Urology 77(1): 93-95, 1996.
Schwartz BF, Swanzy S, Thrasher JB	A Randomized Prospective Comparison of Antibiotic Tissue Levels in the Corpora Cavernosa of Patients Undergoing Penile Prosthesis Implantation Using Gentamicin + Cefazolin Vs Oral Fluoroquinolone for. The Journal of Urology 156(3): 991-994, 1996.
Soderdahl DW	Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction. British J of Urology, 1996.
Soderdahl DW, Knight RW, Hansberry KL	Erectile Dysfunction Following Transurethral Resection of the Prostate. Journal of Urology 156(4): 1354-1356, 1996.
Soderdahl DW, Thrasher JB, Hansberry KL	Bilateral Renal Cell Carcinoma in Autosomal Dominant Polycystic Kidney Disease. Am J Nephrology 516: , 1996.
Thrasher JB, Dodge RK, Robertson JE, Paulson DF	Biologic Hazards of Double Primary Neoplasms Among Patients with Genitourinary Malignancy. North Carolina Medical Journal 57(3): 172-175, 1996.
Thrasher JB, Tennant MK, Twomey PA, Hansberry KL, Wettlaufer JN, Plymate SR	Immunohistochemical Localization of Insulin-Like Growth Factor Binding Proteins 2 and 3 in Prostate Tissue: Clinical Correlations. Journal of Urology 155(3): 999-1004, 1996.

PRESENTATIONS

FISCAL YEAR 96

DEPARTMENT ANESTHESIOLOGY AND OPERATIVE SERVICES

Acarregui-Garrett JM, Dulaveris JE, Garrett MP, Klaus JA	Postsurgical Temperature Trends.	American Association of Nurse Anesthetists Annual Convention, Philadelphia, USA, August 96.
Hermann JD, Bolt SL, Helman JD, Reimer C, Tollefson DFJ	The Effect of Lidocaine and Hydralazine on Radial Artery Diameter and Flow Velocity.	Society of Critical Care Medicine Symposium, New Orleans, USA, February 96.
Shepherd DW, Dampier DS, Daniel PC	Rocuronium: A Comparison of Two Priming Doses.	American Association of Nurse Anesthetists Annual Convention, Philadelphia, USA, August 96.

DEPARTMENT OF CLINICAL INVESTIGATION

Aldous WK, Martin RK	Instructing Physicians in Molecular Biology Techniques.	Society of Armed Forces Medical Laboratory Scientists, 20th Annual Meeting, Washington DC, USA, March 96.
Hamblen E, Sherman RA, Powell JB	The Effect of Premenstrual Syndrome and Primary Dysmenorrhea on Women's Cognitive Functioning and Job Performance Before and After Biofeedback Treatment.	Association for Applied Psychophysiology and Biofeedback, 27th Annual Meeting, Albuquerque, USA, March 96.
Hill C, Wong M, Sherman RA	Variability in Multiple Ambulatory EMG Recordings of Pain Free Subjects.	Association for Applied Psychophysiology and Biofeedback, 27th Annual Meeting, Albuquerque, USA, March 96.
Sherman RA, Arena JG, Evans CB, Hill C, Wong M	Environmental-Temporal Relationships Between Pain and Muscle Tension: Ramifications for Biofeedback Treatment.	Clinical-Applied Surface Electromyography, Annual Meeting, Key West, USA, February 96.
Sherman RA, Karstetter KW, Woerman AL, Damiano M, Hermann-Do KA, Evans CB, Wong M, Robson L	Thermography for CRPS 1 (RSD): Controversial Issues in Diagnosis.	Annual Meeting on Advances in Pain, Orlando, USA, February 96.
Sherman RA, Marden LA MAJ, Stephenson K	The Effect of Pulsed Electromagnetic Fields on Classic Migraine Headaches.	Association for Applied Psychophysiology Annual Meeting, Albuquerque, NM, USA, March 96.

Sherman RA, Robson L, Marden LA MAJ	The Effect of Pulsed Electromagnetic Fields of Classic Migraine Headaches: A Preliminary, Single Group Study.	International Association for the Study of Pain, 8th World Congress on Pain, Vancouver, Canada, August 96.
Sherman RA, Robson L, Marden LA MAJ	Initial Exploration of Pulsing Electromagnetic Fields for Treatment of Migraine Headaches.	Eighth World Congress on Pain, Vancouver, Canada, August 96.
Wong M, Davis GD, Sherman RA	Evaluation of the Treatment of Exercise Induced Urinary Incontinence Among Female Soldiers.	Association for Applied Psychophysiology and Biofeedback, 27th Annual Meeting, Albuquerque, NM, March 96.
DEPARTMENT OF EMERGENCY MEDICINE		
Morres CA	Disaster Medicine Fellowship Curricula: Can We Form an Academic Foundation?.	Society for Academic Emergency Medicine, Denver, USA, May 96.
Pace SA	Prehospital Use of Succinylcholine by Paramedics.	Society for Academic Emergency Medicine, Denver, USA, May 96.
Vandenberg JT, Rudman NT, Ramos DE	Large Diameter Suction Tubing Significantly Improves Simulated Vomitus Evacuation Times.	Society for Academic Emergency Medicine (SAEM) Meeting, Denver, USA, May 96.
DEPARTMENT OF EMERGENCY MEDICINE		
Emerine RW	A Health Risk Appraisal and Needs Assessment of the Active Duty Population on Naval Air Station Whidbey Island.	1996.
DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE		
Eisenhauer MD, Collier HE, Cambier PA	Beneficial Impact of Aorto-Coronary Bypass Graft Markers on Post-Operative Angiography.	Army Chapter, American College of Physicians, Washington DC, USA, October 95.
DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE		
Morris JT	More Unusual Opportunistic Infections in HIV Patients.	12th Annual Scientific Meeting, Army Chapter, American College of Physicians, Reston, USA, October 95.
DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE		
Lesho EP, Jones RE	Hypothyroid Graves' Disease, an Immunologic Chameleon.	American College of Physicians Meeting, San Francisco, USA, April 96.

DEPARTMENT OF MEDICINE, PULMONARY SERVICE

Dillard TA, Knutson SW, Berg BW, Mehm WJ, Phillips YY	Accuracy of Formulae for Predicting Hypoxemia During Air Travel.	American Thoracic Society International Conference, New Orleans, USA, May 96.
Grathwohl KWA, Gibbons RG, Dillard TA, Roth BJ	Videoscopic Placement of Feeding Tubes: Development of a Through the Tube Technique.	American College of Physicians, Army Region, Reston, USA, October 95.
Grathwohl KW, Gibbons RG, Dillard TA, Roth BJ	Videoscopic Placement of Feeding Tubes: Development of a Through the Tube Technique.	American Thoracic Society International Conference, New Orleans, USA, May 96.
Lawless NP, Dillard TA, Torrington KG	Venturi Devices for Hypoxia Inhalation Testing.	American College of Chest Physicians, New York, USA, October 95.
Moores LK, Phillips YY, Bilello KM, Dillard TA	The Effect of Chronic Oral Diltiazem Therapy on Exercise Capacity and Response to Hypoxic Gas Inhalation in Severe COPD.	American College of Chest Physicians, New York, USA, October 95.
Moores LK, Phillips YY, Bilello KM, Dillard TA	The Effect of Acute and Chronic Diltiazem Administration on Pulmonary Gas Exchange and Oxygen Delivery in Severe COPD.	American College of Chest Physicians, New York, USA, October 95.
Pina JS, Roth BJ, Carter ER	Is the Use of Nose Clips Necessary in Adults Performing Routine Spirometry?.	American College of Chest Physicians, New York City, USA, October 95.
Strong JS, Horwhat D, Roth BJ	Exercise Tolerance in Patients with Severe COPD is not Reduced by Use of a Mouthpiece During Exercise Testing.	American Thoracic Society International Conference, New Orleans, USA, May 96.
Zacher LL, Keenan LM, Meyer CA, Gore RL, Pike JD, Horan MP	Prospective Comparison of Computed Tomography and Fiberoptic Bronchoscopy in Patients with Unexplained Hemoptysis and Non-Localizing Chest Roentgenograms.	American College of Chest Physicians, New York, USA, November 95.

DEPARTMENT OF NURSING

Acarregui-Garrett JM, Dulavaris J, Garrett MP, Klaus JA	Postsurgical Temperature Trends.	American Association of Nurse Anesthetists Annual Convention, Philadelphia, USA, August 96.
Acarregui-Garrett JM, Dulaveris J, Garrett MP, Klaus JA	Postsurgical Temperature Trends.	Washington Association of Nurse Anesthetist Annual Convention, Seattle, USA, April 96.

Renaud MT, DePaul D	Fatigue Following Childbirth: Military Family Outcomes.	Celebrating Nursing Research and Scholarship, Pacific Luthern University, Tacoma, USA, November 96.
DEPARTMENT OF OBSTETRICS/GYNECOLOGY		
Macedonia CR, Calhoun BC, Hume RF, Patience TH, Kopelman JN, Maslow AS, Littlefield R, Collins DM	Volumetric Display of Three-Dimensional Ultrasound Data for Telemedicine Applications in Perinatology.	Society of Perinatal Obstetrician Annual Meeting, Kamuela, USA, February 96.
Palacio PE, Wiess TE, Hibbert ML	Life-Threatening Hemorrhage in Expectantly Managed Ectopic Pregnancy with Negative HCG: A Case Report.	Armed Forces District Meeting of the American College of Obstetrics & Gynecology, San Diego, USA, October 95.
Payne JF, Hibbert ML	Persistent Ectopic Pregnancy Following Total Salpingectomy: A Case Report.	American College of Obstetrics & Gynecology, San Diego, USA, October 95.
DEPARTMENT OF PEDIATRICS		
Bauer AJ, Daniel A, Khozeimeh L, Francis GL	Gonadotropin Releasing Hormone Does Not Affect Steroid Hormone Synthesis by JEG-3 Choriocarcinoma Cells.	30th Annual Uniformed Services Pediatric Seminar, McClean, USA, March 96.
PHARMACY SERVICE		
Hart DM, Tomich D, Conrad RC, Craghead RM	Innovations at Madigan Army Medical Center: Expanding Pharmacy Roles with the Tech-Check-Tech Program.	American Society of Health Systems Pharmacists, Midyear Clinical Meeting, Las Vegas, USA, December 95.
Pinski L, Tomich D, Rembold J	Implementing Pharmaceutical Care with a Pharmacist Managed Prescription Renewal Program.	American Society of Health Systems Pharmacists, Midyear Clinical Meeting, Las Vegas, USA, December 95.
PREVENTIVE MEDICINE SERVICE		
Petroski RA, Soderdahl DW	Adrenocortical Carcinoma.	Kimbrough Urologic Seminar Presentation, Washington DC, USA, November 95.
Petroski RA, Soderdahl DW	Meshgraft Urethroplasty.	Kimbrough Urologic Seminar, Washington DC, USA, November 95.

DEPARTMENT OF RADIOLOGY

Fox MG, Rak KM, Lisecki EJ, Castello PH	Radiological Patterns in Total Hip Arthroplasty: Hydroxyapatite-coated and Uncoated Femoral Stem Prothesis.	Radiological Society of North American, Chicago, USA, November 95.
Ho VB	MR of the Thoracic Aorta: Techniques and a Pathologic Spectrum.	Annual Meeting of the American Roentgen Ray Society, San Diego, USA, May 96.
Mansfield LT	Radiology Research: A Primer for Residents.	Association of University Radiologists Annual Meeting, Birmingham, USA, April 96.

DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

Hadley SC	Paranasal Sinus Lymphoma Presenting with Neuro-Ophthalmic Complaints Only.	North American Neuro-Ophthalmology Society (NANOS) 22nd Annual Meeting, Snowbird Resort, USA, February 96.
Hadley SC, Mader TH, Shannon S, Mason KT	Early Cataract Extraction for Military Aviators: The U.S. Army Aviation Epidemiology Data Register.	Association of Research and Vision in Ophthalmology Annual Meeting, Ft Lauderdale, USA, April 96.
May EF, Gilbert BN, Patience TH, Hansen EA	Afferent Pupillary Defect Grading.	North American Neuro-Ophthalmology Society (NANOS) 22nd Annual Meeting, Snowbird Resort, USA, February 96.
Raymond WR, Fannin LA	Safety and Efficacy of Laryngeal Mask Airway Anesthesia in Pediatric Ophthalmology Surgery.	Academy of Ophthalmology, Atlanta, USA, October 95.
Torres MF, Mazzoli RA, Hansen EA, Ng JD, Raymond WR	Combined Porous Implant and Thin Dermis Fat Graft for Complex Socket Reconstruction.	Association of Research and Vision in Ophthalmology Annual Meeting, Ft Lauderdale, USA, April 96.
Witkop GS	Incidence of Trachoma in Eastern Uganda.	Surgeons of America with American Academy of Ophthalmology Meeting, Atlanta, USA, October 95.
Witkop GS, Chismire KJ, George DP	Pre-operative Calculation of Safe Glaucoma Implant Sites.	Association of Research and Vision in Ophthalmology Annual Meeting, Ft Lauderdale, USA, April 96.

Witkop GS, Chismire KJ, George DP	Pre-operative Calculation of Safe Glaucoma Implant Sites.	Walter Reed Tri-Service Biannual Ophthalmology Research Competition, Washington, USA, March 96.
Witkop GS, George DP, Chismire KJ, Leen MM	Anatomic Considerations in Implantation of the Ahmed Glaucoma Valve.	Association of Research and Vision in Ophthalmology Annual Meeting, Ft Lauderdale, USA, April 96.
Wroblewski KJ, Dahlhauser K, Parmley VC, Mader TH	Anterior Capsular Contraction in Phacoemulsification.	Association of Research and Vision in Ophthalmology Annual Meeting, Ft Lauderdal, USA, April 96.
Wroblewski KJ, Hadley SC, Mazzoli RA, Floyd DT, May EF	A Treatable Cause of Visual Loss in Fibrous Dysplasia.	North American Neuro-Ophthalmology Society (NANOS) 22nd Annual Meeting, Snowbird Resort, USA, February 96.
DEPARTMENT OF SURGERY, ORTHOPEDIC SURGERY SERVICE		
Dombroski RT, Asato AJ, Kovac CM, Davis GD, Sherman RA	Incidence of Osteopathic Dysfunction in Non-Gynocologic Female Pelvic Pain, and the Outcome After Osteopathic Treatments.	American Academy of Osteopathy, 1996 Annual Convocation, Atlanta, USA, March 96.
Warme WJ	Structural Bone Allografts in Pediatric Foot Surgery.	SOMOS 37th Annual Meeting, Vail, USA, December 95.
DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE		
Edmond CV	Expert Surgical Assistant[colon] An Intelligent Virtual Environment with Multimodal Input.	Medicine Meets Virtual Reality, San Diego, USA, January 96.
Edmond CV	ENT Surgical Simulator.	Sinus and Allergy Update - Tetons, Jackson Hole, USA, June 96.
Edmond CV	The Substitute Teacher Expert Systems in Medical Training.	Medical Technology Education Conference, Orlando, USA, July 96.
Edmond CV	An ENT Endoscopic Surgical Training Simulator.	Medical Technology Education Conference, Orlando, USA, July 96.
Edmond CV	Otolaryngology Training and Surgical Simulation.	AAOHNS Annual Meeting, Washington DC, USA, September 96.

Edmond CV, Billinghurst M	Expert Systems in Otolaryngology.	AAOHNS Annual Meeting, Washington DC, USA, September 96.
Mesaros GJ	The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas.	American Academy of Otolaryngology-Head and Neck Surgery, Washington DC, USA, September 96.
Song AU	Langerhans Cell Density in Human Oral Mucosa: Relationship to Tobacco, Alcohol Consumption and Squamous Cell Carcinoma.	American Academy of Otolaryngology-Head and Neck Surgery, Washington DC, USA, September 96.
DEPARTMENT OF SURGERY, UROLOGY SERVICE		
Lance RS, Aldous WK, Thrasher JB	Telomerase Activity in Human Transition Cell Carcinoma and Exfoliated Cells in Urinary Cytology Specimens: Prelimenary Findings.	3rd Annual Uniformed Services Urology Research Group Seminar, Denver, USA, March 96.
Salerno SM	Do Antibiotics Alter the Outcome of Ischemic Colitis?.	Washington ACP Meeting, Seattle, USE, December 95.
Salerno SM	Do Antibiotics Alter the Outcome of Ischemic Colitis?.	National ACP Meeting, San Francisco, USA, April 96.
Schwartz BF	Ofloxacin as a Single Agent in Penile Prosthesis Surgery.	American Urological Association Western Section, Seventy-first Annual Meeting, Phoenix, USA, November 95.
Schwartz BF	Prognostic Value of Serum Beta Human Chorionic Gonadotropin Levels in Stage I Seminoma.	American Urological Association Western Section, Seventy-First Annual Meeting, Phoenix, USA, November 95.
Schwartz BF	Randomized Prospective Comparison of Covernosal Antibiotic Levels in Penile Prosthesis Implantation.	James C. Kimbrough Urological Seminar, Forty-Third Annual Meeting, Washington DC, USA, November 95.
Schwartz BF	Bladder Pheochromocytoma.	James C. Kimbrough Urological Seminar, Forty-Third Annual Meeting, Washington DC, USA, December 95.
Schwartz RB, Burke TF	Blood Cultures in Outpatient Pyelonephritis: Necessity or Habit.	Society for Academic Emergency Medicine (SAEM) Meeting, Denver, USA, May 96.
Soderdahl DW	Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction.	Western Section AUA, Scottsdale, USA, November 95.

Soderdahl DW	Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction.	James C. Kimbrough Urological Seminar, Washington DC, USA, November 95.
Thrasher JB	Bilateral Renal Cell Carcinoma in Autosomal Dominant Polycystic Kidney Disease: A Case Report and Literature Review.	American Urological Association, Western Section, Seventy-first Annual Meeting, Scottsdale, USA, November 95.
Thrasher JB	Comparison of Intracavernous Drug-Induced Erection Therapy Versus External Vacuum Devices in the Treatment of Erectile Dysfunction.	American Urological Association, Western Section, Seventy-first Annual Meeting, Scottsdale, USA, November 95.
Thrasher JB	Randomized Prospective Comparison of Cavernosal Antibiotic Levels in Penile Prosthesis Implantation.	James C Kimbrough Urological Seminar, Forty-third Annual Meeting, Washington DC, USA, November 95.
Thrasher JB	Intercavernous Drug Induced Erection Therapy vs External Vacuum Devices in the Treatment of Erectile Dysfunction: A Randomized Crossover Study of Efficacy.	James C Kimbrough Urological Seminar, Forty-third Annual Meeting, Washington DC, USA, November 95.
Thrasher JB	Changes in the Insulin-like Growth Factor System in Prostate Cancer.	James C Kimbrough Urological Seminar, Forty-third Annual Meeting, Washington DC, USA, November 95.
Thrasher JB	Meshgraft Urethroplasty.	James C Kimbrough Urological Seminar, Forty-third Annual Meeting, Washington DC, USA, November 95.
Thrasher JB	Bladder Pheochromocytoma.	James C Kimbrough Urological Seminar, Forty-third Annual Meeting, Washington DC, USA, December 95.
Thrasher JB, Kao T, Garner D, Mooneyhan RD, Moul JW	Multicenter Patient Self-Reported Questionnaire (PSQ) of Incontinence (IN), Impotence (IM), Stricture (S) and Quality of Life (QOL) after Radical Prostatectomy (RP).	American Urological Association, Orlando, USA

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DETAIL SHEETS FOR PROTOCOLS

62ND MEDICAL GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/143 **Status:** On-going

Title: Training of Veterinary Food Inspection Personnel in Field Slaughter and Inspection Methods Utilizing Domestic Swine (Sus scrofa domesticus)

Start Date: 05/26/95 **Est. Completion Date:** Jun 96

Department: 62nd Medical Group **Facility:** MAMC

Principal Investigator: C. H. Martinez

Associate Investigators: None

Key Words: Training:food inspection, Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To train veterinary food inspection personnel in antemortem and postmortem inspection, dispatch, and field slaughter techniques.

Technical Approach: This training protocol will provide experience for food inspection personnel on techniques used within their occupation. A total of two domestic pigs will be used over a 6 month period. After being transported to the training area, the pigs will be inspected using recommended antemortum techniques, stunned using a captive bolt device or mallet and immediately exsanguinated. The methods used are approved by the AVMA Panel on Euthanasia and cause minimal pain or distress to the animals. The pigs will then be eviscerated and inspected using recommended postmortem techniques.

Progress: One session using one pig was held in FY 96.

DETAIL SHEETS FOR PROTOCOLS

ACTIVE DUTY STUDENTS

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/024 **Status:** Completed

Title: The Diagnosis of Ineffective Communication in Acutely Ill, Intubated, Ventilated Adults: Frequency and Factors Related to the Identification of This Nursing Diagnosis

Start Date: 12/15/95 **Est. Completion Date:** Aug 96

Department: Active Duty Students **Facility:** MAMC

Principal Investigator: CPT Denise L. Hopkins, AN

Associate Investigators: Diane M. Pierson, BS, BA, CCRN

Key Words: Communication, nursing diagnosis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To identify the frequency with which ineffective communication is identified as a nursing diagnosis or nursing problem explicitly (i.e., on problem list) or implicitly (deduced from nursing notes) in a population of acutely ill, endotracheally intubated, adult patients. 2) To explore the relationships between some of the factors that surround the intubation and the subsequent identification of the diagnosis of ineffective communication.

Technical Approach: Specifically, the factors to be explored are the length of the patient's intubation, circumstances surrounding intubation, and the acuity of the patient and the unit around the time of intubation and staffing levels. The dependent outcome variable is the frequency of identification of ineffective communication. This variable will not be manipulated, rather reviewed retrospectively in relationship to the frequency of occurrence. A retrospective descriptive correlational design will be used to describe the frequency with which ineffective communication is identified as a nursing diagnosis either explicitly or implicitly. Three groups will emerge, one group having the diagnosis identified explicitly, one group having the diagnosis, identified implicitly, and one group not having the diagnosis identified. These three groups will be compared using ANOVA to test the differences in intubation time and patient/unit acuity. The three groups will be compared for the emergent nature of intubation using a chi-square analysis to determine if the proportion of patients who were intubated emergently differed from the proportion of patients who were intubated nonemergently.

Progress: Fifty records of adult patients who had undergone short-term intubations while experiencing an acute health problem were reviewed retrospectively in order to identify the use of impaired communication either as an explicit or implicit nursing diagnosis. Despite the fact that subjects had an average of five nursing diagnoses, none of the records contained the explicit diagnosis of impaired communication. 36% of the records had the implicit diagnosis. There were no differences in the proportion of patients with and without the diagnosis documented implicitly, regarding the length of intubation, circumstances, patient acuity, or staff workload ratio. The current results demonstrating patient and environment factors do not elicit nursing focus on communication and leave open the possibility that communication-related nursing diagnoses may be receiving inadequate emphasis in critical units, in turn explaining patient reports of difficulty with communication.

DETAIL SHEETS FOR PROTOCOLS

FORT LEWIS, SPECIAL FORCES

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/069	**Status:** On-going
Title: Special Operations Medical NCO Sustainment Training		
Start Date: 03/04/94	**Est. Completion Date:** Jun 96	
Department: Special Forces	**Facility:** MAMC	
Principal Investigator: CPT G. Jeffrey Poffenbarger, MC		
Associate Investigators:	1LT Joseph R. James Jr, SP	
Key Words: Training, medical, special operations,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/19/96

Study Objective: To support required annual Advanced Trauma Life Support type surgical training for all 18D Special Forces medical sergeants. To have exposure, gain experience, and develop proficiency in surgical procedures.

Technical Approach: The following surgical procedures will be performed: Endotracheal intubation, vessel cutdown and catheterization, Soft tissue handling/suturing, chest tube insertion, cricothyroidotomy, pericardiocentesis. All procedures will use goats and support staff from the Department of Clinical Investigation's Laboratory Animal Surgery Service. The trainees will be evaluated through visual observation of satisfactory skill level. Additionally, there will be a 2 day didactic course prior to the animal lab, which will culminate in a written test. After the animal lab all students will undergo a 20 minute oral exam on their performance and details of trauma medicine.

Progress: 24 animals were studied in FY 96, no unexpected loss of animals. 2 training sessions were held, 47 individuals participated in the training.

DETAIL SHEETS FOR PROTOCOLS

UNITED STATES DEPARTMENT OF AGRICULTURE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 92/001	**Status:** On-going
Title: Methods for Assessing Vitamin A Status in Healthy Adults		
Start Date: 10/04/91	**Est. Completion Date:** Jul 92	
Department: USDA	**Facility:** MAMC	
Principal Investigator: Betty Jo Burri, Ph.D.		
Associate Investigators:	Andrew J. Clifford, Ph.D.	
Key Words: liver,vitamin A,isotope technique		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine vitamin A status in healthy free-living adults in the San Francisco area.

Technical Approach: This protocol will consist of studies focusing on three groups of people: (1) women aged 55-60 (2) men aged 55-60 and (3) men aged 18-24. Each group will consist of 30 healthy nonsmokers. These age and sex groups have been selected to include adults with divergent ages and because vitamin A and its analogs can be tetratogenic, making it potentially hazardous to administer analogs to young women. Subjects will be prescreened for serum retinol and holo-retinol binding protein (RBP) in an effort to get at least 15 people in each group with low vitamin A serum concentrations. Subjects will fill out a questionnaire in order to estimate their usual intake of high vitamin A foods over the past year. Body weights and blood pressures will be measured on the first and last days of the study. The vitamin A analogs are to be given on days one (didehydroretinol) and eight (tetradeuterated retinol acetate) of the study. In a pilot study to test the time course of equilibration and elimination of the analogs, three volunteers from each group will be given the cocktails as stated and blood samples taken a 5, 8, and 30 hr, and at 2, 3, 4, 5, 15 days and every 30 days thereafter. This blood would be collected in addition to the blood required for the regular study (pre ingestion, 5 hr, and days 8, 29, and 30). The study will compare three promising new methods for assessing vitamin A status to serum retinol, and to vitamin A liver stores measured by deuterated analogs and by vitamin A2. The new methods tested will be free- and transthyretin-bound holo-retinol binding protein as determined by HPLC, erythrocyte transglutaminase levels, and goblet cell abnormalities. Addendum (Oct 91): All of the testing was done except for tests of the vitamin A2. Vitamin A2 proved to be very difficult to purify, so it was never actually given to the subjects. Then two significant things happened a supply of high quality vitamin A2, approved for human use, was obtained, and it was found that the tetradeuterated analog may interfere with the vitamin A2 test, even when these analogs are given 8 days apart. It is now recommended that the doses of vitamin A2 and other analogs be separated by at least 30 days. Therefore in this study, the vitamin cocktails will be given on day 1 and day 30, with blood draws added as appropriate.

Progress: Fifty-four patients have been entered. This is a longitudinal study in which the patients are not due for follow-up until 1997.

DETAIL SHEETS FOR PROTOCOLS

BASSETT ARMY COMMUNITY HOSPITAL, DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/001	**Status:** Completed
Title: Evaluation of the Benign Nodular Flocculus of the Iris in the Newborn		
Start Date: 10/20/95	**Est. Completion Date:**	
Department: BACH/Pediatrics	**Facility:** MAMC	
Principal Investigator: CPT W. Scott Ashton, MC		
Associate Investigators: LTC Carolyn S. Adkins, AN	CPT Damien R. Delzer, MS	
Key Words: Nodular flocculus, Iris, Newborn		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the incidence and natural history of the benign nodular flocculus of the iris in the newborn.

Technical Approach: Demographic data and the presence or absence of benign nodular flocculus of the iris will be recorded for at least 200 newborn infants examined by the principal investigator. Individuals having iris flocculi will have the number of flocculi recorded for each eye. The incidence of flocculi and 95% confidence limits for this estimate will be determined.

Progress: 100 patients were enrolled, a publication was generated.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF ANESTHESIOLOGY AND OPERATIVE SERVICES

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/075 **Status:** Terminated

Title: Psoas Compartment Catheter vs. PCA for Post-Operative Analgesia After Anterior Cruciate Ligament Reconstruction Surgery

Start Date: 02/17/95 **Est. Completion Date:** Sep 95

Department: Anesthesiology & Operative Svcs **Facility:** MAMC

Principal Investigator: MAJ Stephen L. Bolt, MC

Associate Investigators: CPT Mark C. Weston, MC; Paul J. Teiken, M.D.; LTC John B. Whittemore, AN

Key Words: Analgesia:PO, psoas, PAC, ligament

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate the efficacy of single lower limb nerve plexus block for post-operative pain relief following anterior cruciate ligament (ACL) reconstructive surgery.

Technical Approach: All patients presenting for ACL reconstruction will receive comparable general anesthetics for their surgery. After induction of general anesthesia, the patients will be randomized into two groups for management of post-operative analgesia: a) PCA morphine alone, b) Psoas Compartment Catheter and PCA morphine. The latter group will receive a loading dose of local anesthetic through the Psoas Compartment Catheter, followed by an infusion of local anesthetic. The degree of pain relief achieved by both groups of patients will be assessed at regular intervals via: a) milligrams of morphine dispensed from the PCA pump and b) Visual Analog Pain Scale (VAPS) measurements by a disinterested investigator. We will attempt to demonstrate a 50% reduction (40mm to 20mm on the VAPS) in both postoperative pain scores and narcotic requirement in the Psoas Compartment Catheter population. The sample size is pending power analysis. The data analysis will be performed uslng either the Mann-Whitney U test or t-test.

Progress: Five patients were enrolled in this study; 4 in FY 95 and 1 in FY 96. The protocol was terminated because the investigators did not have the time to pursue it due to increased clinic obligations.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/135	**Status:** Terminated
Title: Epidural Pressures During Continuous Labor Epidural Infusions		
Start Date: 06/16/95	**Est. Completion Date:**	
Department: Anesthesiology & Operative Svcs	**Facility:** MAMC	
Principal Investigator: MAJ James D. Helman, MC		
Associate Investigators:	CPT Michael L. Pylman, MC	
Key Words: Pressure:epidural, labor		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the pressure within the epidural space during an infusion for labor analgesia.

Technical Approach: Epidural pressures will be determined on 16 parturients at one hour intervals starting thirty minutes after placement of their epidural analgesia. This will be accomplished by transducing an in situ epidural catheter using a standard pressure transducer (modified wheatstone bridge). Sixteen parturients will be transduced in the right lateral decubitus position with reference to the cap of the epidural catheter during their labor. The pressure recorded will be the lowest pressure seen during the five minutes of monitoring. Univariant analysis of pressures versus time of infusion. Patient number in study chosen to give confidence interval of 95% based on standard deviation from our previous study and a projected range of 10 torr.

Progress: No new patients were enrolled in FY 96. Ten patients had been entered previously. Results were inconclusive due to the small number of subjects. The protocol was terminated due to the departure of the PI.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/130 **Status:** Completed

Title: The Effect of Lidocaine and Hydralazine on Radial Artery Flow Velocity and Diameter

Start Date: 09/02/94 **Est. Completion Date:**

Department: Anesthesiology & Operative Svcs **Facility:** MAMC

Principal Investigator: CPT John D. Hermann, MC

Associate Investigators: MAJ James D. Helman, MC; MAJ Stephen L. Bolt, MC

Key Words: artery:radial, artery:diameter, artery:flow velocity, lidocaine, hydralazine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if the periarterial infiltration of lidocaine and/or hydralazine near the radial artery at the wrist will either decrease the velocity of flow and/or increase the diameter of the radial artery at the wrist as measured by a duplex/doppler instrument.

Technical Approach: The study will be comprised of 30 healthy volunteers recruited from the MAMC house staff. The study population will initially be comprised of 10 patients in the pilot arm of the study and an additional 20 patients will be studied to confirm the results and to improve the statistical power of the study. Each of the study subjects will serve as their own control. Prior to receiving medication the subjects will have baseline radial artery flow velocity and vessel diameter measurements made and recorded. Each of the subjects will receive the study medication in a random fashion; either normal saline; 1% lidocaine and hydralazine (2 mg/ml). The study will examine the flow velocities in the radial artery with a 5 mHz ATL Duplex scanning device before and after the infiltration of the study medication. An effort will be made to measure arterial diameter with the duplex device and compare pre and post infiltration arterial diameter. The investigators will be blinded to the type of medication being infiltrated periarterially. At the end of the study the syringe codes will be revealed and a comparison of flow velocities between the normal saline, lidocaine and lidocaine/hydralazine will be made. The percent change from baseline will be recorded for all infiltrations and the data will be analyzed using the paired T-test.

Progress: Eleven subjects were entered. Of the test agents, only lidocaine resulted in an increase in radial artery flow velocity, although there was not a similar increase in vessel diameter. Hydralazine did not appear to have a significant effect on flow velocity or diameter.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/042	**Status:** Suspended

Title: Prolonged Analgesia Using Microencapsulated Morphine in A Mouse Model (Mus musculus)

Start Date: 01/19/96	**Est. Completion Date:**
Department: Anesthesiology & Operative Svcs	**Facility:** MAMC

Principal Investigator: CPT Benjamin J. Miller, MC

Associate Investigators: MAJ James D. Helman, MC
MAJ Stephen L. Bolt, MC

Key Words: Morphine:microencapsulated, mouse model,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Sudy Objectives: To determine if microencapsulated morphine, injected intraperitoneally in mice, will produce a sustained analgesic effect using a tail flick test.

Technical Approach: This study will include six separate experiments and will utilize a total of 26 mice. (1) Determination of base line Tail flick latencies. (2) Determination of LD50 of Intraperitoneal injections of plain morphine. (3) Determination of LD50 if IP injected morphine loaded microspheres. (4) Tail flick latency tests with plain morphine. (5) Tail flick latency tests with empty microspheres. (6) Tail flick latency test with morphine loaded microspheres.

Progress: This study has not begun. The investigators are awaiting the results of the **Microsphere Encapsulation of Morphine Sulfate Using a Polymer of Poly-lactide-co-glycolide** protocol before proceeding with this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/017 **Status:** Completed

Title: Microsphere Encapsulation of Morphine Sulfate Using a Polymer of Poly-lactide-co-glycolide

Start Date: 11/17/95 **Est. Completion Date:** Jul 96

Department: Anesthesiology & Operative Svcs **Facility:** MAMC

Principal Investigator: CPT Benjamin J. Miller, MC

Associate Investigators: Katherine H. Moore, Ph.D. MAJ James D. Helman, MC

Key Words: Morphine, encapsulation , poly lactide-co-glycolide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of the proposed study is to produce a sustained-release, injectable morphine.

Technical Approach: The first part of the study would be attending a short course on microsphere production and characterization. After learning the required techniques, morphine microspheres would be produced in the DCI lab. *In vitro* characterization studies would then be performed, again in the DCI laboratory. Samples would be sent to the Army Institute of Research for election scanning microscopy. On completion of, or after obtaining preliminary results, we will then proceed to an animal model study to be proposed in a separate protocol.

Progress: In vitro studies have been completed comparing the kinetics of morphine release from different sizes and polymerization of microspheres. The micropsheres were suspended in phosphate buffered saline and shaked gently at 37°C. Aliguots of buffer were removed periodically to assay by HPLC for morphine levels. All formulations released drug by one hour and continued to release consistent levels of drug for up to 5 days. The project was closed due to reassignment of the principal investigator.

DETAIL SHEETS FOR PROTOCOLS

CLINICAL PSYCHOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/130	**Status:** On-going
Title: MMPI-2 Profiles in Korean Military Dependents		
Start Date: 06/16/95	**Est. Completion Date:** Aug 95	
Department: Clinical Psychology Service	**Facility:** MAMC	
Principal Investigator: CPT Kathleen S. Lester, MS		
Associate Investigators: None		
Key Words: Military dependents:Korean-born, MMPI-2		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the normative scores for the Minnesota Multi-phasic Personalty Inventory-2 (MMPI-2) in Korean dependent wives of active duty soldiers.

Technical Approach: In order to determine the norms for the Korean female spouses of service members, the MMPI-2 will be administered to 50 subjects, age 20 to 70. Subjects will be recruited from the primary care clinics at MAMC by means of referral by their physician and through recruitment advertisements posted in community areas of Ft. Lewis. Subjects consenting to participate will be given a questionnaire, a brief, structured psychiatric interview (mini-SCID), a screening test of English proficiency and the MMPI-2. The mean and standard deviation of the clinical and validity scales will be derived for the group. These scores will be compared with existing norms and, where differences exist, t-tests of significance will be performed. Results will be examined for co-variance of factors of age, number of years in the U.S, and proficiency in English language.

Progress: One subject has been enrolled.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/103 **Status:** On-going

Title: Polymerase Chain Reaction Detection and Cell Culture of Herpes Simplex Virus from Urine of Symptomatic Males with Non-gonococcal Urethritis

Start Date: 04/21/95 **Est. Completion Date:** Oct 95

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: CPT Wade K. Aldous, MS

Associate Investigators: LTC Margot R. Krauss, MC
MAJ Darrell E. Griffin III, MS

Key Words: Herpes simplex, polymerase, non-gonococcal urethritis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the feasibility of using a urine sample for detection and culture of Herpes Simplex Virus (HSV) in patients suspected of having non-gonococcal urethritis (NGU) due to HSV.

Technical Approach: Twenty males presenting with HSV And NGU will be tested for evidence of HSV infection in the urethra. Urine will be submitted from the Dept. of Pathology to the Dept. of Clinical Investigation for analysis. Cells will be collected from the urine by centrifugation and processed for cell culture and for detection by the polymerase chain reaction (PCR) using primers specific for HSV. Results of cell culture will be compared with PCR results. Samples positive for both culture and PCR will be considered true positives and thus will determine the feasibility of using urine samples for HSV detection in NGU patients. This is a descriptive study of a new technique.

Progress: Twelve samples have been received and processed for HSV culture. The PCR portion of the test will begin when 20 samples have been obtained and processed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/025	**Status:** On-going

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

Start Date: 01/20/95	**Est. Completion Date:** Jun 96
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: CPT Wade K. Aldous, MS	
Associate Investigators:	MAJ Rodger K. Martin, MS
Key Words: Molecular biology, training course	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: During FY 96, a total of 19 physicians and one nurse researcher received instruction during two iterations of the course. A total of 283.5 CME credits were awarded to 16 physicians. The course has been altered from a time consuming lecture and lab format to just a lecture format, allowing more physicians to participate and complete the course in a shorter period of time. The expanded lecture format also increased the range of topics discussed in the course. The course was presented in poster format at the SAFMLS 96 meeting held in Washington, DC, March 1996. Since the course was initiated in January 1995, 26 physicians have been trained with 10 of those authoring or co-authoring research protocols dealing directly with the molecular techniques taught in the course.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/058 **Status:** On-going

Title: Detection of Telomerase Activity from Plasmodium falciparum

Start Date: 02/16/96 **Est. Completion Date:** Jan 97

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: CPT Wade K. Aldous, MS

Associate Investigators:
MAJ Curtis L. Yeager, MS
MAJ Rodger K. Martin, MS
MAJ Dennis E. Kyle, MS

Key Words: Telomerase, Plasmodium falciparum, DNA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To modify and to optimize the telomerase repeat amplification protocol (TRAP) employing nonradioactive methods for detection of telomerase activity from the human parasite, P. falciparum. (2) To develop DNA primers specific for P. falciparum telomerase. (3) To detect and to identify by the modified TRAP assay P. falciparum telomerase activity.

Technical Approach: Total protein extractions from normal human testis tissue, erythrocytes, and Plasmodium falciparum will be performed. Parasites will be harvested from in vitro culturesand protein concentrations will be measured. TRAP assays will be performed as described with modifications. PCR amplification of the TRAP assay will be performed. Standard TRAP assays will also be performed. TRAP PCR products will be analyzed on 10% non-denaturing gels. TRAP assays will be performed with a flourescein-labeled forward TS primer for P. flaciparum. Data will be generated in flouregram and chromatogram forms. TRAP assay products will be amplified using the GeneAmp PCR Reagent Kit and will be visualized by ethidium staining in 12% Tris-Glycine acrylamide gels. Standard procedures for DNA hybridization will be performed using the amplified TRAP products. TRAP amplification products will be analyzed by electrophoresis on a 4% agarose gel, visualized by ethidium bromide and UV irradiation. Bands representative of telomeric repeats will be excised from the gel. Purified DNA will be cloned and ligation mixes will be used for transformation into competent cells. Sequencing of repeats will be accomplished and detected with ALF DNA analysis.

Progress: This protocol is being done in collaboration with a project at WRAIR, Division of Experimental Therapeutics. MAMC will run the telomerase assays on various stages of malarial extracts and compare results with work done at WRAIR. The investigators have modified a method widely used in the study of human neoplasias (telomerase repeat amplification protocol, TRAP) to detect telomerase activity in erythrocytic stages of *P. falciparum*. A fluoresceinated primer, specific for falciparum telomeric repeats, was used to facilitate the detection of the resulting PCR products on an automated laser fluorescent DNA sequencer. By using these modifications we have confirmed the presence of parasite-specific telomerase activity in crude extracts of *in vitro-derived P. falciparum*. Additional studies are planned to determine parasite stage-specific expression and to use drugs to inhibit the enzyme.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/162	**Status:** On-going
Title: Indirect Quantitation of Telomerase Activity		
Start Date: 09/20/96	**Est. Completion Date:** Aug 97	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: CPT Wade K. Aldous, MS		
Associate Investigators: M. J. Styner, B.S.	Morgan E. Shook	
Key Words: Proteins, telomerase		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To utilize the F-TRAP assay, the reverse transcriptase assay, the telomerase ELISA, and the TRAPeze methods to determine if any methods produce linear relationships with serially diluted extracts; 2) to pick the best method above based upon reliability, cost, ease of use, and time of use; and 3) to assay several different extracts with controls to find ranges of high and low activity in comparison with tumor specificity and staging.

Technical Approach: A previously extracted protein sample will be subjected to the 4 different methods outlined above in search of the optimal test. The best-test will be used to assay several other protein extracts in order to find ranges of enzyme activity. Values derived from the different extracts will be compared to each other based on tumor specificity and staging.

Progress: This study has just been approved and has not been implemented.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/079 **Status:** Completed

Title: The Detection of Atrial Natriuretic Peptide and Neutral Endopeptidase mRNA from Placentas in Normal and Pre-eclamptic Pregnancies

Start Date: 03/04/94 **Est. Completion Date:** May 94

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: MAJ Rodger K. Martin, MS

Associate Investigators:
MAJ Katherine S. Foley, MC
MAJ Jerome N. Kopelman, MC
MAJ Glenn R. Markenson, MC
LTC Arthur S. Maslow, MC

Key Words: mRNA, atrial natriuretic factor, endopeptidase, placenta

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To ascertain the presence of mRNA for atrial naturietic factor (ANF) and neutral endopeptidase (NEP) in placental tissues.

Technical Approach: Three placentas from uncomplicated, term deliveries and three placentas from pregnancies complicated by pre-eclampsia will be obtained. RNA will be extracted from samples of the umbilical artery and vein, the amnion and chorion, and decidual plate. The presence of ANF or NEP mRNA will be ascertained by northern analysis, RNase protection assay (RPA), or by the reverse transcriptase-polymerase chain reaction (RT-PCR). Samples of the placental tissues will be evaluated by electron microscopy to search for granules similar to those in the cardiac atria, that contain ANF.

Progress: Due to the difficulty of collecting preeclamptic placentas and the fact that the investigators were not able to identify ANF expression in tissues other than one chorion, the project was terminated. A paper was presented at the Conference on Military Perinatal Research at Aspen, CO, Sep 95.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/012 **Status:** Completed

Title: The Relationship of Bacterial Contamination and Interleukin-6 in Amniotic Fluid in Preterm Labor and Delivery

Start Date: 11/04/94 **Est. Completion Date:**

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: MAJ Rodger K. Martin, MS

Associate Investigators:
MAJ Katherine S. Foley, MC
MAJ Glenn R. Markenson, MC
MAJ Michael K. Yancey, MC

Key Words: Pregnancy: bacteria, inerleukin-6, amniotic fluid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the differences in gestational length of pregnancies complicated by preterm labor with and without bacteria in the amniotic fluid as detected by the polymerase chain reaction (PCR). To ascertain the relationship between the presence of bacteria detected using the PCR and elevated concentrations of interleukin-6 (IL-6) in amniotic fluid form preterm deliveries.

Technical Approach: One hundred and fifty women requiring amniocentesis will be enrolled in this collaborative project at the Madigan and the Tripler Army Medical Centers. Amniotic fluid from pregnancies complicated by preterm labor will be obtained only in clinically indicated situations that require analysis to rule out chorioamnionitis. Amniotic fluid will be evaluated for the presence of bacteria utilizing the PCR to amplify a ribosomal consensus sequence of DNA in bacteria. The presence of such sequences in amniotic fluid will be considered as evidence of bacterial contamination. At the time of amniocentesis the fluid will be gram stained and cultured for aerobic and anaerobic bacteria. the fluid obtained will also be evaluated for IL-6 concentration. After delivery, placentas will be sent to pathology. The presence of polymorphonuclear cell in formalin-fixed, paraffin-embedded chorion or amnion will be evidence for chorioamnionitis. The relationship of the outcomes of these tests to preterm delivery will then be assessed as well as the relationship between elevated IL-6 levels and positive PCR studies.

Progress: Due to the late arrival of funds, the investigators were only able to enroll 66 women, rather than the proposed 150 subjects.

Data analysis of the first 54 women entered showed that 9% of amniotic fluid samples were positive by traditional bacterial culture methods and approximately 57% of the samples evaluated by PCR were positive. Pregnancies with evidence of bacterial infections by PCR had a shorter time interval of amniocentesis to delivery and lower birth weights. Human IL-6 assayed by ELISA proved to be a prognostic marker for preterm delivery. Amniotic fluid IL-6 was found to be elevated above 600 pg/mL in 9 samples; all 9 of these subjects delivered preterm. The elevated IL-6 subjects delivered earlier, weighed less, and had longer newborn hospital stays. Of the women with elevated amniotic fluid IL-6, 66% were PCR positive for bacteria whereas only 11% were bacterial culture positive. These data support the utility of the PCR as a diagnostic tool in the evaluation of preterm labor. A new protocol has been revised for further study in this area.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/169 **Status:** On-going

Title: Development of a Method to Study What Proteins Are Regulated by IGF in the PC3 Prostate Cancer Cell Line Using 2-D Gel Electrophoresis and Protein Sequencing

Start Date: 09/21/94 **Est. Completion Date:**

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: Louis A. Matej, B.S.

Associate Investigators: None

Key Words: cancer:prostate, cell line, protein regulation, IGF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to develop a method for using a 2-D Electrophoresis coupled with Protein Sequencing to quantitate and identify proteins produced or inhibited by PC3 Prostate Cancer Cells when regulated by IGF.

Technical Approach: PC3 prostate cancer cells will be grown to confluency at 37°C in RPMI media supplemented with 5% Fetal Bovine Serum and in a 6% humidified CO_2 atmosphere. One culture will be inoculated with IGF at 10-6M; another culture will serve as a normal control. In the media of both the regulated and non-regulated PC3 prostate cell cultures, C^{14} labeled amino acids will be added to allow in the detection of proteins by autoradiography. The cultures will be allowed to incubate for 48 hours.

The media will be pipetted and saved to further study extracellular proteins while the cells will by trypsinized, sonicated in lysing buffer, and the mixture ultracentrifuged to acquire intracellular proteins for further study. The investigator plans to isolate and wash the protein from these solutions by using a dot blot apparatus to bind proteins to a nitrocellulose membrane. The proteins can then be desalted and washed on the membrane. To extract the proteins off the nitrocellulose membrane, we will use 8 M urea in sample buffer.

The IEF (1st dimension) electrophoresis which separates protein by isoelectric point will be carried out using polyacrylamide tube gels having equal amounts of ampholyte pH range 4.0-6.0, ampholyte pH range 6.0-8.0 and ampholyte pH range 7.0-9.0.

The second dimension electrophoresis, which separates protein further by size, will be carried out by layering the tube gel onto a vertical 10 to 20 percent gradient polyacrylamide gel.

The investigator will transfer the proteins onto a PVDF membrane by using an electroblot apparatus followed by staining with coomassie blue and destaining with a methanol/acetic acid/water solution. Autoradiography will then be used to allow more sensitive identification of protein bound to the PVDF membrane. After visual, graphic, and computer analysis of the autoradiographs, purified protein spots will then be cut out of the membrane and sequenced using the ABI protein sequencer. The protein sequences will be used to compare quantities of each protein of interest as well as for identification of the protein.

Progress: This labor intensive protocol is progressing slowly due to the limited amount of time available to the principal investigator.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 87/100	**Status:** Completed
Title: Thyroid Size in Children and Adolescents		
Start Date: 08/21/87	**Est. Completion Date:** Nov 91	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: None		
Key Words: thyroid size,adolescents		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/16/88

Study Objective: To establish normal dimensions ± 2 standard deviations (SD) for thyroid lobe length and width in children and adolescents. A goiter would then be defined as thyroid gland exceeding 2 SD of these dimensions.

Technical Approach: During the course of a routine physical examination, thyroid glands of 300 normal children and adolescents aged 6-20 years (20 at each age, 10 of each sex) will be measured in the following manner. With the neck extended, the thyroid isthmus is located with the index finger. The medial aspect of each lobe is followed to the apparent tip of each lobe. The upper tip of each lobe is located as the patient swallows with the index finger over each tip. The apparent inferior border of each lobe is located as the patient swallows with the index finger over the inferior portion of the gland. The lateral borders of the gland will be located with the index fingers placed medial to the sternocleidomastoid muscle as the gland moves as the patient swallows. The length will be measured as the distance from the apparent tip of each lobe to the apparent inferior border of each lobe. The width will be measured as the distance from the lateral borders of the gland. Means and SD will be calculated for length of each lobe and mid-isthmus width. For validation of measurement accuracy, 30 patients (2 each age, 1 each sex) will have the same measurements determined by thyroid ultrasound.

Progress: Data was collected on 396 patients and is complete. Data analysis will begin in a few weeks. Preliminary analysis shows an increase in thyroid size with pubertal stage and body mass index in both sexes. Norms will be established for each sex and pubertal stage.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/091 **Status:** On-going

Title: A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp(6)-Des-Gly(10)-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing....

Start Date: 07/20/90 **Est. Completion Date:** Nov 92

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: COL Dan C. Moore, MC

Associate Investigators: None

Key Words: precocious puberty,deslorelin,LH

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 08/16/96

Study Objective: To treat patients who have central precocious puberty with Deslorelin in order to suppress pubertal development and excess growth, to restore gonadotropin and sex hormone levels to normal prepubertal levels, and to demonstrate the safety of such treatment.

Technical Approach: Central precocious puberty will be defined as: stage 2 pubic hair or greater, stage 2 breast or genital development or greater, pubertal LH and FSH peak following GnRH stimulation, and absence of peripheral origin of precocity (lack of adrenal or ovarian mass on ultrasound and normal serum hCG). After diagnosis and standard evaluations, patients will be given Deslorelin, 4 mcg/kg SC daily. At three month intervals, patients will be re-evaluated. A physical examination with pubertal staging will be done. Serum sex hormones and gonadotropins (before andost GnRH) will be measured and bone age will be determined. Treatment will be continued until the patient reaches an age at which pubertal development is deemed appropriate (usually 10-11 years) at which time therapy will be discontinued.

Progress: Three patients have been entered on this study. One died due to underlying disease. One patient remains on study. Study drug continues to be effective in preventing puberty.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/003	**Status:** Terminated
Title: Characterization of the Genetic Basis for the Syndrome of Hypoparathyroidism, Deafness, and Renal Hypoplasia		
Start Date: 10/01/93	**Est. Completion Date:** Apr 94	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators:	MAJ Rodger K. Martin, MS	
Key Words: hypoparathyroidism, deafness, renal hypoplasia, DNA		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1200.00	**Periodic Review:** 09/30/96

Study Objective: Using techniques of DNA isolation, PFLP analysis, Southern analysis and probing with cDNA sequences of interest, to identify in chromosome 11, (which contains the PTH gene), genetic variation that is associated with the extremely rare syndrome of hypoparathyroidism, deafness and renal hypoplasia, which has been diagnosed in a family treated by the principal investigator. To date, no genetic etiology for this syndrome has been elucidated.

Technical Approach: Blood will be obtained from a patient with the syndrome of hypoparathyroidism, deafness and renal hypoplasia and from as many family members as possible. Because of the rarity of the syndrome and the non availability of the family locally, lymphocytes will be transformed with EB virus to provide a constant source of genomic DNA. Genomic DNA will be isolated from subjects' lymphocytes, digested with a series of endonucleases and RFLP analysis done, seeking genetic variants that segregate with the patient's restriction fragment digest. Restriction fragment digests will be transferred to membranes for Southern analysis and probed with labelled cDNA probes corresponding to sequences of interest on chromosome 11.

Progress: This protocol was terminated because the patient and family moved from the area before technical problems with establishing an immortal cell line were resolved.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/048 **Status:** Terminated

Title: Treatment use of Oxandrin (Oxandrolone) in Boys with Constitutional Delay of Growth and Puberty

Start Date: 04/03/92 **Est. Completion Date:**

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: COL Dan C. Moore, MC

Associate Investigators: LTC Robert J. Newman, MC

Key Words: delayed maturation and growth, boys, oxandrin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 08/18/95

Study Objective: To provide a means by which boys with constitutionally delayed growth and puberty can be treated with oxandrolone secondarily, data will be collected regarding the effect of therapy on growth and also of significant importance, boys receiving oxandrolone will be monitored for evidence of drug-induced side effects.

Technical Approach: Boys with constitutional delay of growth and puberty will receive oxandrolone orally as prescribed buy the physician. The recommended daily dose based on the published medical literature is up to 0.1 mg/kg. The duration of oxandrolone therapy will be left to the discretion of the physician. However, the published medical literature reports the safe and effective use of oxandrolone at the recommended doses for 3 to 12 months. The primary determinants for cessation of therapy are (1) inappropriate skeletal maturation (2) failure of drug to produce desired effect (3) spontaneous Stage III pubertal development as evidenced by a testicular volume of >10 ml or a length (long axis) of >3.5 cm or (4) adverse effects. Clinic visits not less than every four months will include interval medical history clinical side effects and adverse drug events and a pertinent physical examination. Bone age analysis, hemoglobin, hematocrit, RBC, and IGF-I (somatomedin-C) will be done at baseline, at 6 and 12 months, and annually thereafter.

Progress: This protocol has been terminated due to the lack of subjects. No subjects were entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/081	**Status:** On-going

Title: Genentech National Cooperative Growth Study (NCGS) Post Marketing Surveillance Program for Protropin (Somatrem for Injection) and Nutropin (Somatropin [rDHA Origin)] for Injection)

Start Date: 03/17/95	**Est. Completion Date:** Dec 04
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: COL Dan C. Moore, MC	
Associate Investigators:	LTC Robert J. Newman, MC
Key Words: Growth:delay, Protropin, Nutropin	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To collect long-term safety and efficacy information regarding treatment of children who have growth failure due to a lack of endogenous growth hormone secretion with Protropin and/or Nutropin growth hormone (GH).

Technical Approach: This is a multi-center, open label, post-marketing surveillance study of Protropin and Nutropin in the United States and Canada. Patients are enrolled at the time of their initiation of Protropin or Nutropin therapy and followed throughout their course of therapy. Post-treatment height measurements are collected until adult height is acheived. Since this is a record review and data collection only protocol, the number of patients enrolled will depend on the number requiring treatment for standard medical indications.

Progress: Data for this study have been collected on one patient.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/044 **Status:** Terminated

Title: The Biologic and Genetic Identification of Risk Factors in Breast Lesions and Breast Cancer for Their Clinical Application in the Care of Military Women

Start Date: 02/17/95 **Est. Completion Date:** Dec 96

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: Katherine H. Moore, Ph.D.

Associate Investigators: None

Key Words: Cancer:breast, military women

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To develop methods to study two potential genetic lesions in breast cancer and pre-cancerous breast lesions. The two genetic lesions of interest are HER2/*neu* and p53. To also determine if risk preddictors, HER2/*neu* and p53 mutations can be dtected in pre-malignant and early stage breast cancer tissue. This data will be used to support a grant application in which the goal will ber to determine if examination of biopsy tissue for genetic lesions provides clinically important information for the treatment of breast disease.

Technical Approach: Amplification of the HER2/*neu* and mutations of p53 oncogenes have been associated with poor prognosis in breast cancer. The types of cancers that have been studied, however have tended to be when the cancer has progressed to an advanced stage. We wish to determine if these genetic lesions are present in pre-cancerous lesions and be associated with a reoccurrence of aggressive disease in the same patient in the future. The major problem with doing genetic tests on precancerous lesions is the lack of tissue for conventional genetic analysis (southern blotting, RFLP analysis). The advent of PCR based technology has made the study of small lesions feasible. To develop genetic assays for the amplification of HER2/*neu* and mutations in p53, DNA will be isolated from breast cancer cell lines, including MCF-7, ZR-75-1 and SK-BR-3. The technique of differential PCR will be used to determine gene amplification of HER2/*neu*. A 98 bp portion of the HER2/*neu* gene and a 150 bp portion of a reference gene, interferon g, will be amplified in the same reaction. The level of amplification of HER2/*neu* is reflected by the ratio between the HER2/*neu* PCR product and the g interferon PCR product. Two methods will be used to detect mutations in p53 DNA. One is single strand conformational polymorphism (SSCP), in which small changes in DNA sequence are detectable by changes in PCR fragment mobility of an acrylamide gel. The other method will be direct DNA sequencing of the PCR products. An automated DNA sequencing system will be used for these analyses.

Progress: A PCR based assay was developed to detect the amplification of HER2/*neu* in breast cancer cells. This assay utilized differential PCR of the HER2/*neu* gene and gamma interferon, with the difference in band intensity as a marker for HER2/*neu* amplification. This protocol has been terminated due to failure to obtain grant funding.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/033	**Status:** On-going

Title: Localization and Identification of Sex Hormone Binding Globulin (SHBG) mRNA and SHBG-Related Proteins in Breast Cancer (Production of Monoclonal Antibodies Using Mice)

Start Date: 12/01/95	**Est. Completion Date:** Oct 96
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: Katherine H. Moore, Ph.D.	
Associate Investigators:	CPT Wade K. Aldous, MS
Key Words: Cancer:breast, SHBG, antibodies,Animal Study	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To detect the message (mRNA) for sex hormone binding-globulin (SHBG) in breast tissue sections in-situ. (2) To determine if breast cancer cell lines are producing alternate transcripts of SHBG mRNA, and to characterize these transcripts and their protein product.

Technical Approach: This will be approached by amplifying the mRNA in the tissue sections by the polymerase chain reaction (PCR), first using reverse transcriptase to make cDNA copies of the mRNA in the section. The primer set that our laboratory is currently using to amplify SHBG message from RNA extracted from formalin fixed tissue will be the initial set used. Two control mRNAs will be evaluated, B-2 microglobin (b2) and porphobilinogen deaminase (PBGD). These mRNAs will be amplified in adjacent sections cut from the breast cancer tissue blocks. The amplified cDNA will be visualized through the inclusion of digoxigenin-11 dUTP (DIG) included in the amplification mix. The DIG labeled PCR fragments will be detected using a alkaline phosphatase reaction. A cDNA library will be constructed form ZR-75-1, MCF-7 and MDA-MB-231 breast cancer cell lines. We will screen the library for clones positive for wil type SHBG sequence and alternate sequence using a 550 bp probe. Next, based on the predicted amino acid sequence of the transcripts, peptides will be synthesized and monoclonal antibodies raised against the peptides from the alternate transcripts. These antibodies will be used to examine conditioned media from breast cancer cell lines and cellular extracts of these cells for the presence of protein produced from SHBG alternate mRNA transcripts.

Progress: A cDNA library was produced from MCF-7 breast cancer cells. The library was initially screened by solution hybridization using an oligonucleotide to exon 3 of sex hormone binding globulin. The selected library was subsequently screened with a 500 bp cDNA probe spanning the 5' region of the message. Positive clones are in the process of being subcloned and rescreened. To date, 3 positive clones have been identified. These will be sequenced to determine the complete sequence of SHBG mRNA expressed in breast cancer cells. A paper has been accepted for publication in The Journal of Steroid Biochemistry and Molecular Biology.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/126 **Status:** On-going

Title: Sex Hormone Binding Globulin and Prostate Cancer - Characterization of Alternate mRNA Transcripts

Start Date: 05/19/95 **Est. Completion Date:** Jul 97

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: Katherine H. Moore, Ph.D.

Associate Investigators: CPT Wade K. Aldous, MS
Louis A. Matej, B.S. M. J. Styner, B.S.

Key Words: Cancer:prostate, SEBG, mRNA transcripts

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To characterize the sex hormone binding globulin (SHBG) mRNA produced by prostate cancer cells. This will be accomplished by characterizing the SHBG products amplified by PCR, and ultimately the full length transcripts. 2) To determine if SHBG mRNA is translated into protein. This will be accomplished by metabolically labeling the proteins in the cells and detecting by immunoprecipitation. A long range objective is to develop an antibody against the protein product of an altered SHBG mRNA, and use this antibody to determine if the proposed altered transcript is translated into functional protein.

Technical Approach: We will examine prostate cancer cell lines for the presence of SHBG mRNA. In addition, we will construct a cDNA library to fully characterize the SHBG transcripts produced by prostate cancer cells. We plan to examine the proteins manufactured by prostate cancer cell using immunoprecipitation to determine if the cells are producing SHBG protein. This study will thus characterize a potential oncogene for prostate cancer and lead to a greater understanding of the mechanism of cancer formation. This is a descriptive study. The DNA sequences will be compared with known sequences using MacVector.

Progress: The reverse transcriptase-polymerase chain reaction (rtPCR) was used to study the expression of SHBG in prostate cancer cell lines and benign prostate hypertrophy cells. SHBG binds steroids with high affinity and may play an additional role in regulating the growth of prostate cells. rtPCR analysis of total RNA produced two bands, which were cloned and sequenced. The smaller band was found to be the product of alternate processing of the mRNA, with exon seven removed and a single base deletion at the start of exon 8. This modification is predicted to produce an altered amino acid sequence in the carboxy tail of the protein, removing the glycosylation sites and producing a truncated protein. The sequence of the large PCR band from PCR analysis of RNA from the prostate cancer cell line, DU-145, was identical to wild-type SHBG. Sequence analysis of the large band amplified from the benign prostate hypertrophy tissue by PCR revealed two polymorphisms that did not alter the predicted amino acid composition.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/084	**Status:** On-going

Title: Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine Sus scrofa, Goat Capra hircus, Rabbit Oryctolagus cuniculus, Ferret Mustela putorius furo, Rat Rattus ...

Start Date: 02/09/94	**Est. Completion Date:** Feb 97
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: MAJ Ronald E. Nielsen, VC	
Associate Investigators:	CPT Stephen Caldwell, VC
Key Words: Training:vet techs,Animal Study	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$200.00	**Periodic Review:** 09/30/96

Study Objective: 1) To help the DCI technical staff to remain proficient in basic technical skills as well as emergency care procedures that may arise during normal animal care. 2) To teach investigators and technicians the basics of animal restraint and manipulations. 3) To teach DCI technical staff basic surgical skills that will enable them to better assist investigators.

Technical Approach: The DCI technical staff trainees will be instructed in proper handling and restraint techniques used with the Swine Sus scrofa, Goat Capra hircus, Rabbit Oryctolagus cuniculus, Ferret Mustela putorius furo, Rat Rattus norvegicus, and Mouse Mus musculus. Trainees will be taught basic surgical skills, to include endotracheal intubation; blood collection and injections; vessel cutdown and catheterization; soft tissue handling and suturing; anesthetic regimens, and necropsy procedures.

Progress: No training session were held in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/143	**Status:** Completed
Title: Adolescent Risk Behavior and the Influence of Parents and Education		
Start Date: 09/02/94	**Est. Completion Date:**	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: Troy H. Patience, B.S.		
Associate Investigators:	MAJ Brent V. Nelson, MC	
Key Words: risk behavior:adolescents, parents, education		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1. To determine the level of involvement of a sampling of 7th grade students in alcohol use, illegal drug use, sexual activity, and gang participation. 2. Assess student and parent general knowledge concerning alcohol use, illegal drug use, sexual activity, and gang participation. 3. Survey parental involvement in providing students with information and guidance. 4. Compare individual student's report of interaction with parents concerning the above topics, with their parent's report of interaction. 5. Determine if parent's level of general knowledge concerning alcohol above, illegal drug use, sexual activity, and gang activities, and parental involvement in providing students with information and guidance, have any effect on adolescent risk taking behavior.

Technical Approach: Approximately 1000 7th grade students and their parents will be surveyed in this study. Each student will be given a packet that includes a student survey, numbered student response sheet, parent survey, numbered parent response sheet with a number corresponding to the student response sheet, stamped envelope with MAMC address, stamped envelope with no address. Parents will complete their survey, place it in the unaddressed envelope and the student will place that envelope and their own response sheet in the addressed envelope. This will insure the student and the parent surveys are paired while still maintaining anonymity.

Survey results will be entered into a database for calculation of responses. Chi-square distribution will be used to compare parent and student paired responses, with statistical significance accepted at $p \leq 0.05$. General knowledge questions will be tabulated for parent and student in a percentage correct format.

Progress: The PI left Madigan in FY 95. The protocol was to be transferred to another Family Practice physician in order to obtain additional information; however, no one has had the time to pursue this further and it has been discontinued. The results of the 215 seventh grade students who were surveyed indicate that there is a considerable difference between the direction that parents believe they are giving their adolescent and the message that the student is receiving. There did not appear to be any relationship between what students know about risk behavior and their actual behavior. Many parents have not communicated their expectations to their children as clearly as they believe. For those risk behaviors where parent expectations matched student perceptions, there were significantly lower rates of student participation in this risk behavior.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/014 **Status:** On-going

Title: Relationships Between A Female Soldier's Military Occupational Specialty (MOS) and Birth Outcomes

Start Date: 11/04/94 **Est. Completion Date:** Jan 96

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: LTC Richard A. Sherman, MS

Associate Investigators:
CPT Robert J. Palowski, MS
MAJ Noble, MC
CPT Joseph F. Creedon Jr., MS
CPT Jennifer Aro, MC
Roxie Johnson, NP

Key Words: Female soldiers:birth outcomes, MOS

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this investigation is to attempt to quantify risk utilizing Risk Ratio and Odds Ratio risk estimates and establish baseline rates for the offspring of female soldiers by Career Management Field (CMF) or MOS for the following outcomes: spontaneous abortions, ectopic pregnancies, intrauterine fetal demise, preterm birth, low birth weight infant, and as a mechanism to intervene in these adverse outcomes.

Technical Approach: A prospective cohort study will be performed at the following locations: Ft. Carson, Ft. Hood, Ft. Lewis, Ft. Bragg, Ft. Campbell, and Ft. Riley. Respondents will be enrolled during OB registration classes form 1 October 1994 through 31 January 1995 and then followed through September 1995 to allow the subjects to progress through their pregnancies and develop outcomes. All pregnant soldiers and pregnant wives and daughters of soldiers limited to those eligible for care. Demographic variables will be ascertained by way of a proctored questionnaire given to the mother at the time of the initial OB registration. Outcome data will be obtained through the use of a questionnaire located in the OB record, which will be compiled in the newborn nursery. The number of subjects required to provide sufficient power is estimated to be 5,000 composed of 1,670 soldiers and a comparison group of 3,330 spouses and daughters. The CMF/MOS's likely to meet these requirements are 91B and 92A. Soldier jobs could also be classified into the following categories for analysis: Medical Maintenance, Administrative, Logistics, Food Service, Law Enforcement, Communications, and Other.

Progress: Eight hundred and fifty patients entered the study and filled out the questionnaire. No further subjects will be entered. Data from current subjects are being recorded as they deliver. All data will be combined with data from the other military sites at the end of the collection period.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/139	**Status:** On-going
Title: Pilot Study for: Wound Healing Using Pulsed Electromagnetic Field Therapy		
Start Date: 04/21/95	**Est. Completion Date:**	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: LTC John B. Whittemore, AN	CPT Thomas K. Curry, MC	
Key Words: Pulsed Electromagnetic Field Therapy, wound healing		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The overall objective is to determine whether pulsing electromagnetic fields (PEMFs) can potentiate post operative recovery by increasing the rate of incisional wound healing and decreasing pain management requirements in patients undergoing abdominal and vascular surgery whose wounds are left open for secondary closure. The objective of this particular study is to perform a pilot which will provide trained staff and practiced methodologies for a larger study.

Technical Approach: This project is designed as a pilot to test the objectives as described and to prepare personnel and methods for a larger study with more subjects. The study is designed as a semi-double blind, randomized, two-group experimental repeated measures design. Ten subjects will be randomly assigned to two groups of five each. One group will receive PEMF treatment and the other will receive placebo treatment. The study will be double-blinded for the PEMF technician as well as the evaluators. Subjects will be males or females, over 18 years of age, who have undergone abdominal or vascular surgery at MAMC and who have incisions healing by secondary intention. Patient information will be collected pertaining to pre-existing disorders that may act as confounding variables to normal wound healing. All eligible subjects will be sequentially entered into the study until the groups are full. Wound healing will be assessed by ASEPSIS (a wound healing and infection assessment), videothermography, photography, and plenography (a computer program used to trace and compare wound outlines). Post operative incisional pain will be assessed by a Visual Analog Scale and post-operative analgesic usage. Each variable will be initially analyzed separately. The non-parametric variables will be analyzed using a two-way, repeated measures, non-parametric analysis of variance. The parametric variables will be analyzed with a parametric repeated measures ANOVA.

Progress: No patients have been entered in this study due to non-availability of technical support at this time.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/153	**Status:** On-going
Title: Use of Pulsing Electromagnetic Fields to Potentiate Healing of Stable, Open Ulcers on the Lower Limbs and Feet		
Start Date: 06/16/95	**Est. Completion Date:** Dec 97	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: MAJ Arnoldas S. Kungys, MC Melissa Wong, BA	LTC Delbert E. Casey Jones, MC Estelle Hamblen, BA, MHA	
Key Words: Pulsing electromagnetic fields, ulcers, feet, lower limbs		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether pulsing electromagnetic fields (PEMFs) can potentiate healing of stable, open ulcers on the lower limbs when used simultaneously with standard treatments relative to the rate of healing with placebo PEMF and standard treatment.

Technical Approach: Skin ulcers on the feet and legs are a highly significant clinical problem for patients with compromised neurovascular systems such as diabetics. We will perform a double blind study in which subjects will be randomly assigned to placebo PEMF and standard treatment or real PEMF and standard treatment. The patients will be those with diadnosed metabolic abnormalies (almost all will be diabetic) and haveskin ulcers on their feet and lower legs which have not healed during the previous three months. Patients will be stratified by grade (I/I, III, and IV), location and diameter (< 1cm, 2.01 to 3.0 cm and >3.0 cm) of the ulcer as well as age and athen rendomly placed in either a placebo or real PEMF group. PEMF therapy (or placebo PEMF) therapy) will be performed five days per week for one hour per day until the ulcer heals or six weeks. Rate of ulcer healing will be measured by photographing the ulcer on the first day of treatment and once every seven days for the duration of participation. A special high resolution, set distance, light controlled camera in conjunction with a plenometer to measure the cross-sectional area of the ulcer as recorded on the photographs will be used. Videothermograms will be taken nearly simultaneously with the light photographs from a standard distance using standard settings to evaluate changes in near-surface blood flow (very highly correlated with healing rate). A power analysis of previous results shows that 3 subjects will be needed in each group assuning (a) that we predict the PEMF group will do better (one-tailed test) and (b) an 80% chance of finding a difference between the two groups at a 0.05 level of significance. A total of about 80 subjects will be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

Progress: Four diabetic patients with five open ulcers which had been stable in size for at least three months have been entered. Three healed entirely within three weeks with daily exposure to pulsing electromagnetic field and the fourth healed in eight weeks.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/019 **Status:** Terminated

Title: Developmt/Infection Resistant External Fixater Sys & A Tibially Implanted, Percutaneous Limb Prosthetic Holder/Overlapping Ph III & IV: Tests of Resistance to Infection & Skin Ingrowth In a Goat Model

Start Date: 11/18/94 **Est. Completion Date:** Dec 97

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: LTC Richard A. Sherman, MS

Associate Investigators:
LTC Edward J. Lisecki, MC
LTC Delbert E. Casey Jones, MC
Stephen Cook, Ph.D.

Key Words: External fixater:infection resistant; limb prosthesis:tibia,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The overall objectives for this program are to (a) develop a prosthetic attachment system for amputees which can be directly implanted into the major weight bearing bone and be extended through the skin (percutaneously) and (b) develop an external fixater pin coating which will resist infection for at least one year. Specific objectives of this study are to determine whether goats will develop infections when hydroxyapatite (HA) coated or uncoated screws are implanted into bone through the skin and left in place for eight months. HA is a substance normally found in bones which is used to coat artificial hips and knees in order to get bone to grow into the prostheses. The other specific objective is to determine whether a percutaneously implanted prosthetic will function under normal patterns of weight and movement without infections, loosening or other problems for at least one year.

Technical Approach: This study will utilize a total of 14 goats to test the objectives stated above. For the first specific objective, HA coated and uncoated screws will be percutaneously placed into the radius of ten goats with the shanks of the screws protruding 1/2 to 3/4 inch through the skin. The screws will be left in place 8 months. Biweekly blood work and daily observations of the site along with daily observation of the goats behavior and gait will insure that infections are diagnosed and treated immediately. After eight months, the screws will be removed and signs of chronic infection and tracts along the shanks will be noted. For the second specific objective, four goats will have HA coated, prosthetic limbs implanted after amputation of the left front leg below the goat's wrist. The goats will be monitored daily for discomfort and infection and intervention will be made as necessary. The animals will be maintained for as much of their natural lives as funding will afford for continued observation.

Progress: This protocol was terminated because funding was not obtained.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/020	**Status:** Terminated
Title: Development of an Infection Resistant External Fixater		
Start Date: 11/18/94	**Est. Completion Date:** Dec 97	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: LTC Edward J. Lisecki, MC	LTC Delbert E. Casey Jones, MC Stephen Cook, Ph.D.	
Key Words: External fixaters:infection resistant		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether patients having standard fixaters coated with Hydroxyapatite (HA) will have significantly fewer infections than those having the same external fixaters not coated with HA.

Technical Approach: The proposed protocol is intended to solve the infection problem with external fixaters and work toward developing a percutaneously implanted prosthetic holder which would eliminate most of the reasons lower limb amputees are debilitated. This protocol is approved at Fitzsimmons Army Medical Center (FAMC). It was originally approved as protocol 90/208A in 1990 and has been re-approved since by both the human and animal use committee. It now carries the designation 94/208A with FAMC's animal use committee. We plan to perform the human use and goat transcutaneous rod portions of the study at Madigan. The goat prosthetic holder would be mounted on goats at FAMC. The goats would be transported to Madigan for long term holding after they stabilize. The human portion of the proposed study will not begin until the goat transcutaneous rod portion has been completed and the FDA has approved implanting HA coated external fixaters into humans for purposes of the study. Considerable detail about the animal portions of the study are presented in this protocol to support the proposed human work. This protocol will not be performed without outside funding.

Progress: This protocol was terminated because funding was not obtained.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/126 **Status:** On-going

Title: Incidence and Impact of Headaches Among Users of Medical and Dental Facilities at Fort Lewis

Start Date: 05/17/96 **Est. Completion Date:** Oct 96

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: LTC Richard A. Sherman, MS

Associate Investigators:
MAJ Richard T. Dombroski, MC
Steven A. Pace, MD
1LT Jan L. Sprauge, AN
Melissa Wong, BA
MAJ Linda A. Marden, MC
LTC Ann M. V. Bianchi, AN
CDR Brian J. Kelly, MC
Linda Robson, BA

Key Words: Headache, Ft Lewis, WA, medical facility, dental facility

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the incidence an impact of headaches and low back pain among people eligible for care at military medical facilities. To estimate the utilization of medical facilities at Fort Lewis for treatment of headaches and low back pain. To estimate the cost of treating headaches and low back pain to the medical facilities at Fort Lewis.

Technical Approach: The proposed study had three parts: 1) distribute a two page survey of headache and low back pain activity and impact to a representative sample of people eligible for care at Ft. Lewis medical facilities. It will be distributed to people waiting in the Pharmacy, Pediatrics, Family Practice, Dental Clinics, Adult Primary Care Clinic, and the TMCs, as well as during annual physical exams in OB/GYN and Physical Exam. Additionally, it will be offered to over 2,000 ROTC Cadets in the summer. A power analysis of the response variability will be conducted after 1,000 responses and used to guide continued distribution. 2) Daily patient records from the ER, the TMCs, Family Practice and the Adult Primary Care Clinic will be prospectively reviewed for two months to identify patients with non-trauma headaches and their record will be reviewed for the history of treatment over the last two years. 3) A list of medications primarily prescribed for headaches will be compiled and the pharmacy will prepare (a) a record of how much of these prescriptions have been dispensed over the last two years and their costs and (b) a list of the people receiving these medicines. Every fifth name on a random sample of 500 people receiving those medications will be evaluated to insure that the medications are used for headaches.

Progress: Surveys of headache and low back pain activity have been sent to approximately 2300 individuals eligible for care at Madigan. The daily patient records from the ER, the TMCs, Family Practice, and the Adult Primary Care Clinic are being reviewed to identify records of patients who came for treatment of non-traumatic headache to determine their history of using medical facilities for treatment over the past two years. A list of medications, primarily prescribed for treatment of headache and low back pain, has been compiled and the pharmacy is preparing a report. A random, representative sample of people receiving these medicines is being generated and the pharmacists are evaluating their records to determine the percent of patients for whom the medication is prescribed for headache or back pain.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/019	**Status:** On-going
Title: Treatment of Aura-Inaugurated Migraine Headache (Classic Migraine) with Pulsing Electromagnetic Fields: A Pilot Efficacy Study		
Start Date: 11/17/95	**Est. Completion Date:** Sep 96	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: Linda Robson, BA	MAJ Linda A. Marden, MC	
Key Words: Migraine, PEMF		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/15/96

Study Objective: To determine whether classic migraine headaches can be treated with pulsing electromagnetic field (PEMF) therapy. This pilot will only determine whether the application of PEMF appears to have a clinically important effect. If it appears to have such an effect, larger, controlled studies will be proposed which will determine the extent and duration of the effect.

Technical Approach: We propose to have ten patients of either sex between the ages of 18 and 70 with at least a two year history of having classic migraines at least once per week keep a daily log of the frequency and intensity of headaches as well as medication use for two weeks. They will then be exposed to PEMF on the thigh at a power/frequency setting 6/600 for one hour per day, five days per week for three weeks. Analysis of headache activity will be performed by making a composite rating for each subject for each of the three rated periods (before, during, and after intervention). Activity for each period will be calculated for each variable by simply adding up the ratings (e.g. total hours of pain for the period) and by constructing a composite score equal to frequency times intensity for each period. The parametric measures (e.g. hours of pain) will be compared using a parametric, one way, repeated measures analysis of variance while non-parametric measures (e.g. pain intensity) will be evaluated using the non-parametric equivalent.

Progress: Thirteen subjects with long histories of poorly controlled migraine headaches at least once per week were studied. For the 11 subjects having standard migraines with or without visual auras, migraine headaches decreased significantly or stopped. This change has been maintained for one year. There were no changes in headache activity for the two subjects having trauma induced migraines. A paper was presented at the March 1996 meeting of the Association for Applied Psychophysiology.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/085 **Status:** On-going

Title: Treatment of Headaches with Pulsing Electromagnetic Fields: A Multigroup, Double-Blind, Placebo-Controlled, Crossover Study

Start Date: 03/15/96 **Est. Completion Date:** Mar 97

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: LTC Richard A. Sherman, MS

Associate Investigators: MAJ Linda A. Marden, MC
Linda Robson, BA

Key Words: Headache, PEMF, migraine, tension

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the duration and impact of pulsing electromagnetic field (PEMF) therapy on migraine and tension headache activity.

Technical Approach: We propose to have adult patients of either sex between the ages of 18 and 70 with at least a two year history of having headaches at least once per week keep a daily log of the frequency and intensity of headaches as well as medication use for two weeks. They will be stratified by type of headache (either migraine with aura, migraine without aura, migraine associated with the menstrual cycle, tension headache, and mixed migraine - tension headache) and randomized into actual or placebo PEMF therapy. They will then be exposed to PEMF (real or placebo) on the thigh at a power/frequency setting of 6/600 for one hour per day, five days per week for two weeks. Neither the therapist nor the patient will know which group they are in. A two week stabilization period will follow the two weeks of real or placebo therapy. Patients will keep a headache log during this period. The next stage will cross-over the subjects. At the end of this period, patients will keep a two week follow-up log and be followed-up by phone at one month, three months, and six months after the end of therapy. Patients will be instructed to call us when their headaches have returned to pre-treatment levels. Standard treatment will be offered at that time. Success is usually defined as at least a 50% decrease in headache activity as calculated from a composite score based on frequency, duration, and intensity with a commensurate decrease in medication use. We will perform a power analysis after the first five patients complete the post-treatment log to determine the number which will probably be required. We will request permission to increase our number of subjects if more than a total of 100 subjects are required to differentiate between groups if the differences are such that differentiating between groups would be worthwhile.

Progress: Eight subjects kept a three week log of headache activity and were then randomly assigned to received two weeks of real or placebo PEMF exposures. Headache activity decreased when exposed to the actual fields, but not much when exposed to the placebo. Patients with long histories of migraine headaches exposed to PEMF's showed an almost complete cessation of headache activity during and after actual exposure. The effect was dose dependent, was not a placebo response, and did not occur among people with headaches of traumatic origin. Thus, it is worth performing large controlled studies to determine whether this intervention is actually effective. A paper was presented at the Eighth World Congress on Pain in August 1996.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/151	**Status:** On-going
Title: Short-term Stability and Habituation of Human Finger Blood-Flow		
Start Date: 09/20/96	**Est. Completion Date:** Sep 96	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: Melissa Wong, BA	Linda Robson, BA	
Key Words: Blood flow:finger		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the short term stability (half an hour) of human finger blood flow and any habituation which may occur to the recording environment over the course of three recording sessions. This is necessary in order to determine how long patients need to sit quietly after being instrumented for finger temperature recordings before stabilization occurs and interventions can begin. Changes in length of time required for stabilization across sessions as habituation occurs also needs to be determined so the amount of time required can be anticipated and planned for in multi-session treatments and studies.

Technical Approach: Fingertip temperature has been used as an index of sympathetic/vascular relaxation-stress response at least since the 1930s. Ten subjects who are healthy employees of Madigan AMC will walk from their places of work to the test room in Orthopedic Clinic and be seated upright in a comfortable recliner. A thermistor probe will immediately be taped to the left edge of the left index finger just above the distal joint and temperatures will be documented every thirty seconds for one half hour. The hand with the probe attached will be kept relatively still on the padded arm of the chair for the entire recording period. A videothermograph will be focused on the hand to produce continuous recordings of near surface blood flow in the hand. Participants will be asked to minimize movement and talking while being encouraged to sit quietly and relax with eyes open or closed as they wish. Each subject will participate in three of these half hour sessions at the same time of day once per week for three weeks. Pilot data show that ten subjects should be sufficient to establish the amount of variability which can be expected. Recordings made by the thermistor and the videothermograph will be correlated. Confidence intervals for variability will be established and the data will be displayed in both tabular and chart form so clinicians and investigators can use their own stabilization criteria to establish an optimal stabilization period for their own needs.

Progress: Ten patients have been entered in the study, but none has completed the protocol to date.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/010	**Status:** Completed

Title: Evaluation of the Performance Impact and Treatment of Exercise Induced Urinary Incontinence Among female Soldiers

Start Date: 11/04/94	**Est. Completion Date:** Apr 96
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: LTC Richard A. Sherman, MS	
Associate Investigators:	LTC Richard A. Sherman, MS

Key Words: Female soldiers:incontinence, exercise, performance impact

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To determine the incidence of exercise induced urinary incontinence among female soldiers, 2) the impact of urinary incontinence upon female soldiers' ability to perform their exercises and tasks, 3) the effectiveness of standard treatments for exercise induced stress and urge urinary incontinence, and 4) the effectiveness of urinary tract biofeedback and exercise training for stress and urge urinary incontinence.

Technical Approach: Study participants will perform a simulated PT-test after drinking 500 ml (1 pint) of an electrolyte balanced fluid. A pre-weighed absorbent pad will be worn and then placed in a plastic bag following completion of the PT-test for weighing to determine how much urine was lost. Tests will be conducted to determine a diagnosis of stress incontinence or motor/urge incontinence.

Patients will be randomized to one of two groups. Group 1 will do Kegel Exercises twice a day (10 minutes each session) for four weeks. Group 2 will do Kegel Exercises twice a day (10 minutes each session) for four weeks plus biofeedback training (30 minute treatments three times per week). Both groups will also receive a 20 minute tape recorded exercise to use twice per day, which will help recognize when the muscles are tenser than they should be.

Following the four weeks, patients will be reevaluated to determine if surgery is still necessary for stress incontinent patients or medication for motor/urge incontinent patients. Patients going on to surgery or medication will be reevaluated after recovery and stabilization of the problem. These tests will be repeated again approximately six months later.

Progress: Results of an incidence survey indicated that about one third of the 450 female soldiers experience problematic urinary incontinence during exercise and field training activities. Thirty-nine female soldiers who reported exercise induced urinary incontinence were entered in the study. Patient reports as well as post-treatment urodynamic and physical examinations indicated that all subjects improved significantly. However, five subjects in the biofeedback group and three in the Kegel group still desired surgery or medicinal treatment. All subjects initially diagnosed with detrusor dysfunction had normal readings at the end of the study.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/131	**Status:** On-going
Title: Treatment of Inflammation Related Low Back Pain with Pulsing Electromagnetic Fields: A Pilot Efficacy Study		
Start Date: 06/21/96	**Est. Completion Date:** May 97	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: LTC Richard A. Sherman, MS		
Associate Investigators: CPT Marc J. Michaud, MC	LCDR Clayton Tuerner, MC	
Key Words: Low back pain, PEMF, inflammation		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether inflammation related to low back pain can be treated with pulsing electromagnetic field (PEMF) therapy. This pilot will only determine whether the application of PEMF appears to have a clinically important effect. If it appears to have such an effect, larger, controlled studies will be proposed which will determine the extent and duration of the effect.

Technical Approach: We propose to have ten adult patients of either sex between the ages of 18 and 70 with at least a two year history of having chronic, daily musculoskeletal low back pain with symptoms of inflammation keep a daily log of the frequency and intensity of back pain as well as medication use for two weeks. They will then be exposed to PEMF over the lower back at a power/frequency setting of 6/600 for one hour per day, five days per week for two weeks. This should be more than sufficient time to produce an effect. They will continue keeping the pain log during and for two weeks after the PEMF exposure. The trial will be considered successful if half of the patients report any combination of at least a fifty percent decrease in pain with no change in medication or a twenty-five percent decrease in pain with reduced use of pain medications. Patients will have a videothermographic evaluation of their lower backs before and after treatment to assess changes in inflammation. Analysis of changes in back pain will be performed by comparing each subject's pain during each of the three rated periods. Parametric measures (length of pain) will be compared will be measured using parametric one-way, repeated measures analysis of variance while the non-parametric measures (pain intensity) will be evaluated using the nonparametric equivalent. Changes in temperature patterns of the low back will be evaluated using a paired t-test of changes in the difference in absolute temperature between the left and right sides of a three cm square area centered over the bulk of the paraspinal muscles at L4 IAW Psychophysiology Laboratory SOPs.

Progress: Ten patients have been entered in the study, but none has completed the protocol to date.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/158 **Status:** On-going

Title: Pilot Study For: Environmental-Temporal Relationships Between Changes in (a) Paraspinal Muscle Tension and Low Back Pain and (b) Trapezius Muscle Tension and Migraine and Tension Headache Intensity

Start Date: 06/16/95 **Est. Completion Date:** Feb 97

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: LTC Richard A. Sherman, MS

Associate Investigators:
Christie Hill
Estelle Hamblen, BA, MHA
Antje F. W. Goeken, Psy.D.
Melissa Wong, BA
Linda Robson, BA
Kimberly A. Hermann-Do, BS, MHA

Key Words: Muscle tension:paraspinal, Muscle tension:trapezius, migraine, low back pain

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To determine whether there is a temporal relationship between changes in paraspinal muscle tension and changes in musculoskeletal low back pain in patients' normal environments. 2) To determine whether there is a temporal relationship between changes in trapezius muscle tension and changes in intensity of migraine and tension headaches in patients' normal environments. 3) To determine whether environmental - temporal relationships between (a) musculoskeletal low back pain and paraspinal muscle tension pain and (b) trapezius muscle tension and migraine and tension headache change after successful biofeedback therapy.

Technical Approach: There will be ten subjects in each group with the groups consisting of patients diagnosed as having tension headaches, musculoskeletal low back pain, migraine headaches, or mixed migraine-tension headaches (a total of 40 patients). Ten subjects per group are likely to be needed to detect consistent temporal relationships between pain and muscle tension reliably because the previous data were highly variable and idiosyncratic. Assignment to groups will be by diagnosis only as there are no controls, etc. The subjects will all be patients referred from the TMC's at Ft. Lewis or the Neurology and Family Practice clinics at Madigan AMC who meet the diagnostic criteria for entrance into the study. They will be between 18 and 55 years of age, be otherwise healthy, and of either sex. Each subject will have four consecutive days of ambulatory recordings during all waking hours before and after standard muscle tension awareness and control treatment which will take approximately six weeks. Headache patients will have their bilateral trapezius muscled tension recorded while low back pain patients will have their paraspinal muscles recorded. The motion sensor will be placed in the center of the back between the shoulder blades for all patients. The recorded will beep every hour to remind the subjects to record their pain levels and type of activity being engaged in. the beeper does not stop until a pain rating is entered on the keyboard. The intervention/treatment is not experimental and will be performed (and its success rated) according the Surgical Research Service SOPs.

Progress: Twenty five subjects have been entered. Preliminary data for five subjects showed statistically significant differences between the subjects, but these differences were not consistently found within subjects when tested on separate days. Because there are few significant differences when one subject is recorded while performing the same tasks repeatedly on two days and virtually none when performing the tests repeatedly on the same day, the device can be used to reliably record muscle tension in one subject. Significant differences found between days of recording up to one week apart would probably be due to changes in some factor affecting muscle activity other than time. Because different pain free people consistently produced significantly different readings, little can be said about using the device to differentiate between people who are in pain and those who are pain free. A paper was presented at the Association for Applied Psychophysiology Annual Meeting, March 1996.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/052	**Status:** Completed
Title: Seroprevalence of Cryptosporidium Infection Among Active Duty soldiers		
Start Date: 01/19/96	**Est. Completion Date:** May 96	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: MAJ Curtis L. Yeager, MS		
Associate Investigators: MAJ David P. Goldman, MC	LTC Margot R. Krauss, MC	
Key Words: Cryptosporidium, drinking water, immunoblot technique		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To ascertain the serologic prevalence of cryptosporidium infection among active duty troops using an immunoblot technique. To determine if there are any differences in prevalence based on the source of drinking water. To determine if there are differences in prevalence based on history of recent deployments.

Technical Approach: This study will employ a recently developed technique of detecting immunologic response to cryptosporidium referred to as the enzyme linked immunoelectrotransfer blot (EITB), which is thought to be superior to ELISA and to direct-testing of stool for cryptosporidium. Convenience samples will be drawn from those who present for routine HIV testing. Soldiers will be asked to complete a self-administered questionnaire. 200 microliters of serum will be removed for the HIV sample and placed in a container for transport to the lab. No additional blood is required. Part of the serum will be examined using the EITB, specifically looking for IgA and IgG responses to the cryptosporidium antigen. Positive responses to IgA will be evidence of recent exposure, up to 60 days prior to sampling. Positive responses to IgG will be evidence of exposure in the previous 6-12 months. The results of the questionnaire with information about potential exposures will be correlated to antibody response. Results of EITB will be compared with questionnaire data on history of deployment, water source, and history of diarrheal disease. This is a descriptive study to estimate prevalence of cryptosporidium infection based on a relatively new technique. The chi-square test will be employed to compare proportions of those deployed vs non-deployed and those drinking ground water vs surface water.

Progress: 294 soldiers comprised the final study group. The seroprevalence of *Cryptosporidium* infection in this sample of US Army personnel was somewhat lower than that estimated for the US population using the ELISA testing, consistent with previous evidence demonstrating immunoblot to be more sensitive and specific for serodiagnosis of this infection. Among all factors previously identified as risk factors for *Cryptosporidium* infection, only having a family members involved in a daycare setting was associated with seropositivity, emphasizing the importance of person-to-person transmission and secondary infections in the epidemiology of this parasitic infection.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF DENTISTRY

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/046	**Status:** On-going

Title: Evaluation of the Efficacy of Post-operative Antibiotics After Orthognathic Surgery

Start Date: 01/19/96	**Est. Completion Date:** Nov 96
Department: Dentistry	**Facility:** MAMC
Principal Investigator: MAJ Thomas J. Borris, DE	
Associate Investigators: COL Andrew A. Vorono, DE	LTC Charles R. Weber, DC MAJ Timothy Bandrowsky, DE

Key Words: Surgery:orthognathic, penicillin G, penicillin VK, cefaxolin, cephradine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the efficacy of a standard perioperative antibiotic regiment with and without a one week postoperative antibiotic regimen for patients undergoing orthognathic surgery in a prospective, randomized, double-blind study.

Technical Approach: Either isolated mandibular bilateral sagittal split ramus osteotomies, isolated maxillary Lefort I osteotomies, or a combination of the two procedures will be performed on all patients enrolled in the study. Patients in each operative group will be further subdivided randomly into one of two groups. The experimental group will receive prophylactic antibiotics as follows: one preoperative dose and intraoperative doses at two hour intervals for the duration of the surgery. The control group will receive the same preoperative and perioperative regimen along with a seven day oral postoperative regimen. The patients will be monitored for objective signs of infection, and WBC counts will be drawn preoperatively and post-operatively at one week.

Progress: Twenty-three (approximately 50% of required patients) have been enrolled in the study. Of the ones who have completed the study, only four met the study's definition of a postoperative infection. One of these patients required incision and drainage of the swelling; the remaining patients were asymptomatic and required no additional treatment.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/014	**Status:** On-going
Title: Patients Who Leave A Military Hospital Emergency Department Without Being Seen by a Physician		
Start Date: 11/17/95	**Est. Completion Date:** Feb 96	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: CPT Richard D. Brantner, MC		
Associate Investigators:	CPT Constance A. Lavieri-Reynolds, MC	
Key Words: Emergency treatment, patient not seen by a physician, outcome		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To develop identifiers that may aid in early recognition of patients who leave the emergency department woithout being seen. (2) To compare the medical outcomes of patients who leave without being seen to determine if they are at risk for poorer outcomes than patients who stay to be seen by a physician.

Technical Approach: This study will involve all patients who register for care in the MAMC Department of Emergency Medicine who leave prior to being seen by a physician. The sample size is estimated to be approximately 500-600 patients over the course of 6 months. The patients will be identified through the QA/QI system already established and begins when the triage nurse call the patient's name three times without a response. In this system, the chart is reviewed, an attempt is made to contact the patient, and the patient is then discharged out of the computer system. Under this protocol, patients who leave without being seen will receive additional attempts to contact by phone or mail for 3 days following their ER check-in. Charts will be collected and reviewed for particular characteristics which will be recorded. Patients contacted within the three days will be asked to answer a questionnaire which includes questions on their demographics, reason for leaving the ER, length of wait before leaving, further treatment sought and current status. Questionnaires will be given either telephonically or by mail. These will be compared to patients who went through with an ER visit and answered the same questionnaire. The characteristics and medical outcomes of the two groups will be compared using the student's t-test, chi-square and regression analysis for statistical significance.

Progress: This study has not been started due to a lack of secretarial and other support.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/120 **Status:** On-going

Title: The Randomized Use of Helium-Oxygen Mixture for the Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease. A Blinded Trial

Start Date: 06/09/93 **Est. Completion Date:** Dec 93

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Richard D. Brantner, MC

Associate Investigators:
CPT David A. Della-Giustina, MC
MAJ Bernard J. Roth, MC
CPT James W. Thompson, MC
MAJ Timothy R. Murray, MC

Key Words: COPD, helium,oxygen

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$800.00	**Periodic Review:** 04/21/95

Study Objective: To determine the therapeutic role of Heliox administration in the treatment of acute exacerbation of chronic obstructive pulmonary disease.

Technical Approach: Patients presenting with an acute exacerbation of COPD and requiring urgent treatment and agree to participate will be randomized to receive either Heliox (a mixture of 75% helium and 25% oxygen) or nitrogen-oxygen (a mixture of 75% nitrogen and 25% oxygen). Pulse oximetry will be monitored and any patient whose level falls to less than 90% will receive supplemental oxygen at a rate sufficient to raise pulse oximetry to at least 90%. Spirometry will be performed to measure FEV_1, FVC, and PEFR. Base line arterial blood gas analysis will be performed and an upright portable chest x-ray will be obtained. Patients will be asked to score the severity of symptoms and the time to relief of those symptoms. All patients will receive nebulized albuterol treatments every thirty minutes for a total of 3 treatments. Patients will be re-evaluated after each treatment and at the end of the 90 minutes study period all patients will be placed on room air. Ten minutes after discontinuation of heliox or nitrogen-oxygen treatment, an arterial blood gas will be obtained, spirometry performed and the patients will be instructed not to discuss or divulge the mode of treatment they received. Patients will be evaluated at this time by a pulmonologist who will be blinded as to the treatment used. After evaluation of the patient, baseline and end of study data a determination will be made for 1) probable admission, 2) possible admission, 3) or admission not necessary.

Biographical data will be evaluated using the t-test. The subjective rate of improvement in symptoms between the groups will be analyzed using the Mann-Whitney U Test and percentage improvement in FEV_1 will be compared using regression analysis.

Progress: Forty patients were entered this year for a total of 88 subjects.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/116	**Status:** On-going

Title: Multicenter, Prospective, Double-Blind Randomized Comparative Trial to Evaluate the Treatment Effects of Ciprofloxacin for 7 Days, Compared with Standard Therapy for 14 Days, In...acute Pyelonephritis

Start Date: 06/03/94	**Est. Completion Date:** Jul 95
Department: Emergency Medicine	**Facility:** MAMC
Principal Investigator: MAJ Thomas F. Burke, MC	

Associate Investigators:

COL Eugene T. Etzkorn, MC
Carlos Falcon, M.D.
David E. Bell
COL Ronald H. Cooper, MC
LTC Joseph T. Morris III, MC
MAJ Darrell E. Griffin III, MS
MAJ William T. Hurley, MC

Key Words: pyelonephritis, ciprofloxacin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To compare the treatment effects of ciprofloxacin (IV single dose/PO or PO) versus standard therapy (IV single dose/PO or PO) as outpatient management in premenopausal females with acute uncomplicated pyelonephritris. The efficacy and tolerability of a seven day treatment of ciprofloxacin will be compared with a fourteen day treatment with standard therapy. In addition, healthcare resource utilization will be evaluated related to treatment drop-outs, failures/relapses, as well as adverse events between both treatment arms (direct costs). Patient perception will be collected by recording patient's speed of recovery and return to normal activity.

Technical Approach: Premenopausal women with clinical signs and symptoms of acute pyelonephritis and pyuria are eligible to participate in this study. After enrollment, study drug (ciprofloxacin or Trimethoprim/Sulfamethoxazole) may be administered as an initial single IV. dose, or oral dose, followed by oral therapy for a total duration of therapy of 14 days of active study medication for the control arm, versus 7 days of active drug for the investigational arm, followed by 7 days of placebo. All patients enrolled in the trial (including failures and drop-outs) will be followed until 4-6 weeks following the completion of study drug. The primary outcome parameter will be bacteriological and clinical efficacy. A secondary parameter is the overall costs associated with pyelonephritis treatment of the two regimens. Patient perceptions will be collected by questioning the patient regarding their response to treatment.

Progress: Fifty-eight patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/074 **Status:** Completed

Title: A Multi-center, Prospective Study of the Microbiology and Treatment of Infected Dog and Cat Bite Wounds

Start Date: 03/04/94 **Est. Completion Date:** Jun 95

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: MAJ Thomas F. Burke, MC

Associate Investigators: CPT Jack K. Handley, MC
CPT William Evans, MC

Key Words:

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the relative presence of various zoonotic and non-zoonotic pathogens in the microbiology of infected cat and dog bites.

Technical Approach: This is a multi-center study. Patients who have sustained a dog or cat bite would infection presenting for care more than 12 hours after being bitten will be invited to participate in this study. Volunteers will have one set of both aerobic and anaerobic wound culture(s) specimens to be sent to a reference lab. A complete blood count, blood cultures, and soft tissue and bone x-rays are not part of the study but are suggested when indicated. A history and physical examination will be performed upon study entry. Specifically noted in the history will be the type of and age of biting animal (dog or cat), the time of the wound, the time of onset of the wound infection and fever if present, and the presence of any immunocompromising conditions. Also noted will be any local wound care, the number and location of wounds, the presence and measured area of erythema, the presence of lymphangitis, the presence of swelling , the presence of purulent drainage, fluctuance and/or abscess formation. Any surgical procedures or debridements will be noted. The study endpoint will be the microbiological characterization of the pathogens associated with 100 dog and 50 cat bites. A tabulation of parenteral and/or oral antibiotic administered will be made. Recording of discontinuation or initial antibiotics because of clinical failure will also be made. Correlation of clinical failure and antibiotic susceptibilities will be analyzed.

Progress: Eighteen subjects were entered at MAMC. MAMC tied with Maricopa Medical Center for enrolling the greatest number of subjects. Several interesting isolates from both the dog and cat bites have been identified. Papers are being prepared for submission to Clinical Infectious Diseases and the Journal of Clinical Microbiology.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/057	**Status:** Completed
Title: Assessment of the Efficacy and Safety of Eliprodil in Patients with Acute Ischemic Stroke		
Start Date: 02/16/96	**Est. Completion Date:** Oct 97	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: MAJ Thomas F. Burke, MC		
Associate Investigators: CPT Gary W. Beaver, MC LTC Max B. Duncan Jr., MC MAJ Michael A. Elliott, MC	MAJ John W. McBurney, MC CPT Jon L. Hobbs, MC MAJ Linda A. Marden, MC Steven A. Pace, MD	
Key Words: Stroke:ischemic, eliprodil		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the safety and efficacy of eliprodil (relative to placebo) in limiting the impairment in the patient's functional abilities following an acute ischemic stroke in the distribution of the carotid artery. To evaluate the effect of eliprodil on mortality during the first 90 days after stroke onset.

Technical Approach: This is a double-blind, randomized, parallel-group, placebo-controlled, multicenter study of the safety and efficacy of eliprodil in the reduction of injury associated with an acute ischemic stroke in the distribution of the carotid artery. Patients with evidence of an acute ischemic stroke in the territory of the carotid artery will be randomized in a 1:1 ratio to one of two treatment groups. Infusion of study drug must be initiated within eight hours of the onset of symptoms. Patients will be randomized to receive either intravenous eliprodil every 12 hours for 10 doses, or matching IV placebo every 12 hours for 10 doses. Patients will receive 10 doses of double-blind study medication during the five day treatment period and then will be followed for an additional 85 days during the follow-up evaluation period with visits occurring 30 and 90 days post-onset of the stroke. Phone contacts will be made to the patient or the care giver at 14 and 60 days post-onset of the stroke. The total duration of the study is 90 days. During the treatment period and the follow-up evaluation period, patients will be assessed with the Barthel Index, NIH Stroke Scale, Modified Rankin Scale, general health questionnaires and CT scans of the head. Electrocardiograms, laboratory assessments, clinical examinations, and adverse event assessments will also be done throughout the study.

Progress: This study was terminated by the sponsor due to a lack of efficacy in European trials. No safety concerns have been raised. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/135 **Status:** Completed

Title: Multicenter, Randomized, Double-Blind, Parallel Trial, Comparing the Efficacy and Safety of a Single IV Dose (1.5 mg/kg) of Selfotel with Placebo in Patients Age 40-85 Years with Acute Ischemic Stroke

Start Date: 08/05/94 **Est. Completion Date:**

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: MAJ Thomas F. Burke, MC

Associate Investigators:
MAJ Jonathon Newmark, MC
Richard B. Schwarts, M.D.
CPT Jon L. Hobbs, MC
Maggie M. Swansberg, M.D.
Eric Hassid, M.D.
MAJ John W. McBurney, MC
CPT Leo W. Kesting, MC
MAJ William T. Hurley, MC
CPT Gary W. Beaver, MC
Joseph N. Piper, M.D.
Carlos L. Rodrigues, M.D.

Key Words: stroke:ischemic, Selfotel, placebo

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To evaluate the efficacy and safety of a single 1.5 mg/kg dose of selfotel relative to placebo in improving the 90-day functional outcome of acute ischemic stroke patients. 2) To determine whether selfotel improves the 30-day and 90-day outcome compared with placebo. 3) To determine whether selfotel reduces mortality from acute ischemic stroke compared with placebo.

Technical Approach: There will be three periods to this trial: Screening/Treatment, Acute Monitoring, and Follow-up. Screening/Treatment Period: The Screening/Treatment period begins when the patient is admitted to the Emergency Room. This trial will enroll patients 40-85 years with a clinical diagnosis of paretic hemispheric acute ischemic stroke. Baseline neurologic symptoms will be documented with the Scandinavian stroke Scale and the National Institutes of Health (NIH) Stroke Scale. Screening procedures and treatment must be accomplished as soon as possible and no longer than six hours from the onset of the patient's stroke symptoms. Patients will be randomized to 1.5 mg/kg selfotel or placebo. A single dose of trial drug will be given. Acute Monitoring Period: The Acute Monitoring period begins immediately after trial drug administration and ends on Day 8 or hospital discharge (if earlier). During this acute period, the patients will be monitored for safety and neurologic function. Follow-up Period: The Follow-up period begins after Day 8 or when the patient is discharged from the hospital (if earlier). Clinic visits will be made on Trial Days 30 and 90 when efficacy will be determined using the Barthel Index, NIH and Scandinavian Stroke Scales.

Progress: This protocol was closed by the sponsor pending further benefit/risk assessment. Three patients were enrolled at MAMC with no serious adverse events reported.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/189	**Status:** On-going
Title: Analgesia for Reduction of Acute Glenohumeral Dislocation: Intra-articular Lidocaine Versus Intravenous Fentanyl		
Start Date: 09/15/95	**Est. Completion Date:** Aug 96	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: CPT Joseph R. Hoffman, MC		
Associate Investigators: MAJ Marco Coppola, MC	CPT Richard Butler, MC CPT David A. Siegel, MC	
Key Words: Glenohumeral dislocation, lidocaine, Fentanyl		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: We intend to contrast the analgesic efficacy of intra-articular lidocaine versus intravenous fentanyl in an adult population suffering from acute glenohumeral dislocation.

Technical Approach: A sample of 40 consenting patients (male and female) meeting diagnostic and inclusion criteria would be enrolled in the study. They would be randomized to receive either intravenous fentanyl or intra-articular lidocaine as analgesia for the reduction of their shoulder dislocation. Reduction would be performed by a standardized technique and their shoulder immobilized for post-reduction radiographs. Patients would be asked to rate their pain at presentation, pain at the administration of analgesia, pain of reduction, level of sedation, and pain at time of discharge on a visual analog scale. The clinician would also rate the ease of reduction. Data would undergo analysis of variance (ANOVA). The patient's score and the physician's score would be subjected to regression correlation.

Progress: Five patients have been entered at MAMC and an additional 19 have been entered under the same protocol at Darnell Army Community Hospital, Ft Hood.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/062 **Status:** On-going

Title: Double-Blind, Randomized, Comparative, Multicenter Study of Zagam (Sparfloxacin) vs. Biaxin (Clarithromycin) in the Treatment of Community-Acquired Pneumonia

Start Date: 02/16/96 **Est. Completion Date:**

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: Steven A. Pace, MD

Associate Investigators:
D. W. Schroeder
MAJ Thomas F. Burke, MC
J. Halper

Key Words: Pneumonia, sparfloxacin, clarithromycin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the efficacy and safety of sparfloxacin (RP 65206) compared with clarithromycin when administered orally for 10 consecutive days in the treatment of patients with community acquired pneumonia.

Technical Approach: This is a double-blind, randomized, double-dummy, comparative, multicenter study of sparfloxacin versus clarithromycin in the treatment of patients with community-acquired pneumonia. A total of 380 patients will be recruited from 30 participating cites. After meeting the inclusion/exclusion criteria and giving informed consent, patients will be randomly assigned to receive either a loading dose of 400 mg sparfloxacin (two 200 mg tablets) followed by sparfloxacin 200 mg (one 200 mg tablet) QD, or clarithromycin 500 mg q 12h, each for 10 days. A double-dummy system will be used such that matching comparator placebos will be given concurrently with the active drug during the treatment period. Patients will be required to visit the study site at baseline, on day 4 during treatment, on day 20 (10 days after treatment) and for long-term follow-up on day 38 (28 days after treatment). Efficacy will be assessed as the clinical response. Safety of sparfloxacin and clarithromycin will be assessed using subjective patient reports, clinical evaluations and laboratory tests.

Progress: Three patients have been enrolled and completed the study. One patient was enrolled whose pneumonia did not radiographically clear. They were subsequently diagnosed with an endobronchial, non-small cell carcinoma. This was appropriately reported as an adverse event though it was not drug related.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/152	**Status:** On-going
Title: Pediatric Intubation Training Utilizing the Ferret Model		
Start Date: 08/16/94	**Est. Completion Date:**	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: Steven A. Pace, MD		
Associate Investigators: MAJ Lawrence A. Wilson, MC COL Patrick C. Kelly, MC MAJ Thomas D. Carver, MC	MAJ Thomas F. Burke, MC MAJ Mary P. Fairchok, MC R.V. Jarrett MAJ Roger M. Hinson, MC	
Key Words: Intubation:training, animal model, ferret,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To enhance the clinical skills of health care providers in managing pediatric airways, specifically endotracheal intubation.

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: Three PALS courses were held in FY 96 with trainees from Pediatrics and Emergency Medicine.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/183 **Status:** Completed

Title: A Double-Blind, Randomized, Placebo-Controlled, Multicenter, Parallel Group Study to Demonstrate the Efficacy and Safety of GG167 in the Prevention and/or Progression of Influenza A and B Viral ....

Start Date: 09/15/95 **Est. Completion Date:** Mar 96

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: Steven A. Pace, MD

Associate Investigators:
MAJ William S. Powell, MC
MAJ William J. Frohna, MC
CPT Nathan T. Rudman, MC

Key Words: GG167, influenza, safety, efficacy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate the efficacy of GG167 given by the inhaled, intranasal, and inhaled plus intranasal routes, in the prevention and/or progression of symptomatic disease caused by influenza A and B viral infection. Also, to further assess the safety of GG167 given by the inhaled, intranasal, and inhaled plus intranasal routes.

Technical Approach: This will be a double-blind, randomized, placebo-controlled, multi-center, parallel-group study to be conducted at 100 centers worldwide. Approximately 840 patients will be randomized to receive study medication twice daily or four times daily for five days and will attend a post-treatment visit on Day 6 and a follow-up visit on Day 21. Efficacy evaluation will based on the presence of symptomatic influenza, daily symptom and severity assessments recorded by the patient on a Diary Card, global assessment of symptoms and temperature. Safety will be evaluated by baseline and post-treatment routine blood analysis and follow-up (if indicated) and adverse event monitoring during the study period. The primary endpoint is the proportion of patients with laboratory confirmed influenza plus at least two clinically significant influenza symptoms of greater than mild severity. The primary population for analysis will be the Intent-to-Treat population that 15% placebo patients will have symptomatic influenza and assume a clinically relevant difference as a decrease to less than or equal to 5% of patients with symptomatic influenza for the GG167 treatment group. Primary significance tests will be performed on data from all centers worldwide.

Progress: Enrollment to this protocol was closed on 25 Feb 96. Four patients were randomized to drug at MAMC with no adverse events.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/165	**Status:** On-going
Title: Emergency Surgical Procedures Laboratory Training Utilizing the Goat (Capra hircus)		
Start Date: 09/21/94	**Est. Completion Date:** Oct 97	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: Steven A. Pace, MD		
Associate Investigators: MAJ Lawrence A. Wilson, MC	MAJ William J. Frohna, MC	
Key Words: Emergency surgical procedrues: training, goat,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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) Cricothyroidotomy, 3) Pericardiocentesis, 4) Diagnostic peritoneal lavage, 5) Venous cutdown, 6) Thoracotomy.

Progress: The training course was performed twice in FY 96 for Emergency Medicine physicians.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/185 **Status:** Completed

Title: A Double-Blind, Randomized, Placebo-Controlled, Multicenter, Parallel Group Study to Investigate the Efficacy and Safety of GG167 Administered Twice and Four Times a Day for the Treatment of Inf

Start Date: 09/15/95 **Est. Completion Date:**

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: Steven A. Pace, MD

Associate Investigators:
MAJ William J. Frohna, MC
CPT Nathan T. Rudman, MC
MAJ William S. Powell, MC

Key Words: GG167, influenza

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the efficacy of GG167 given by the inhaled and intranasal routes in the treatment of influenza A and B viral infections. To compare the efficacy of GG167 administered four times a day to twice a day in the treatment of influenza A and B viral infections. To evaluate the safety of GG167.

Technical Approach: This will be a randomized, placebo-controlled, multi-center, parallel-group study which will be double-blind to active or placebo treatment but not to dosing schedule. Approximately 720 patients will be randomized to receive study medication twice daily or four times daily for five days or to placebo treatment groups for both schedules and will attend a Post-treatment visit on Day 6 and a follow-up visit on day 21. Males or females $\geq$ 13 years of age with a duration of influenza-like illness of $\leq$ 48 hours (this must include feverishness and at least two of the following: myalgia, headache, cough, sore throat) prior to receiving the first dose of study medication will be included. Efficacy measurements will include daily symptom assessments in a diary card, global assessment of symptoms, temperature, use of relief medications, incidence of secondary infections and use of anti-infective medications. Safety will be evaluated using laboratory analysis of blood and clinical adverse events inquiries. The primary endpoint is the time until alleviation of clinically significant symptoms of influenza within the qualified Intend-to-treat population of all patients randomized to treatment. Placebo groups will be combined for statistical analysis. Statistical tests for efficacy will be pairwise comparisons of GG167 qds and GG167 bd against placebo. Time to alleviation will be analyzed using an extended Mantell-Haezel test, stratified for center. Other parameters will be tested using analysis of variance, the Fischer's Exact-test, or other appropriate statistical method.

Progress: Twelve patients at MAMC were randomized. One patient was dropped because of an adverse event that was felt to be possibly related to the study medication.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/005	**Status:** Completed
Title: SMARTT: Serial Markers: Acute MI, and Rapid Treatment Trial		
Start Date: 10/20/95	**Est. Completion Date:** Aug 96	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: Steven A. Pace, MD		
Associate Investigators: Eric Friedland, M.D.	MAJ Brent A. Smith, MC	
Key Words: Serial markers, acute MI, myoglobin, creatine kinase		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To determine whether the rapid reporting of serum indicators of acute necrosis (both myoglobin and creatine kinase - myocardial (CK-MB) isoenzyme) will increase the appropriate use of thrombolytic therapy in eligible patients with acute myocardial infarction (MI) and ST-segment elevation or new bundle branch block (BBB) on the 12-lead ECG. 2) To determine if the above markers will increase the use of thrombolytic therapy or primary PTCA in patients with ST elevation and BBB. 3) To determine whether rapid reporting of these indicators to emergency physicians will affect admission and release decisions in patients with and without acute MI. 4) To determine whether the availability and rapid reporting of these indicators influence time to treatment in patients receiving thrombolytic therapy.

Technical Approach: Patients over the age of 25 years presenting to the Madigan emergency department with the chief complaint of chest pain (atraumatic) suggestive of MI or ischemia will be randomly assigned to either Group 1 or Group 2. Group 1 patients will have the results of CK-MB taken at the time of emergency department presentation reported to the provider on a stat (approximately one hour) basis. Group 2 patients will have the results of CK-MB and myoglobin taken at the time of emergency department presentation and one hour later reported to the provider. Data will be collected on historical factors, ECG analyses, admission and discharge rates, myocardial infarction "rule in" rates, treatments and procedures administered, and the results of serum marker analyses in all patients at time of presentation to the emergency department and one hour later. Admitted patients will be followed in the hospital and discharged patients will be contacted by mail, telephone, or follow-up visit. The primary endpoint will be the proportion of patients with acute MI who are treated with thrombolytic therapy within 3 hours of randomization.

Progress: Approximately 50 patients were entered at MAMC. Data will be forwarded to a central location for analysis.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/025 **Status:** Completed

Title: Analysis of Oropharyngeal Suction Efficiency in Relation to Suction Tube Diameter

Start Date: 12/15/95 **Est. Completion Date:** Dec 95

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT James T. Vandenberg, MC

Associate Investigators: CPT Nathan T. Rudman, MC
CPT David E. Ramos, MC

Key Words: Suction:oropharyngeal, tube diameter

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine which of three suction apparatuses is most efficient at evacuating liquids of varying viscosities and simulated vomitus.

Technical Approach: Three difference suction apparatuses using standard wall pressure, regulators and reservoirs will be compared for material evacuation time. Suction tubing size and the canister lid port size are the dependent variables to be studied. The time required to evacuate 90 mls of water, activated charcoal, and chunky simulated vomitus from a 110 ml cup will be recorded. Analysis of variance will be used to compare evacuation times for all three test situations. Analysis of variance will be used to compare the evacuation times between each of the suction apparatus. Three different types of materials will be used in this experiment, however, comparisons will only be made between the different suction apparatus. A post hoc test will be used for any differences of ANOVA. A p value of less that 0.05 will be considered significant. Using power analysis, a sample size of four is adequate.

Progress: Six tests were performed with each system on each substance. The study demonstrated that 3/4 inch suction tubing attached to the 1 inch pour spout is superior to the standard 1/4 inch tubing and connection ports currently used. The greater than 1- fold reduction in evacuation time of the more viscous and particulate materials may have important clinical implications in preventing or minimizing the complications from aspiration. This new technique could easily be used in prehospital, emergency department, and operating room settings. A paper was presented at the Society of Academic Emergency Medicine Annual Meeting, May 96 and a manuscript has been submitted for publication.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF FAMILY PRACTICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/127 **Status:** On-going

Title: Incidence of Exercise Induced Hematuria After the Army Physical Fitness Test (APFT)

Start Date: 06/21/96 **Est. Completion Date:** Aug 96

Department: Family Practice **Facility:** MAMC

Principal Investigator: CPT Yong H. Chun, MC

Associate Investigators: MAJ Charles Payne, MC

Key Words: Hematuria, exercise-induced, APFT

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To determine the incidence of hematuria in a young healthy population. (2) To determine the effect of routine exercise such as the APFT on urinalysis for blood and protein. (3) To modify a guideline for assessment of painless hematuria after routine exercise.

Technical Approach: The purpose of this study will be to identify the incidence of exercise-induced hematuria secondary to routine physical training and develop guidelines for proper urine collection and triage of patients found to have hematuria after exercise. 500 male and female ROTC Cadets will be recruited during routine physical examinations which includes a urinalysis. A questionnaire will be completed and urine will be collected following a standard APFT. Urinalysis will check for blood and protein. If positive for blood, the specimen will be forwarded for microscopic study to determine of >3 RBC/HPF are present. If so, the participant will be asked to provide specimens at 24 hrs, 48 hrs, 72 hrs, and 1 week after the APFT. The data will be collected and analyzed as part of a descriptive study.

Progress: Urine specimens have been collected on 95 subjects in accordance with the study plan. Data analysis is in process.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/056	**Status:** On-going

Title: Incidence of Unintended Pregnancy in Female Soldiers Presenting to OB Orientation at Madigan Army Medical Center From March 1996 to February 1997

Start Date: 02/16/96	**Est. Completion Date:** Feb 97
Department: Family Practice	**Facility:** MAMC

Principal Investigator: LTC Jeffrey B. Clark, MC

Associate Investigators: None

Key Words: Pregnancy:unintended, female soldiers

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To determine the incidence of unintended pregnancy in active-duty females presenting to OB orientation. (2) To determine if the soldier was using contraception if the pregnancy was unintended. (3) To determine if the soldier was using the method of contraception correctly. (4) To determine why a contraception was not being used if the pregnancy was unintended.

Technical Approach: Pregnant soldiers will be surveyed during MAMC OB orientation. Participants will complete the questionnaire, and return it to the OB orientation coordinator. The following information will be analyzed using descriptive statistics: (1) Demographic characteristics of the respondents by age, grade, marital status, and race, (2) Frequency of unintended pregnancy both total and stratified (3) Frequency of unintended pregnancy in those not using contraception or using it incorrectly.

Progress: Approximately 200 subjects have been entered in the study. Subject enrollment will continue. Preliminary results show that 61% of officers and 70% of noncommissioned officers reported that their pregnancy was intended. In contrast, 64% of the junior enlisted reported that their pregnancy was unintended and 65% reported that they were not using any form of birth control. The most common reasons for not using birth control were fear of side effects or stopping of contraception because of side effects. The most common failed contraceptive method was the male condom. Prevention programs should target the subpopulation of soldiers with unintended pregnancies and focus on increasing the use of effective contraception.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/047 **Status:** Terminated

Title: Healing of Sprained Ankles Using Pulsed Electromagnetic Field Therapy

Start Date: 05/19/95 **Est. Completion Date:** Sep 95

Department: Family Practice **Facility:** MAMC

Principal Investigator: MAJ Richard T. Dombroski, MC

Associate Investigators:
MAJ James D. Terrio, MC
MAJ Arnoldas S. Kungys, MC
Estelle Hamblen, BA, MHA
LTC Richard A. Sherman, MS
MAJ Kirk Willard, MC
Linda Robson, BA
Melissa Wong, BA

Key Words: Pulsed Electromagnetic Field Therapy, ankle sprains

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether pulsing electomagnetic fields (PEMFs) can be useful in potentiating recovery from grade I and II sprained ankles when used in conjunction with standard techniques.

Technical Approach: This project is designed to confirm the results of an earlier, relatively small study performed by the Army. That study showed that soldiers exposed to PEMF's just after spraining their ankles recovered more quickly than those who were not exposed to them. This project is a multicenter study supported by Electropharmacology, INC. Approximately 40 subjects will partcipate at Madigan AMC and will have objective measures of recovery including range of motion (assessed by goniometry), pain assessement (by visual analog scale), level of activity, presence of swelling (by volumetric measure) and use of ice and medications. Soldiers between the ages of 18 and 50, diagnosed as having had either a Grade I or Grade II ankle sprain within 48 hours of evaluation will be ranndomly divided into (a) standard treatment plus active PEMF therapy or (b) standard treatment plus placebo PEMF therapy. Each patient's ankle will be placed under the device for 30 minutes for two consecutive days and swelling and pain will be assessed during a follow-up on day three. Changes in swelling will be analyzed using a non-paramentric two way repeated measures analysis of variance in which the repeated measure will be the subject's swelling at each evaluation and the independent measure will be the active vs. placebo group. Changes in pain, pressure, function, and differences in rate of initial swelling and then subsequent decrease, will be determined using a non-parametric correlation. Differences in amount of ambulation, range of motion and pain medication taken will be calculated using repeated measures analysis of variance and a slope analysis.

Progress: This protocol was terminated due to a lack of funding and insufficient data for analysis. Eighteen patients were enrolled.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/021	**Status:** Completed

Title: A Health Risk Appraisal and Needs Assessment of the Active Duty Population on Naval Air Station Whidbey Island

Start Date: 11/17/95	**Est. Completion Date:** Feb 96
Department: Family Practice	**Facility:** MAMC
Principal Investigator: CMDR Richard W. Emerine, MC	
Associate Investigators:	LCDR John Filmore, MS

Key Words: Health risk, health needs, Naval Air Station Whidbey Island

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To perform a descriptive study of the health risk appraisal and a health needs assessment of a random sample of the active duty population attached to Naval Air Station (NAS) Whidbey Island.

Technical Approach: We will sample 30% of the servicemembers attached to NAS Whidbey Island. Subjects will be stratified by rank and sex. Varying percentages of each group will be randomly surveyed using the health risk appraisal form and receive a Needs Assessment. This assessment will allow us to describe the various demographics and major health risks for this population. This will assist in hypothesis generation, facilitate the local Health Promotion Program at NHOH/NAS Whidbey Island and provide generalizable data to be used to further develop health promotion programs throughout the Navy and possibly the military. Measures for central tendency will include the mode for nominal data, median for ordinal data and mean for ratios. A measure of variability will include the range and standard deviation. Contingency tables will assist in comparing the rates of distribution of particular variables. Chi square and contingency tables for nominal and categorical data, ANOVA and "T" tests for continuous variables and correlation coefficients or Pearson's "r" will be used for ordinal, interval and ratio scale data.

Progress: Approximately 2940 sailors and Marines were randomly sampled. Mean age was 27.9 years with 73% males, 75% white, non-Hispanics, 62% married, and 98% had at least a high school degree, which is consistent with that of the total Navy population. The active duty population exceeded the HP 2000 objective for exercising at least three times per week by 18-30% across all age groups. However, an alarming 50-62% failed to achieve this objective despite a mandate from the Chief, Naval Operations, that all active duty personnel exercise at least three times per week. Current smokers and overweight adults failed to meet the HP 2000 objectives. The perceived desires for health promotion programs were congruent with their identified health risks. Nearly half of the respondents were interested and desired a health promotion program. Over one-third of smokers ranked the personal health goal to stop smoking as their first and most important health concern. The Navy's health promotion program needs to reemphasize adequate exercise, smoking cessation, and help for overweight personnel.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/079	**Status:** On-going
Title: Operational Medical Database Investigation		
Start Date: 03/15/96	**Est. Completion Date:** Feb 97	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: CPT Mark D. Harris, MC		
Associate Investigators:	LTC Brian R. Johnson, MC	
Key Words: Database:medical		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To discover what primary care doctors are currently using for a medical database in operational environments. 2) To discover what primary care physicians believe are the characteristics of the perfect operational medical database.

Technical Approach: One thousand male and female active duty Army, Navy and Air Force family practitioners and GMOs between the ages of 20-65 will be recruited. We plan to first create an operational medical database questionnaire to use as a pretest questionnaire with members of the MAMC Department of Family Practice. Once the protocol is approved, we will mail out a final questionnaire. Respondents will answer anonymously, but will return a separate, included card to indicate when they have returned the survey so that I know who has returned one. A second survey will be sent to those from whom I have not received a completed survey. Three to four months after the initial mailing, data will be tabulated, analyzed, presented and published.

Progress: Approximately 450 questionnaires have been returned and data entry is in progress. A third mailing has been sent out to try to obtain more responses.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/078 **Status:** Completed

Title: Marketing the Residency Program: What Do Prospective Applicants Look For in a Family Practice Program

Start Date: 03/15/96 **Est. Completion Date:** Mar 96

Department: Family Practice **Facility:** MAMC

Principal Investigator: LCDR Robert C. Marshall, MC USNR

Associate Investigators: None

Key Words: Family Practice, Residency, Marketing

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To canvas all physician applicants to military Family Practice residencies in order to ascertain what factors were most influential in their ranking and choice of the available military programs in Family Practice.

Technical Approach: All applicants to R-1 positions in military Family Practice residency programs (Army, Air Force and Navy) will be mailed a questionnaire. The questionnaire will contain demographic questions, open-ended questions about the three most important factors in choosing a residency program, questions about how they learned about Family Practice and then 43 closed-ended questions about what they thought were the important factors in choosing a program. The combination of open-ended and closed-ended questions allows internal checking for validity and reliability. All questionnaires will be anonymous (identifiers will be used for follow-up mailings only). Once received, all questionnaires will be analyzed for trends and statistical significance. Factors will be rank ordered in terms of importance for both open-ended and closed-ended questions. From this data, more effective means of attracting the quality medical students needed for Family Practice residency positions can be developed.

Progress: One hundred and eighty-seven questionnaires were mailed out and 160 returned for an 85% return rate (after two mailings and reminder post cards). Data analysis is complete and a paper is being prepared for presentation as well as publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/149 **Status:** On-going

Title: Primary Prevention of Otitis Media Using a Parental Education Model to Reduce Risk Factors

Start Date: 06/16/95 **Est. Completion Date:**

Department: Family Practice **Facility:** MAMC

Principal Investigator: LCDR Robert C. Marshall, MC USNR

Associate Investigators: LT Mark Flynn, MC USNR
LT Joan Morris, NC USN

Key Words: Otitis media, education

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to reduce the incidence of acute otitis media by educating parents to modify known risk factors.

Technical Approach: All infants born at Naval Hospitals Bremerton and Oak Harbor for the month of April, May, June and July 1995 will be screened for exclusion criteria or Tri-care assignment to primary care portal outside of USNH Bremerton or Oak Harbor. If acceptable, the patient will be stratified and randomized to intervention and control groups. Each infant will be given a random number derived from a random number table. The control group will receive usual information on child care. In addition to this information, the intervention group will also receive a parental handout on risk factor modification of known behaviors that increase the risk of otitis media and a 10-15 minute talk by a nursery nurse or corpsperson about modifying these factors. All parents will complete a newborn risk factor questionnaire. At each well baby visit, ER visit and acute clinic visit, the child will be evaluated for otitis media using published criteria for diagnosis and a check-off sheet. Parents and infants in both groups will receive only routine care and counseling subsequent to the initial encounter. Follow-up questionnaires will be mailed at 6 and 12 months.

Progress: Forty-five patients have been enrolled at Naval Hospital Oak Harbor and 97 at Naval Hospital Bremerton. Numerous difficulties have been encountered. Many patients have declined enrollment for various reasons and many times the clinics have not completed the necessary forms, plus the Pediatrics Clinic at Bremerton is not accepting new patients. A second mailing to a majority of patients was recently undertaken with about a 5% "return to sender rate". Enrollment will continue with a goal of at least 250 patients enrolled.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/177	**Status:** On-going
Title: Comparison of Manipulative Treatment and Conservative Measures in the Management of Carpal Tunnel Syndrome (CTS)		
Start Date: 09/15/95	**Est. Completion Date:** Jun 96	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: CPT David C. Martin, MC		
Associate Investigators: LTC Brian R. Johnson, MC R. K. Evans	COL Shashi J. Kumar, MC CPT Mary V. Biglow, MC	
Key Words: Carpal tunnel syndrome, manipulation, home exercise program		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/19/96

Study Objective: The objectivde of this study is to show that manipulation of the wrist and/or the thoracic outlet in compbination with a home exercise program can alter the symptoms, function and/or nerve conduction latencies in carpal tunnel syndrome. It will be a ropspective, randomized, controled and partially blinded clinical trial.

Technical Approach: The subjects for the study will be consecutively drawn from a pool of patients referred to the Madigan Physical Medicine Department. All patients with suspected CTS will be given nerve conduction studies by the same physiatrist (S.K.). The patients with abnormal nerve conduction studies will be asked to enroll. All enrollees will be evaluated for level of function and mobility by an independent blinded investigator (D.M.) at the start and end of the study period. They will fill out questionnaires for demographic information, pain level, mobility and function. The individuals will be randomly assigned to the treatment or control group and will be blinded as to which group they are in. All subjects will be seen by the same physician (B.J.) weekly for the first month and every other week for the next two months for a total three month study period. At each visit, the control group will be asked to fill out pain scales and will be evaluated for range of motion. The treatment group will be asked to fill out pain scales and then treated using osteopathic methods (Sucher, 1993, 1995). The treatment group will also be instructed in a home exercise program. In addition to a final evaluation by D.M., each participant will be asked to fill out the questionnaires again and will be given repeat nerve conduction studies by the same physiatrist (S.K.) who will also be blinded.

Progress: Dr. Martin is in the process of making required changes to obtain final IRB approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/013 **Status:** Completed

Title: Exercise Blood Pressure and Heart Rate Response in Pregnancy As A Predictor of Preeclampsia

Start Date: 11/06/92 **Est. Completion Date:**

Department: Family Practice **Facility:** MAMC

Principal Investigator: CPT Craig M. Meier, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
MAJ Wade A. Lillegard, MC
CPT Janus D. Butcher, MC
CPT David N. Crouch, MC
LTC John P. Kugler, MC
CPT Monte C. Uyemura, MC
CPT Brain C. Harrington, MC

Key Words: preeclampsia, exercise, heart rate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/21/94

Study Objective: To determine if blood pressure and heart rate response to exercise can be used to predict the development of preeclampsia in pregnant women.

Technical Approach: An estimated 200 obstetric patients seen at MAMC Departments of OB/GYN and Family Practice who are nulliparous and have no history of hypertension, diabetes, heart disease or thyroid disease prior to pregnancy will be enrolled. Stationary bicycle exercise stress test will be performed prior to 20 weeks gestation. Blood pressure and heart rate response to exercise, the independent variables, will be monitored and documented at prescribed intervals during the test. The dependent variable will be the development of preeclampsia, and will be recorded as categorical data.

Progress: Three hundred and fifty women were studied. Preeclamptics were more likely to reach the maximum heart rate during exercise. They also exhibit a higher resting MAP starting at about week 16. Their average resting MAP rises with gestational age up to 20 weeks, while for normals it declines. Clinicians could exercise women who demonstrate serially rising MAPs after the 16th week of pregnancy. Those women with an above average heart rate response may be at increased risk of developing preeclampsia and thus could be targeted for preventive therapy. This research found discriminating features for the development of preeclampsia at a point earlier in pregnancy than looked at by most other screening studies. Future investigations should apply this theory to a group of early pregnancies and seek to improve sensitivity and specificity by combining with other screening modalities such as utero-placental doppler flow studies.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/130	**Status:** On-going

Title: Determining the Need for Teaching Interns About Professional Boundaries in the Physician-Patient Relationship

Start Date: 06/21/96	**Est. Completion Date:** Jul 96
Department: Family Practice	**Facility:** MAMC

Principal Investigator: LTC William F. Miser, MC

Associate Investigators: COL Paul Evans, MC
LTC David C. MacDonald, MC

Key Words: Physician,Patient relationship, professional boundaries, training

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: We want to know if interns have received any training during medical school on professional boundaries in the physician-patient relationship. The information obtained form this study will be the basis for the development of an educational curriculum dealing with these topics.

Technical Approach: This is a one-time, cross-sectional survey. During the inial orientation this academic year, the Directors of Medical Education at each military training institution will distribute an anonymous questionnaire to a total of approximately 750 interns among the various sites. The questionnaire and the resulting educational curriculum will address several issues in the physician-patient relationship to include (1) romantic or sexual relationships between a physician and a patient, (2) what to do with a seductive patient in the office, (3) what to do if they feel sexually aroused by a patient, and (4) the use of chaperones in patient care. We also want to explore their attitudes toward dating or having sexual relationships with current and former patients. Finally, we want to know if they have ever had a patient make a sexual advancement toward them as a medical student, and if, when in medical school, they knew of any medical student, residents, or attendings who had a sexual relationship with a patient. The interns will be allowed to ask questions dealing with the survey which will not be identified with the respondents.

Progress: Seventeen of the 24 military hospitals that conduct graduate medical education agreed to participate in this study. The investigator is awaiting data from 5 other hospitals before doing the final data analysis. Preliminary analysis indicates that a significant number of medical students are not being trained in this area. A larger percentage of students who trained at the Uniformed Services University of the Health Sciences reported training in this area than among other students. More training is needed at the medical school and residency level to address this topic.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/053	**Status:** On-going
Title: The Annual Pap Smear Screen: Knowledge by Women Soldiers		
Start Date: 01/19/96	**Est. Completion Date:** Dec 96	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: MAJ Heidi P. Terrio, MC		
Associate Investigators: LTC William F. Miser, MC	LTC Donald M. Bradshaw, MC LTC Jeffrey D. Gunzenhauser, MC	
Key Words: Pap smear, annual exam, women soldiers		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To determine the number of active duty women who comply with regulations by receiving an annual Pap smear. (2) To determine factors influencing active duty Pap smear screening. (3) To compare the cervical cancer risk factor differences between women who have/have not received an annual Pap. (4) To compare age-specific atypia rates to their reported history of risk factors as indicated on the questionnaire for those women who have had a Pap at Fort Lewis. (5) To determine the percentage of women who know if their Pap had abnormality. (6) To determine the sexual behavior of women soldiers, their average number of sexual partners, the percentage that are in a monogamous relationship, the types of contraception that are used, and the percentage who obtain an elective termination of pregnancy.

Technical Approach: SIDPERS database will be used to identify all active duty women on Fort Lewis stationed at all units except the AMEDD units. Of the approximate 2100 active duty women from field units, 600 of these women will be age stratified, then randomly selected by a computer program. Survey will be sent to their unit address. COPATH database from MAMC cytology section will be used to confirm Pap smear in the last year and abnormality for those who had their Pap smear at Fort Lewis. We will also correlate the risk factors of the sample of women who have had their pap at MAMC to their cytologic and pathology results dating as far back as Oct 92 when the COPATH database began. Descriptive statistics will be used for demographic data, access to care information and risk factor data. In the evaluation of risk factors between the two groups of women, the women who have attained an annual Pap versus those who have either not had a Pap or who have not had one in greater than a year, multivariate analysis will be used, as well as, a one tailed t-test for a comparison of the cumulative score between the two groups. Chi-square analysis will be employed in the analysis of assessing the knowledge of abnormality of their own Pap smear.

Progress: Six hundred soldiers from field units at Ft. Lewis were surveyed with a 71% response rate. The nonresponders were demographically similar and had similar rates of obtaining PAP smears. The sample was racially diverse and well educated (80% with at least some college), 52% were married, and the mean age was 27 years. Seventy-eight percent responded that they had been informed of the results of their last PAP smear. These female soldiers have several high risk behaviors which help explain their higher atypical PAP smear rate. The higher number of lifetime partners and lack of condom use, also increased these womens' risk for an STD or unintended pregnancy. Further analysis is planned in the area of access to testing, knowledge of the purpose of a PAP smear, and question about sexual behavior.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/090	**Status:** On-going
Title: Treatment of Nocturnal Leg Muscle Cramps: A Double-Blind Placebo-Controlled Trial of Magnesium Oxide		
Start Date: 04/19/96	**Est. Completion Date:** Jul 96	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: LTC Bruce A. Woolman, MC		
Associate Investigators: CPT John P. Barrett, MC	MAJ Alan J. Barker, MC	
Key Words: Muscle:nocturanl cramps, muscle:leg, magnesium oxide		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the effectiveness of magnesium oxide in reducing or eliminating nocturnal leg muscle cramps when compared to placebo.

Technical Approach: No current pharmacologic agent is approved for use in the treatment or prevention of nocturnal leg muscle cramps. Quinine appears to be an effective remedy but sufficient evidence for its efficacy and safety are lacking. Magnesium supplementation has been given trial in Europe for the treatment of night leg cramps. No studies have been done in this country to assess the efficacy of magnesium. Patients with a history of nocturnal leg muscle cramps and who are experiencing 2 or more cramps per week will be considered for enrollment in this study. Patients will be primarily identified from Family Practice Clinic physician panels with open invitation to other interested patients who are eligible DOD beneficiaries not followed in MAMC FP Clinic. Subjects will be observed via a 2 week symptom diary prior to treatment for 2-weeks with either magnesium oxide or placebo. During the full four weeks of the study, patients will keep a daily symptom diary that will be given to one of the investigators at each clinic visit. These symptom diaries will record the number, severity and duration of muscle cramps experience. The data obtained will be analyzed for statistical significance.

Progress: No patients have been entered. The medication and placebos have not been received.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/022 **Status:** Completed

Title: Characteristics of Family Practice at an Army Family Practice Residency Clinic

Start Date: 12/15/95 **Est. Completion Date:** May 96

Department: Family Practice **Facility:** MAMC

Principal Investigator: MAJ Mary J. Wyman, MC

Associate Investigators: None

Key Words: Family practice:characteristics, Family practice:U.S. Army

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the characteristics of family practice seen at an Army family practice residency clinic with respect to patient demographic information, diagnoses given, lab tests and x-rays ordered, prescriptions and consults written, type of visit, disposition, and to delineate what associations, if any, exist between increasing levels of training and style of practice.

Technical Approach: Data collected on about 45,000 patient encounters in the family practice clinic at Tripler Army Medical Center (TAMC) from 7/91-6/95 will be analyzed with respect to patient demographic data, diagnoses given, number of labs, xrays, consultations, and prescriptions ordered, level of training of the physician seeing the patient, whether the patient was seen by their assigned physician, deposition and follow-up on the patient, and length of the visit using a descriptive correlational approach. The correlational aspects will include looking at any differences which occur between staff and residents in their practice style. The data base would also allow a cross sequential analysis, in that one could follow year group cohorts of physicians as they proceed through their residency to look for "generational" changes.

Progress: Family practice diagnoses in the military medical centers with residency programs are similar to those in civilian and military non-residency hospitals. The average visits per year per patient were approximately four. The high utilizers account for 30% of the headache diagnoses and 25% of the depression diagnoses.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/150	**Status:** On-going
Title: Characteristics of Outstanding Teachers of Primary Care Medicine in the U.S. Military		
Start Date: 08/16/96	**Est. Completion Date:** Dec 96	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: COL Joseph F. Yetter III, MC		
Associate Investigators: None		
Key Words: Teachers, Primary Care Medicine, Military		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the characteristics of outstanding teachers of primary care medicine in the U.S. military.

Technical Approach: We will send a letter and a survey form to each chief of each department of primary care (Family Practice, Internal Medicine, and Pediatrics) at every Army, Navy, and Air Force teaching hospital where there are rersidency programs in their respective specialties. The letter inroduces the research project, requests surveys be given to these teachers, and explains that we will request the name of the oustanding teacher later. Two months later, we will send follow-up letters to the same chiefs of departments, requesting the name of the outstanding teacher, as well as additional information and participation by teaching chiefs and chief residents. For each slected outstanding teacher, two controls will be randomly selected from the list of physicians from the same department. All responses will be added into a data base without designation as outstanding teacher or control. Responses of the selected outstanding teachers will be compared with the responses of the controls.

Progress: In late spring and early summer 1996, all programs in family practice, internal medicine, and pediatrics in the Army, Navy, and Air Force were asked to give the survey to their teaching staff. In June, names of selected outstanding teachers were requested. Data continue to arrive and results are being entered. No results are yet available.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, ALLERGY/IMMUNOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/050 **Status:** Completed

Title: A Double-Blind, Randomied Study Comparing the Efficacy and Safety of Fexofenadine and Placebo in Black Patients with Seasonal Allergic Rhinitis

Start Date: 01/19/96 **Est. Completion Date:** Mar 97

Department: Medicine, Allergy/Immunology Service **Facility:** MAMC

Principal Investigator: MAJ Marcia L. Muggelberg, MC

Associate Investigators:
COL David G. Schall, MC
MAJ Ray E. Jensen, MC
MAJ Evan J. Matheson, MC

Key Words: Rhinitis:seasonal, fexofenadine, black patients

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To assess the efficacy of fexofenadine and placebo as measured by total symptom score (TSS) and to assess the safety profile of the drugs when used by black patients with seasonal allergic rhinitis. (2) To assess patient responses to quality of life, work, classroom, and activity impairment questions at designated visits during the study.

Technical Approach: This multicenter study is a two-arm, parallel, double-blind, randomized study with a placebo baseline period followed by a 2 week treatment period. Baseline demographic and clinical characteristics will be compared for patients randomized to each treatment group. Wilcoxon rank-sum tests will be used to compare continuous parameters and chi-square tests will be used to compare categorical parameters.

Progress: This study was closed to enrollment on 1 Jul 96. Eighteen patients were consented at MAMC and 13 patients were given the run-in drug. Six patients were randomized to the study drug. All patients have completed their follow-up visits.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/167	**Status:** Completed
Title: Heart Failure Management Clinic: A Cost and Benefits Outcomes Analysis Study		
Start Date: 09/15/95	**Est. Completion Date:** Jul 96	
Department: Medicine, Cardiology Svc	**Facility:** MAMC	
Principal Investigator: MAJ Maureen A. Arendt, MC		
Associate Investigators: Phyliss A. Hill, MN/MPH	LTC Catherine M. Schempp, MC	
Key Words: Heart Failure, clinic cost vs benefit		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The proposed research has been developed to evaluate the effect of an intensive, multidisciplinary outpatient approach to the management of the patient with severe heart failure.

Technical Approach: The Heart Failure Management Clinic (HFMC) is designed to improve the outpatient management of patients with symptomatic left ventricular (LV) systolic dysfunction not amenable to surgical correction. These patients have histories of recurrent hospital admissions. Participants will receive ongoing intensive outpatient medical and nursing management combined with structured health education by a multidisciplinary team. Research has shown that with intensive patient education, close outpatient follow-up, and careful manipulation of standard pharmaceutical therapy the number of hospitalizations or emergency room visits can be reduced as well as improvement in the patient's quality of life.

The goal of HFMC is to stabilize the patients' health status. Stability as defined by the number of hospitalizations or emergency room visits will be measured and compared to a comparable group of patients receiving the current standard of care. Functional status and quality of life measurements will be obtained throughout the program.

A total of 60 patients with the diagnosis of congestive heart failure will be enrolled. Patients will be identified by chart review. The first 30 patients that are identified will be placed in the treatment group, the next 30 patients in the control group. The treatment group will attend a series of four one-hour structured education classes on a weekly basis. All subjects will complete questionnaires addressing quality of life issues.

Progress: Principal Investigator failed to submit the requested Annual Report Progress by date notified. This protocol will be suspended until the Principal Investigator complies with reporting requirements as established by MAMC Regulation 40-117.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/144 **Status:** Completed

Title: BOAT (Balloon versus Optimal Atherectomy): A Randomized Multicenter Trial of Optimal Directional Coronary Atherectomy versus Balloon Angioplasty

Start Date: 06/16/95 **Est. Completion Date:** Jul 96

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: MAJ Patrick A. Cambier, MC

Associate Investigators: Doug Stewart, M.D.
COL Roger F. Chamusco, MC

Key Words: BOAT, Atherectomy, balloon vs optimal

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of this study is to demonstrate that it is possible to provide larger acute results safely with directional coronary atherectomy (acute residual stenosis ≤15% by QCA) compared to conventional balloon angioplasty, an that such improved results translate into reduced angiographic re-stenosis and diminished clinical need for revascularization.

Technical Approach: This is a multi-center, prospective, randomized trial which will enroll 1000 patients with *de novo* lesions in native coronary arteries, who meet entry criteria. Patients will consent to either balloon angioplasty for directional atherectomy who have an indication for coronary revasularization. Upon completion of the procedure, surveillance will be maintained along with a follow-up coronary angiogram 6 months post-procedure. Patients who warrant percutaneous revascularization of multiple lesions in one or more major epicardial coronary arteries (i.e., multi-vessel with multiple lesions) are ineligible. Comparative safety monitoring such as myocardial infarct, need for emergent coronary bypass surgery, and death will also be made. Secondary endpoints including economic impact, and a quality of life comparisons will also be explored. The study endpoints will be drawn from acute and late angiographic (6 month) and late clinical (1 year) outcomes. The primary re-stenosis endpoints, and all secondary endpoints will be analyzed on an intent-to-treat basis, i.e. each outcome will be attributed to the randomized arm regardless of the sequence of procedures that occur.

Progress: Three subjects were entered in this study at MAMC. All patients have completed follow-up. Directional atherectomy was found to be as safe and efficacious as balloon angioplasty. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/002 **Status:** Completed

Title: Efegatran Sulfate as an Adjunct to Streptokinase vs Heparin as an Adjunct to Tissue Plasminogen Activator in Patients with Acute Myocardial Infarction: A Dose-Finding Study

Start Date: 10/21/94 **Est. Completion Date:** Jul 95

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: MAJ Patrick A. Cambier, MC

Associate Investigators:

COL Roger F. Chamusco, MC
LTC Karl C. Stajduhar, MC
MAJ Maureen A. Arendt, MC
LTC John M. Bauman, MC
CPT Michael A. Rave, MC
W. Douglas Weaver, M.D.
LTC Alice M. Mascette, MC
MAJ Herman E. Collier III, MC
Steven A. Pace, MD
MAJ Christine Sapuntzoff, AN
MAJ Mark E. Peele, MC

Key Words: Myocardial Infarction, efegatran, heparin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: This study will demonstrate whether the direct acting thrombin inhibitor efegatran, when combined with intravenous streptokinase, can be demonstrated to produce equal or superior 90-minute coronary patency and lower reocclusion rates than heparin and recombinant tissue plasminogen activator (t-PA) alone in acute myocardial infarction.

Technical Approach: Patients will be randomized to receive either TPA and heparin or streptokinase and efegatran in an attempt to quickly dissolve the clot. TPA will be given IV over 90 minutes for a total dose not to exceed 100mg. The heparin will be given IV as a 5000 unit bolus followed by 1000 units/hour for 72 to 96 hours. Streptokinase (1.5 million units) will be given IV over 60 minutes. Efegatran will be given IV (0.3 mg/kg/hr) for 72 to 96 hours. To verify the vessel is opening, a heart catheterization will be performed.

Progress: Twenty-two patients were enrolled at MAMC. The total number enrolled from all sites was 247. The study was closed to patient enrollment because the sponsor believes that enough data have been collected for meaningful results. Several adverse events occurred which the principal investigator reported as not related to the study drug. All were appropriately reported to the IRB and to the study sponsor.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/037 **Status:** On-going

Title: Impact of Aorto-Coronary Bypass Graft Markers on Graft Patency: A Prospective Trial

Start Date: 12/15/95 **Est. Completion Date:** Jun 97

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: MAJ Michael D. Eisenhauer, MC

Associate Investigators:
MAJ Herman E. Collier III, MC
LTC Blaine R. Heric, MC
CPT Louis C. Coyle, MC
MAJ Patrick A. Cambier, MC
LTC Alice M. Mascette, MC
T. L. Eisenhauer
Bonnie Goodman

Key Words: Grafts:aorto-coronary, patency

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To address the impact of AOCGM placement on graft patency in responce to the widespread opinion that they may adversely affect graft patency.

Technical Approach: A power analysis has been performed to estimate required sample size. To detect a 10% adverse effect on graft patency, we estimate that 296 patients would be required, and to detect a 15% adverse effect, 132 patients would be required. Our sample size of 200 exceeds that needed to detect a 15% difference, and approaches that samlple size needed to detect a 10% difference. Options include (1) extending the protocol for 6 months (if necessary after statistical evaluation has been completed for the first 200 cases), and (2) inviting BAMC to become involved with the protocol. All data will be compiled on a Microsoft EXCEL or ACCESS spreadsheet, allowing import or export of data to available software-statistical programs, including MacIntosh programs currently in use by MAMC's Department of Clinical Investigations. A weighted student's t-test will be performed to compare patency rates obtained from the 6-month angiography. Patient characteristics between the "marked" and "unmarked" (i.e.: experimental and control) groups will be compared with Chi-square testing. If profile characteristics are low in frequency, Fisher's Exact-testing will be substituted. P-values of <0.05 will be required to define statistical significance.

Progress: Enrollment to date is 78 patients of an expected 300. 35 have completed the protocol's 6 month follow-up with CAB and have been evaluated for 6 month angiography. Expect enrollment rates to increase given San Diego Navy Hospital recent approval of protocol. BAMC has also been invited to join.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/003	**Status:** Completed
Title: Impact of Aortocoronary Graft Markers on Post-operative Angiography		
Start Date: 10/20/95	**Est. Completion Date:** Dec 95	
Department: Medicine, Cardiology Svc	**Facility:** MAMC	
Principal Investigator: MAJ Michael D. Eisenhauer, MC		
Associate Investigators:	MAJ Herman E. Collier III, MC	
Key Words: Angiography, aortocoronary graft markers		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether the use of radio-opaque Aortocoronary Graft Markers are associated with reduced radiation exposure, contrast exposure, and economic cost during coronary angiography in patients with prior Coronary Artery Bypass Grafting.

Technical Approach: A retrospective chart review of all coronary angiograms performed between January, 1989 and June, 1995 will be performed to identify cases in which previous Coronary Artery Bypass Grafting (CABG) has been performed. Approximately 5,500 charts will be reviewed to identify approximately 400-500 such cases. Matched cohorts of patients with and without Aortocoronary Graft Markers will be compared. Data collected will include: 1) length of fluoroscopy time required, 2) volume and type of contrast media used, 3) whether left ventriculogram was performed, 4) whether ascending aortogram was performed, 5) amount of additional contrast material required if ascending aortogram was performed, 6) number of saphenous vein grafts placed at time of surgery, 7) number of saphenous vein grafts remaining patent at time of angiography, 8) whether Internal Mammary Artery (RIMA or LIMA) graft was placed and imaged, and 9) number of diagnostic catheters required to image all native coronaries and surgical grafts. In addition, angiograms or chest x-rays of all subjects will be reviewed to determine if Aortocoronary Graft Markers which are radio-opaque were placed during previous CABG.

Progress: Evaluated 414 patient records. Determined significant benefit related to the presence of graft markers on subsequent angiograms - 30% to radiation exposure to pt, 25% to contrast exposure to pt, 18% to disposable equipment required (as a marker of precedural expense). This project led directly to the initiation of a prospective, multicenter, randomized trial.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/099	**Status:** Terminated
Title: The Effect of Coronary Angiography on Subsequent Left Ventriculography		
Start Date: 05/06/94	**Est. Completion Date:** Sep 94	
Department: Medicine, Cardiology Svc	**Facility:** MAMC	
Principal Investigator: LTC Alice M. Mascette, MC		
Associate Investigators:	COL Roger F. Chamusco, MC	
Key Words:		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the results of left ventriculography performed after coronary arteriography, compared to that performed before, in patients undergoing cardiac catheterization at Madigan.

Technical Approach: Patients scheduled to undergo elective cardiac catheterization will have an additional left ventriculogram performed at the time of heart catheterization. Left ventriculography performed before coronary arteriography will be compared with left ventriculography performed after coronary arteriography using the patient as his/her own control. Left ventriculograms will be analyzed by blinded observers for overall ejection fraction and regional wall motion analysis using existing computerized programs and compared using paired t-test

Progress: Four patients were enrolled at MAMC. Data for wall motion proved to be too difficult to collect with the present computer software.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/141 **Status:** On-going

Title: A Phase II, Randomized, Open-Label, Multicenter, International, Angiographic Trial of the Efficacy of TNK-tPA Compared with Accelerated Activase Alterplase rt-PA in Acute Myocardial Infarction.....

Start Date: 07/19/96 **Est. Completion Date:** Aug 97

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: LTC Alice M. Mascette, MC

Associate Investigators:
COL Roger F. Chamusco, MC
MAJ Maureen A. Arendt, MC
W. Douglas Weaver, M.D.
LTC Karl C. Stajduhar, MC
CPT J. Olson, MC

Key Words: Myocardial infarction, TNK-tPA, Activase Alterplase rt-PA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The study is designed to determine the efficacy of TNK-tPA, a new thrombolytic agent, in the treatment of acute myocardial infarction, as compared with rt-PA. The primary objective of this study is to determine the percentage of subjects with TIMI grade 3 flow (normal, brisk blood flow) in the infarct-related artery (IRA) by angiography at 90 minutes after the start of treatment with bolus TNK-tPA (30 or 50 mg) compared with accelerated dosing of rt-PA (Activase-® Alteplase). Secondary objectives of this study are: 1) To evaluate IRA patency (TIMI grade flow and TIMI frame count) at 60, 75 and 90 minutes; 2) to evaluate the safety and clinical efficacy of TNK-tPA; 3) to evaluate the effects of TNK-tPA on coagulation and fibrinogenolysis; and 4) to evaluate the formation of antibodies against TNK-tPA.

Technical Approach: This is a phase II, randomized, open-label, multicenter trial designed to compare the efficacy of a new thrombolytic agent, recombinant TNK-tPA (two doses) versus a standard front-loaded infusion of rt-PA in the treatment of acute myocardial infarction. The primary endpoint is normal (TIMI 3) blood flow in the infarct related artery as judged by 90 minute angiography. Secondary objectives include evaluation of safety and efficacy of TNK-tPA, its effect on coagulation and fibrinogenolysis and antibody formation, and artery patency at earlier angiograms if performed. Concomitant therapy with heparin and aspirin will be given as per usual practice after thrombolytic therapy, and other medical therapy is at the discretion of the treating physician. Further intervention or revascularization is at the discretion of the treating physician. Blood samples for coagulation profiles, antibodies, and serum markers for myocardial damage will be drawn over the first 48 hours. A blood sample for antibody formation will be drawn on outpatient follow-up at 30 days; subjects who test positive for antibodies against TNK-tPA at 30 days will have an antibody sample repeated at 90 days.

Progress: This is a new study which has not been started. It is awaiting MEDCOM approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/149 **Status:** On-going

Title: ST Segment Depression in Localizing Regional Myocardial Ischemia in Unstable Angina

Start Date: 08/16/96 **Est. Completion Date:** Jan 97

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: CPT John A. McHenry, MC

Associate Investigators:
LTC Vernon C. Parmley, MC
Christopher Wolfe, M.D.
LTC Karl C. Stajduhar, MC
Nora Goldschlager, M.D.

Key Words: ST segment, depression, myocardial ischemia, angina

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if regional myocardial ischemia in unstable angina can be specifically localized based on the representative ECG leads demonstrating ST-segment depression.

Technical Approach: The major focus of this study is to determine whether labile ST-T wave depression in the setting of unstable angina can be used with any accuracy in localizing ischemic regions of myocardium threatened by impending infarction. Such repolarization abnormalities are known to not localize with exercise induced ischemia, but this has yet to be determined with certainty in the setting of unstable angina.

To evaluate this we anticipate enrolling a total of 200 patients in a 6 month period among three trial centers. Patients will be treated according to standard of care practice in the treatment of unstable angina. Patients considered to be high risk will undergo cardiac catherization in the usual fashion.

ECG's showing labile ST segment depression during symptoms will be interpreted according to the myocardial segments they represent. Patients who additionally undergo coronary angiography will be entered into the study in the order of presentation with determinations then being made for coronary anatomy and the culprit vessel.

Interpretations of ischemic regions of myocardium, as determined by coronary anatomy and/or radionuclide scintigraphy, will be compared with ischemic regions determined by ECG criteria. Statistical determinations will then be made of the population makeup, coronary anatomy and the relation (if any) between the myocardial segments represented by the ECG's and the actual vessel involved.

Progress: Seventy-three patients have been enrolled. Preliminary data from 55 subjects have been accepted for presentation. Of these 55 patients, the mean age was 62.5 years, with 76% male and 24% female. ST Depression (STD): 41% of the patients had anterior ST depression, 48% had lateral changes and 11% had inferior changes. Associations: 77% with anterior STD demonstrated culprit LAC lesions yielding a positive predictive value of 77% ($p<0.0001$). Positive predictive value for lateral and inferior changes were 29% (p=NS) for circumflex disease and 67% ($p<0.0004$) for PDA disease, respectively. Negative Predictive Values (NPV): The absence of anterior STD gave a 90% NPV for Lad culprit disease ($p<0.0001$), the absence of inferior STD gave a 87% NPV for PDA disease ($p<0.0004$) and the absence of lateral STD did not have a statistically significant NPV for circumflex disease.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/180 **Status:** Terminated

Title: Stress Echocardiography in the Evaluation of Asymptomatic Aircrew Members for Significant Coronary Artery Disease

Start Date: 08/18/95 **Est. Completion Date:** Jun 96

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: MAJ James P. Olson, MC

Associate Investigators: MAJ Edward E. Collier III, MC
MAJ Maureen A. Arendt, MC

Key Words: Coronary artery disease, stress echocardiography

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the sensitivity and specificity of exercise echocardiography and exercise ^{201}TI scintigraphy in the evaluation of asymptomatic aircrew members who have been referred to the Cardiology Service for suspected coronary artery disease.

Technical Approach: Our study population will consist of 20-40 active duty US Army aviators. Subjects will be those aviators who have been referred to the Cardiology Service for cardiac catheterization to determine the presence or absence of significant coronary artery disease. Each subject will undergo an exercise echocardiogram and exercise ^{201}TI scintigraphy prior to diagnostic angiography. We will also determine the presence or absence of fluoroscopic or cineangiographic calcification in the coronary artery distribution. Images will be interpreted by two experience cardiologists who are blinded to thallium, echocardiographic and clinical data. For this study, significant coronary artery disease will be defined as one or more stenosis of equal to or greater than 50% in any major coronary artery, including large diagonal and marginal branches. The study will also be defined as abnormal if no lesion is equal to or greater than 50% but the aggregate of lesions identified is equal to or greater than 120%. Data will be collected from each case. Numerical variables will be compared using t-test and yes/no or normal/abnormal variables will be compared using the chi-square test. We will then determine the sensitivity, specificity and predictive value to each diagnostic modality.

Progress: This protocol was terminated due to the inability to recruit patients when the patients began to be systematically referred to WRAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/043 **Status:** Terminated

Title: Effects of Chronic Smoking and Transdermal Nicotine Replacement Therapy on Hemostatic Function in Humans

Start Date: 03/17/95 **Est. Completion Date:** Jun 95

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: CPT Thomas M. Roe, MC

Associate Investigators: CPT Scott A. Sample, MC

Key Words: Smoking, nicotine replacement therapy, hemostasis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the effects of smoking and transdermal nicotine therapy on the hemostatic function of healthy men and women.

Technical Approach: Healthy male and female volunteers undergoing routine periodic physical examination or participating in smoking cessation programs using nicotine replacement therapy will donate blood samples. The blood will be prepared for assay measurement of tissue plasminogen activators, tissue plasminogen activator inhibitor 1, fibrinopeptide A, platelet factor IV, beta thromboglobulin and thrombin-antithrombin III complex. 120 subjects will be included and will be divided into control, smoking and nicotine replacement therapy groups. Assays will be performed in duplicate for each specimen tested. The data will then undergo standard statistical analysis to determine statistical significance.

Progress: This protocol was originally conducted by CPT Scott Sample and then assigned to CPT Thomas Roe, when CPT Sample PCS'd. Due to the work load and his own imminent departure, CPT Roe was unable to enter more patients in the study in FY 96. The protocol was discontinued when CPT Roe left MAMC. Previously, 68 patients had been enrolled with preliminary data analysis showing that smoking activates the coagulation system more than nicotine alone, gender differences in hemostasis are diminished by smoking, and smokeless tobacco causes platelet activation and not fibrin activation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/069 **Status:** On-going

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

Start Date: 02/16/96 **Est. Completion Date:** Mar 01

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: LTC Karl C. Stajduhar, MC

Associate Investigators:
COL Roger F. Chamusco, MC
MAJ Herman E. Collier III, MC
MAJ Michael D. Eisenhauer, MC
MAJ James P. Olson, MC
MAJ Patrick A. Cambier, MC
LTC Alice M. Mascette, MC
MAJ Maureen A. Arendt, MC
CPT John A. McHenry, MC
CPT Thomas M. Roe, MC

Key Words: Atrial fibrillation, drug therapy, heart rate control, heart rhythm control

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: Three patients have been enrolled at MAMC. Subject recruitment is going well nationwide.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/068 **Status:** On-going

Title: A Double-Blind, Placebo Controlled, Randomized, Dose Response Study of Oral dl-Sotalol Hydrochloride for the Maintenance of Sinus Rhythm in Subjects with Prior Symptomatic Atrial Fibrillation or ....

Start Date: 02/17/95 **Est. Completion Date:** Apr 97

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: LTC Karl C. Stajduhar, MC

Associate Investigators:

COL Roger F. Chamusco, MC
MAJ Herman E. Collier III, MC
CPT Michael A. Rave, MC
CPT Scott A. Sample, MC
CPT Thomas M. Roe, MC
MAJ Patrick A. Cambier, MC
LTC Alice M. Mascette, MC
MAJ Maureen A. Arendt, MC
MAJ Mark E. Peele, MC
MAJ James P. Olson, MC
MAJ Michael D. Eisenhauer, MC

Key Words: Sinus rhythm, atrial fibrillation, dl-Sotalol Hydrochloride

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm.

Technical Approach: Multicenter, double-blind, placebo controlled, randomized, dose response study to evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm. Six subjects will be randomly assigned to receive one of the three fixed dose regimens of dl-sotalol Hcl (80 mg, 120 mg or 160 mg) or placebo administered every 12 hours orally. The study will consist of double-blind and open-label phases. Treatment will last for 12 months. In the analysis of time to AFIB/AFL, the log-rank test will be used. The proportions of subjects free of AFIB/AFL for two treatments groups will be compared at 6 months and 12 months using the product-limit estimates. The corresponding variances will be compted using Greenwood's formula. This method adjusts for dropouts or censored data.

Progress: Eight patients were enrolled in FY 96 for a total of 15 subjects. Two patients are currently in follow-up.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/169 **Status:** On-going

Title: A Multicenter, Randomized, Parallel, Double-Blind Study to Investigate the Safety and Clinical Efficacy of MK-383 Alone and MK-383 in Combination with Heparin vs. Heparin Alone in Patients with ....

Start Date: 07/21/95 **Est. Completion Date:** Dec 95

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: LTC Karl C. Stajduhar, MC

Associate Investigators:
LTC Alice M. Mascette, MC
MAJ Herman E. Collier III, MC
CPT J. Olson, MC
MAJ Michael D. Eisenhauer, MC
COL Roger F. Chamusco, MC
MAJ Patrick A. Cambier, MC
MAJ Maureen A. Arendt, MC
CPT Thomas M. Roe, MC
CPT John A. McHenry, MC

Key Words: Myocardial infarction, MK-383, Heparin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To examine the efficacy of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in reducing the combined occurrence of the following clinical events: refractory ischemic conditions (refractory ischemia; hemodynamic instability; or severe, prolonged or repetitive anginal pain at rest requiring urgent invasive intervention within 12 hours of symptom onset), new myocardial infarction or death (through 7 days after initiation of study drugs) in high-risk patients with unstable angina/non-Q-wave myocardial infarction (UAP/NQWMI). the incidence of these endpoints will be examined at 48 hours, through 7 days after initiation of study drug, and at 30 days. 2) To examine the safety and tolerability of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in high-risk patients with UAP/NQWMI receiving aspirin and antianginal medications, in the absence of cardiac catherization. 3) to examine the safety and tolerability of MK-383 in combination with heparin compared with heparin alone in an invasive setting(cardiac catherization). 4) To examine the effect of MK-383 in combination with heparin in reducing the maximal extent of angiographically-apparent thrombus compared to heparin alone.

Technical Approach: this multicenter, randomized, double-blind study will examine the safety and clinical efficacy of Mk-383 alone and MK-383 in combination with heparin versus heparin alone, in patients with high-risk unstable angina/non-Q-wave myocardial infarction. Patients meeting entry criteria will be randomized to receive either MK-383 alone (group A), heparin alone (group B), or MK-383 and heparin (group C). Patients will be stratified depending on whether or not they are on a continuous intravenous infusion of heparin at the time of randomization. All patients will receive conventional antianginal therapy consisting for nitrates, betablockers or calcium channel blockers, as deemed necessary by the responsible physician. During the initial 48-hour period of study drug infusion, patients will not undergo cardiac catherization unless clinically indicated by development of refractory ischemia or new myocardial infarction. After 48 hours, all patients are expected to undergo coronary angiography (unless contraindicated) because of their high-risk clinical condition. Study drug may continue, be discontinued and resumed, or discontinued entirely depending upon the findings at time of catherization. Study drugs may be infused for up to 96 hours (in patients who undergo PTCA/atherectomy no later than Hour 96 while on study drug, the study drug may be administered for up to a total of 108 hours after initiation). All patients will remain under close supervision until 24 hours after discontinuation of the study drug (or until clinically stable). All randomized patients will be followed for 30 days after study drug initiation and also at 6 months. Data to include vital signs, periodic laboratory evaluation, ECG and physical examination findings, adverse clinical events, refractory ischemia, new myocardial infarction, and death will be recorded on all patients. A composite goal of 1260 patients has been established. During the study period, Madigan seeks to enroll between 10 and 25 patients.

Progress: This study is closed to patient entry. Four subjects were entered in this study. Two have completed the study and two will complete the study in October. No adverse events have occurred.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/082 **Status:** Suspended

Title: Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Transcatheter Coronary Revascularization Procedures

Start Date: 03/15/96 **Est. Completion Date:** Jun 96

Department: Medicine, Cardiology Svc **Facility:** MAMC

Principal Investigator: LTC Karl C. Stajduhar, MC

Associate Investigators: CPT Thomas M. Roe, MC
MAJ Patrick A. Cambier, MC

Key Words: Coronary revascularization, bradycardia, hypotension

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The intent of this study is to determine whether the bradycardia and hypotensive response that is commonly encountered during transcatheter coronary revascularization procedures can be prevented by intravenous aminophylline administration. A secondary objective is to determine is aminophylline's attenuation of this adverse hemodynamic response dependent on the type of intervention performed (i.e. is the hemodynamic response the same for percutaneous transcatheter angioplasty (PTCA), directional coronary atherectomy (DCA), and rotational coronary atherectomy (RTCA)).

Technical Approach: This study will enroll selected patients undergoing one of the three types of transcatheter coronary revascularization (PTCA, RTCA, DCA). We intend to enroll 50-150 patients. Patients will have orthostatic vital signs recorded to establish that they are euvolemic prior to receiving standard pre-procedure medications. Standard cardiac catheterization procedures will be followed. After intraarterial access is obtained, baseline hemodynamic data will be recorded. Prior to the actual revascularization procedure the patient will be randomized in a double blind fashion to receive either aminophylline 5 mg/kg IV over 5-10 minutes or the equivalent volume of saline placebo. A 15 second strip of the ECG and blood pressure will be recorded just prior to initiation of the revascularization procedure and for the duration of procedure. The pre-procedure heart rate and blood pressure, and minimum heart rate and blood pressure during the procedure, will be determined. A comparison will be made between the absolute and percentage change in heart rate and blood pressure during the procedure in the treated vs. placebo group. Also reported will be the need for additional therapies to treat hypotension and bradycardia (e.g. atropine, fluid boluses, or the need for temporary pacing) in each group. The data will also be analyzed to determine if there is a difference in the hemodynamic effects by type of revascularization procedure performed in the placebo group.

Progress: When the PI was reassigned, the investigator was changed from CPT Thomas Roe to Dr. Stajduhar. It was put in a suspended status at that time pending the outcome of a similar protocol (MAMC #96073). No patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/073	**Status:** On-going
Title: Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Intracoronary Administration of High Osmolar Contrast Agents		
Start Date: 02/16/96	**Est. Completion Date:** Jun 96	
Department: Medicine, Cardiology Svc	**Facility:** MAMC	
Principal Investigator: LTC Karl C. Stajduhar, MC		
Associate Investigators: MAJ Patrick A. Cambier, MC	CPT Thomas M. Roe, MC Jacquelline Gillet, RN	
Key Words: Contrast agent, aminophylline, bradycardia, hypotension		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: The intent of this study is to determine whether the bradycardia and hypotensive response that is commonly encountered during intracoronary injection of high osmolar contrast agents can be prevented by intravenous aminophylline administration. A secondary objective is to determine whether intracoronary injection of high osmolar contrast agents ipsilateral to the origin of the sinus nodal (SA) artery leads to an increased incidence of bradycardia and hypotension.

Technical Approach: We intend to enroll 50-200 consecutive patients undergoing an elective cardiac catheterization. Patients will be consented at the time of their standard pre-catheterization appointment by the cardiac catheterization lab nurse. Patients will have orthostatic vital signs recorded to establish that they are euvolemic prior to receiving standard pre-catheterization medications. Standard cardiac catheterization procedures will be followed. After intraarterial access is obtained, baseline hemodynamic data will be recorded. Prior to the initial injection of contrast media, the patient will be randomized in a double blind fashion to receive either aminophylline 5 mg/kg IV over 5-10 minutes or the equivalent volume of saline placebo. A 15 second strip of the ECG and blood pressure will be recorded just prior to injection of contrast in both the left and right coronary arterial systems, and for one minute post injection. The pre-contrast heart rate and blood pressure, and minimum heart rate and blood pressure during contrast injection, will be determined. A comparison will be made between the absolute and percentage change in heart rate and blood pressure during contrast injection in the treated vs. placebo group. Also reported will be the need for additional therapies to treat hypotension and bradycardia (e.g. atropine, fluid boluses, need to change contrast agents, or the need for temporary pacing) in each group. The angiograms will be studied to determine the origin of the sinoatrial (SA) artery (left or right coronary artery). The data will be analyzed to determine whether intracoronary injection ipsilateral to the origin of the SA artery will manifest greater incidence of bradycardia and hypotension.

Progress: Twenty-nine patients have been enrolled to date, with data analysis ongoing. Study code remains sealed under direction of the Pharmacy. Progress is slow but steady in recruiting subjects.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, CRITICAL CARE SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/005	**Status:** Completed

Title: Effect of Empiric Low-Dose Amphotericin B or Fluconazole on the Development of disseminated Candidiasis in an Intensive Care Unit

Start Date: 10/01/93	**Est. Completion Date:** Jul 95
Department: Medicine, Critical Care Svc	**Facility:** MAMC

Principal Investigator: CPT Joseph S. Pina, MC

Associate Investigators: CPT Gregory S. Witkop, MC
MAJ Lewis L. Low, MC

Key Words: Candidiasis, amphotericin B, Fluconazole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objective: To determine the efficacy of low-dose amphotericin B (AmB) or Fluconazole (Flu) in preventing the development of disseminated candidiasis.

Technical Approach: There will be two study groups, one receiving low-dose AmB 0.3 mg/kg/day, and the other receiving Flu 200 mg IV q24h. Those patients who do not receive either regimen will serve as the control group and will receive the standard of care given in the "community", i.e. treat local Candida infections with local treatment until dissemination occurs, whereby full dose AmB is employed. Hematologic, chemistry, and microbiologic monitoring will be performed. The two treatment groups will be compared to the control group, utilizing the chi-square test. There will be no comparison between the two treatment groups themselves. Survival analysis will be used to compare the time until appearance of disseminated candidiasis between treatment groups.

Progress: Fifteen additional subjects were enrolled in FY 96 for a total of 27 participants. The PI is PCSing; therefore, the protocol has been discontinued. Data have been sent to the University of Florida to be included with data from the study done at that site.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/023 **Status:** Completed

Title: Investigations into the Mechanisms of Phospholipid Synthesis in Human Spermatozoa

Start Date: 11/21/86 **Est. Completion Date:** Dec 87

Department: Med, Endocrinology Svc **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators:
CPT Kevin J. Carlin, MC
MAJ Charles J. Hannan, MC
Stephen R. Plymate, M.D.

Key Words: spermatozoa,phospholipid synthesis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1600.00	**Periodic Review:** 10/21/88

Study Objective: To determine if sperm can replenish phospholipids after they have been partially hydrolyzed to the lyso-forms by the action of phospholipases A2 or A1 and to attempt to identify and characterize sperm acyl transferase.

Technical Approach: Acyl transferase, acyl CoA:1-acyl-sn-glycero-3-phosphocholine O-acyl transferase will be screened by coincubating human sperm with labeled fatty acids, CoASH, ATP, Mg^{2+}, and Tris. The reaction will be terminated by delipidating the sperm with $CHCl_3$: MeOH, and the organic phase will be chromatographed on silica gel TLC plates. These plates will be developed and spots will be scraped and counted. If the labeled fatty acid is found to be contained within a phospholipid region, cofunctioning of ligase and acyl transferase will be assumed to occur. Studies to characterize acyl transferase activity will be performed using an assay based on the liberation of CoASH which reacts with DTNB, resulting in a change in absorption at 414 nm. Either palmitoyl or docosahexaenoyl CoA will be used as the acyl donor to lyso-phosphatidyl choline. The conversion of lyso-phosphatidyl choline to phosphatidyl choline will be chromatographed. This assay will be optimized for pH, ionic strength, substrate levels and amount of enzyme before kinetic constants are determined. For carnitine-dependent transacylation, D, L-palmitoyl carnitine and lyso-phosphatidyl choline will be coincubated with washed sperm, delipidated and the products chromatographed as above. If the amount of lyso-phosphatidyl choline declines while phosphatidyl choline increases, a carnitine dependent mechanism will be presumed to exist. Alternatively, carnitine dependency could be screened by using 3H-palmitoyl carnitine to look for labeled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabeled 22:6 with 3H-16:0 and following the appearance of 16:0 in phosphatidyl choline. Conversely, the effect of 16:0 on 14C-22:6 will be studied.

Progress: No further bench work was completed on this protocol this FY. All data have been compiled and a manuscript has been submitted.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/093 **Status:** Terminated

Title: Hyperactivation in Cryopreserved Spermatozoa: Effects of Progesterone and Various Membrane-Active Agents

Start Date: 08/07/92 **Est. Completion Date:**

Department: Med, Endocrinology Svc **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators:
CPT M. Ahmed, MC
CPT Wilma I. Larsen, MC
CPT David H. Harrison, MC
COL Robert E. Jones, MC
CPT J. Olson, MC
CPT Colleen C. Foos, MC
MAJ Alicia Y. Armstrong, MC

Key Words: spermatozoa, cyropresavation, hyperactivation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the optimal incubation buffer (human follicular fluid versus a synthetic, defined media, both supplemented with varying concentrations of progesterone) to induce hyperactivated motility in cryopreserved human sperm. Once the optimal hyperactivation conditions are determined, the effects of a variety of different classes of agents (calcium channel blockers, free fatty acids, platelet activating factor, and the synthetic phospholipase A2 inhibitors, U73,343 and U73,122,) on hyperactivated motility and motility during capacitation will be assessed.

Technical Approach: Cryopreserved sperm will be counted via computer assisted semen analysis (CASA), washed, reassessed, and incubated in a capacitating buffer containing Ham's F10 with 3.5% bovine serum albumin. After capacitation, the sperm will be incubated in similar media supplemented with diluted (1/20) human follicular fluid (HFF) (the hyperactivation step). A CASA evaluation of hyperactivation will be performed. Swim-up capacitation and hyperactivation will be performed for all test substances. The HFF will be stripped of steroids and varying concentrations of progesterone will be added to examine the role of progesterone in inducing hyperactivation. Following the completion of the progesterone portion of the study, the effects of various compounds (calcium channel blockers, phospholipase A2 inhibitors, free fatty acids, and platelet activating factor) on hyperactivated motility will be evaluated. Depending on the type of data analyzed, either Chi-square or repeated measures ANOVA will be used for statistical analysis.

Progress: This protocol was terminated due to the retirement of the PI. No work was done on this protocol this FY.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 90/038	**Status:** Completed
Title: Detailed Studies Into Membrane Lipid Synthesis in Human Sperm		
Start Date: 02/16/90	**Est. Completion Date:** Feb 99	
Department: Med, Endocrinology Svc	**Facility:** MAMC	
Principal Investigator: COL Robert E. Jones, MC		
Associate Investigators: CPT Brenda K. Bell, MC	Stephen R. Plymate, M.D.	
Key Words: lipid synthesis,human sperm		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $3494.00	**Periodic Review:** 04/05/91

Study Objective: To elucidate the biochemical pathways for membrane lipid synthesis (excluding cholesterol) present in freshly ejaculated human spermatozoa from donors of proven fertility.

Technical Approach: Sperm will be washed and the sample diluted to achieve a concentration of $2x10^8$ sperm/ml. The incubation buffer, optimized for fatty acid activation, will consist of 380 mM TRIS [pH 8.4], 20 mM ATP, 20 mM $MgCl_2$, 0.1 mM coenzyme A (CoASH), 5 mM dithiothreitol, and 10-50 m M fatty acid, either 3H-9,10-16:0, 14C-1-16 0, or 14C-1-22 6. The reaction will be initiated by the addition of 107 sperm. Blank incubations will be performed in the absence of CoASH or the specific starting substrate to investigate the metabolic mechanisms of lipid turnover. Methylation of phosphatidylethanolamine (PE) will be measured by incubating 3H-methyl-S-adenosylmethionine (SAM) with diacyl PE or a 14C labeled fatty acid, 3H-SAM and 1-acyl-2-lyso PE. Another pathway for plasmalogen or ether lipid synthesis in nongerminal tissues will be assessed by incubating sperm with 14C-22:6, 1-palmitoyl32-lyso PI (phosphatidylinositol) or -PC (phosphatidylcholine) and 3H-1-hexadecanol in the aforementioned buffer. Alternatively, 3H-hexadecanol, 14C-22:6, unlabeled 16:0 will be coincubated with dihydroxyacetone phosphate (DHAP). The reaction will be terminated after 1 hour and lipids will be extracted and dried. Incorporation of labeled fatty acids into sphingomyelin (SM) will be determined by detection of the fatty acyl radiolabel in the SM region of the thin layer chromatography (TLC) plates. After resolubilization in chloroform and methanol, lipids will be separated on LK5 TLC plates. Standards will be run on each plate and spots corresponding to standards will be scraped and counted. Plasmalogen formation will be assessed by performing mild acid hydrolysis on the extracted phospholipids prior to TLC or before rechromatography and determining DPM's in the fatty aldehyde and lysophospholipid regions. The presence of ether lipids will be determined by their resistance to alkaline and enzymatic hydrolysis prior to TLC. Mono and diacyl phospholipid synthesis will be assessed by free fatty acid release from SM and by using phospholipases A2 (PLA2) and B (PLB).

Progress: No further lab work was done on this protocol this FY. Previous data were analyzed and a manuscript prepared.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/083 **Status:** On-going

Title: The Polar T3 Syndrome: Metabolic and Cognitive Manifestations, Their Hormonal Regulation and Impact Upon Performance

Start Date: 03/15/96 **Est. Completion Date:** Oct 97

Department: Med, Endocrinology Svc **Facility:** MAMC

Principal Investigator: LTC Homer J. Lemar Jr., MC

Associate Investigators: COL H. Lester Reed, MC
CPT Nhan V. Do, MC

Key Words: Polar T3 Syndrome, hypothroxinemia, thyroxine, memory, mood, muscle efficiency, energy utiliation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This is a subportion of the blanket protocol "The Polar T_3 Syndrome: Metabolic and Cognitive Manifestations, Their Hormonal Regulation and Impact Upon Performance". In this subportion we will: (1) Evaluate the response of central nervous system hypothyroxinemia in the development of the Polar Triiodothyronine (T_3) Syndrome to thyroxine (T_4) administration using the cognitive parameters of memory and mood; (2) Define the role of decreasing skeletal muscle efficiency in the increased energy requirements observed in the Polar T_3 Syndrome; and (3) Evaluate the effect of thyroxine supplementation on muscle efficiency and energy utilization during development of the Polar T_3 Syndrome.

Technical Approach: Sixteen military and civilian health care beneficiaries including men and women who are between 18 and 55 years old and are members of the winter-over crew in McMurdo, Antarctica will be recruited for the study. Subjects will perform monthly exercise, mood, and cognitive testing beginning one month prior to departure and continuing through their entire 11 month stay in McMurdo. The parameters that will be examined include changes in muscle oxygen utilization, changes in thyroid functions, and changes in cognitive, memory, and mood during the development of the Polar T_3 Syndrome. One of the characteristics of the Polar T_3 is a low T_4 state in the CNS that may be responsible for the characteristic decline in mood and memory during winter seasons in circumpolar regions. It is proposed that T_4 supplementation can correct the low T_4 state in the CNS and thus attenuate the syndrome. All subjects will be placed on placebo for the first 6 months of the study, then one-half of the subjects will be switched from placebo to levothyroxine 50 mg per day in a double blind fashion. Thyroid functions will be monitored monthly throughout the study. Subjects will serve as their own controls for analysis of mood and cognitive data. Comparisons will also be made between levothyroxine and placebo groups for the exercise, mood, and cognitive testings.

Progress: Fourteen subjects have been entered. Baseline history, physicals, labs, and exercise testing have been completed and all subjects have been started on placebo.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/146	**Status:** On-going

Title: Triiodothyrinine Serum Kinetics: A New Nonisotopic Method for Field and Clinical Use

Start Date: 06/21/96	**Est. Completion Date:** Nov 97
Department: Med, Endocrinology Svc	**Facility:** MAMC

Principal Investigator: LTC Homer J. Lemar Jr., MC

Associate Investigators:	COL H. Lester Reed, MC
CPT Nhan V. Do, MC	LTC Marc G. Cote, MC

Key Words: Triiodothyronine, kinetics, T3(non-radioactive)

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This is a subportion of the umbrella protocol "The Polar T3 Syndrome: Metabolic and Cognitive Manifestations, their Hormonal Regulation and Impact Upon Performance" National Science Foundation grant #94-18466, Opp #89-22832. In this subportion we will determine if triiodothyronine (T3) kinetics studies using intravenous non-radioactively labeled T3 compare well with oral T3 and the gold standard of [125I]T3 kinetics. If this intravenous (iv) methodology closely approximates he T3 kinetic parameters obtained with isotope studies, it will provide a safe and easily usable technique to help define, manage, and better characterize the polar T3 syndrome during "field" studies carried out in the isolated regions of the Antarctic, subarctic and arctic.

Technical Approach: T3 kinetic parameter calculations will be performed using the iv administration of 30 mg of T3 to eight healthy male or female volunteer subjects. This technique will be validated at Madigan Army Medical Center. Both compartmental and noncompartmental analysis of the iv nonlabeled T3 disappearance will be carried out and compared with tracer 125I[T3] techniques, as well as oral nonlabeled T3 (50 mcg) administration in the same eight subjects as done in previous studies. The iv tracer studies will use 40-100 microcuries of 125I[T3], after thyroidal uptake blockade with potassium iodide using methodology we have previously reported for humans and swine. The compartmental and noncompartmental analysis of these kinetic parameters will be performed with SAAM methodology and three compartment mammillary model used as we have recently reported. The sampling times, isotope handling, hormone RIA assays, patient preparation and statistical analysis will be similar to our previous studies.

In brief, the isotope studies will be conducted for 96 hours, the IV non-labeled T3 studies for 72 h, and the oral T3 studies for 24 h with interval sampling. An exception to our earlier studies will be the sampling following nonlabeled iv T3 where blood will be obtained at 5 minutes, 15 minutes, 30 minutes and then each 30 minutes up to 10 hours as with the oral T3 studies. This study introduces the novel technique of IV T3 kinetic analysis using no radioactivity exposure. A paired comparison with other previously reported techniques by our group will provide the necessary contrast.

Progress: This a relatively new protocol with patient enrollment expected to commence in November 1996.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, GASTROENTEROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/026 **Status:** On-going

Title: A Double-Blind Trial of Omeprazole versus Placebo for Prophylaxis of Sclerotherapy-Associated Esophageal Ulcer

Start Date: 11/17/95 **Est. Completion Date:**

Department: Med, Gastroenterology Svc **Facility:** MAMC

Principal Investigator: MAJ John G. Carrougher, MC

Associate Investigators:
Michael B. Kimmey, M.D.
Margaret Shuhart, M.D.
Kris V. Kowdley, M.D.
John Sekijima, M.D.
Lonny Hecker, M.D.

Key Words: Ulcer:sclerotherapy, Omeprazole, Placebo

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether treatment with omeprazole (Prilosec) results in prevention or more rapid healing of esophageal ulcers associated with sclerotherapy.

Technical Approach: Patients undergoing sclerotherapy for bleeding esophageal varices will be invited to participate. Participants will be randomized within 24 hours after the initial sclerotherapy to receive either omeprazole at a dose of 40 mg/day, or an identical placebo. The treatment period will be six weeks in duration, during which time the subjects will be monitored for the development of esophageal ulcers as seen during routine upper gastrointestinal endoscopy done for the purpose of repeat sclerotherapy. All other treatment will be continued in the normal manner. During this study, the patients will be given a brief questionnaire prior to each endoscopy to determine the presence of any symptoms associated with sclerotherapy, such as dysphagia or heartburn. Esophageal variceal sclerotherapy will be performed in the routine manner. All other testing and treatment will be performed as needed for the clinical care of the patients. Sample will be chosen to achieve an a of 0.05, and a b of 0.1. For a difference in ulcer rate of 40% in the prophylaxis group, based on an ulcer rate of 20% in the omeprazole group and 60 in the placebo group, this would require 44 patients. Student's t-test will be used for calculating means of continuous variables, and the chi-square test or z-statistic will be used to calculate differences in complication rates among various Child's-Pugh class patients. Survival data will be analyzed using Kaplan-Meier statistics.

Progress: One patient has been enrolled in this study with no complications.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/182 **Status:** Completed

Title: Evaluation of the Performance of Fecal Occult Blood Tests in High Risk Patients Undergoing Colonoscopy

Start Date: 08/18/95 **Est. Completion Date:**

Department: Med, Gastroenterology Svc **Facility:** MAMC

Principal Investigator: LTC Robert H. Sudduth, MC

Associate Investigators:
Daniel C. Sadowski, M.D.
Lucio Bertario, M.D.
Michael Epstein, M.D.
Paul Rozen, M.D.
Reinhard Gnauck, M.D.
Don C. Rockey, M.D.
Gary Zuckerman, M.D.

Key Words: Occult blood, FlexSure, HemeSelect, Hemoccult, Hemoccult SENSA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of this study is to compare the sensitivity of the different fecal occult blood tests (FOBTs) for the detection of colorectal neoplasia in a high risk population. The data collected will support regulatory submissions for the FlexSure^{R} OBT (FS) in the USA.

Technical Approach: This is a multi-center study involving private and institutional gastroenterology practices. 250 colonoscopy patients who meet the inclusion criteria will be recruited to participate. Using established mechanisms that may be unique for each study center, patients will be asked to collect samples from three consecutive bowel movements while observing certain dietary and drug restrictions (no red meat, high peroxidase-containing vegetables, vitamin C, aspirin and non-steroidal anti-inflammatory drugs). Generally, stool collections will be done prior to colonoscopy, except as noted in the inclusion criteria. After consenting, patients will be provided a FOBT kit. The kit will have all the necessary materials and instructions for collecting their stool samples. The completed kits are then returned to a designated site or laboratory at the study center. All FOBTs will be developed at the study center except for HemeSelect^{R}. Results of FOBTs and clinical findings will be reviewed and correlated. The test positivity rate on patients confirmed to have colorectal neoplasia (colorectal cancer and adenomas $\geq$ 1cm) will be the measurement of the test sensitivity. The negative predictive values for each of the tests will also be compared.

Progress: Fifty patients were entered in this multicenter study. Data have been sent to California where data analysis and manuscript preparation are in progress.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/164	**Status:** On-going
Title: Epidemiology of Gallbladder Sludge and Stones in Pregnancy		
Start Date: 09/20/96	**Est. Completion Date:** Sep 02	
Department: Med, Gastroenterology Svc	**Facility:** MAMC	
Principal Investigator: LTC Amy M. Tsuchida, MC		

Associate Investigators:

MAJ Kazunori Yamamoto, MC
LTC Byron C. Calhoun, MC
Beth W. Alderman, M.D., MPH
Edward J. Boyko, M.D., Ph.D.
Katherine H. Moore, Ph.D.
Sum P. Lee, M.D., Ph.D
LTC Roderick T. Hume Jr., MC
Scott J. Schulte, M.D.
Gerard Schallenberg, M.D.
Gail Jarvik, M.D.

Key Words: Gallbladder, sludge, pregnancy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: No patients have been enrolled in this new study, which is awaiting final approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/067 **Status:** Completed

Title: A Study to Evaluate the Effects of Therapy with Lansoprazole and Clarithromycin and/or Amoxicillin on the Eradication of Helicobacter pylori and the Recurrence of Duodenal Ulcer

Start Date: 02/17/95 **Est. Completion Date:** Mar 96

Department: Med, Gastroenterology Svc **Facility:** MAMC

Principal Investigator: LTC Amy M. Tsuchida, MC

Associate Investigators:
MAJ Kazunori Yamamoto, MC
LTC Robert H. Sudduth, MC
MAJ John G. Carrougher, MC

Key Words: Ulcer:duodenal, Helicobactger pylori, Lansoprazole, Clarithromycin, Amoxicillin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the safety and efficacy of monotherapy with lansoprazole, dual therapy with lansoprazole and amoxicillin or lansoprazole and clarithromycin, and triple therapy with lansoprazole, clarithromycin, and amoxicillin for the eradication of *Helicobactor pylori* from the gastric mucosa of patients with active duodenal ulcer or a history of duodenal ulcer.

Technical Approach: In this Phase III, randomized, double-blind, parallel-group, active-controlled study , patients will be treated with the aforementioned therapies for 14 days. Patients will be stratified by baseline duodenal ulcer (DU) status and randomly assigned in an equal ratio such that 65 patients will be assigned to each of six treatment groups. Patients with a DU or a history of DU endoscopically proven within the past year and who have a positive result for the presence of antibodies to *H. pylori* will undergo an endoscopy within seven days prior to initiating study treatment. Duodenal ulcer(s), if present, will be documented, gastric biopsy specimens will be taken from the antrum and the body of the stomach for culture and histology of *H. pylori*, and an additional biopsy specimen will be taken from the greater curvature of the antrum for the rapid urease test. If a patient is positive for *H. pylori* by rapid urease test, the patient will be entered in the study. If a patient is negative for *H. pylori* by rapid urease test but is subsequently determined to be *H. pylori* positive by histology, the patient will be considered *H. pylori* positive and will enter the study.
All patients completing the Week 6 visit with healed DU will return to the study center for evaluation at three and six months after completion of active treatment.

Progress: This study was closed to patient enrollment 1 Apr 96. Twenty-two patients were consented at MAMC. Ten patients were randomized to study. There was one serious adverse event, but the study drug was not considered the cause. All patients have completed follow-up visits.

Date: 30 Sep 96	**Protocol No.:** 96/093	**Status:** On-going

Title: A Multicenter Randomized, Double-Blind, Evaluation of Helicobacter pylori Eradication Following Oral GR122311X in Combination with Clarithromycin Compared to Omepraole in Combination with Clarithromycin ...

Start Date: 04/19/96 **Est. Completion Date:** Jun 97

Department: Med, Gastroenterology Svc **Facility:** MAMC

Principal Investigator: LTC Amy M. Tsuchida, MC

Associate Investigators:
MAJ Kazunori Yamamoto, MC
LTC Robert H. Sudduth, MC
MAJ John G. Carrougher, MC

Key Words: Helicobacter plyori, GR122311X, clarithromycin, omeprazole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To compare the following treatment groups with regard to *H. pylori* eradication rates: (a) GR122311 x 400 mg BID + clarithromycin 500 mg TID for 14 days, then GR122311 x 400 mg BID for an additional 14 days, (b) Omeprazole 40 mg QD + clarithromycin 500 mg TID for 14 days, then omeprazole 20 mg QD for an additional 14 days. 2) To compare the treatment groups with regard to duodenal ulcer healing, ulcer pain severity, antacid consumption, safety and tolerability.

Technical Approach: This is a randomized, double-blind, parallel group, double-dummy, active controlled, multicenter study. Subjects with ulcer-like pain will be tested for

serum antibodies to H. pylori using the FlexSure™ HP serology test. Subjects with a positive test result will undergo an esophagogastroduodenoscopy (EGD), with biopsies for CLOtest®, *H. pylori* histology and culture, and antibiotic susceptibility. Subjects with a positive CLOtest® result and with endoscopic evidence of at least one duodenal ulcer will be assigned to one of two treatment groups. Subjects will be treated for 28 days. One month after treatment discontinuation, subjects will be re-endoscoped to determine duodenal ulcer healing and biopsies will be taken to determine *H. pylori* status and antibiotic susceptibility.

Progress: No patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/086 **Status:** On-going

Title: The Location of the Esophageal Lesion Responsible for Dysphagia. How Accurate is the Patient's History?

Start Date: 04/01/94 **Est. Completion Date:** Jan 94

Department: Med, Gastroenterology Svc **Facility:** MAMC

Principal Investigator: MAJ Kazunori Yamamoto, MC

Associate Investigators:
CPT Eric T. Fajardo, MC
LTC Gregory N. Bender, MC
MAJ Michael F. Lyons II, MC
CPT Thomas P. Peller, MC
LTC Amy M. Tsuchida, MC

Key Words: dysphagia, esophageal lesion

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$31.65	**Periodic Review:** 09/30/96

Study Objective: To correlate the patient's localization of the site of food impaction with the site of the lesion by endoscope and barium swallow.

Technical Approach: The patients entered into this study will receive a directed history and physical exam as well as a CBC and thyroid function test. As part of the history, the patients will be asked to fill out a questionnaire on which foods they can swallow easily. Each food will be given a numeric value as follows: soup (1), mashed potatoes (2), peas (3), peeled apple (4), meat (5), wholemeal bread (6). A dysphagia score of 0-20 will then be established. After this initial exam the patients will receive an esophagogastroduedenoscopy (EGD) and barium swallow study per standard gastroenterology and radiology protocols. The physicians participating in the study will be blinded to the results of previous tests. The patients will be educated to the risks and benefits of the procedures and informed consent will be obtained. At the time of the procedure the patient will be asked to localize the site where food sticks or hangs up. A radiographic marker will then be placed over this/these point(s). Endoscopy and barium swallow will then be performed in the standard fashion. The site of the culprit esophageal lesion will be documented roentgenographically. We will compare the site of the lesion on the x-ray with the nipple marker. A correct localization will be defined as the nipple marker lying within two centimeters of the lesion on x-ray. Data will be analyzed descriptively by comparing the site of lesions on endoscopy and swallowing study with the external x-ray markers.

Progress: Twenty-six patients have been entered, nine of whom were found to have no endoscopically apparent lesions (non-obstructive dysphagia). Of the 17 patients who had endoscopically demonstrable lesions, all were found to have strictures or esophageal rings. There was wide variation in the level of subjective dysphagia as procured by history compared to the level of the endoscopic lesion. In 9 instances, the subjective level of dysphagia was within 6 mm of the endoscopic lesion. In 5 cases, the subjective level was greater than 12 cm from the actual level of the lesion. In all 5 cases, the lesion was at the level of the gastroesophageal junction and the subjective level of dysphagia was at the suprasternal notch. At this time, the code for the barium swallow has not been broken.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/057 **Status:** Completed

Title: A Randomized, Double-Blind, Acyclovir-Controlled, Multicenter Study to Assess the Safety, Efficacy, and Pharmacokinetics of IV Penciclovir for the Treatment of Mucocutaneous Herpes Simplex Infection..

Start Date: 02/04/94 **Est. Completion Date:** Feb 95

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
MAJ James S. D. Hu, MC
LTC Robert B. Ellis, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
LTC Howard Davidson, MC
MAJ Richard F. Williams, MC

Key Words: herpes simplex, immunocompromised, penciclovir, intravenous

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To compare the safety and efficacy of intravenous penciclovir, at a dose of 5 mg/kg 2-3 times daily for 7 days, with 5 mg/kg intravenous acyclovir 3 times daily for 7 days in the treatment of mucocutaneous herpes simples infection in immunocompromised patients.

To study the population pharmacokinetics of intravenous penciclovir at a dose of 5 mg/kg 2 and 3 times daily in immunocompromised patients with mucocutaneous herpes simples infection.

Technical Approach: This is a randomized, three dose arm, parallel-group, multicenter study. Double-blind treatment will be allocated sequentially by means of a fixed, equally balanced randomization code by the pharmacist. Patients at least eighteen years of age with a clinical mucocutaneous herpes simples infection and are immunocompromised will receive intravenous penciclovir, at a dose of 5 mg/kg either two or three times daily for 7 day, will be compared with intravenous acyclovir at a dose of 5 mg/kg three times daily for 7 days.

Patients will be evaluated daily during the 7 day treatment period and thereafter every other day until complete healing (re-epithelialization of lesions) has occurred, for clinical signs and symptoms, assessment of herpetic lesions and viral culturing. Laboratory tests will be conducted at baseline, at the end of the treatment period and one week after the treatment period. Four blood samples for population pharmacokinetic studies will be taken on one of the full treatment days only.

Data collected from the study will be evaluated by the sponsor.

Progress: No patients were entered due to failure to meet enrollment criteria.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/080 **Status:** Completed

Title: Letrozole (CGS 20267) Comparison of Two Doses (0.5 mg and 2.5 mg) of Letrozole versus Megestrol Acetate in Postmenopausal Women With Advanced Breast Cancer, Protocol 02

Start Date: 04/01/94 **Est. Completion Date:** Oct 99

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
MAJ John R. Caton, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC
LTC Howard Davidson, MC
James H. Timmons, MD
LTC Luke M. Stapleton, MC
LTC Robert D. Vallion, MC
MAJ James S. D. Hu, MC

Key Words: Cancer:breast, Letrozole, megestrol acetate, postmenopausal

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: 1) To compare the anti-tumor efficacy, as evaluated by the primary variable of objective response rate, and the secondary variables of duration of response, time to treatment failure (TTF), time to progression (TTP) and time to death among the three treatment arms (daily) doses of 0.5 mg letrozole, 2.5 mg letrozole, or 50 mg megestrol acetate (q.i.d.). 2) To compare tolerability and toxicity of daily doses of 0.5 mg letrozole, 2.5 mg letrozole and 40 mg megestrol acetate q.i.d. 3) To assess information on population pharmacokinetics, including evaluation of trough estrogen levels during treatment, with daily doses of 0.5 mg and 2.5 mg letrozole.

Technical Approach: This is a multicenter, multinational, randomized, parallel-group, double-blind trial in postmenopausal women with advanced breast cancer who have failed on antiestrogen as an adjuvant or advanced disease therapy. Patients will receive either one tablet letrozole 0.5 mg or 2.5 mg once daily in the morning plus one placebo capsule matching megestrol acetate q.i.d. or one 40 mg capsule megestrol acetate q.i.d. plus one placebo tablet matching letrozole once daily in the morning. Patient evaluations will be done at baseline (prior to treatment), after 2 weeks, 1, 2, 3, 4, 5 and 6 months and every 3 months thereafter until the code is broken to the participating investigators which will occur after the last patient has been enrolled for 18 months. In addition any patient who manifests an objective tumor response will have her full tumor evaluations repeated at least 4 weeks but no later than the next scheduled tumor assessment after the initial observation of response to confirm the presence of the response. Patients who respond to treatment (complete response, partial response or stable disease) will continue the treatment until the double-blind code is broken or there is disease progression, whichever comes first. After this period, the patients will be followed periodically for the purpose of collecting survival data for a total period of 5 years after initiation of treatment of the first patient on trial.

Progress: Two patients were entered on this study. Both had disease progression while on study medication and were taken off study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/055 **Status:** On-going

Title: Agrelin (Anagrelide) for Patients With Thrombocythemia

Start Date: 02/04/94 **Est. Completion Date:** Jan 97

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: thrombocythemia, Agrelin, safety, efficacy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 01/19/96

Study Objective: To assess the safety and efficacy of Anagrelide in patients suffering from thrombocythemia of various etiologies.

Technical Approach: Patients who are 18 years or older, free of infection and have thrombocythemia due to a myeloproliferative disorder will be asked to participate. Those consenting will have a physical examination, complete blood count and serum chemistry and then be dispensed a three-month supply of drug. During treatment with Anagrelide, blood counts should be determined as often as needed to assure patient safety. Other test will be done as clinically indicated. Any patient whose thrombocythemia is unchanged (± 20%) after two weeks of treatment will be removed from the study. Those patients receiving benefit may remain on the study until the drug is released by the FDA or all trials are terminated. The data derived from the study will be analyzed by the sponsor.

Progress: Two patients were enrolled in previous years. One patient with polycythemia sera and high platelet counts; continues to have platelet counts controlled by Anagrelide and is clinically stable. One patient never achieved a durable response and was removed from the study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/017 **Status:** On-going

Title: Evaluation of Immunity to Breast Cancer

Start Date: 02/04/94 **Est. Completion Date:** Nov 94

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Mark E. Robson, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:breast, immunity

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$18.00	**Periodic Review:** 09/30/96

Study Objective: To determine the significance/relationship of CD4 helper/inducer T cell response in the presence of H2N positive/negative cancers in an attempt to determine how the immune system responds to breast cancer.

Technical Approach: Patients with breast cancer will have samples of tumor tissue obtained at the time of surgery for Her-2/neu. Blood will be obtained at the same time to evaluate for an anti-Her-2/neu T-lymphocyte response. Further venipunctures will be performed monthly during the 5 year follow-up period to continue evaluation for an anti-Her-2/neu T-lymphocyte response.

Progress: Blood samples have been collected on seven patients to evaluate immune response to breast cancer cell antigens. Data are insufficient for conclusions at this time.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/099 **Status:** On-going

Title: Phase III Trial of 3-Hour versus 96-Hour Infusions of Paclitaxel from NaPro/Baker Norton in Patients with Refractory Metastatic Breast Cancer, and an Assessment of 96-Hour Infusions in 3-Hour Failures

Start Date: 03/17/95 **Est. Completion Date:** Nov 96

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:breast, paclitaxel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: 1) To confirm the established therapeutic effects of paclitaxel in refractory metastatic breast cancer patients given the approved dose and schedule of a new source of this novel chemotherapeutic agent. 2) To confirm the safety profile and patient tolerance characteristics of paclitaxel under the widely accepted therapeutic regimen, to offer a new regimen of paclitaxel (by 96-hour infusion) as a rescue therapy for patients progressing on the standard paclitaxel regimen, and to confirm the reported higher efficacy of the 96-hour infusion regimen of paclitaxel in a subset of patients selected randomly de novo.

Technical Approach: This is a multi-center, open-label, Phase II/III, trial evaluating 3-hour and 96-hour infusions of paclitaxel from NaPro/Baker Norton. The study population is women with metastatic breast cancer who have failed a maximum of two prior chemotherapy regimens, only one of which may have been as treatment for metastatic disease. The study will enroll 200 patients, approximately 75% of whom are expected to have been exposed to anthracyclines. Patients will be stratified on the basis of measurable versus evaluable disease. Patients will be randomized to the 3-hour and 96-hour infusions in each strata on a 3 to 1 ratio. Patients randomized to the treatment group using the 3-hour schedule will crossover to the 96-hour schedule when there is evidence of rapid progression. Rapid progression is defined as increase of disease within a maximum of 4 cycles of 3-hour paclitaxel infusion. Estimation of the response rate to a 3-hour infusion will be determined in 150 patients. The second objective of obtaining estimates of the response rate to a 96-hour infusion will be obtained in an additional 50 patients. The assignment of patients to infusion schedules will be done by randomization. Sample size was base on response rates of 26% and 48%.

Progress: Two patients have been entered on this study. One patient was discontinued due to a drop in performance status and subsequently died >30 days after her first dose. The second patient, on day 4, cycle 8, at time of disconnection from 96 hour cycle had a white, solid precipitate aspirated from her Groshong catheter. At the beginning of cycle 9, the aspirate was again noted at the time of bag and tubing change. The precipitate was identified as paclitaxel upon analysis. Patient was taken off study and followed per standard care, event reported to sponsor. The consent form was revised.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/162	**Status:** On-going
Title: The Characterization of Breast Cancer Susceptibility Genes in Males and Their Kindred		
Start Date: 08/18/95	**Est. Completion Date:** Sep 98	
Department: Medicine, Hematology/Oncology Service	**Facility:** MAMC	
Principal Investigator: MAJ John R. Caton, MC		
Associate Investigators: Amelia Langston, M.D.	LTC Robert B. Ellis, MC Elaine Ostrander, Ph.D.	
Key Words: Cancer:breast, genes:BRCA1, BRCA2, AT, p53, RB, ras		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: Using male breast cancer patients as probands we will characterize the known breast cancer susceptibility genes BRCA1, BRCA2, AT and additional genes such at p53, RB and ras in the affected individuals and their families.

Technical Approach: The data obtained from a previous study of the Automated Central Tumor Registry database (ACTUR) revealed 123 total cases of male breast cancer within the Department of Defense (DOD) healthcare system. Those patients with a family history of breast cancer are currently in the process of evaluation under a previous IRB approved protocol. The next step involves collecting samples of blood from each living male breast cancer patient and family members of both living and deceased patients as deemed appropriate for study. Additionally, formalin fixed paraffin imbedded tumor blocks will be collected on as many patients as possible. Once the specimens are collected the blood will be processed at Madigan Army Medical Center. Both DNA and buffy coat cells will be extracted and frozen for storage. Aliquots of these specimens along with portions of tumor blocks will be blinded with regard to clinical information and sent to Dr. Ostrander's lab at Fred Hutchinson Cancer Research Center for analysis. This analysis will initially include screening for mutations in BRCA1, BRCA2 (when cloned) and the Ataxia-Telangiectasia gene (AT) using the patient DNA extracted from the blood sample. The tumor blocks would be tested for the loss of heterozygosity for markers on chromosomes 13q covering both the BRCA2 and Retinoblastoma (RB) genes, chromosome 11 for the AT gene and chromosome 17 regions covering the p53 and BRCA1 genes. Data collected from these studies would then be matched with the clinical information in order to derive information regarding cancer susceptibility, prognosis and basic mechanisms of carcinogenesis.

Progress: Twenty-five subjects have been enrolled. Blood samples from these patients are undergoing genetic analysis.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/118	**Status:** Completed
Title: The Natural History of Male Breast Cancer		
Start Date: 04/21/95	**Est. Completion Date:** Apr 95	
Department: Medicine, Hematology/Oncology Service	**Facility:** MAMC	
Principal Investigator: MAJ John R. Caton, MC		
Associate Investigators: MAJ Timothy P. Rearden, MC	LTC Robert B. Ellis, MC	
Key Words: Cancer:breast, Cancer:natural history		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To establish a comprehensive, complete database of information on male breast cancer patients diagnosed and treated in the Department of Defense.

Technical Approach: The Automated Central Tumor Registry (ACTUR) for the Department of Defense contains information on all cancer cases. This database was previously searched and 123 individuals with male breast cancer identified. Unfortunately, the database contains very little information other than names and addresses. A survey has been constructed for the patients to complete and will yield large amounts of information concerning epidemiology, natural history hereditary patterns, and treatment . The data will also be the foundation for other studies on the molecular basis of male breast cancer and comparison to female tumors.

Progress: A total of 126 cases were identified at 33 military medical facilities. The majority of patients presented with Stage I or II breast cancer (85%). Overall survival at 5 years and 10 years was 70% and 51%, respectively. Axillary lymph node involvement was not a predictor of adverse overall or disease-free survival. The overall survival of node negative patients at 10 years was 58%, compared to a 10 year survival of node positive patients of 59%. Patients treated with adjuvant therapy had a trend towards improved survival compared to patients who received local therapy alone. The difference in survival at 5 years was 14% and at 10 years was 10% ($p = 0.4$). The investigators conclude that the prognosis of breast cancer in men is similar to female breast cancer and the benefits of treating node positive patients with systemic adjuvant therapy are similar as well. In the absence of randomized trials, it is recommended that males with breast cancer be treated with adjuvant therapy according to guidelines established in females. A paper has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/187	**Status:** On-going

Title: A Study to Evaluate the Effect of Cisplatin/Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment of Goals in Accessible Tumors of Any Histology

Start Date: 09/15/95	**Est. Completion Date:** Nov 96
Department: Medicine, Hematology/Oncology Service	**Facility:** MAMC

Principal Investigator: MAJ John R. Caton, MC

Associate Investigators:

MAJ James S. D. Hu, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
LTC Robert L. Sheffler, MC

Key Words: Tumors, Cisplatin,Epinephrine Injectable Gel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the effect of MPI 5010 on local tumor volume and local tumor volume per patient. To assess achievement of an identified primary treatment goal selected for the most troublesome tumor following up to 6 weekly treatments of MPI 5010. To observe the time to response and the time to progression for the most troublesome tumor after treatment with MPI 5010. To assess improvement and stabilization in quality of life as measured by FACT-G/H&N. To evaluate the histopathology of injected lesions that respond to local treatment with MPI 5010.

Technical Approach: This will be a multi-center, open label study in approximately 60-65 evaluable patients with measurable and histopathologically confirmed accessible tumors of any histology except squamous cell carcinoma of the head and neck. Prior to the enrollment, the investigator must identify the patients's most troublesome tumor and one improvable primary treatment goal for that tumor. Patients with tumors measuring at least 0.5 cm^3 will be treated with 0.5 mL MPI 5010/cm^3 of tumor volume weekly for up to 6 treatments within 8 weeks or until patient objective complete response, which ever occurs first. Patients will return for an evaluation weekly for 4 weeks after the last treatment. Patients with a 100% reduction in volume of all treated tumors at the end of the Treatment Phase will be followed monthly for an additional 5 months or until time of tumor progression. Re-treatment of a tumor in follow-up in the case of disease or symptom progression may be performed if, in the opinion of the investigator, it will benefit the patient. Data analysis will include progress toward treatment goal, quality of life, tumor response, dosing, and safety. Appropriate statistical tools will be employed to measure and test each parameter in support of the objectives.

Progress: Two patients have been randomized. Neither patient responded well to the treatment and were subsequently dropped from the study and treated with other agents.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/049 **Status:** Terminated

Title: A Stratified, Randomized, Double-Blind Comparison of Oral Ondansetron and Compazine Spansules in the Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Chemotherapy

Start Date: 12/16/94 **Est. Completion Date:** Aug 95

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
MAJ Richard F. Williams, MC

Key Words:

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the efficacy and safety of 8mg oral ondansetron BID with 15mg Compazine Spansules BID in the prevention of nausea and vomiting associated with a cyclophosphamide-based chemotherapy regimen. This study will also assess the impact of nausea, vomiting, and sleepiness on the productivity and activity levels of the subject population. The quality of life related to cancer and emesis will be compared between the two treatment groups.

Technical Approach: This will be a stratified, randomized, double-blind, multicenter, comparative trial. The treatment period begins with the administration of the first does of study drug, 30 minutes prior to initiation of cyclophosphamide or doxorubicin (whichever occurs first), and continues until midnight on Study Day 3. A posttreatment final visit will occur after the end of the three day treatment period (Days 4-8). A total of 372 evaluable chemotherapy-naive subjects will be enrolled in this multicenter trial. Eligible subjects will have a histologically proven cancer, be scheduled to receive a cyclophosphamide-based regimen of chemotherapy, and meet all other eligibility criteria. All subjects will receive cyclophosphamide ($\geq$ 500mg/m^2) and either doxorubicin ($\geq$ 40mg/m^2) or methotrexate ($\geq$30 mg/m^2) administered over a period of less than 2 hours per agent. Thirty minutes prior to the administration of the chemotherapy regimen subjects will receive the first dose of study drug. Subjects will be randomized (1:1) to one of the following treatment arms for oral administration of study drug: 8 mg Ondansetron (BID x 3 days) + 15 mg Placebo Compazine Spansules (BID x 3 days) or 8 mg Placebo Ondansetron (BID x 3 days) + 15 mg Compazine Spansules (BID x 3 days). Efficacy data will be collected for each subject up until Study Day 3. The primary efficacy variable is the number of subjects with zero emetic episodes. Clinical adverse events will be recorded up until Study Day 3.

Progress: This study has been closed by the sponsor due to administrative reasons. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/049 **Status:** On-going

Title: An Open-Label, Long-Term, Multicenter Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough or Incident Pain in Cancer Patients Previously Enrolled in Other OTFC Studies

Start Date: 01/19/96 **Est. Completion Date:** Mar 97

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ James S. D. Hu, MC
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Pain:cancer, fentanyl citrate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To establish the long-term safety and tolerance of OTFC in cancer patients experiencing breakthrough or incident pain while taking other opioids.

Technical Approach: The study will be conducted using an open-label, uncontrolled design in cancer patients. Cancer patients successfully completing other appropriate studies of OTFC will be eligible for this study. When patients experience breakthrough pain, they may treat up to 4 episodes each day with OTFC. Patients will be given a supply of OTFC units, all the same dosage strength, to treat breakthrough or incident pain for one month. The patient will be contacted at least weekly by telephone by a study physician or nurse and will be seen by study personnel at least monthly. After each contact, the investigator will decide whether or not the patient requires a larger or smaller dose of study medication to relieve breakthrough pain using a single OTFC unit. Patients may remain in the study for up to four months if they continue to experience breakthrough pain and are able to provide complete and accurate information on the safety and efficacy of the study medication. Patients will record in a daily diary the use of OTFC and any other medications, assess the performance of the study medication in relieving breakthrough or incident pain, and report any adverse events they experience. Demographics, medical history, physical exam, and laboratory results will be summarized using descriptive statistics.

Progress: Five patients were entered in this long-term trial and two currently remain active. Two patients dropped out of the study for personal reasons and one was discontinued because of disease progression.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/048 **Status:** Completed

Title: A Multicenter, Double-Blind, Placebo-Controlled, Crossover Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough Pain in Cancer Patients Taking Stable Doses of Opiods

Start Date: 01/19/96 **Est. Completion Date:** Mar 97

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ James S. D. Hu, MC
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Pain:cancer, pain:breakthrough, fentanyl citrate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate that oral transmucosal fentanyl citrate (OTFC) provides more effective relief from breakthrough pain than placebo in opioid tolerant cancer patients.

Technical Approach: This study will be conducted using a double-blind, crossover, randomized, placebo controlled design. Twenty to thirty centers will each enroll approximately 5 patients, for a total of 100 evaluable patients. In an initial open-label phase, patients will be titrated to a dose of OTFC that generally controls their breakthrough pain. Only those patients who can successfully use the OTFC in this way will proceed to the blinded phase of the study. In the second phase, patients will be given a supply of 10 pre-numbered oral transmucosal (TO) units. Three units will be placebo and 7 of the units will be the OTFC dose found to be effective in the open-label phase. The units will be identical in appearance and the order of administration will be random. Patients will be instructed to take 1 unit, in the designated order, for each episode of breakthrough pain they experience. Demographic variables will be summarized descriptively. The data from the double-blind phase will also be statistically analyzed to compare active to placebo.

Progress: This study was closed to enrollment 15 July 96. Nine patients were consented at MAMC; 6 completed the study, 2 were dropped due to rapidly escalating pain, and 1 patient did not meet the screening criteria and did not receive the medication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/118 **Status:** On-going

Title: Phase II Study of Single Agent Thiotepa for Advanced, Hormone-Refractory Prostate Carcinoma

Start Date: 06/03/94 **Est. Completion Date:** Dec 96

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
MAJ J. Brantley Thrasher, MC
MAJ Richard C. Tenglin, MC
Celestia S. Higano, MD
MAJ Timothy P. Rearden, MC

Key Words: Cancer:prostate, thiotepa

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to evaluate the efficacy and toxicities of single agent thiotepa for advanced hormone-refractory prostate carcinoma.

Technical Approach: This is a non-randomized phase II study. All eligible patients with metastatic, hormone-refractory prostate cancer who are considered by their physicians to have a chance to benefit and also agree to participate will be entered. Patients will be initially staged with abdominal/pelvic C.T. scans, bone scans, chest radiographs, serum PSA, serum PAP, BUN, creatinine, liver function tests and complete blood count. All patients will receive thiotepa 50 mg/m^2 by intravenous administration at 28 - day intervals. Patients will be continued on therapy until: 1) disease progression is documented; 2) Unacceptable toxicities occur; or 3) the patient refuses further treatment for any reason. Any patient obtaining a complete response will receive two (2) additional courses of thiotepa past CR, and then be followed off therapy.

Progress: Study has enrolled 3 subjects (1 in 1994 and 2 in 1995).

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/133 **Status:** On-going

Title: A Double-Blind, Randomized, Phase 3, Multicenter Study of Suramin and Hydrocortisone vs Hydrocortisone and Placebo in the Treatment of Patients with Metastatic, Hormone-Refractory Prostate Carcinoma

Start Date: 05/19/95 **Est. Completion Date:** Jul 96

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Luke M. Stapleton, MC
MAJ J. Brantley Thrasher, MC
LTC Robert D. Vallion, MC
LTC Robert B. Ellis, MC
James H. Timmons, MD

Key Words: Cancer:prostate, Suramin, Hydrocortisone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 05/17/96

Study Objective: To determine suramin's effect on pain, performance status, PSA, disease response, quality of life and survival in patients with hormone-refractory prostate carcinoma. Also to evaluate the safety of suramin.

Technical Approach: This study will be a double-blind, randomized, placebo-controlled, multi-center study of suramin plus hydrocortisone therapy versus placebo plus hydrocortisone therapy in 20 MAMC patients (total of 186 per treatment group) with prostatic carcinoma who have failed at least 1 course of prior hormonal manipulation. The primary outcome measurements will include changes in PSA level, disease response, quality of life, survival, time to progression, time to response and duration of responses. Patients will be stratified prospectively on the basis of PSA levels and presence of measurable disease and then randomly assigned to the suramin or placebo treatment groups. Patients will be given fixed doses of suramin or placebo, infused intravenously over a 1-hour period over a 78-day treatment period. Both arms will receive concomitant hydrocortisone. Primary efficacy determination will be determined on the basis of changes relative to baseline in pain score, analgesic use and performance status. Secondary efficacy measurements will be made on the basis of changes relative to baseline in other BPI scales, PSA changes, measurable disease response, and quality of life. Descriptive statistics will be provided for all demographic, efficacy and safety parameters. All tests will be 2-sided and conducted at the 5% level of significance. The level of significance will not be adjusted for the planned comparisons. Appropriate statistical methods will be applied to the various parameters and will include analysis of covariance, Cochran-Mantel-Haenszel analysis, and the Wilcoxon test.

Progress: Two patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/170 **Status:** On-going

Title: Phase 3 Trial of Gemcitabine Plus Cisplatin Versus Cisplatin Alone in Patients with Metastatic Non-Small Cell Lung Cancer

Start Date: 07/21/95 **Est. Completion Date:** Sep 96

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: LTC Luke M. Stapleton, MC

Associate Investigators:
MAJ James S. D. Hu, MC
LTC Robert B. Ellis, MC
MAJ John R. Caton, MC
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:non-small cell lung, gemcitabine, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of this study is to compare the survival of patients with Stage III and IV metastatic MSCLC treated with cisplatin alone to that of patients treated with the combination of cisplatin and gemcitabine.

Technical Approach: This is a randomized study of cisplatin monotherapy versus the combination of cisplatin and gemcitabine in patients with locally advanced (unresectable Stage IIIA or IIIB), or metastatic NSCLC who have received no prior chemotherapy regimens. Approximately 520 patients will be enrolled in this study and be randomized to receive either Regimen A or Regimen B. Regimen A is defined as follows: gemcitabine will be administered intravenously once each week for 3 weeks, followed by a 1-week rest period, and cisplatin will be administered intravenously once each cycle immediately after the first gemcitabine infusion of that cycle. This 4-week schedule defines a cycle of treatment. Multiple cycles will be administered. Regimen B is defined as follows: cisplatin will be administered intravenously once each cycle. Patients may receive a maximum of 6 cycles. It is anticipated that 10 to 15 patients will participate at Madigan.

Progress: Two patients have been randomized to single agent cisplatin and both have had progressive disease. One patient is currently receiving cisplatin and gemcitabine with a partial response. No further patients will be enrolled in this trial as there is now a study showing that Taxol and carboplatin in combination are superior to treatment with cisplatin alone.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/138 **Status:** On-going

Title: The Effect of Tamoxifen and Ionizing Radiation on Expression of Bcl-2, Bcl-x, and p53 in Breast Cancer Cells In Vitro

Start Date: 06/16/95 **Est. Completion Date:** Mar 96

Department: Medicine, Hematology/Oncology Service **Facility:** MAMC

Principal Investigator: MAJ Richard F. Williams, MC

Associate Investigators:
MAJ Nyun C. Han, MC
Katherine H. Moore, Ph.D.
LTC Robert B. Ellis, MC
MAJ Mark D. Brissette, MC

Key Words: Cancer:breast, oncogenes, tamoxifen, radiation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to define the molecular mechanism by which antitumor agents such as estrogen receptor antagonists and ionizing radiation initiate programmed cell death (apoptosis) in cultured breast cancer cells. Specific objectives are to examine the treated breast cancer culture cells for morphologic and biochemical evidence of apoptosis and to determine the time course for apoptotic death as well as that for changes in the level of bcl2 and p53 in the cells. Thereby, we will determine if changes in the level of these factors precede the onset of apoptotic death and provide evidence for the importance of modulation of the expression of these proteins as antitumor effects of these agents. Also, changes in other bcl2-related factors such as bax and bcl-x will be examined.

Technical Approach: Three breast cancer cell lines, MCF-7, MDA-MB-231, and ZR-75 cells, are currently available and express varying levels of estrogen receptor, bcl-2 and /or p53 molecules. Cells form each of these lines will be grown in the presence of estrogen for 24 hours, after which the medium will be treated with either tamoxifen or 4-hydroxytamoxifen, at 0.1 and 1.0 micromolar for six days. For the effects of radiation, cell will be grown in estrogen for 24 hours and then irradiated. At 24 hour intervals, cells from each experimental condition will be harvested and examine for apoptosis and for the level of expression of bcl2, bcl-x and p53. Morphologic and biochemical evidence for apoptosis in these cultures will be obtained by light microscopy and DNA agarose gel electrophoresis. Flow cytometry will be used to determine the fraction of apoptotic cells. Expression of the protein products of the three oncogenes will be determined by quantitative Western blot electrophoresis. The mean values and standard deviations for three separate cultures with each treatment at each time point will be determined. Statistical analysis will be performed using two way analysis of variance methods.

Progress: Apoptosis & bcl-2 assays are being analyzed. Expect completion of technical portion of protocol in mid 1997.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/132 **Status:** On-going

Title: An Open-Label, Multicenter Study of Clinafloxicin in the Treatment of Infective Endocarditis

Start Date: 05/19/95 **Est. Completion Date:** Jul 97

Department: Medicine, Infectious Disease Service **Facility:** MAMC

Principal Investigator: COL Ronald H. Cooper, MC

Associate Investigators: None

Key Words: Endocarditis, Clinafloxicin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 05/17/96

Study Objective: To assess the efficacy of clinafloxacin in the treatment of patients with infective endocarditis.

Technical Approach: This study will evaluate the safety and efficacy of clinafloxacin in 50 patients (5 to 10 from MAMC) with infective endocarditis of bacterial etiology for survival rate, time to defervescence, time to sterile blood cultures and development of resistant pathogens. The dosage will be clinafloxacin 200 mg intravenously or by mouth every 12 hours for 4 to 6 weeks, up to 12 weeks maximum. The primary efficacy parameter is the microbiological eradication rate. Patients will be stratified on the basis of (1) right-sided vs left-sided endocarditis, (2) native valve versus prosthetic valve infection, and (3) pathogen recovered from blood cultured.

Progress: No patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/131 **Status:** Completed

Title: A Double-Blind Multinational Trial Comparing Sorivudine [BV-araU] vs Acyclovir for the Treatment of Acute Localized Zoster and the Effect on Zoster-Associated Pain in Immunocompetent Subjects

Start Date: 05/19/95 **Est. Completion Date:** Jul 97

Department: Medicine, Infectious Disease Service **Facility:** MAMC

Principal Investigator: COL Ronald H. Cooper, MC

Associate Investigators:
COL Eugene T. Etzkorn, MC
MAJ Thomas F. Burke, MC
LTC Joseph T. Morris III, MC

Key Words: Zoster, Sorivudine, Acyclovir, immunocompetent

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the safety and efficacy of sorivudine 40 mg once daily for 7 days vs. acyclovir 800 mg every four hours five times daily for 7 days in the treatment of acute localized zoster and the effects on zoster-associated pain and on healing of the skin lesions in immunocompetent subjects with trigeminal zoster or > 50 years of age.

Technical Approach: This is a randomized, double-blind comparative safety and efficacy trial of sorivudine vs. acyclovir in the treatment of acute localized zoster and the effect of zoster-associated pain and quality of life in immunocompetent subjects. It is anticipated that at least 348 subjects from approximately 35 centers will be enrolled into this trial. The subjects must have a localized rash consistent with zoster present for $\leq$ 72 hours: have trigeminal zoster or be >50 years of age; and have no evidence of an immunocompromising condition by medical history, physical examination or treatment history. Once stratified, the subjects will be randomized to either active sorivudine with acyclovir placebo or active acyclovir with sorivudine placebo. Subjects will be evaluated during and following treatment to determine their response to therapy. Clinical assessments will follow a rigid schedule with additional visits at the end of months 2 and 3 for those patients with continuing symptoms of post-herpetic neuralgia. Patients will be telephoned weekly to reinforce completion of diaries for assessments of efficacy, quality of life and pharmacoeconomic parameters. Clinical and laboratory adverse events will be assessed throughout the acute phase (Days 1-28) of the study. The two treatment groups will be compared with respect to the primary efficacy endpoint of total time (days) with severe or moderate pain associated with zoster during the six month study period using the Wilcoxon Rank-sum test.

Progress: One patient was entered in this study at MAMC with no complications.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/156	**Status:** On-going

Title: A Pilot Study of the Semmes-Weinstein Monofilament for Diagnosing Peripheral Neuropathy in Diabetics: Inter-rater Reproducibility and Comparison with Standard Clinical Examination

Start Date: 09/20/96	**Est. Completion Date:** Nov 96
Department: Medicine, Internal Medicine Service	**Facility:** MAMC

Principal Investigator: MAJ Jeffrey L. Jackson, MC

Associate Investigators: None

Key Words: Diabetes, Semmes-Weinstein monofilament, neuropathy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess the inter-rater reproducibility and to compare the Semmes-Weinstein monofilament in the detection of peripheral neuropathy in diabetics.

Technical Approach: Loss of foot sensation is a common complication of diabetes mellitus and may lead to ulceration, infections, and amputation. A simple device consisting of a monofilament mounted on a plastic stick has been developed to enable the clinician to detect protective sensation in the foot. In this pilot study, we will examine basic measurement properties of this device: how reproducible are the results of foot examination by two examiners, using the monofilament and standard physical examination? The study will consist of two five-minute examinations by two physicians of each subject's feet during a single clinic visit for each subject. This will be a pilot study for a possible future multi-center physical examination study by the U.S.-Canadian Research Group on the Clinical Examination.

Progress: Three patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/161 **Status:** On-going

Title: The Relationship Between Intensity of Anticoagulation and Complications

Start Date: 09/20/96 **Est. Completion Date:** Jul 97

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: MAJ Jeffrey L. Jackson, MC

Associate Investigators: None

Key Words: Anticoagulation, coumarin, thrombosis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To measure the relationship between the intensity of anticoagulation with coumadin and potential bleeding and thrombotic complications.

Technical Approach: The coumadin data base at MAMC is an automated system for following patients taking coumadin. The system changed methods of tracking degree of anticoagulation in 1993 to the International Normalized Ratio (INR). There are approximately 800 patients in this data set which have been followed for up to three years. Data elements present within this data set include patient demographics, indication for initiation of coumadin, the target INR, the actual recorded INR values, the doses of coumadin given and, for patients withdrawn from coumadin, the indication for withdrawal. I propose to extract these data elements and analyze the INR values with respect to the optimal INR. Generally speaking the two significant outcomes of interest are cerebral vascular accidents, generally indicative of inadequate coumadinization and bleeding complications from overzealous treatment. The hope is to define an optimal INR to minimize both complications. Combined databases of MAMC and WRAMC total 2300 total patients which will be retrospectively analyzed. The total number of patient-years will be subdivided by INR intervals of 0.5. For each patient, the fluctuation of INR around the target value is measured at regular intervals. We will assume that the INR changes in a linear fashion between measurements and will allocate a specific INR accordingly, to each day. Days will then be grouped according to INR intervals and summed for all patients--this will generate patient-years at different intensities. If there is greater than 8 weeks between two measurements, no INR will be allocated, since this duration may make the linear assumption invalid. The ratio of the number of events that took place when the prothrombin time is in a particular INR range to the number of patient-years during which the INR is at this level in the patient population will e the fundamental unit of analysis. 95% confidence intervals for the incidence rates will be calculated with the assumption of Poisson distribution. Logistic regression analysis using demographic and INR data to model predicted likelihood of a complication. Cox proportional hazard model will be used to assess the likelihood of failure using both demographic and INR data.

Progress: This is a new study which has not been implemented.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/155	**Status:** On-going
Title: Symptom Related Expectations in A Rheumatology Clinic Setting		
Start Date: 09/20/96	**Est. Completion Date:** Aug 97	
Department: Medicine, Internal Medicine Service	**Facility:** MAMC	
Principal Investigator: MAJ Jeffrey L. Jackson, MC		
Associate Investigators:	MAJ Edmund H Hornstein, MC	
Key Words: Rheumatology, symptoms		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: a) To determine the prevalence of mood, anxiety and somatoform disorders in patients making an initial visit to a rheumatology subspecialty clinic; b) to determine whether a relationship exists between mental disorders and the likelihood of objective abnormal findings on physical examination or laboratory; and c) to determine whether a relationship exists between mental disorders and the likelihood of organic rheumatologic diagnosis.

Technical Approach: 75 patients presenting with a new consult to the rheumatology clinic will be asked to participate. After obtaining verbal consent, patients with fill out a questionnaire on symptom-related expectations as well as the PRIME-MD screen. After the visit, rheumatologists will complete a one-page questionnaire on their clinical assessment. The data will be encoded into a database using the EPI-INFO system developed by the CDC for epidemiological studies. Simple descriptive analysis, such as frequency of various psychiatric disorders, mean ages, frequency of specific rheumatologic diagnosis, will be performed. The chi-square statistic can also be performed to analyze the relationship between the presence or absence of a psychiatric disorder and the presence of organic pathology. Predictors of likelihood of having either a disorder or objective findings will be performed using logistic regression techniques using STATA statistical packages. We previously found that patients undergoing EGD without a psychiatric disorder had abnormalities present 45% of the time, compared to 15% in patients with a psychiatric disorder. Assuming that this 30% difference also holds in rheumatologic patients and further assuming a 50% prevalence of psychiatric disorders, sample size calculations (assuming alpha=0.05, beta=0.20, HO: 0.45%, H1: 0.15%) would be 35 patients, requiring a total of 70 patients.

Progress: Fifteen patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/066 **Status:** Terminated

Title: Using Systems Methodology to Model and Deploy Ambulatory Care Resources

Start Date: 03/04/94 **Est. Completion Date:** Oct 96

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: MAJ Duane J. Jeffers, MC

Associate Investigators:
W. Paul Nichol, M.D.
Scott Iverson, MD
Tesfai Gabre-Kidan, MD
Kenric W. Hammond, MD

Key Words:

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) Modify and validate two computer simulation models of ambulatory care resource allocation nearing completion at the Seattle VA Medical Center (SVAMC) ambulatory care clinic; and 2) adapt these "source" models for the ambulatory care clinics at the Madigan Army Medical Center (MAMC) and American Lake VA Medical Center (ALVAMC), as well as 3) perform sensitivity analysis and preliminary validation.

Technical Approach: Existing computer simulation models of the Ambulatory Care Service at SVAMC will be further refined and adapted to the MAMC and ALVAMC Ambulatory Care Services over a period of two and one-half years. The adaptation process includes surveying interested parties at the two sites, collecting the necessary data, and changing the "source" model. Sensitivity analysis, which assesses how the models respond to parameter changes, will be performed on all three models using the data to construct the models as well as data collected subsequently. Preliminary validation of the model with the aim of determining how well the model represents the system in question will also take place. Surveys will be conducted to investigate the impact of the model development process on organizational behavior. The models will be used, in a future project, to suggest intervention(s) to reconfigure one or more of the ambulatory care clinics, whereupon the intervention will be implemented and assessed.

Progress: The computer models were developed, but were not sufficiently robust to warrant conducting the rest of the project. The project did not receive further funding from the VA, and therefore the project has been terminated.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/018 **Status:** Completed

Title: Impact of Adult Primary Care Clinic (APCC) on the Health Status of Patients and the Resource Utilization of MAMC

Start Date: 11/05/93 **Est. Completion Date:** Oct 95

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: MAJ Duane J. Jeffers, MC

Associate Investigators:
MAJ Sabrina A. Benjamin, MC
CPT Robert V. Gibbons, MC
LTC Jackie W. Saye, AN
COL Eric B. Schoomaker, MC
MAJ Francis J. Landry, MC
LTC M. Lupo, RN
Rhonda J. McColpin, DAC

Key Words: resource utilization, adult primary care clinic

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1600.00	**Periodic Review:** 09/30/96

Study Objective: To determine the impact of a primary care clinic operating with managed care principles (the Adult Primary Care Clinic), on the health status of patients and overall resource utilization by enrolled clinic patients within a tertiary care medical center.

Technical Approach: Approximately 100 patients from a pool of 14,500 being enrolled into the Adult Primary Care Clinic will be selected by random number table to provide the sample. The study will measure two main outcomes: 1) The health status of patients and 2) Hospital Resource Utilization using predetermined yardsticks. A 12 month retrospective and prospective chart review will be used to determine resource utilization.

Comparison of before and after rates of compliance will be analyzed by chi-square analysis for categorical variables. Analysis of resource utilization will be done by paired t-test and multiple linear regression.

Progress: Final data analysis was completed and a presentation was presented.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/048 **Status:** On-going

Title: The Effect of Left Ventricular Hypertrophy on Diastolic Function at Rest and After Exercise

Start Date: 12/16/94 **Est. Completion Date:** Sep 95

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: CPT Kenneth M. LeClerc, MC

Associate Investigators: CPT Stephen J. Fleet, MC; MAJ Patrick A. Cambier, MC; CPT Eric M. Osgard, MC

Key Words: Hypertrophy, diastolic function, exercise, rest

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate dastolic function in two populations with left ventricular hypertrophy (LVT) at rest, after acute exercise testing, and following aerobic exercise training.

Technical Approach: A predetermined number (15-50 per group) of younger subjects (<45 years of age) with either isolated pathologic LVH (i.e. attributed to a primary medical problem) or physiologic LVH (attributable to exercise training) will undergo elective echocardiographic evaluation at rest and immediately after maximal exercise testing. Measures of diastolic function wil be compared between these two groups. In addition, both groups will electively undergo a prescribed aerobic exercise program for 10 weeks and the effect on dastolic function will be re-assessed echocardiographically and differences within and between groups will be described. The echocardiographic studies will be analyzed by blinded observers for assessment of diastolic function using existing computerized analysis and compared using paired and unpaired T-tests.

Progress: 11 patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/091 **Status:** On-going

Title: Can Antibody Response to Pneumococcal Vaccination Be Enhanced by Pretreatment with Vitamin B12

Start Date: 04/19/96 **Est. Completion Date:** Oct 96

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: MAJ Emil P. Lesho, MC

Associate Investigators: COL Ronald H. Cooper, MC

Key Words: Penumococcus, vaccination, vitamin B12

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if prior treatment with cobalamin enhances immunogenic response to pneumococcal vaccination in immunocompetent patients.

Technical Approach: Patients who are determined to require pneumococcal vaccination as part of routine health maintenance will be asked if they wish to participate in a study to see if the effectiveness of the vaccination can be enhanced with vitamin B12. If so, informed consent will be obtained, and at least 40 patients will be randomized into 2 groups of 20 patients each. Overall nutritional, immunologic, vitamin B12 status will be assessed. One group will receive hydroxocobalamin injection, the other will receive sterile saline as the placebo. One to two weeks later, the patients will then have cobalamin levels reassessed to see if replacement was successful. Those in the treatment group will be given another dose of B12 along with their routine pneumococcal immunization. Those in the control group will be given the placebo along with the pneumococcal vaccine. One to two months after this, patients will then have quantitative pneumococcal serotype titers re-measured. ANOVA with pre and post antibody titers as the within groups variable will be primary method of data analysis. Nonparametric rank-sum test will be used to compare the differences in antibody titers between the two patient groups. Regression analysis in which the change in antibody titers is the outcome variable will also be used.

Progress: This protocol has not been started due to delays in obtaining funding.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/077 **Status:** Completed

Title: The Accuracy of pH Determination of Pleural Fluid by pH Paper as Compared to the Arterial Blood Gas Analyer - a Pilot Study

Start Date: 03/15/96 **Est. Completion Date:** Feb 97

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: MAJ Emil P. Lesho, MC

Associate Investigators: MAJ Bernard J. Roth, MC

Key Words: pH determinations, pleural fluid, pH paper, arterial blood gas analyer

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To access the accuracy of pH determination of pleural fluid using pH paper.

Technical Approach: At present, a complete power analysis cannot be performed due to insufficient raw data from previous studies. If unable to do a power analysis after additional data gathering efforts, this will be a pilot study of 25-50 patients. Patients who are determined to need thoracentesis as part of routine standard of care will have part of their pleural fluid sample sent to the respiratory care division to have the pH of the sample determined using an ABG machine. It will not be necessary to remove any additional fluid from the patient to do this, rather 0.2 ml from the fluid which has already been drawn off will be sent for ABG pH analysis. This data will be compared to the pH of the sample determined in the usual fashion by pH sensitive litmus paper. Data will be analyzed using the paired t-test and McNemar's test of correlated proportions.

Progress: Thirty subjects who underwent diagnostic or therapeutic thoracenteses as part of routine standard of care had two separate 1 cc aliquots of pleural fluid drawn. One sample had the pH measured using pHydron Vivid 6-8 brand litmus paper from MicroEssential Labs. The other aliquot had the pH measured using the blood gas analyzer. Mean pH values for the both of the two measurement techniques equated 7.35, but pH measured with pH paper was more variable (SD=0.41) than with the blood gas analyzer (SD=0.08). There was no significant correlation between values obtained with the two techniques over the pH range studied. These data indicate that the pH paper technique is associated with a high measurement error that hinders its capability to distinguish small differences in pH accurately. Results of this pilot study suggest that serious consideration should be given to changing the current method of measuring pleural fluid pH at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/105 **Status:** Completed

Title: Do Antibiotics Alter the Outcome of Ischemic Colitis?

Start Date: 06/21/96 **Est. Completion Date:** Jun 96

Department:
Medicine, Internal Medicine Service

Facility: MAMC

Principal Investigator: CPT Stephen M. Salerno

Associate Investigators:
LTC Robert H. Sudduth, MC
LTC Amy M. Tsuchida, MC
MAJ John G. Carrougher, MC
MAJ Kazunori Yamamoto, MC

Key Words: Colitis:ischemic, antibiotics, outcome

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the utility of antibiotic use in the therapy of ischemic colitis in two groups with varying clinical severity. As a secondary goal, the prevalence of clinical signs and symptoms and various laboratory parameters will be recorded.

Technical Approach: This is a retrospective case-control study comparing odds ratios for short term and long term complications of 100 patients receiving and not receiving antibiotics for endoscopically proven ischemic colitis. Subgroup analysis of patients with mild and severe initial presentations will also be performed. Patients charts will be screened for inclusion criteria. Data to be collected from acceptable cases will include antibiotics on admission and throughout stay, vital signs, blood work, electrolytes, presence of free air, presence of ileus, presence of peritoneal signs on exam, number of re-bleeding episodes in hospital, surgery, time to symptom resolution, time to discharge, ICU vs. ward hospitalization, complications up to one year from acute episode, and the number of units transfused. The chart will be classified as either severe ischemic colitis or mild ischemic colitis with either short term complications or long term complications. The Chi square test will be used to compare short and long term outcomes of patients who received and who did not receive antibiotics.

Progress: Sixty-six subjects were studied in a retrospective chart review. There was no significant difference in short term mortality, but a trend (not statistically significant) was noted in decreased complications in the subjects receiving antibiotics.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/037 **Status:** Completed

Title: A New Method of Diagnosing and Treating Patients With Dyspepsia and Antibodies to Helicobacter pylori

Start Date: 12/17/93 **Est. Completion Date:** Jan 95

Department: Medicine, Internal Medicine Service **Facility:** MAMC

Principal Investigator: CPT Garry H. Schwartz, MC

Associate Investigators:
LTC Amy M. Tsuchida, MC
CPT Thomas P. Peller, MC
CPT Eric J. Ormseth, MC
MAJ Michael F. Lyons II, MC
MAJ Kazunori Yamamoto, MC
LTC Gregory N. Bender, MC
LTC Robert H. Sudduth, MC

Key Words: dyspepsia, H. pylori, diagnosis, treatment

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To develop a cost effective algorithmic approach (ie. clinical pathway) that will predict which patients can be safely diagnosed and treated in a single outpatient visit for Helicobacter pylori induced symptoms of dyspepsia.

Technical Approach: Patients (300) with symptoms consistent with dyspepsia will be enrolled in the protocol. Patients will fill out a questionnaire designed to screen for those patients with symptoms consistent with dyspepsia. Those enrolled will all go through an esophageal-gastroduodenoscopy (EGD). Those patients with evidence of peptic ulcer disease will be so identified. Biopsies of gastric mucosa will be taken from all patients and sent to the lab for analysis of gastritis as well as for the presence of *H. pylori* using histologic methods. At endoscopy, biopsy material will also be tested for *H. pylori* using the CLO test. In addition, the ELISA and Flex Sure antibody tests for *H. pylori* will be performed. The patients will then be routed through radiology where they will receive an UGI barium study while at the same time a nasogastric tube (NGT) intubation of the esophagus and stomach and biopsies for *H. pylori* will be taken. Patients who do not have evidence of PUD, but with a positive diagnosis for *H. pylori*, will be randomized to four treatment arms each lasting two weeks. In the first, patients will be treated with the current standard at MAMC Gastroenterology Service, that being a two week course of amoxicillin and omeprazole. The second group of patients will be treated with a combination of metronidazole, peptobismal, and tetracycline plus omeprazole. Patients will be treated with omeprazole alone in the third arm, and in the fourth arm patients will be treated with a placebo. All patients will be treated for two weeks. Patients with evidence of PUD and with a positive diagnosis for *H. pylori* will be randomized to one of the first three treatment arms mentioned above. They will not be given a placebo. At the completion of the two week treatment all patients will then be given 28 days of ranitidine 150 mg twice daily, then 14 days of once daily treatment. Patients will then be followed at 2, 4, 8, 12, 20, 24, 28 and 32 weeks after treatment. A follow-up worksheet will be updated by the study coordinator. Follow-up serological blood test using the same *H. Pylori* antibody test will be performed. They will have a repeat EGD at 12 weeks after day #1 of treatment at which time they will have repeat biopsies for *H. pylori* and to assess ulcer healing if they originally had PUD. Data will be analyzed using Kappa test to determine sensitivities, specificities, and positive and negative predictive values.

Progress: Fifty-three subjects were studied. *H. pylori* is present in a significant number of patients with nonulcerative dyspepsia. While the use of noninvasive testing has proven to be accurate in patients with peptic ulcer disease, its utility in nonulcerative dyspepsia may be less reliable due to its lower sensitivity. Enzyme immunoassay and FlexSure HP appear to have similar detection rates for *H. pylori,* with FlexSure HP adding the advantage of being office-based, thus providing immediate results. An abstract has been accepted for presentation at the 1996 Army ACP Meeting.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/070 **Status:** On-going

Title: Optimal Bowel Preparation for Flexible Sigmoidoscopy: Hypertonic Phosphate Enemas with and Without Use of Oral Magnesium Citrate or Tap Water Enemas

Start Date: 02/16/96 **Est. Completion Date:** Mar 97

Department:
Medicine, Internal Medicine Service

Facility: MAMC

Principal Investigator: CPT Jeffrey S. Strong, MC

Associate Investigators:
CPT Eric M. Osgard, MC
MAJ John G. Carrougher, MC
LTC Robert H. Sudduth, MC
MAJ David J. Waddell, MC
LTC Amy M. Tsuchida, MC
MAJ Kazunori Yamamoto, MC

Key Words: Sigmoidoscopy, enemas:hypertonic phosphate, enemas:oral magnesium citrate, enemas:tap water

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of this project is to study the effect of addition of oral magnesium citrate to a standard two enema flexible sigmoidoscopy preparation, and to confirm prior work which has shown no advantage of a two enema preparation over a one enema preparation.

Technical Approach: A direct comparison of the commonly used regimens that are proposed in the current study has not been reported. A power analysis was performed using data reported comparing one verses two HPEs, again, which revealed no statistical difference. A 25% difference in rated preparation quality was felt to be clinically significant by the investigators, generating an estimate of 50 patients required per group, based on a total of 2 groups. Since this study will involve three groups, we estimate needing approximately 75-100 patients per group. We plan to perform an initial analysis after 75 patients are done in each group. The particular regimen that patients receive is dependent primarily on the institution to which they present. Thus, the regimen performed is based primarily upon the biases of the endoscopist or nurse educators. The proposed study should provide information upon which a scientifically based recommendation can be made regarding the need to perform an additional enema, or to add oral magnesium citrate.

Progress: To date, 110 patients have been enrolled and approximately 40 have completed the study. An abstract is to be submitted to the ACP reporting preliminary data of the first 37 patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/109 **Status:** On-going

Title: Coronary Artery Calcification Detected with Computed Radiography as a Marker for Obstructive Coronary Artery Disease

Start Date: 05/17/96 **Est. Completion Date:** Dec 96

Department:
Medicine, Internal Medicine Service

Facility: MAMC

Principal Investigator: LT Eric B. Stuart, MC

Associate Investigators:
MAJ Cristopher A. Meyer, MC
CPT Jeffrey S. Strong, MC
MAJ Michael D. Eisenhauer, MC
Douglas J. Collins, MD

Key Words: coronary artery disease, calcification, computed radiography

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To determine if chest radiography using a computed radiographic system (MDIS) can detect coronary artery calcification which correlates with significant coronary artery obstruction by cardiac catheterization. 2) To determine if non-radiologists can interpret a computed chest x-ray image for coronary artery calcification with a clinically significant level of accuracy.

Technical Approach: Approximately 200-300 patients presenting to the cardiology service who are referred for coronary catheterization will be asked to participate. All patients undergoing coronary angiography will have their screening computed chest radiograph reviewed for evidence of coronary artery calcification. During the coronary angiography procedure, just prior to the injection of radiocontrast dye into the coronary arteries, a fluoroscopic view of the heart will be recorded on film. The sensitivity and specificity of coronary artery calcification detected by computed chest radiography, by fluoroscopy, and by the combination of the two, will be compared to the detection of obstructive coronary artery disease by coronary angiography. Comparisons and likelihood ratios will be used to evaluate data and most will be presented in table format.

Progress: Five patients have been enrolled.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/007	**Status:** On-going
Title: Ophthalmic Anesthesia in Trigeminal Neuralgia		
Start Date: 10/20/95	**Est. Completion Date:** Oct 96	
Department: Medicine, Neurology Service	**Facility:** MAMC	
Principal Investigator: CPT Gary W. Beaver, MC		
Associate Investigators:	MAJ Eugene F. May, MC	
Key Words: Neuralgia, anesthesia, proparacaine		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To investigate the benefit of ophthalmic anesthesia in the treatment of trigeminal neuralgia.

Technical Approach: This study will be a double-blind, placebo-controlled trial at multiple military medical centers. Approximately 80 patients will be enrolled study wide, with 25 planned for entry at MAMC. Patients will be randomly assigned to either the test or placebo group. Two drops of either 0.5% proparacaine or saline will be placed onto the cornea ipsilateral to the neuralgia. Patients will receive an additional two drops on day 7 and day 14. Prior to treatment, each patient will be asked her/his frequency of pain attacks and pain severity, and patients will be contacted by phone on days 3, 10, and 30 to collect follow-up data on pain frequency and severity.

Progress: One patient has been enrolled. Accrual has been slower than usual plus the PI was in an off-site rotation for several months.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/019 **Status:** Terminated

Title: Use of CSF D-dimer Assay to Differentiate Subarachnoid Hemorrhage From Traumatic Lumbar Puncture

Start Date: 11/05/93 **Est. Completion Date:** Jun 94

Department:
Medicine, Neurology Service

Facility: MAMC

Principal Investigator: MAJ Michael A. Elliott, MC

Associate Investigators:
LTC William L. Clayton III, MC
Richard R. Larson, MT, AMT
CPT David J. Wilke, MC
MAJ David C. Lipps, MC
MAJ Mark D. Brissette, MC
CPT Dale T. Waldner, MC

Key Words: Assay:D-dimer, subarachnoid hemorrhage, lumbar puncture

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$100.00	**Periodic Review:** 09/30/96

Study Objective: To prospectively determine the sensitivity and specificity of the CSF D-dimer assay in differentiating subarachnoid hemorrhage from traumatic lumbar puncture.

Technical Approach: This study will analyze cerebrospinal fluid (CSF) and plasma samples from 100 patients with a clinical history suggestive of subarachnoid hemorrhage (SAH). A lumbar puncture is done as part of the standard diagnostic workup. The fluid will be tested for D-dimer, xanthochromia and cell counts in addition to routine chemistries. A D-dimer will be obtained simultaneously from a peripheral blood sample that is routinely obtained for PT/PTT. The diagnosis of SAH will be determined by a combination of results from CT, LP, neuroimaging, and autopsy, which will serve as our "gold standard". Traumatic LP will be determined by the findings as noted above, plus the absence of SAH by standard diagnostic means.

Progress: This study was terminated due to lack of subjects. Since the prevelance of this disease process is so small, it was felt that it would be impossible to generate enough data for analysis. Six subjects were enrolled before termination.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/053 **Status:** Completed

Title: The Clinical Significance of Unilateral Rebound Nystagmus

Start Date: 05/19/95 **Est. Completion Date:** Apr 95

Department: Medicine, Neurology Service **Facility:** MAMC

Principal Investigator: MAJ Linda A. Marden, MC

Associate Investigators: MAJ Eugene F. May, MC

Key Words: nystagmus:unilateral rebound, nystagmus:bilateral rebound

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To examine the clinical associations and localizing significance of unilateral rebound nystagmus.

Technical Approach: A review of 149 subjects with unilateral rebound nystagmus (URN) on neuroophthalmologic examination will be peformed. These subjects will be divided into groups with URN from the right side or URN from the left side.Other abnormalities found on neuroophthalmologic examiniation will be analyzed for each group of patients. Additional clinical information will be obtained from records review, including imaging study results, presenting symptoms, known diagnoses, and will be analyzed for trends. This information will be analyzed descriptively to correlate localizing information and associated occular motility findings.

Progress: No further records were reviewed in FY 96. Data analysis suggests that unlike bilateral rebound nystagmus, which is highly correlated with cerebellar disease, the presence of unilateral rebound nystagmus is more likely a sign of brainstem pathology. The correlation of unilateral rebound nystagmus with headshaking nystagmus, primary position nystagmus, and unilateral gaze-evoked nystagmus, all in the same direction, suggests a common etiology, most likely an asymmetry in the function of the brainstem vestibular system. Data analysis is complete and a manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/063	**Status:** Completed
Title: Familial Syndrome of Nystagmus Without Episodic Symptoms: Description of Two Families		
Start Date: 02/16/96	**Est. Completion Date:** Apr 96	
Department: Medicine, Neurology Service	**Facility:** MAMC	
Principal Investigator: MAJ Eugene F. May, MC		
Associate Investigators: CPT David J. Wilke, MC	LTC William F. Coughlin III, MC Stephen J. Peroutka, M.D., Ph.D.	
Key Words: Nystagmus:familial, genetics		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the neurologic, eye movement, neuroradiologic, and genetic findings in two families affected with an autosomal dominant nystagmus syndrome and to explore its clinical and genetic relationship with other familial nystagmus syndromes.

Technical Approach: This study will involve 10 subjects in two families; 6 are known to have nystagmus; 3 do not have nystagmus; the status of one subject is unknown. The study will obtain historical, ocular motility, genetic and neuroimaging data on these family members. Historical data will be collected by interviewing each family member to obtain evidence of a history if migraines, attacks of vertigo, or symptoms suggestive of central nervous system disease. Ocular motility examination will include clinical assessment of primary-position, gaze evoked, headshaking, and rebound nystagmus; saccades; smooth pursuit; vestibulo-ocular reflex (VOR); and vestibulo-ocular reflex suppression (VORS). DNA linkage analysis will also be performed on all consenting family members. Three samples of blood (4cc each) or a single buccal swab will be collected on each individual and sent to Spectra Biomedical, Inc. Spectra Biomedical will utilize microsatellite markers and the polymerase chain reaction to perform the DNA linkage analysis. Microsatellite markers have been selected based on the suspected region of the FHM gene on chromosome 19. Lod scores, or the logarithm of the odds that two loci are linked, will then be calculated for each marker. Magnetic Resonance Imaging will consist of saggital and axial T1-weighted images through the posterior fossa of each patient using 5 mm cuts. The subject's scans and control scans will be analyzed independently by three neuroradiologists on the staff at MAMC.

Progress: Evaluation of eye movements has been performed on six affected members of two pedigrees. Affected family members had downbeating nystagmus, gaze evoked nystagmus in all directions, and rebound nystagmus. Vestibulo-ocular reflex and its cancellation, optokinetic nystagmus, and smooth pursuit were impaired. In one pedigree, low frequency vestibulo-ocular reflex gain was increased. MRI's showed mild vermian atrophy. Genetically, there did not appear to be linkage to the familial hemiplegic migraine (FHM)/hereditary paroxysmal cerebellar ataxia (HPCA) region of chromosome 19. The investigators conclude that autosomal dominant syndrome of vertical and horizontal nystagmus is likely caused by dysgenesis or degeneration of the vestibulocerebellum. Although the ocular motility pattern in this cerebellar syndrome is identical to that in FHM and HPCA, it appears to be genetically distinct.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/129 **Status:** Suspended

Title: The Assessment of Motor Recovery After Stroke Induced Hemiplegia

Start Date: 08/05/94 **Est. Completion Date:** Aug 94

Department: Medicine, Neurology Service **Facility:** MAMC

Principal Investigator: MAJ Jonathon Newmark, MC

Associate Investigators: CPT Eric I. Hassid, MC

Key Words: hemiplegia, stroke, motor recovery

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: We hope to determine whether or not there exist certain consistent patterns of motor recovery after stroke. We also hope to be able to prognosticate about extent of motor recovery with relation to lesion site and size.

Technical Approach: Select patients from the neurology service who have sustained their first non-hemorrhagic stroke affecting motor function will obtain an MRI of the brain at about the 7 day post event mark for purposes of accurate neuroanatomical localization. These patients will be evaluated weekly to assess motor recovery. No additional studies which would not be part of good stroke care will be done. Clinical and statistical significance will be done by a statistician. The initial data analysis will be longitudinal, modeled upon that of Twitchell. Should trends develop of statistical significance, standard tests including ANOVA will be used as data points.

Progress: Patient accrual may or may not have added more than the 12 subjects that were entered the previous fiscal year. The PI has been on extended TDY and is attempting to figure out the data that had been collected while he was gone.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, PULMONARY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/099 **Status:** On-going

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

Start Date: 08/17/90 **Est. Completion Date:**

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: CPT Donald M. Collins, MC

Associate Investigators:
MAJ Bernard J. Roth, MC
LTC William H. Cragun, MC
CPT Stephen M. Salerno

Key Words: pleural effusion,albumin,congestive heart failure

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: 6 subjects have been entered onto protocol in FY 96, for a total of 14 subjects.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/029 **Status:** On-going

Title: A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation

Start Date: 12/17/93 **Est. Completion Date:** May 94

Department: Medicine, Critical Care Svc **Facility:** MAMC

Principal Investigator: CPT Kurt W. A. Grathwohl, MC

Associate Investigators:
MAJ George N. Giacoppe Jr., MC
CPT Jeremy R. Blanchard, MC
MAJ James D. Pike, MC
MAJ Francis J. Landry, MC
MAJ Lewis L. Low, MC

Key Words: ventilation, airway occlusion pressure

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The main objective of this study is to ascertain the usefulness of the PO.1 as a weaning parameter in predicting success or failure of patients upon extubation. The secondary objective is to validate the Rapid Shallow Breathing Index as described by Yang and Tobin.

Technical Approach: Weaning parameters will be obtained and documented by a Respiratory Care Practioner (RCP) on patients in the surgical and medical ICU at MAMC. Individual progress toward weaning and extubation will be determined by the primary physician/team. When it is determined the patient is ready for extubation, a second set of weaning parameters will be obtained immediately prior to extubation. Weaning parameters will only be collected on patients at rest and who have not been stimulated within the prior 10 minutes. The parameters will be obtained by utilizing the Respiratory Mechanics Package on the Infrasonics Adult Star as required by MAMC policy. Only the data obtained from patients on the Infrasonic Adult STAR mechanical ventilator will be used so that our results are reproducible since other available ventilators do not easily measure the PO.1. The first 50 patient's will be used to form ROC curves to develop threshold values for the prediction of success or failure of extubation which can then be prospectively applied. A successful weaning/extubation will be defined as one in which the patient does not have to be reintubated within 24 hours.

Progress: No more patients were entered in FY 96. Approximately 70 had been entered in previous years. The PI does not plan to enter more patients; however, he has requested that the protocol be left open so that he can perform the data analysis in FY 97.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/146 **Status:** Completed

Title: Videoscopic Placement of Feeding Tubes: Development of a Through the Tube Technique

Start Date: 06/16/95 **Est. Completion Date:** May 98

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: CPT Kurt W. A. Grathwohl, MC

Associate Investigators:
CPT James W. Thompson, MC
MAJ Bernard J. Roth, MC
LTC Thomas A. Dillard, MC
CPT Robert V. Gibbons, MC
CPT James D. Horwhat, MC
MAJ Patrick A. Cambier, MC

Key Words: Feeding tubes: videoscopic placement, through-the-tube technique

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe a new technique for placement of small bowel feeding tubes.

Technical Approach: Ten ICU patients will be studied. An angiofiberscope (Olympus AF 22A) is placed through the center of a Corpak 10 F feeding tube which will be inserted under direct videoscopic guidance through the mouth or nose, into the esophagus and stomach. Thirty ml of viscous lidocaine or cetacaine spray will be used per standard procedure to provide local anesthesia of the mouth, pharynx and hypopharynx. The subject will be initially placed into Fowlers position and subsequently may be positioned into the lateral decubitus position. Air will be insufflated through the feeding tube into the stomach to allow visualization of the characteristic stomach anatomy. Using the deflectional capability of the angioscope, the tube/scope system will be advanced until the pylorus is identified. Once the pylorus is identified, the feeding tube will be advanced into the small bowel. Placement of the tube will be confirmed by the characteristic valvulae conniventes of the duodenum. A radiograph will be performed to confirm positive placement in the small bowel.

Progress: Eight healthy volunteers (Group 1) and 9 critically ill patients (Group 2) were studied. A total of 19 feeding tubes were placed; two Group 2 patients had feeding tubes placed on two separate occasions. Enteric structures were visualized clearly through the feeding tube. Based on visual landmarks, the feeding tube was advanced through the pylorus and into the duodenum. Transpyloric tube placement was confirmed videoscopically and radiographically. In three Group 1 subjects, the feeding tube entered the first part of the duodenum and in the remainder it passed into or beyond the second portion of the duodenum. In 8 of 11 attempts on the Group 2 patients, the feeding tubes were advanced to the distal duodenum or jejunum. The time required for Group 2 ranged from 2-43 minutes with a mean of 18 minutes. The feeding tubes remained in place 10 ± 4 days and patients met their estimated caloric needs within 24 hours. Residuals were < 5 ml. There were no episodes of aspiration. This new technique has the potential for rapid, accurate, and safe feeding tube placement.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/138 **Status:** On-going

Title: Active Inspiration/Expiration versus Tidal Volume Breathing During Transbronchial Biopsy

Start Date: 08/16/96 **Est. Completion Date:**

Department:
Medicine, Pulmonary Service

Facility: MAMC

Principal Investigator: CPT Kurt W. A. Grathwohl, MC

Associate Investigators:
MAJ Bernard J. Roth, MC
LTC Thomas A. Dillard, MC
MAJ Timothy R. Murray, MC
Suzette Gagnon-Bailey, M.D.

Key Words: Transbronchial biopsy, inspiration,expiration breathing method, tidal volume breathing method

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare to yield, results and complications of two currently used techniques for transbronchial biopsy.

Technical Approach: All patients referred in the pulmonary clinic for bronchoscopy will be enrolled. Bronchoscopy will be performed in the usual manner. Patients will have a minimum of 6 transbronchial biopsies performed. They will be randomized to have the first three biopsies performed by either the active inspiration/expiration method or the tidal volume breathing method. After 3 biopsies are performed, the patient will be crossed over to the method not previously performed to obtain the next three biopsies. If more biopsies are needed, the attending physician can utilize any method at their discretion although the subsequent biopsy samples will not be included in data analysis. The attending pulmonologist or nurse will record the number of attempts for each and the appearance and quantity of sample grossly. Hemorrhage, pain, dyspnea, change in vital signs, and need for stopping the procedure will be recorded after each attempt. Two containers will be identified to the investigators although the examining pathologist will be blinded to the method performed. The pathologist will identify the number and size of samples in each as well as note the presence of alveolar tissue and the pathologic diagnosis if any. We will enroll 100 patients over one year. The differences between number of adequate samples and size will be compared using the paired student t-test. Other variables such as presence of alveoli and presence of complications (i.e. chest pain, bleeding, dyspnea, etc.) will be compared using the chi square test.

Progress: The protocol has just been started. One subject has been entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/162 **Status:** Completed

Title: Exercise Capacity Following Radiation Therapy in Patients With Stages II and III Non-small Cell Lung Cancer

Start Date: 09/03/93 **Est. Completion Date:** Jun 95

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Timothy R. Murray, MC

Associate Investigators: MAJ Rahul N. Dewan, MC; MAJ Bernard J. Roth, MC; LTC Steven S. Wilson, MC

Key Words: cancer:lung, radiation therapy, exercise capacity

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$6390.00	**Periodic Review:** 09/30/96

Study Objective: To study the physiologic effect of therapeutic radiation of the lung on exercise capacity in patients with stage II or III non-small cell lung cancer.

Technical Approach: All subjects will be evaluated within two weeks of initiation of radiation therapy (RT) and then 3, 6 and 12 months after initiation of RT. At each visit the subject will receive a brief history and physical exam and be asked to complete a questionnaire that will subjectively assess functional status. This data will be assessed and compared to objective data obtained from an exercise test conducted on a stationary, calibrated and electronically braked cycle. At exercise testing, subjects will be assessed at rest and at incremental work rates increasing at a fixed rate to between 20 and 50 watts per minute. Inhaled and exhaled gases will be measured. Vital signs will be documents every 20 seconds during exercise. Radiation treatment history will include total dose and calculation of lung volume irradiated.

Data will be examined for interval changes and correlated with radiation dose. A subset analysis will be attempted on patients receiving chemotherapy.

Progress: Fourteen patients were entered. Significant changes in maximal oxygen consumption and pulmonary function were identified. The trend of rising V_e/Vco_2 at anaerobic threshold with stable V_e suggests increased alveolar dead space and falling Vo_2/hr suggests decreased cardiac stroke volume. These findings imply a multifactorial etiology to the decreased exercise performance seen following therapeutic radiation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/004 **Status:** On-going

Title: Controlled Prospective Evaluation of Intrapulmonary Percussive Ventilation with Standard Chest Physiotherapy

Start Date: 10/20/95 **Est. Completion Date:** Dec 97

Department:
Medicine, Pulmonary Service

Facility: MAMC

Principal Investigator: Nora A. Regan

Associate Investigators:
Michael G. Winter, RRT
MAJ Timothy R. Murray, MC
LTC Thomas A. Dillard, MC

Key Words: Pulmonary percussive ventilation, standard chest physiotherapy, secretions, atelectasis, complications

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/18/96

Study Objective: To compare the effectiveness of Intrapulmonary Percussive Ventilation (IPV) with standard Chest Physiotherapy (CPT) for treatment of lobar atelectasis or secretion mobilization in patients with compromised clearance mechanisms.

Technical Approach: Two hundred patients having immobile airway secretions who are ordered for CPT will be randomly assigned to receive either standard CPT or IPV therapy. IPV therapy is the delivery through the mouth of high-frequency oscillations in air flow, combined with in-line nebulization of beta agonist or normal saline. Major endpoints will be spirometry parameters, oxygenation, sputum production (amount and characteristics) and radiographic changes as well as duration of treatments and RT workloads.

Progress: Five patients have been entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/011 **Status:** Terminated

Title: The Short-Term Use of a Helium-Oxygen Mixture in Adults Hospitalized with Acute, Severe Asthma

Start Date: 10/20/95 **Est. Completion Date:** Feb 96

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Bernard J. Roth, MC

Associate Investigators: CPT James W. Thompson, MC; LTC Edward R. Carter, MC

Key Words: Asthma, helium-oxygen, short term

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to determine whether the inhalation of a helium-oxygen mixture (heliox) will improve pulmonary function and respiratory clinical status in adults hospitalized with severe asthma.

Technical Approach: We plan to enroll 15 subjects in this randomized, double blind, prospective, crossover study. Patients between 18-75 years of age admitted to the hospital for treatment of asthma will be asked to participate. The patients will be stabilized, and baseline pulmonary function tests, clinical score, heart rate, and pulsus paradoxus will be recorded. They will then be randomized to inhale either 30%oxygen-70%helium gas mixture or 30%oxygen-70%nitrogen (oxygen enriched air) first. After breathing the first gas via a face mask for 20 minutes, pulmonary function testing, assessment of clinical score, pulsus paradoxus and the other measurements will be repeated again. After a 10 minute period patients will then breath the second gas mixture for 20 minutes, and all the measurements will be repeated. After stopping the second gas mixture patients will rest for another 20 minutes, and all measurements will be measured for a 4th and final time. The patients, their families and all health care professionals with the exception of the respiratory therapist will be blinded to the order of administration of the two treatment regimens. Differences in continuous variables (i.e. FEV1 and heart rate) will be analyzed with the two sample Student t-test, and difference in clinical scores (mean) will be assessed with the Wilcoxon rank sum test.

Progress: This protocol was originally submitted by Dr. James Thompson who was reassigned before the study began. Dr. Roth assumed the role of PI hoping that a new resident or fellow would wish to continue the protocol. It has been terminated since he has been unable to find a new PI. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/015 **Status:** On-going

Title: Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure

Start Date: 12/07/90 **Est. Completion Date:**

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Bernard J. Roth, MC

Associate Investigators: MAJ Bruce S. Grover, MC; LTC William H. Cragun, MC

Key Words: positive pressure ventilation,air flow obstruction,nasal mask

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$260.00	**Periodic Review:** 09/30/96

Study Objective: To determine if one eight hour period per week of ventilatory rest via nasal mask positive pressure ventilation will improve pulmonary function and exercise tolerance in patients with chronic air flow obstruction and chronic respiratory failure marked by an elevated arterial carbon dioxide.

Technical Approach: The study population will be both sexes, age >18 years, with severe COPD. The following baseline values will be obtained: age, weight, height, smoking status, medication list, chest x-ray, spirometry, formal lung volumes, MIP, MEP, DLCO, arterial blood gas measurement, pulse oximetry, end-tidal capnography, thyroid function tests, CBC, electrolytes, Karnofsky scale, dyspnea index, and 12 minutes walking distance. Spirometry, pulse oximetry, and end-tidal capnography will be repeated once weekly for four weeks. After four weeks, baseline studies will be repeated and an overnight polysomnography will be performed which includes electroencephalogram, electromyogram, electro-oculogram, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous capnograpny. At this time the patient will be tested to determine if he tolerates intermittent positive pressure ventilation through a nose mask (nIPPV). Patients who tolerate nIPPV will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAP and nIPPV patients using Student's T-test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or $PaCO_2$ will be considered a positive result of nIPPV.

Progress: No new patients were entered in this study during FY 96 due to a lack of personnel to assist in the study. Six patients have been entered in previous years.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/110 **Status:** Completed

Title: The Specificity of Methacholine Challenge in ROTC Cadets

Start Date: 05/17/96 **Est. Completion Date:** Jun 96

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Bernard J. Roth, MC

Associate Investigators: LTC Thomas A. Dillard, MC
Lynn Hammers

Key Words: Asthma, methacholine, ROC cadets

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine how often ROTC cadets who do not give a history suggestive of asthma have a positive methacholine challenge.

Technical Approach: We propose to have 2 cadets who have a negative history and physical exam be sent with every cadet who has a history suggestive of asthma to determine the potential false positive rate of the methacholine challenge. They would be sent to pulmonary with a consultation stating "R/O Asthma". The principal investigator would then ask the next 2 cadets with normal history and physicals if they would like to participate in the study. Serial cadets will be asked until 2 are found willing to participate. They will also be sent to the Pulmonary Clinic with consultations stating "R/O Asthma". The Cadets, both patient and controls, will be identified by a number and will present to the Pulmonary Clinic with that number only and not their name. On arrival to the Pulmonary Clinic, the cadets will be asked to fill out a questionnaire on asthma symptoms and known causes of a false positive methacholine challenge. They then will get spirometry and a bronchodilator trial if obstructed, or a methacholine challenge if spirometry is normal. The control Cadets will be released from the clinic without ever identifying them by name or sharing results of their test with them. The actual patients will be identified by name and interviewed with the results of their pulmonary function tests. The number of positive challenge tests in control cadets will be determined and the questionnaire data will be compared to see if any historical data were predictive of a positive test.

Progress: Seventy-one control patients had the methacholine challenge, and 14% had positive tests. Data analysis is nearing completion. The data are being analyzed to test correlation of positive tests with positive responses or questionnaire, but no correlation is expected.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/172 **Status:** On-going

Title: The Value of Questionnaire Responses and Body Measurements in the Prediction of Obstructive Sleep Apnea in a Young Physically Fit Population

Start Date: 09/15/95 **Est. Completion Date:** Jun 96

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Bernard J. Roth, MC

Associate Investigators: MAJ Joseph D. Kern, MC; Vishesh Kapur, M.D.

Key Words: Sleep apnea, questionnaire. body measurements

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study has two primary aims: to determine the prevalence of various symptoms and their specificity in obstructive sleep apnea syndrome (OSAS), and to examine the association of neck circumference, body mass index (BMI) and specific symptoms with sleep disordered breathing. Secondary aims are to determine if hypothyroidism needs to be excluded in individuals from this population being evaluated for OSAS, and to estimate period prevalence of OSAS in this population.

Technical Approach: Consecutive patients between the ages of 18 to 35 referred to MAMC for polysomnography will be eligible for inclusion in this cross sectional study. 200 eligible consenting participates will complete a symptom questionnaire and undergo a brief examination that includes neck circumference, blood pressure, weight and height measurements, and have serum thyroid stimulating hormone (TSH) evaluation prior to overnight polysomnography. An equal number of controls randomly sampled at routine health visits will complete the symptom questionnaire and have neck circumference, weight and height measurements performed. Questionnaire responses and anthropometric measurements will be compared between patients with OSAS and patients without OSAS and controls using the student's t-test at α=0.05. Sensitivity and specificity will be calculated for questionnaire responses. Questionnaire responses along with BMI, neck circumference (corrected for height), and hypertension will be evaluated using multiple linear regression techniques using apnea hypopnea index as the dependent variable. In addition, each of these factors will be evaluated individually by simple linear regression. The r and slope obtained for corrected neck circumference and BMI from linear regression will be compared with previously published estimates from other populations using the t-test. The prevalence of hypothyroidism in all patients evaluated by polysomnography and just those with OSAS will be compared to the estimated prevalence in this age group (0) and the prevalence at a which screening for hypothyroidism is commonly recommended (2-5%) using the student's t-test. A period prevalence will be calculated by dividing the number of cases detected in one year by the total referral population.

Progress: Fifty patients have been entered in the study, all in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/024 **Status:** On-going

Title: Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging

Start Date: 01/03/92 **Est. Completion Date:**

Department: Medicine, Pulmonary Service **Facility:** MAMC

Principal Investigator: MAJ Bernard J. Roth, MC

Associate Investigators:
LTC Miquel J. Rovira, MC
MAJ Frank A. Zimba, MC
MAJ Kevin L. Quinn, MC
LTC Steven S. Wilson, MC

Key Words: cancer, bronchogenic, MRI

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the incidence of clinically occult brain metastasis in patients with resectable primary bronchogenic carcinoma.

Technical Approach: The subjects (100) for this protocol will be patients >18 years of age with primary bronchogenic carcinoma, Stage IIIa or less as determined by chest CT, who are neurologically intact. The patient will undergo a complete clinical neurological history and physical exam and enhanced cranial MRI to screen for brain metastasis. Patients with evidence of significant CNS pathology will be divided into four groups: (1) solitary lesion amenable to neurosurgical resection (2) significant brain pathology other than metastatic disease that would delay or preclude therapy (3) brain metastasis and (4) metastasis outside the brain. Patients in group 1 or 2 will undergo neurosurgical and/or radiation therapy evaluation for possible curative or palliative therapy. Patients in group 3 or 4 will undergo radiation therapy and/or hematology-oncology evaluation for possible palliative therapy. Patients in whom MRI revealed suspicious areas which are not definitely characteristic for metastasis will undergo brain biopsy using stereotactic localization. Patients refusing brain biopsy will be followed closely with periodic follow-up enhanced cranial MRI every three months. MRI and clinical data will be evaluated to determine the overall incidence of clinically occult brain metastases and the presence (if any) of any significant differences among primary cell types.

Progress: Six additional patients were entered in this study for a total of 30 subjects. The accrual goal is 50 subjects. WRAMC has been added as a site to assist in accrual of sufficient patients.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF NURSING

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/016	**Status:** Completed
Title: Postsurgical Temperature Trends		
Start Date: 11/17/95	**Est. Completion Date:** Jun 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: CPT Julie M. Acarregui-Garrett, AN		
Associate Investigators: CPT Michael P. Garrett, AN	CPT John E. Dulaveris, AN 1LT Julie A. Klaus, AN	
Key Words: Temperature, postsurgical, abdominal laparoscopy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to identify if there is a significant temperature change during the transport period form the OR to the recovery room.

Technical Approach: Our study will focus on the temperature changes during the transport period to determine if a significant decrease in temperature occurs. This will be a non-experimental descriptive study that will observe temperatures in male and female patients undergoing abdominal laparoscopic surgery between 18 and 60 years of age. The patients will be of the ASA I or II classification and a convenience sample size of 60 will be used. Descriptive statistics will be used to analyze the temperature data. Means and standard deviations will be calculated for the following time periods: immediate post-surgical (baseline), post-extubation, pre-transport and post-transport to the PACU. The dependent variable is temperature and the independent variable is time. The study will use repeated measures ANOVA for analysis. The strengths of this design are repeated measures and subjects serving as their own control. The outcome for the hypothesis will be categorized in the form of either "accept" or "reject" the null hypothesis. Statistical significance will be set at $p \leq 0.05$.

Progress: The study has been completed and a thesis has been successfully defended at the University of Texas Health Sciences Center at Houston. The data collection tool, which was designed specifically for this study, functioned well. The study design was thorough and operationally performed as anticipated. Fifty four females and six males were studied. Repeated measures ANOVA failed to demonstrate statistical significance when analyzing change in temperature over time; however, a downward trend in temperature over time was noted. There was a minimal temperature decrease during the postoperative period, which the investigators suggest could be caused by maintenance of patient temperature intraoperatively >35° Celsius and the relatively short transport time to the PACU. A paper was presented to the national, as well as the state, Association for Nurse Anesthetists Annual Convention.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/154	**Status:** Completed
Title: A Descriptive Study of the Development of Critical Pathways in the Perioperative Nursing Department in Two Pacific Northwest Hospitals		
Start Date: 08/18/95	**Est. Completion Date:** Sep 95	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: CPT Barbara J. Acselrod, AN		
Associate Investigators: None		
Key Words: Critical pathways: perioperative nursing		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study is concerned with discovering what steps are used by perioperative nursing departments in the development of critical patnways. In addition, the study is concerned with the relationship, if any, between the actual steps used and written literature on the subject. Further, a final concern is what influence did any standard have on the development of critical pathways (example AORN standards)

Technical Approach: This study is a description of the development of critical pathways in the perioperative nursing department in two Pacific Northwest hospitals. The purposes of the study were to describe the development of critical pathways in the perioperative nursing department of an acute care hospital and to campare the development of critical pathways to the current literature on the subject. Data collected were examined from the perspective provided by an integrated model based on systems theory and the New England Medical Center Hospital's "Nursing Case Management Model".

The study used a jpurposive convienience sample of two perioperative nursing departments. Participants were the individuals designated as coordinators for the development of critical pathways within the departments. Data were collected through face-to-face interview and analysis of documents within a comparative case study design. The actual development of critical pathways was compared to principles and prescriptions for developing critical paths as reported in the literature.

Progress: Study results revealed that perioperative nursing departments are developing critical pathways based on limited non-empirical research and published literature. Coordinator/developers are using other bases for development such as experience, focus panel "lessons learned," and non-published "how to develop" instructional guides. The Joint Commission on Accreditation of Health Care Organizations and other standards have indirect influence on the development of the critical pathways method. Investigation revealed that the development of critical pathways within the perioperative nursing department is both consistent and inconsistent with the cited literature on the subject.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/106 **Status:** Completed

Title: Family Home Visitation Program: The Nurse as Coach

Start Date: 05/07/93 **Est. Completion Date:** Jul 95

Department: Nursing **Facility:** MAMC

Principal Investigator: MAJ Kimberly K. Armstrong, AN

Associate Investigators:
Frances M. Lewis, RN, Ph.D.
MAJ Stacey B. Young-McCaughan, AN
Diane D. Stajduhar, RN
Sandra L. Underhill, RN, Ph.D.
1LT Barbara F. Wall, AN

Key Words: Cancer: breast, home visitation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To test the effectiveness of a home intervention program for child-rearing families experiencing non-metastatic breast cancer in the mother; (2) to test a causal model of nurses' coaching behavior underlying the intervention; (3) to test the cost-effectiveness of the intervention.

Technical Approach: Subjects will be recruited whose mothers were recently diagnosed (6 months or less) with early stage breast cancer and have had either breast conserving surgery or simple modified mastectomy. Subjects will be living in a partnered relationship and have 1 or more school-age children living at home. A total of 100 families will be recruited and randomly assigned to either the Experimental or Control group.

The Experimental Group will receive home visits and the Control or Evaluation Group will receive "treatment as usual" from physicians and clinic nurses. The initial visits (by the Nurse Coach Team) will last one to one and one half hours, on 3 occasions, during which time experienced nurses will talk about the breast cancer, the concerns or issues related to it, and ways which might prove helpful in managing the experience. Each visit will include a joint session, individual sessions and a concluding joint session with the mother and partner.

The Couples' Evaluation Team Visits are made on four occasions. Each visit from that team will involve the completion of questionnaires and an interview about their experiences as a result of the breast cancer. After permission is granted the school aged children living at home will be asked to complete several questionnaires about self esteem and their relationships with their parents and friends.

The outcome analysis will employ multivariate analysis and which can detect differences between the Experimental and the Control groups.

This study will be conducted in conjunction with the University of Washington.

Progress: The study has been closed. Two subjects were entered from MAMC. The results of data analysis are not known.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/123	**Status:** Completed
Title: Intensive Care Unit Nurse Perceptions of the Graphical User-Interface to Support Medication Record Retrieval Tasks		
Start Date: 06/21/96	**Est. Completion Date:** Jun 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: MAJ Robert L. Boucher, AN		
Associate Investigators:	Libertad B. Rovira, RN, BS, MN(C)	
Key Words: Nurses, medications, computer interface		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The research questions in this proposed study are: 1) What are the perceptions of intensive care unit (ICU) nurses of the graphical user-interface (GUI) to support medication record retrieval tasks; and (2) What nurse characteristics are related to nurses' perceived scores of (a) the graphical user-interface, (b) the two primary tasks related to retrieving the medication record, and (c) the ten sub-tasks related to retrieving the medication record.

Technical Approach: A convenience sample of 30 registered nurses (RN's) across three critical care units (ICU, IMCU & CCU) will be surveyed to evaluate their perceptions of Clinicomp's graphical user-interface used to support the medication administration process. Critical care nurses will be asked to assign a usability rating (e.g., 1=least helpful; 2=minimally helpful; 3=moderately helpful; 4=somewhat helpful; 5=most helpful) to sub-tasks required to complete the retrieval of a patient's medication record. Data collected will be recorded by the investigator using the GUI Usability Rating survey as the nurse is retrieving the medication record from the clinical information system (CIS) in real-time (e.g., while using). In addition, a set of nursing characteristics (e.g. previous computer experience, age, etc.) of each RN will be collected to compare with the usability ratings of the graphical user-interface. This process is expected to take approximately 45 minutes per RN subject. Data will be extracted from the RN demographic survey and the GUI Usability Rating survey. Data from the RN demographic survey will be used to develop categories for comparison of RN characteristics and usability responses. The GUI Usability Rating survey includes an ordinal rating scale in which participants are asked to rate each computer interface action as to the extent of it's helpfulness in retrieving the medication record. Frequency distribution will be used to display the data according to the purposes of this study. Content analysis will be used to analyze participant's self-reported data in the "explain rating" column of the GUI Usability Survey.

Progress: Thirty ICU nurses were studied. Study findings indicate that ICU nurses have positive perceptions toward the GUI as a support for medication record retrieval tasks. Total perception scores across 18 sub-tasks ranged from moderately helpful to most helpful. Of the 18 sub-tasks, total perception scores of six frequently performed sub-tasks ranged from moderately helpful to somewhat helpful. The only statistically significant relationship was between years using the clinical information system and sub-task 3 (find medication record). Other findings reported nurses' perceived barriers with direct access to the PRN medication record.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/100 **Status:** On-going

Title: Postoperative Wound Healing: Hydration and Oxygenation

Start Date: 05/06/94 **Est. Completion Date:** Oct 96

Department: Nursing **Facility:** MAMC

Principal Investigator: Stacey L. Heiner, BSN, RN

Associate Investigators:
Lori A. Loan, MSN, RNC
LTC Brenda I. Mygrant, AN
LTC Blaine R. Heric, MC
JoAnne D. Whitney, Ph.D., RN
COL Daniel G. Cavanaugh, MC
LTC Pamela J. Hildreth, AN
Diane M. Pierson, BS, BA, CCRN

Key Words: wound healing:hydration, wound healing:oxygenation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/17/95

Study Objective: To (1) Compare an augmented fluid replacement protocol to a conventional fluid replacement protocol after open-heart surgery for its effects on: a. subcutaneous tissue oxygen levels; b. subcutaneous tissue perfusion; and c. wound healing indicators in wound tissue samples including: 1) hydroxyproline accumulation measured by high pressure liquid chromatography; and 2) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation on postoperative day 7.

Technical Approach: This is a randomized 2 group (80 subjects per group) experimental design. The control group will receive the standard protocol for postoperative intravenous fluid. The experimental group will receive fluid augmentation with an additional intravenous infusion of 20 cc/hr of 5% Dextrose in water. The biochemical and cellular markers of healing will be measured 7 days postoperatively. The tissue indicators of oxygen and perfusion will be measured on the day of surgery and for the next 2 postoperative days. Sternal and leg wound assessments will be made for the first five days during hospitalization. For subjects discharged before the 7th postoperative day the ePTFE implant will be removed on the 7th postoperative day during a clinic visit. Descriptive statistics (mean, standard deviation) will be used to summarize sample description variables. Student's t-tests or chi-square analysis will be performed on the variables measured pre-intervention to ensure randomization of the two groups.

Progress: A no cost extension has been approved by the Tri-Service Nursing Research Group through 30 Sep 97. Subject recruitment and data collection will continue until approximately 31 Jul 97. Ninety four (94) subjects have been enrolled; 8 have been dropped. Five subjects became ineligible due to surgical complications not related to the protocol. Two subjects were dropped due to equipment problems and another returned home to Alaska. Data collection on patients enrolled to date is complete, HPLC analysis and histologic evaluation of patches are currently underway.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/112	**Status:** On-going
Title: Wound Healing: The Effect of Supplemental Oxygen Therapy		
Start Date: 05/17/96	**Est. Completion Date:** Sep 97	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: Stacey L. Heiner, BSN, RN		
Associate Investigators: Lori A. Loan, MSN, RNC	JoAnne D. Whitney, Ph.D., RN LTC Brenda I. Mygrant, AN	
Key Words: Wound healing, oxygen therapy		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The aim of nursing research is to maximize positive patient outcomes through research-based nursing interventions. This study will provide a foundation of developing nursing standards based on evaluation of the independent variable, inhaled supplemental oxygen, and it's role in wound healing. Wound healing, a complex phenomenon involving modiable and non-modiable person variables, can be affected by research-based nursing interventions.

Technical Approach: The proposed pilot study utilizes a randomized, two group experimental repeated measures design. subjects are randomly assigned to either the control or the intervention group using computer generated random number blocks of 6. This assures that there are not large imbalances between groups at any point in the study. The control group will receive only room air, which is current standard therapy. The intervention group will receive supplemental oxygen at 28% in the form of 2 liter per minute via nasal cannula for 36 hours postoperatively. Subjects will be randomized upon admission to the surgical ward. Subjects will be recruited from those who undergo cervical fusion and/or excision of cervical intervertebral disc, either through the Neurosurgery or the Orthopedic Surgery Services. Based on existing data, it is hoped that 24 subjects can be recruited over the one year study period.

Progress: No patients have been entered on this study as it has just received approval of funding by the Tri-Service Nursing Research Group.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/132 **Status:** On-going

Title: Pressure Ulcer Prevention: Comparing Support Surfaces

Start Date: 06/21/96 **Est. Completion Date:** Sep 99

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Pamela J. Hildreth, AN

Associate Investigators:
LTC Brenda I. Mygrant, AN
LTC Linda H. Yoder, AN
Gladys Cobb, BSN, MSN

Key Words: Ulcer prevention, Kinair bed, EHOB waffle mattress

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) Determine the demographic characteristics that differ between patients who do and those who do not develop pressure ulcers. 2) Compare the incidence of pressure ulcers between the patients on the KinAir® bed and patients on the EHOB WAFFLE® mattress. 3) Determine the difference in length of stay and monetary expenditure for individuals within the two support surface groups who do not develop pressure ulcers. 4) Determine the difference in length of stay and monetary expenditure for individuals within the two support surface groups who do develop pressure ulcers.

Technical Approach: The proposed study is a prospective, quasi-experimental design, in which subjects who are at risk for pressure ulcer development will be randomly assigned to one of two support surfaces. Data will be collected for a period of at least one week or until the subject is discharged, expires, or is no longer considered at risk. Data to be collected will include pressure sore risk using the Braden Scale for Predicting Pressure Sore Risk, daily skin integrity assessments, and information on pressure ulcer development and subsequent ulcer progression using the Pressure Sore Status Tool, as well as data on selected demographic variables. The study will be conducted in multi-site settings. The primary site for the study will be Madigan Army Medical Center and Brooke Army Medical Center (BAMC) is the study's secondary site. Using data obtained from the Wound Care Specialists at both MAMC and BAMC, it is anticipated that approximately 4 eligible subjects will be admitted to BAMC per week. Because the proposed study offers daily care from a research team devoted to maintaining skin integrity, a 75% consent rate is predicted. This equates to enrollment of 3 subjects per week at MAMC and 2 per week at BAMC. An attrition rate of approximately 10% is anticipated based on preliminary data from the Tri-Services Nursing Research Group funded study "Pressure Ulcers: Patient Outcomes on Kinair Bed or EHOB Mattress." Recruitment will occur for twenty-eight months and enrollment of 560 subjects is anticipated.

Progress: This protocol has not been started as funding by the Tri-Service Nursing Research Group has only very recently been approved.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/122	**Status:** On-going
Title: A Grounded Theory Analysis of Patient Satisfaction in the Military		
Start Date: 06/21/96	**Est. Completion Date:** Sep 97	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: COL Bonnie L. M. Jennings, AN		
Associate Investigators: Lori A. Loan, MSN, RNC	COL Frances D. Anderson, AN Debra DePaul, RN	
Key Words: Patient satisfaction, military, TRICARE		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: The primary purpose of this study is to describe the experiences, expectations, and preferences of military health care beneficiaries, as related to health care in the TRICARE environment. The overall goal of this study is to describe, through grounded theory method, the precess by which military health care beneficiaries arrive at their perceptions of satisfaction or dissatisfaction with their health care experience.

Technical Approach: The purpose of this study is to generate hypotheses regarding how military health care beneficiaries arrive at their perceptions of their health care experience. Approximately 30 military beneficiaries who reside within the 40 mile MAMC catchment will be purposely selected form the DEERS roster. Theoretical sampling dictates that the variety of experiences existing in the empiric care would will be represented. The sample size, however, will be dictated by ongoing data collection. Subjects will be interviewed to describe their experiences and expectations as they relate to obtaining health care, and to elucidate what level of preferences they will allow as minimally tolerated. All interviews will be audiotaped and transcribed. Data analysis will be done concurrently with the interviews. It will consist of open coding (conceptualizing and categorizing data), axial coding (establishing relationships between categories), selective coding (emergence of the dominant category), and theoretical integration (reflection of the emerging theory and description of the phenomenon under study.

Progress: No patients have been entered. Original grant application was denied. The PI is attempting to obtain alternative funding.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/125 **Status:** On-going

Title: A Survey of Access to Care in the TRICARE Environment

Start Date: 06/21/96 **Est. Completion Date:** Sep 98

Department: Nursing **Facility:** MAMC

Principal Investigator: COL Bonnie L. M. Jennings, AN

Associate Investigators:
Lori A. Loan, MSN, RNC
COL Frances D. Anderson, AN
Suzanne K. Wilson, MSN, RN

Key Words: TRICARE, access to care, Madigan Army Medical Center

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe access to health care in the TRICARE environment.

Technical Approach: Using a stratified sample of 7,680 military beneficiaries from the MAMC 40 mile catchment areas, this descriptive survey aims to describe access to health care in the TRICARE environment. The research questions are: (1) How do military beneficiaries (consumers) in the MAMC 40 mile catchment area evaluate access to health care? (2) How do military beneficiaries in each of the consumer groups evaluate access to health care? (3)How do members of each of the components of TRICARE evaluate access to health care? (4) Do consumer evaluations of access to care differ according to TRICARE component? Randomly selected beneficiaries from the four TRICARE components will complete and return a mailed questionnaire. Instruments selected for use in the study include the PSQ-III, the General Health Perceptions scale from the SF-36, and select sociodemographic questions from the 1994-1995 Annual Health Care Survey for DoD Beneficiaries. The instruments were chosen for their appropriateness and their high levels of reliability and validity. Data form the survey will be analyzed using descriptive statistics and one-way ANOVA.

Progress: No patients have been entered. The study has just received funding from Tri-Service Nursing Research.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/101 **Status:** Completed

Title: A Survey of Patient Satisfaction and Loyalty in Military Beneficiaries Evacuated From the TRICARE Prime-MAMC Waiting List

Start Date: 05/17/96 **Est. Completion Date:** Sep 96

Department: Nursing **Facility:** MAMC

Principal Investigator: COL Bonnie L. M. Jennings, AN

Associate Investigators:
Debra DePaul, RN
Troy H. Patience, B.S.
Lori A. Loan, MSN, RNC
Stacey L. Heiner, BSN, RN
Suzanne K. Wilson, MSN, RN

Key Words: TRICARE, satisfaction, loyalty

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to evaluate consumer motivation for changing TRICARE Prime portal of care. The study plans to describe military health care beneficiaries choosing to change portal of care to those choosing not to change portal of care. Descriptions will be made on the following beneficiary attributes: (1) patient satisfaction with health care at Group Health Cooperative; (2) reason for changing TRICARE Prime portal of care; (3) experience with and expectations of health care at MAMC; and (4) sociodemographic characteristics.

Technical Approach: The study plans to describe military health care beneficiaries choosing to change portal of care (n=171) and those choosing not to change portal of care (n=120). The following beneficiary attributes will be described: (1) patient satisfaction with health care at Group Health Cooperative; (2) reason for changing TRICARE Prime portal of care; (3) experience with and expectations of health care at MAMC; and (4) sociodemographic characteristics. The data collection phase of the study will consist of acquiring the waiting list names and phone numbers from Foundation Health, computer randomization of names from the list, and data collection via telephone survey. Inter-rater reliability will be done on 10% of the telephone calls. Mean+SD of satisfaction scores for the entire PSQ III and for each subscale will be determined. Reason for changing TRICARE Prime portal of care will be analyzed qualitatively by identifying common themes and concepts.

Progress: The major reason beneficiaries chose to return to MAMC was loyalty (60%). Secondary reasons for changing site included cost (12%) and travel distance (10%). Other reasons included "don't like civilian provider" (8%), "my privilege" (5%), "family reasons" (2%), and continuity (1%). Contrary to pre-study assumptions and the opposite findings from the civilian sector, there was a low percentage of people changing sites because of cost. **Most participants stated that they would return to MAMC even if a co-payment was required (89%).** There was no correlation between the participant's yearly income and responses to this question. Reasons for not returning to MAMC were "don't like MAMC" (38%), travel distance (31%), Group Health loyalty (15%), "bad time to switch" (8%), and "my privilege" (5%). Specific concerns related to long waits to see the health care provider (13%), long waits to get an appointment (41%), non-specific long waits (33%), and bad service (13%).

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/117	**Status:** On-going
Title: Exogenous Surfactant Therapy in Premature Infants		
Start Date: 06/09/93	**Est. Completion Date:** Sep 94	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: Lori A. Loan, MSN, RNC		
Associate Investigators: LTC Barbara S. Turner, AN LTC Deborah J. Leander, AN	LTC Joanna C. Beachy, MC CPT William D. Glover, AN	
Key Words: surfactant, premature infants		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To examine two types of surfactant (Exosurf & Survanta), 3 methods of administration, and the resulting neonatal physiologic responses and outcomes. A secondary aim will be to determine the relationships between type of surfactant and administration technique, nursing assessed neonatal clinical cues of a hemodynamically significant patent ductus arteriosus, and neonatal outcomes.

Technical Approach: This is a prospective, quasi-experimental study, in which selected physiologic parameters will be monitored during exogenous surfactant administration in a convenience sample of 24 premature infants. Subjects will be randomly divided into one of three administration groups. A control group receiving no surfactant would not be appropriate as it would mean the infants would receive less than the standard of care.

The convenience sample will consist of 24 neonates, with the diagnosis of RDS, who will receive exogenous surfactant using rescue therapy. The three groups will be: 1) n=12, Exosurf administered by sideport adapter. 2) n=6, Survanta administered by feeding tube through endotracheal tube. 3) n=6, Survanta administered through double lumen ET tube. After consent is obtained and electronic monitors applied, baseline data will be collected for 10 minutes after which either Survanta or Exosurf will be administered by the predetermined route. The infant will be ventilated during the procedure using NICU SOPs. At completion of the surfactant administration, data collection will continue for 2 hours. Nurses will be free to make whatever adjustments they deem necessary in response to the lung compliance changes using their own judgment or in consultation with the physician.

Descriptive statistics obtained from the data will be categorized into critical ranges for each of the data collection periods. Demographic data will be coded and analyzed.

Progress: A total of 60 patients have been studied. Data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/175	**Status:** On-going
Title: A Comparison of Skin Microbes Under Two Types of Temperature Probe Covers Used on Premature Newborns		
Start Date: 08/18/95	**Est. Completion Date:** Sep 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: Lori A. Loan, MSN, RNC		
Associate Investigators: MAJ Pamela S. Birgenheier, AN Suzanne K. Wilson, MSN, RN	Debra DePaul, RN CPT Wade K. Aldous, MS	
Key Words: Microbes, probe covers, NICU		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This is a descriptive pilot study to determine if the temperature probe covers in current use in the NICU contribute to nosocomial infections by providing an environment for normal skin microbes to colonies.

Technical Approach: Two types of probe covers are currently used in the MAMC NICU. One type has a reflective exterior surface and a type of foam tape adhesive on the interior surface (Probe Cover A). The second type also has a reflective exterior but has a hydrogel adherent surface (Probe Cover B). Probe covers will be placed on 20 premature newborns (28 to 34 weeks gestational age) following their first bath, within 24-36 hours of life. The newborns will be separated into two groups of ten each and will serve as their own controls. The first group will wear Probe Cover A. The second group will wear Probe Cover B. Probe covers will be removed on the third day of wear. Probe covers and the skin under the probe will be swabbed for bacterial growth. An exposed patch of skin opposite from the probe cover will be swabbed as a background (control) check of skin bacteria. Culture swabs will be placed in saline and serial dilutions will be made before plating onto sheep blood agar (SBA) and mannitol salt agar (MSA) plates for detection and enumeration of skin flora. Significant differences in bacterial types and amount will be noted between exposed skin and the two types of probe-covered sites. The basic parametric procedure for testing differences in groups is the t-test. The paired t-test will compare results from skin under Probe Cover A with uncovered and skin under Probe Cover B. The Mann-Whitney-U test will be used to test the difference between the two independent samples.

Progress: Microbiological tests have been completed for nine subjects.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/124 **Status:** Completed

Title: A Nursing Resource Management Tool: An Application of the Neonatal Therapeutic Intervention Scoring System

Start Date: 06/21/96 **Est. Completion Date:** Apr 97

Department: Nursing **Facility:** MAMC

Principal Investigator: Lori A. Loan, MSN, RNC

Associate Investigators: Kristie K. Marbut

Key Words: Neonatal Therapeutic Intervention Scoring System, hospital stay, ventilation, lung disease, mortality

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to validate the use of the admission-day NTISS score as a predictor of length of hospital stay in the Neonatal Intensive Care Unit, which could assist in resource utilization and management. A secondary purpose is the use of the admission day NTISS score as a predictor of 1) number of ventilation days, 2) chronic lung disease and 3) newborn mortality.

Technical Approach: This study is secondary analysis of a portion of the data collected from a prospective, quasi-experimental study entitled: "Exogenous Surfactant Therapy in Premature Infants," Principal Investigator: Dr. Barbara S. Turner (COL) (1992-1995). The secondary analysis will be based on the relationship between the independent variable, the admission-day NTISS score and the dependent variables: 1) length of hospital stay (LOS), 2) number of ventilator days, 3) respiratory morbidity, and 4) mortality. Admission-day NTISS scores were tabulated at the time the infant was enrolled in the original study and documented on a demographic data collection form. The admission-day NTISS score was later transferred from the form to a subject numbered log book. The original consent form requested permission from parents to enter their child's medical records after discharge. This was necessary to collect data about length of hospital stay, number of ventilator days, diagnosis of CLD or BPD or whether or not the newborn died during the initial hospital stay. The information collected from the records review was also entered in the subject numbered log book. The log book information will be analyzed for the relationship the admission-day NTISS and 1) length of hospital stay, 2) number of ventilator days, 3) discharge diagnosis of CLD or BPD, and 4) mortality. Descriptive statistics will be used for demographic data. Linear regression will be used for the continuous variables, and ROC analysis will be used for the dichotomous variables to identify the NTISS score that best separates positive and negative cases.

Progress: The findings did not support the results of the original developers of the TNISS tool. This study was limited by the small sample size (n=60), missing data from the original study files, and the homogeneous nature of the patient population. Second level analysis did support birth weight and gestational age assessment to continue to be an accurate risk estimate in the ill and/or premature newborn.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/190	**Status:** On-going
Title: The Effects of Thermocouple Sensor Placement on Neonatal Skin Temperature Measurement		
Start Date: 09/15/95	**Est. Completion Date:** Oct 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: Lori A. Loan, MSN, RNC		
Associate Investigators: Susan T. Blackburn, Ph.D., RN, FAAN	Lauran T. Taquino, RN, MS Karen A. Thomas, Ph.D., RN	
Key Words: Skin temperature, neonatal, thermocouple sensor placement		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objectives of this study are to compare temperature readings from probes placed on peripheral skin sites with readings of axilla temperature, and to compare temperature readings form probes placed on the abdomen and back during periods when the infant is lying -on and not lying-on the temperature probes. Also, to evaluate the effects of body size on accuracy of temperature probe measurements from selected sites, and when the infant is lying-on versus not lying-on the probe.

Technical Approach: This descriptive study is designed to objectively evaluate several common nursing practices and beliefs regarding the care of neonates and the placement of temperature probes. The study seek to provide a physiologic basis to support and validate nursing practice. Four body sites will be studied simultaneously through the use of a small thermocouple sensor and two channel continuous readout device. Data will be collected for one hour with the subject in each of two common positions, supine and prone. Environmental temperature and basic demographic data will also be collected for each subject and study period. The study period will consist of approximately 2.5 hours for each study subject and will not interfere with or alter the standard neonatal nursing and medical care of that infant. This study is sponsored by the local chapter of the national professional association for neonatal nursing and is designated to support data collection in multiple hospital sites. Data from all sites will be aggregated for the purpose of analysis and reporting. Descriptive statistics will be use initially to examine differences in temperature readings from the four sensors. Further analysis will examine clinically and statistically significant changes in temperature between the four sites and between lying-on and not lying-on the sensors. comparisons will also be made of differences in temperature values between sites and between infants of different weight groups.

Progress: No patient subjects have been entered. Training of research staff continues at Children's Hospital in Seattle, WA.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/137	**Status:** On-going
Title: Single Woman's Breast Cancer Program		
Start Date: 07/19/96	**Est. Completion Date:** Jun 98	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: Lori A. Loan, MSN, RNC		
Associate Investigators:	Nancy F. Woods, Ph.D., RN	
Key Words: Cancer:breast, single women		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: There are five study purposes: to (1) test the effectiveness of a home-based counseling intervention for single women with early stage breast cancer with dependent children; (2) investigate the causal model underlying the intervention; (3) explore time related patterns of change in individual study participants; (4) develop a discriminant function that effectively categorizes women and children most able to benefit from the intervention; and (5) test the cost-effectiveness of the intervention. The goal of the intervention is to improve psychosocial adjustment and quality of life in single women with early stage breast cancer and their dependent children.

Technical Approach: This study will enroll 200 single females who have a recent diagnosis (11 months or less) of early-stage breast cancer (Stage 0, 1 or 2). Subjects will be inpatients or outpatients, from medical, surgical or radiation oncology departments. Subjects will be randomized prior to initial contact so that the woman is invited to participate in either the coached or evaluation group. When subjects have agreed to participate, an in-home appointment is made with the evaluation nurse. Consent is obtained on the first visit and questionnaires are administered. Child participation is desirable but not mandatory. Initial explanation to the child is always is left to the mother, but the nurse will provide additional information and obtain written consent from the child, if willing. All families receive 4 evaluation visits. Women randomized to the coached group receive an additional 5 in-home visits by the coach. At the end of the study, all women receive thank you a letter and those who were randomized to the evaluation group receive $20 for each visit and an informational packet about breast cancer. Data will be analyzed by 5 major methods: formal statistical tests of the effect of the intervention (MANCOVA); investigation of the explanatory model underlying the intervention (structural equation modeling); exploration of time-related patterns of change in individuals (trend analysis and latent growth model); discriminant analysis and cost-effectiveness analysis. All of these data analytic components constitute outcome analyses and there will also be a process evaluation component.

Progress: Nurse training has been completed. Patient enrollment to commence within the next few weeks.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/076	**Status:** On-going
Title: Gastric/Jejunal Feeding: Nutritional Outcomes and Pneumonia		
Start Date: 05/17/96	**Est. Completion Date:** Sep 98	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: MAJ Mary S. McCarthy, AN		
Associate Investigators: CPT Kurt W. A. Grathwohl, MC	MAJ Bernard J. Roth, MC 1LT Faith U. Watanabe, SP	
Key Words: Feeding:gastric, Feeding:jejunal, pneumonia		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To compare nutritional outcome between patients randomized to gastric or jejunal tube feeders as measured by: a) daily caloric intake, b) subjective global assessment, c) biochemical parameters, d) delayed cutaneous tests and e) indirect calorimetry. 2) To compare rates of nosocomial pneumonia between gastric and jejunal fed patients as measured by: a) new & persistent infiltrate on chest x-ray (CXR), b) fever, c) sputum culture, d) leukocytosis, and e) brochoscopically directed protected specimen brush. 3) To compare colonization rates between a subset of gastric and jejunal fed patients, at three sites (oropharynx, trachea, stomatch); specific focus being Gram-negative bacilli, as measured by quantitative and qualitative microbiology analysis.

Technical Approach: This proposed study is a replication of a prior study done by Montecalvo et al. (Appendix A) in the medical model. Areas of interest include modifiable and non-modifiable person factors, social and physical environmental factors, physiological factors, pathophysiological factors, behavioral factors, symptoms, congitions/emotions, and drives/sensations. Infants who are prescibed a feeding tube in one of two places, the stomach or the small intestine. Both methods are commonly used in this hospital. If you are to receive tube feedings in the stomach your doctor will pass a soft, flexible tube down your nose or mouth into your stomach. If you are to receive tube feedings in the small intestine, a radiologist will pass a soft, flexible tube down your nose or mouth using a lighted scope to guide the tube placement into your small intestine. It is the policy of this hospital to confirm the placement of the tube by xray before feedings can begin. This is ordered by the physician and will be performed whether or not you participate in this study. Shortly after having the tube in place, the principal investigator or the project director will conduct a noninvasive metabolic test at the bedside to estimate your calorie needs for tube feeding. This test measures the amount of energy you use while you are ill in the ICU. It will be performed each week. In addition, specimens of blood, urine, sputum and stomach contents will be obtained to evaluate your nutritional status and monitor for infection or bleeding. Lastly, your health record will be examined by the investigator or the project director for the following information: pertinent medical history, admission vital signs, current medications, height and weight, and tube feeding regimen.

Progress: No patients entered at this time. The protocol has only recently received notification of grant approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/027 **Status:** Completed

Title: Effects of Separation on Families During Hospitalization

Start Date: 11/17/95 **Est. Completion Date:** Aug 95

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Thomas H. Miller, AN

Associate Investigators:
MAJ Barbara Lawson, AN
COL Cynthia A. Gurney, AN
LTC Janice Agazio, AN
Deborah Wills, MSN, RN
SSG James T. Reeder Jr., NC

Key Words: Family separation:hospitalization, medical evacuation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To systematically identify the stressors associated with family separations during the circumstances of medical evaluation or treatment, identify the coping mechanisms and resources used by families to mediate these stressors, and to determine the effects of the separation on family function.

Technical Approach: This study is a prospective two-group comparison using methodological triangulation. This study will also be testing a hypothesized causal model developed from the theoretical model. In the separated sample, a subset of the families will participate in the descriptive qualitative component of the design. Subjects will be recruited from pediatric admissions to MAMC to obtain a matched sample for age and diagnostic type. There will be two groups. Group I will be families with children medically evacuated (where the distance is greater than 200 miles or three to four hours travel time from the facility). Group II will be families admitted from the local area. As data will be collected from other sites, a total of 500 subjects will be recruited. Descriptive statistics will be used to describe the samples in Group I and Group II. Descriptive statistics will be used to summarize the range and frequency data to include mean, standard deviation, and distribution of responses. Cronbach's Alpha will be used to verify reliabilities on each of the instruments and the subscales. Pearson correlation coefficients will be obtained between each of the preliminary study variables (resources, demographics, stressors, and perception) and then each against coping. MANOVA will be used to test the instrument subscales' relationship to family functioning for differences between the Group I and Group II. Qualitative data will not be collected at MAMC.

Progress: Twenty-nine patients were entered at MAMC in this multicenter study, with 8 completing the surveys. The protocol was terminated at Madigan in August 1996, because significantly more patients were available at Walter Reed AMC; therefore, they received the additional funds. All data have been transferred to Walter Reed to be analyzed with the data collected there.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/015	**Status:** Terminated
Title: Preterm Labor: PCR Method Identifying Amniotic Fluid Bacteria		
Start Date: 11/17/95	**Est. Completion Date:** Sep 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Thomas H. Miller, AN		
Associate Investigators: MAJ Glenn R. Markenson, MC MAJ Nathan J. Hoeldtke, MC MAJ Curtis L. Yeager, MS	CPT Wade K. Aldous, MS MAJ Katherine S. Foley, MC CPT Jason L. Blaser, MS MAJ Rodger K. Martin, MS	
Key Words: Bacteria, Amniotic fluid, polymerase chain reaction		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To develop additional bacteria-specific DNA primer sets to differentiate and to positively identify the microorganisms in the bacteria PCR positive group.

Technical Approach: We will continue to enroll patients in this study at the William H. Beaumont Army Medical Center (WHBAMC), TAMC, and MAMC. Together with our previous study population of patients, we hope to exceed 100 preterm amniotic fluid samples in the study. Preterm labor will be defined as the onset of uterine contractions that result in cervical change prior to the completion of the 37th week of gestation with intact membranes. New amniotic fluid from preterm labor patients will be aspirated aseptically and split into fractions. One fraction will be processed for PCR using eubacterial and Mycoplasma DNA primer sets. An aliquot of the second fraction will be cultured for aerobic and anaerobic bacteria at the host institution where the amniocentesis is performed. In addition, new patient samples will have an aliquot of the fluid sent to an independent laboratory for Mycoplasma testing. Previously collected samples have been cultured from bacteria and Mycoplasma and that data has been entered into the database. Samples collected at the TAMC and WHBAMC will be process and shipped frozen on dry ice to the Department of Clinical Investigation (DCI) at the MAMC for further analyses by PCR studies. Samples from MAMC will be generally processed within 24 hours upon amniocentesis within the DCI.

Progress: This protocol was terminated because grant funding was not approved.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/128	**Status:** On-going
Title: Natural Killer Cell Activation in Women with Early Stage Breast Cancer		
Start Date: 06/21/96	**Est. Completion Date:** May 97	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Thomas H. Miller, AN		
Associate Investigators:	Betty J. Gallucci, Ph.D., RN	
Key Words: Cancer:breast, killer cell activation		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To obtain preliminary data for the Research Proposal entitled "Natural Killer Cell Activation in Women with Early Stage Breast Cancer" to be submitted for the DOD Breast Cancer Research Initiative July 15, 1996. The major critique of the same proposal, which was submitted in September 1995, was that no preliminary data was available.

Technical Approach: For this preliminary study, 10-20 female subjects will be recruited form those patients obtaining a breast biopsy at MAMC or volunteers recruited by advertisement. Those patients interested will be advised to contact the researchers and be screened for inclusion/exclusion criteria. The women will have blood drawn for testing at the University of Washington School of Nursing Laboratory. Sixty to 100 ml of venous blood will be collected into heparinized vacuum tubes. Appropriate cells will be separated an tested for NK cell cytotoxicity and activation antigen expression. Students t-test and a two-say analysis of variance for repeated measures will be used to detect difference in the mean activation antigen expression before and after IL-2 incubation.

Progress: Data collection has not yet begun.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/133	**Status:** Terminated
Title: Soldier Toughening: NK Cell and Neuroendocrine Patterns		
Start Date: 07/19/96	**Est. Completion Date:** Sep 97	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Thomas H. Miller, AN		
Associate Investigators:	Betty J. Gallucci, Ph.D., RN	
Key Words: Killer cell activation, Special Forces, hormonal levels		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) Compare the NK cell responses (before, during and post exercise) to high intensity exercise (70-80% VO_2max) between toughened Special Forces and non-Special Forces soldiers. 2) Compare the hormonal response to a high intensity exercise challenge between toughened Special Forces and non-Special Forces soldiers. The baseline levels of serum cortisol and catecholamines as well as the magnitude of changes from baseline will be quantified and compared in the two groups of soldiers, before, during and after exercise.

Technical Approach: Our study proposes to identify the patterns associated with toughened Special Forces soldiers to elucidate the cellular responses that might affect health and readiness of our Armed Forces. Changes in the functions of NK cell (e.g., in levels of lysis, or secretion of cytokines) are accompanied by changes in the activation antigens expressed on the NK cell surface. We will examine the differences in activation antigen expression before, during and after exercise in two groups of soldiers. Sixty soldiers (30 in each group) will be recruited and their maximal cardiorespiratory fitness will be assessed. The soldier will exercise at 70-80% $V0_2$ max for 60 minutes. NK cell activity, epinephrine, norepinephrine and cortisol will be measured by blood drawings at -30, 0, 30, 60, 120 and 240 minutes after exercise. A one page appraisal questionnaire will be completed that assesses their perception of the exercise challenge. NK cells will be tested with the standard cytotoxicity assay or labeled with mAb to activation antigens. Flow cytometry will be used to quantify the expression of the antigens. This study will identify patterns of neuroendocrine and immune activation that will be the basis for the scientific prescription of nursing therapies to enhance wellness through immune responses.

Progress: This protocol was terminated because grant funding was not approved.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/176 **Status:** Completed

Title: The Effect of Perceived Social Support on the Competency Level of U.S. Army Perioperative Nursing Students

Start Date: 09/15/95 **Est. Completion Date:** Mar 96

Department: Nursing **Facility:** MAMC

Principal Investigator: MAJ Jane E. Newman, AN

Associate Investigators: LTC Rita Corcoran, AN

Key Words: Competency:nursing students, social support

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to determine if a relationship exists between the US Army perioperative students' perceived social support received during their 16 week course of instruction and their competency level upon completion of the course.

Technical Approach: The Interpersonal Relationship Inventory will be used to evaluate the student subjects' perceived social support and each perioperative course instructor will evaluate the students' competency level based on a 100 point scale (1 being worst and 100 being best). The students' competency level will be annotated on the CompetencyLevel Numeric Rating Form. Knowing the relationship between perceived social support and the competency levels in perioperative students will provide information to Army educators about the quality of social support available for perioperative students from resident staff nurses. In a profession that experiences frequent staffing shortages and position justification, it is necessay to support the education process that develops new specialists. Upon receiving returned questionnaires and subject evaluation forms, descritpive statistical analysis will be used to comple the demographic data and develop a profile of the subjects. Inferential statistics will be used to compare the selected variables. Correlational statistics will be used to demonstrate the relationship between perceived social support and competency level. The Person Product-moment correlation will be used to test that a correlation between perceived social support and competency level if different from zero, or that a relationship exists between the two variables.

Progress: The Interpersonal Relationship Inventory was used to evaluate the subjects' perceived social support. Three perioperative course instructors recorded the students' competency level ratings based on a 100 point scale with one representing the lowest level and 100 representing the highest. The students' competency level ratings were annotated on the Competency Level Numeric Rating Form. Sources of support were identified for each subject, with parents and friends cited most frequently as support persons. Although a positive relationship was found between perceived social support and competency and an inverse relationship was found between conflicted support and competency, neither relationship was statistically significant. One implication was that resident perioperative nursing staff may need to be targeted to receive instruction and education on perceptorship and social support behaviors.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/101	**Status:** On-going
Title: Fatigue Following Childbirth: Military Family Outcomes		
Start Date: 05/06/94	**Est. Completion Date:** Sep 95	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Gertdell Phyall, AN		
Associate Investigators:		
Marcia G. Killien, Ph.D.	Debra DePaul, RN	
Karen A. Thomas, Ph.D., RN	Susan T. Blackburn, Ph.D., RN, FAAN	
LTC Michelle T. Renaud, AN	Lori A. Loan, MSN, RNC	
Lorna R. Imbruglio, BSN, MSN	Jeanette Zaichkin, BSN	
Martha J. Lentz, BSN, MN, Ph.D.	Sue E. Chambers, RN	
	Julianna Ellis	
Key Words: birth:fatigue, birth:military		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/15/95

Study Objective: To determine if an advanced practice nursing intervention to reduce fatigue will promote job well-being, parenting ability, and infant outcomes among military active duty personnel and their spouses/partners following the birth of an infant.

Technical Approach: Pregnant females and their spouses/partners (if applicable) will be recruited during weeks 28-32 of gestation in the prenatal clinic at MAMC. Data will be collected at six time points: prenatally at time of enrollment and post birth when the infant is 24-48 hours, 2 weeks, 2 months, 4 months, 6 months or age. Time measures correspond to typical timing of clinic visits. During the clinic visit, parents will complete a packet of questionnaires specific to each time of measure and active military status. If only one parent attends the clinic visit, the other parent will complete their part of the questionnaire packet at home and return it by mail. Following birth, infant neurobehavioral status will be assessed by trained study personnel at 24-48 hours of age. At 4 & 6 months of age parent-infant interaction will be assessed during the clinic visit using the NCATS observational tool. At 6 months of age infant development will be assessed by trained study personnel using the CAT/CLAMS-r and Denver II assessment instruments. Experimental subjects will begin the fatigue modulating intervention following the initial assessment at Time 1. Throughout the study experimental subjects will receive care from the project's advanced nurse practitioners. Continuos monitoring of the intervention's integrity and effectiveness will allow the nurse practitioner to reinforce and modify the intervention as appropriate.

Progress: A total of 1398 pregnant women were approached for participation in the study; 852 subject families agreed to participate, but only 392 successfully met the study criteria. Of these, 296 families completed the first two questionnaires. Of these, 119 subject families have completed the study and 67 subject families are at various stages of the study, with 110 failing to return further questionnaires. Preliminary data from the first two collection points indicate that there do not appear to be differences between experimental and control women in age, income, ethnicity, physical training scores, and weight, and no significant difference between experimental and control men in age, education, income, physical training scores, and weight.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/115	**Status:** On-going
Title: Neonatal Outcomes in a Modified NICU Environment		
Start Date: 06/09/93	**Est. Completion Date:** Sep 94	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Michelle T. Renaud, AN		
Associate Investigators: Susan T. Blackburn, Ph.D., RN, FAAN	LTC Joanna C. Beachy, MC Karen A. Thomas, Ph.D., RN	
Key Words: Neonates, modified NICU		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To evaluate the effects of a modified NICU environment on physiological and neurobehavioral parameters in two groups of preterm infants and in high risk full term infants during hospitalization and post discharge; (2) to evaluate the effects of a modified NICU environment on infant-caregiver synchrony and stressors in the period of transition from hospital to home, and post-discharge.

Technical Approach: This is a continuation project of an ongoing study. This project extends longitudinal follow-up through the addition of a home visit and incorporates parent behavioral responses as factors relevant to infant outcomes. At the Post-Discharge Clinic Visit, 2 - 3 weeks following discharge, the mother will be asked to complete the Transition from NICU to Home Questionnaire during the infant's regularly scheduled follow-up visit. The home visit will be scheduled at the parents convenience at 82 weeks post discharge. At the home visit, the infant's neurobehavioral status will be assessed using the Brazelton Newborn Assessment Scale (BNBNS) and the infant's sleep-wake pattern will be recorded using the Newborn Child Assessment Sleep Activity (NCASA) record. Parents will complete the Parenting Stress Index (PSI) during the home visit. Parent-infant interaction during a feeding will be observed using the Nursing Child Assessment Feeding Schedule (NCASF). Home visits will be arranged to accommodate the feeding schedule.

ANOVA and repeated measures ANOVA will be used to test group differences in the BNBAS, NCAFS, PSI and Transition from NICU to Home Questionnaire. The 24-hour recordings of sleep obtained by the NCASA will be summarized and differences in total sleep and wake time, number of awakenings, and synchrony to day-night pattern will be tested using ANOVA and repeated measures ANOVA. Cyclicity of NCASA data will be determined within subject using cosinor analysis.

Progress: One hundred twenty six subjects were entered and data collection is complete. Data analysis is in progress, with a final report expected by 31 Dec 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/148	**Status:** On-going
Title: Feasibility and Patient Satisfaction with Wearing an Eye Mask and Ear Plugs During Regular Sleep Times While in the Coronary Care Unit		
Start Date: 08/16/96	**Est. Completion Date:** Oct 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: CPT Mary E. Riley, AN		
Associate Investigators: None		
Key Words: Sleep, CCU, eye mask, ear plugs		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to describe the feasibility and patient satisfaction with wearing an eye mask and ear plugs during the person's regular sleeping time while in an Intensive Care Unit (ICU).

Technical Approach: Subjects for this study will include all ICU admissions except for those patients either undergoing cardiac admissions or who are currently involved in another study. A minimum of 30 subjects will be used for the study. A fourteen-item questionnaire will be administered every morning for up to three consecutive days during their ICU stay. The subjects will be asked their level of satisfaction with the use of the eye masks and ear plugs and also their overall ICU experience. Descriptive statistics will be used to describe and summarize results obtained from the questionnaires. The means, frequencies, and percentages of scores for each item on the questionnaire will be calculated. Demographic data will be displayed in a table with the calculated means, standard deviations, modes, and medians as appropriate.

Progress: Twenty two subjects have been asked to participate in the study with eight subjects agreeing to participate. Of the eight participants, two participated in data collection for two consecutive nights and the other six for only one night. Two subjects asked not to continue because they did not want to be disturbed for another night and six subjects were transferred from the ICU before the second night. Subjects thus far have shown a slight preference for the use of the silk eye mask compared to the ear plugs.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/013 **Status:** Completed

Title: Primary Care Demonstration Project: Measurement of Provider Practice Styles and Clinet Outcomes

Start Date: 11/17/95 **Est. Completion Date:**

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Jackie W. Saye, AN

Associate Investigators:
Vicki L. Byers, RN, Ph.D.
MAJ Debra D. Mark, AN
Mary Z. Mays, Ph.D.

Key Words: provider practices, multidisciplinary team, client outcomes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The proposed study will assess the practice styles of members of a multidisciplinary team of providers composed of physicians, nurse practitioners and physician assistants and how those styles influence client outcome variables.

Technical Approach: The military medical system is changing from a focus on impatient care to outpatient primary care. This pilot study will fill gaps in the literature and generate hypotheses for future studies concerning effective practice styles and efficient utilization of physicians, nurse practitioners and physician assistants. This large-scale, repeated measures, correlational pilot study has been designed to: (a) investigate key technical and interpersonal components of provider style and their association with client satisfaction and health status; (b) extend the reliability and validity of measuring instruments; and (c) avoid issues of sampling bias that have reduced the credibility of earlier investigations of client satisfaction. Sampling and data collection methods include self-reporting and objective and analytical measures obtained through questionnaires and existing records. They will be used retrospectively to quantify client outcomes, provider practice styles, client/provider demographics, and organizational attributes. Analysis of variance, regression analysis, discriminant analysis, and structural equation modeling techniques will be used to answer nine specific research questions.

Progress: Two hundred twenty six (226) clients and 58 providers (26 physicians, 19 nurse practitioners, and 13 physician assistants) were studied. Providers completed six practice style questionnaires that measured their practice model, confidence, autonomy, collaboration practices, attitudes towards giving information, and job satisfaction. Clients completed four outcome questionnaires that measured their functional status, health status, attitudes toward seeking information and satisfaction with health care services. The questionnaires use in this study to measure client outcomes and provider practice styles all demonstrated good reliability and validity in a primary care setting. They should serve as effective tools for evaluating health care systems that provide primary care services.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/079	**Status:** On-going
Title: Soldier HIV Behavior Modification		
Start Date: 02/17/95	**Est. Completion Date:** Sep 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: LTC Catherine M. Schempp, MC		
Associate Investigators: Debra Pontius	Ann E. Hyder LTC Roberta E. Dyer	
Key Words: HIV, behavior		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: 1) What is the current knowledge level concerning HIV and AIDS within the units, and does knowledge level change after the intervention? 2) What are the current beliefs toward HIV and AIDS, and risk behaviors regarding sexual practices, within the units and do beliefs and risk behaviors change after the intervention? 3) At the unit level is a peer led HIV education program more effective than the current nurse led HIV education program at increasing adaptive intentions and attitudes toward safe sex practices? These aims will be addressed utilizing the Health Belief Model as the theoretical framework.

Technical Approach: The purpose of this study is to determine if the use of a peer leader as opposed to the HIV nurse or the size of the group receiving the intervention makes any change in the outcome measures of knowledge of HIV and AIDS, beliefs toward HIV and AIDS, and risk behaviors. The theoretical model for this proposal is the Health Belief Model. The design of the study will include four groups receiving the intervention and a control group. The units requesting HIV education classes will be assigned to either a large or small group depending on the size of the unit and will receive the intervention from either the peer leader or the HIV nurse. This study will involve approximately 35 units with approximately 1700 soldiers. The units will be further stratified by their mission to allow for differences based on individual requirements to meet the unit mission. The control group will consist of units that do not request HIV education classes during the intervention period. The research questions will be analyzed using analysis of variance upon the data gathered from three questionnaires, and post hoc tests will be performed on significant differences. The first questionnaire will be administered prior to the intervention and will consist of a comprehensive assessment of knowledge, beliefs and risk behaviors. The second questionnaire will be administered immediately after the intervention and will focus on knowledge. The third questionnaire will be administered after three months and will focus on beliefs and risk behavior.

Progress: Three "Train the Trainer" courses were taught providing 41 potential peer instructors. Seventy-five units have been taught, including 17 peer taught and 8 control. The final questionnaires have been mailed to approximately 20 groups. Control groups continue to be recruited. A request for a no-cost extension was submitted to Tri-Service Nursing Research Group and has been granted for September 1997. Data has been collected from approximately 2300 subjects.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/028	**Status:** Completed
Title: Rocuronium: A Comparison of Two Priming Doses		
Start Date: 11/17/95	**Est. Completion Date:** May 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: CPT David W. Shepherd, AN		
Associate Investigators: CPT Paul C. Daniel, AN	MAJ Donna S. Dampier, AN	
Key Words: Rocuronium, priming dose, elective procedures		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the onset times of rocuronium between two groups, one using a 10% priming dose and the other a 12% priming dose with a 3 minute interval between the priming dose and the principle dose.

Technical Approach: This study will utilize 70 ASA I and II, male and female subjects between the ages of 18 and 45 who are undergoing elective surgical procedures. Subjects will be evenly divided into two groups. During the induction period each subject will receive a normal intubating dose of rocuronium (0.6 mg/kg). Subjects is group A will receive 10% of the intubating dose as the priming dose followed by the remaining 90% as the principle dose. Subjects in group B will receive 12% of the intubating dose as the priming dose followed by the remaining 88% as the principle dose. The time interval between the priming and the principle dose will be three minutes. The time of onset is defined as the time period between the administration of the principle dose to the time that three of four twitches on a Train of Four measurement (TOF) are lost. Data will be analyzed using simple descriptive statistics to include mean and standard deviation. The inferential statistical test will be a one-sided student's test for statistical significance. Pearson's r correlations will be performed on demographic data to assess differences among subgroups in the sample.

Progress: There was a significant difference between the two groups with time of onset of 157 ± 60 sec. for the 10% group and 123 ± 63 sec. for the 12% group. A significant effect of gender on outcomes was also noted, with males having a significant decrease in time of onset, while females displayed no difference. The investigators have concluded that increasing the priming dose from 10 - 12% can reduce the time of onset of rocuronium. The times reported in this study differ from reported times of onset from other studies. These differences may be due to the use of objective measurement of TOF in this study. Other researchers have used subjective quantification of either TOF or intubating conditions as the criteria for onset. It is notable that many anesthesia care providers in this study were able to successfully intubate prior to the onset criteria being met. The authors suspect that the sensitivity of this tool may be such that the loss of three twitches may not correlate well with relaxation of laryngeal muscles. Gender differences on the response to an increased priming dose warrants further study. This study was presented at the American Association of Nurse Anesthetists Annual Meeting.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/089	**Status:** Terminated
Title: Ergonomic Awareness and Analysis Tool for Women		
Start Date: 05/17/96	**Est. Completion Date:** Sep 97	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: COL Jo Ellen Vanatta, AN		
Associate Investigators:	Daniel J. Pond	
Key Words: Ergonomics, female soldiers		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this research and development project is to extend ErgoEASER (a set of ergonomic education and analysis tools developed by Pacific Northwest National Laboratory under the collaborative sponsorship of the US Department of Energy, US Department of Defense, and US Department of Labor) to include health care/patient handling ergonomics and to enhance the awareness of ergonomic issues that apply to military health care professionals. The portion of the proposed work that will be performed at Madigan Army Medical Center consists of (i) identifying representative patient handling procedures and associated ergonomic risks and (ii) obtaining video and still photography of patient-handling activities.

Technical Approach: The proposed work will involve video and still photography of patient-handling activities at Madigan Army Medical Center. Representative patient handling activities identified to date include: moving patient from wheelchair to bed, moving patient from bed to wheelchair, moving patient from chair to bed, moving patient from bed to chair, moving patient from bed to gurney, moving patient from gurney to bed, repositioning/lifting patient in bed, repositioning/lifting patient in wheelchair, repositioning/lifting patient in chair, making bed with patient in it, helping patient into/out of vehicle, supporting patient while standing/walking

Progress: This study was terminated because external funding (Tri-service Nursing Research Group) was not approved.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/054 **Status:** Completed

Title: Descriptive Study of Military Families with Children Who Are Medically Fragile: A Needs Assessment

Start Date: 02/16/96 **Est. Completion Date:** Apr 96

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC William O. Walker, Jr., MC

Associate Investigators: MAJ Muriel D. Metcalf, AN

Key Words: Military family, children, special needs

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the demands placed on military families with children who are medically fragile.

Technical Approach: Letters will be mailed to all eligible parents from the pool of parents in the Developmental Pediatric Clinic inviting them to participate during a routine clinic visit. At their next clinic visit, trained staff in the clinic will explain and present an information statement to the parents about the survey. A second letter will be sent part way through the study as a thank you and a reminder. Questionnaires are anonymous with no personal identifiers. Parents may return the questionnaire to the front desk of the clinic or return it in a postage-paid envelope from home. Data will be analyzed using SPSS or similar computer programs. Descriptive statistics and percentages will be used to describe the findings. The data will then be used in a descriptive report that explains the demands as described in the objectives.

Progress: Findings from the study showed that military families with medically fragile children experience two-fold demands. The first in the form of caring for the child, and second in responding to military life. Respondents to the survey were mainly young, enlisted-member wives. Mothers are the primary care providers and often lacked adequate support systems, care support, and respite care. Child care requirements were often the full time job for the mother, preventing, limiting, or interrupting employment outside the home. Responsibilities of military life greatly intensify the daily challenges for the families. Demands placed on the active duty member received precedence over child care demands, greatly limiting the active duty member's ability to assist with the medically fragile child. These families endure more frequent and longer separations because of the child's condition. Family members experience frustration with the increased responsibility, sadness, anger, and child care problems. Study results indicate both a need for medical and military case management as well as greater support for the family members. This study was the basis of a thesis for a Master's in Nursing Science at the University of Washington.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/165	**Status:** Completed
Title: Profile of Army Nurse Managers Conflict Handling Modes in the Hospital Setting		
Start Date: 12/15/95	**Est. Completion Date:** Jan 96	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: MAJ Julie K. Weber, AN		
Associate Investigators:	CPT Thomas A. Darisse, MC	
Key Words: Conflict:nurse management, resolution		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this pilot descriptive study is to describe nurse managers' selection of conflict handling styles for facilitating conflict resolution in the hospital setting.

Technical Approach: This is a pilot study that will use a descriptive survey to determine the incidence and use of different conflict handling modes by Army nurse managers and staff nurses in conflict situations. A sample size of 30 (15 staff nurses and 15 nurse managers, i.e., head nurses and nursing supervisors) is sought. This method is being used to establish a foundation to conduct further research by this investigator on conflict resolution and negotiation skills for military nurse managers. Conflict handling modes will be measured using the Thomas-Kilmann Conflict MODE Instrument. Results will reveal information about the individuals most frequently used and least used conflict handling strategies. Data analysis will focus on summarizing characteristics of the demographic data, profile of conflict handling modes, and the relationships between demographic data and conflict handling modes.

Progress: Protocol was completed, but no other information is available.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/136	**Status:** On-going
Title: Teen Pregnancy		
Start Date: 07/19/96	**Est. Completion Date:** Jun 97	
Department: Obstetrics/Gynecology	**Facility:** MAMC	
Principal Investigator: LTC Byron C. Calhoun, MC		
Associate Investigators: CAPT Anne McEwen, MC	MAJ Nathan J. Hoeldtke, MC	
Key Words: Pregnancy, teen, special clinic		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate that unique and comprehensive teen clinics in the military provide improved outcomes.

Technical Approach: Pregnancy in teens remains a conundrum. Various studies provide confusing results regarding comprehensive clinics and pregnancy outcomes. Our study seeks to expand the investigation into teen pregnancy by providing a platform of a comprehensive clinic compared to married teenagers in routine obstetrical clinics in a cohort of single women between the ages of 20-24 years. We believe that we will find an improved outcome in the teenagers in the focused clinic. Demographic data including age, race, gravidity/parity, tobacco use, and substance abuse will be analyzed. Outcome will be examined utilizing week gestation at delivery, fetal birth weights, APGARS, anemia, NICU admission days, deliveries < 2500 gms, mode of delivery, intrauterine growth delay, c-section rates, preeclampsia, gestational diabetics, large for gestational age (>4000 gms), deliveries after 42 weeks, and delivery complications (i.e., postpartum hemorrhage, chorioamnionitis). Retrospective chart review will be used to compare the cohorts. Descriptive statistics, as well as multivariate analysis, will be used to examine the data.

Progress: Approximately 600 patients have been entered in this study. Patient enrollment is complete and the investigators are working with a data base to determine clinical outcome.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/129 **Status:** On-going

Title: The Non-invasive Detection and Characterization of Anal Incontinence in the Parous Female Population

Start Date: 06/16/95 **Est. Completion Date:**

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: COL Gary D. Davis, MC

Associate Investigators:
CPT Clinton S. Beverly, MC
LTC Bradley G. Bute, MC
LTC Phillip L. Mallory II, MC

Key Words: Incontinence:anal, pregnancy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study attempts to determine the frequency and nature of obstetric-related anal incontinence by using non-invasive techniques. Anal sphincter and pudendal nerve status would be assessed and correlated with patient questionnaire complaints and manometric measurement of function.

Technical Approach: Permanent anal incontinence is reported to complicate 4-6 percent of vaginal deliveries and has been blamed on pudendal nerve injury or sphincter muscle damage. A non-invasive study of 300 pregnant women during and after pregnancy is proposed to attempt to differentiate between neuronal, muscular or combination injuries which produce incontinence. Volunteer subjects would be assessed for: pudendal nerve terminal motor latency as a measure of innervation, manometric variables as an indicator of function and transanal ultrasound as a morphologic study. Comparison of results before and after delivery would help determine the cause of obstetric-related anal incontinence. Standardized anorectal physiology data would be recorded for each patient to include resting pressure, maximal squeeze pressure, presence of rectoanoinhibitory reflex, sphincter length, and sensory threshold. Statistical analysis will evaluate for differences being due to chance with less than five percent being considered significant ($p \leq 0.05$). Tests for ordinate and continuous variables will be employed as appropriate.

Progress: Two patients have been entered at MAMC. Accrual is slow due to a lack of personnel trained to use the equipment.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/038	**Status:** On-going
Title: Ambulatory Recording of Urodynamic Functioning in Female Soldiers During Training		
Start Date: 12/15/95	**Est. Completion Date:** Jun 96	
Department: Obstetrics/Gynecology	**Facility:** MAMC	
Principal Investigator: COL Gary D. Davis, MC		
Associate Investigators: LTC Richard A. Sherman, MS	CPT Lynda S. Gilliam, MC	
Key Words: Incontinence, female soldiers, computer aided measurement system		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether ambulatory urodynamic recordings from female soldier's participating in the actual situations which elicit urinary incontinence will: (1) show that (A) some female soldiers undergoing the rigors of airborne training will demonstrate urodynamic changes as well as physical findings when urinary incontinence develops or progress, (2) show that female soldiers who complain of incontinence, but demonstrate no abnormalities on laboratory urodynamic testing will demonstrate ambulatory urodynamic abnormalities when performing the activities they report as eliciting the incontinence, (3) demonstrate different patterns of ambulatory urodynamic abnormalities when compared to similar female soldiers who complain of incontinence but demonstrate abnormalities in the standard urodynamic laboratory, and in comparison to continent female soldiers, and (d) show that incontinent female soldiers who only demonstrate ambulatory urodynamic abnormalities will show different patterns before and after successful treatment for urinary incontinence.

Technical Approach: 100 female soldiers will be recruited by questionanaire or from clinic. We will perform ambulatory recordings to (1) compare urodynamic patterns of normal and incontinent female soldiers, (2) to compare urodynamic patterns of incontinent female soldiers before and after successful treatment, and (3) review ambulatory recordings of incontinent female solders who do not demonstrate incontinence in the laboratory urodynamic setting.

Progress: Twenty three subjects have been entered. To date, subjects have shown very abnormal contractions of various muscles while in the normal environment. These contractions lead to sudden urges and leaks. Subjects are being trained to recognize and prevent these abnormal contractions.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/084 **Status:** On-going

Title: Incidence of Exercise Related Musculoskeletal Injuries vs Phase of the Menstrual Cycle

Start Date: 03/15/96 **Est. Completion Date:** Jun 96

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: COL Gary D. Davis, MC

Associate Investigators:
LTC Richard A. Sherman, MS
LTC Delbert E. Casey Jones, MC
L. Lilliam

Key Words: Musculoskeletal injury, exercise, menstrual cycle

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the relationship between exercise related musculoskeletal injuries and the phase of the menstrual cycle.

Technical Approach: An unanticipated finding of our studies on urinary incontinence among female soldiers supported by the Defense Women's Health Research Program was that the incidence is much worse and more prevalent during the luteal phase of the menstrual cycle. At least one civilian study has found that more women are injured while playing soccer during the luteal phase. There is some evidence that ligaments are stretched more during this phase possibly due to the presence of more progesterone. If ligaments are actually being significantly stretched/weakened during this phase, a disproportionate rate of exercise related injuries would occur during the luteal phase. We propose to determine whether this relationship exists to an important extent by asking all female soldiers who sustain exercise related musculoskeletal injuries at Fort Lewis how long it has been since their last period to determine where they are in their cycles. The subjects will also have their blood drawn the morning after the injury and once again during the follicular phase of their next menstrual cycle (Day 8 of the menstrual cycle), to assay for concentrations of metabolites of estrogen and progesterone. This will objectively document the phase of the cycle as well as supply quantifiable information concerning hormone levels. Disproportionately low occurrence rates among female soldiers who do not go through a luteal phase for any reason will be evaluated as well.

Progress: Four patients have been entered. Accrual is slow due to a lack of support personnel.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/011 **Status:** Terminated

Title: The Incidence of Spontaneous Abortion in Obese Patients: A Retrospective Chart Review

Start Date: 09/02/94 **Est. Completion Date:** Jun 94

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: CPT Karen E. Hayes, MC

Associate Investigators: CPT David H. Harrison, MC
MAJ Alicia Y. Armstrong, MC

Key Words: Abortion, obesity

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the response rates of metastatic or locally advanced breast cancer with administration of four cycles of high doses of Taxol as a three hour infusion with Rhu-G-CSF support. 2) To evaluate the feasibility of administering this regimen for at least four cycles.

Technical Approach: Women with metastatic Stage IV or locally advanced Stage IIIb breast cancer, with measurable disease, will be eligible for this study. Although patients may have received adjuvant chemotherapy, they should not have received any chemotherapy for metastatic disease. All patients will receive a premedication regimen prior to taxol administration. Taxol will be administered as a three hour continuous infusion at a dose of 250 mg/m^2; the infusion will be repeated every 3 weeks. Rhu-G-CSF will be given at 5 ug/kg subcutaneously from day 2 of every cycle. After completion of the four cycles, further treatment, including continuation of Taxol will be at the discretion of the investigator.

Progress: This protocol has been terminated at MAMC. Original PI (LTC Armstrong) could provide no information on the study. CPT Hayes has been reassigned and can not be located. No records of this study ever being implemented can be located, and the Chief, OB Service at MAMC, stated that no protocol by this name is being done at MAMC at present.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/106 **Status:** Completed

Title: Feto-placental Vasculature Response to Fetal Compartment Acidosis and Acidosis with Hypoxia in the Dual Perfuesed Human Placental Cotyledon Model

Start Date: 06/21/96 **Est. Completion Date:** Jun 96

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: MAJ Nathan J. Hoeldtke, MC

Associate Investigators:
LTC Roderick T. Hume Jr., MC
Katherine H. Moore, Ph.D.
MAJ Peter G. Napolitano, MC
LTC Byron C. Calhoun, MC

Key Words: Fetal acidosis, hypoxia, vasculature response, cotyledon model

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To investigate the effect of (1) acidotic fetal perfusate alone and (2) acidotic and hypoxic fetal perfusate together on the fetoplacental vasculature in a dually perfused, isolated human placental cotyledon model. This will be investigated by evaluating changes in baseline perfusion pressure of the fetal circuit and changes following angiotensin II challenge.

Technical Approach: We will utilize the dual perfused, isolated human placental cotyledon model to assess the effect of an acidotic fetoplacental vascular perfusion medium on the baseline perfusion pressure and response of the perfusion pressure to physiologic doses of angiotensin II. We will repeat the same experiment with an acidotic and hypoxic perfusion medium. We will perfuse cotyledons of 7 placentas for each of the two types of media. Placentas will be obtained from uncomplicated vaginal deliveries and cesarean sections on MAMC labor and delivery. Two cotyledons from each placenta will be used, one to serve as a control cotyledon and the other as a study cotyledon. A random number table will determine which perfusion medium will serve as the study perfusate for each placenta. Both the maternal side and the fetal side of each cotyledon will initially be perfused with a perfusate and each fetal circuit will be challenged with angiotensin II and the response recorded. The study cotyledon will then have the fetal circuit switched to a perfusate which is either acidotic or acidotic and hypoxic. Each fetal circuit will again be challenged with angiotensin II and the response recorded. After a brief recovery period the angiotensin II challenge will be repeated and the response recorded. The study fetal circuit will then be re-perfused with the original perfusate, allowed a recovery period, and each fetal circuit will again be challenged with angiotensin II and the response recorded. During the initial perfusion, study perfusion, and recovery perfusion, the pH, pO_2, and pCO_2 of the inflow perfusate and maternal and fetal effluents will be evaluated and recorded. The perfused cotyledons will be dissected from the surrounding placental tissue and weighed at the end of each experiment. Paired *t*-test will be utilized to compare differences between the mean perfusion pressures after stimulation with angiotensin II. Differences in cotyledon weights and baseline pressures will also be analyzed with a paired *t*-test. Linear regression analysis will be performed to determine correlation between cotyledon weights and pressure changes.

Progress: Dually perfused cotyledons from 14 placentas were studied with either an acidotic fetal circuit perfusate (n=7) or an acidotic hypoxic fetal circuit perfusate (n=7). The fetoplacental perfusion pressure and pressor response to angiotensin II were not affected by fetal circuit acidosis or acidosis-hypoxia. This suggests that neither fetal acidosis, nor fetal acidosis combined with hypoxia, has a direct effect on fetoplacental vascular tone.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 92/101	**Status:** Suspended
Title: Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy		
Start Date: 09/04/92	**Est. Completion Date:** Mar 94	
Department: Obstetrics/Gynecology	**Facility:** MAMC	
Principal Investigator: LTC Roderick T. Hume Jr., MC		
Associate Investigators: LTC Glenn C. Tripp, MC	Millie Herd, AN MAJ Jerome N. Kopelman, MC	
Key Words: herpes simplex virus, pregnancy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate infants of sero-converters by means of Denver Developmental Tests and type specific HSV antibodies by Western blot in order to answer the following questions: does maternal HSV-2 seroconversion during pregnancy without evidence of asymptomatic shedding of the virus from the genital tract at the onset of labor or evidence of acute neonatal HSV infection result in significant neurodevelopmental disability in the offspring; and can asymptomatic HSV seroconversion in the newborn occur as a result of in utero infection or undetected perinatal transmission without evidence of acute neonatal infection.

Technical Approach: About 3% of women who are HSV seronegative at the first prenatal visit are HSV seropositive at the time of delivery. If the maternal HSV cultures were negative on admission to the labor suite and the neonatal conjunctival and nasopharyngeal cultures were negative on day 2 of life, the newborns are discharged from the hospital at 1-5 days postpartum. The only long term follow-up performed has been routine pediatric care. However, any long term neurodevelopmental consequences to the uninfected offspring of women experiencing an asymptomatic first episode of genital HSV during pregnancy are unknown. This study will be done in conjunction with Children's Hospital, Seattle, WA, and the University of Washington. Approximately 20 children will be studied at Madigan. At six months of age, the child will be administered the modified Denver Developmental Test, and a blood sample will be drawn to measure type-specific HSV antibodies by Western blot. By six months of age, passively acquired maternal antibody should be completely metabolized. HSV antibody present at this time should represent an asymptomatic congenital or neonatal infection and seroconversion. Information regarding the mother's demographic profile and pregnancy history, her serologic and virologic profiles, and the infant data (e.g., birth weight, gestational age) will also be obtained.

Progress: One hundred eighty four patients have been enrolled in this multicenter protocol since it was implemented. The data have been forwarded to the University of Washington for analysis. The protocol has been put in a suspended status until a decision is made whether to update this protocol or to rewrite as a new protocol since some of the objectives have changed due to information already obtained.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/159 **Status:** Completed

Title: Three Dimensional Ultrasound

Start Date: 07/21/95 **Est. Completion Date:** Jun 96

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: CPT Christian R. Macedonia, MC

Associate Investigators:
MAJ Jerome N. Kopelman, MC
COL Dan C. Moore, MC
LTC Arthur S. Maslow, MC
Troy H. Patience, B.S.

Key Words: Ultrasound, 3D

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess the feasibility and quality of three dimensional reconstruction of conventional two-dimensional ultrasound images using a low-cost and transportable system.

Technical Approach: We propose to use a continuous running acquisition process for three dimensional ultrasonographic data visualization. The process involves the use of a worm drive linear translation device coupled to a conventional two-dimensional ultrasound transducer. this transducer sends conventional 2 dimensional ultrasonographic data streams to a standard 2D image processor. The RGB output from that processor is downloaded into a 3D graphics workstation where it is rendered into a three dimensional image. This image can then be manipulated to provide novel views of internal anatomy. It can also be used to make size and weight estimations of internal organs for preoperative planning.

Progress: 24 gravid volunteers were enrolled. Each had conventional 2D screening ultrasound at 16-20 weeks gestation. Using the continuous lines acquisition method, image stacks containing multiple parallel 2D sonographic frames were obtained. Volume visualization was then accomplished using several public domain software packages and commercially obtained stereo projection glasses. These data sets were successfully transformed into TIFF, PICT, and MPEG compression formats for remote "tele-consulting." The investigators were able to successfully demonstrate that continuous linear acquisition of standard 2D ultrasound used in combination with widely available visualization engines and data compression provided a new means of tele-consultation for perinatologists. This research in 3D ultrasound demonstrates that inexpensive modifications to standard 2D ultrasound equipment may provide a means of enhancing tele-consultation in maternal fetal medicine.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/074	**Status:** Completed
Title: The Effects of Low Dose Acetylsalicylic Acid Infusion on Perfusion Pressure in the Dual Perfused Isolated Human Placental Cotyledon Model		
Start Date: 02/16/96	**Est. Completion Date:** May 96	
Department: Obstetrics/Gynecology	**Facility:** MAMC	
Principal Investigator: MAJ Peter G. Napolitano, MC		
Associate Investigators: LTC Roderick T. Hume Jr., MC LTC Byron C. Calhoun, MC	MAJ Nathan J. Hoeldtke, MC Katherine H. Moore, Ph.D.	
Key Words: Placenta, perfusion pressure, acetylsalicylic acid		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To study the effect of acetylsalicylic acid (ASA) on the maternal and fetal components of the human placenta, via the dually perfused isolated human cotyledon. The properties investigated will include changes in perfusion pressure and the production of endothelial derived vasoactive substance before, during and after treatment of the chorionic vessels with Angiotensin II. The purpose of the current study design is to isolate the endothelial compartmental response to the effects to Angiotensin II when modulated by the effects of low dose ASA free of circulating platelets.

Technical Approach: Ten to 15 placentas from uncomplicated pregnancies will be acquired. After visual inspections for lacerations or infarcts, the fetal surface will be inspected for a chorionic artery and vein pair supplying a cotyledon which will be cannulated. A circular section of placenta 8 cm in diameter will be clamped into a specifically designed holder to prevent leakage from the cut edges. Two cotyledons will be prepared from each placenta. After perfusion is established using a standard saline perfusate and a baseline steady rate is maintained for 30 minutes, one of the perfusates will be switched to include ASA an the other will not. After 20 minutes, a bolus of Angiotensin II will be injected into both cotyledons. There will be a total of four collection periods during which pressure readings and four different perfusion samples will be collected for a total of 16 samples. Statistical analysis will be done by analysis of variance with repeated measures to determine significance between treatment and control cotyledons for pressure changes after two doses of Angiotensin II. Differences in cotyledon weights and baseline pressures will be evaluated with the paired t-test. Linear regression analysis will be used to determine the correlation between cotyledon weights and pressure changes. ANOVA will also be used to determine significance between treatment and control values of prostacylin, thromboxane B2, lipid peroxide, an nitric acid.

Progress: Fourteen placentas were obtained from uncomplicated term pregnancies and 12 perfusions were completed. There was no difference in perfusion pressure response between cotyledons pretreated with ASA and control cotyledons when 50 mcg of angiotensin II was injected into the intervillous space. There was no difference between cotyledons in pressure response to $1 \times 10^{-11.5}$ moles of angiotensin II injected into the fetal circuit. However, there was a decrease in the pressor response to 1×10^{-10} moles of angiotensin II in the cotyledons pretreated with ASA. The investigators conclude that low-dose aspirin infused into the intervillous space decreased vasoconstriction elicited by angiotensin II in the fetal placental compartment. This suggests that maternal low dose aspirin therapy has effect in the fetoplacental circulation in addition to its effects in the maternal circulation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/085 **Status:** On-going

Title: Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig (Sus scrofa) and Goat (Capri hircus)

Start Date: 02/09/94 **Est. Completion Date:** Feb 97

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators:
LTC David J. Magelssen, MC
MAJ Alicia Y. Armstrong, MC
COL Paul N. Smith, MC
MAJ Rosemary L. Casey, MC
MAJ Mary C. Nace, MC

Key Words: Surgical management:gynecology, endoscopy, pig, goat,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: 1) To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. 2) To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. 3) To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans.

Technical Approach: With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

Progress: One laboratory session, utilizing four goats, was held during FY 96. The residents involved were familiarized with the techniques of enterotomy closure, bowel resection, ureteroneocystostomy, and cystostomy closure.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/051	**Status:** On-going
Title: Caesarean Section Pain Study		
Start Date: 01/19/96	**Est. Completion Date:** Apr 96	
Department: Obstetrics/Gynecology	**Facility:** MAMC	
Principal Investigator: CPT Jeffrey A. Rondeau, MC		
Associate Investigators: LTC Byron C. Calhoun, MC CPT Frederick W. Larsen, MC CPT Shelley B. James, AN	LTC Joseph J. Mancuso Jr., MC MAJ Nathan J. Hoeldtke, MC CPT Byron D. Gatlin, MC	
Key Words: Pain:cesarean, perioperative local anesthetic, IV narcotic therapy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To attempt to determine if perioperative local anesthetic injected into the incision line and the ilioinguinal nerves will improve post-operative pain control compared to standard intravenous narcotic therapy.

Technical Approach: This is a prospective, double-blinded study. After subjects are randomized to one of two study groups, spinal anesthesia using 1.6 cc of 0.75% bupivacaine with 0.2 mg epinephrine and 25 micrograms of fentanyl will be performed. After an adequate surgical block is obtained, 10 cc 0.5% bupivacaine with epinephrine 1:200,000 or saline control will be infiltrated along the proposed line of incision with an additional 5 cc placed to perform a bilateral ilioinguinal block (10cc total). A total of 20 cc of study solution or normal saline will be used prior to incision. Just prior to closure, the wound will be irrigated with 10cc of 0.5% bupivacaine with epinephrine 1:200,000 or saline control for a total of 30cc of study solution. The patient will receive perioperative prophylactic antibiotics using either Ancef 1gm IV or Cleocin 900mg IV as per protocol of the Department of Obstetrics. Post-operatively the patient will be placed on PCA (patient controlled anesthesia) using morphine with a concentration of 1mg/ml. The PCA will not be activated until the patient desires pain control. When reporting discomfort, the patient will receive a bolus of 5mg of morphine intravenously followed by activation of the PCA device. A continuous infusion will not be used so that actual narcotic requirement can be documented. The PCA dose and lockout interval will be 2mg and 8 minutes, respectively. If uncomfortable, the patient may receive a 5mg morphine bolus every four hours as needed. The patient will be given a flow sheet on which she will record verbal analogue pain scores at 1, 4, 8, 12 18, 24 hours postoperatively. The quantity of narcotic analgesic will also be tabulated for a 24 hour period at the same time interval as pain scores are assigned by the patient. Verbal analgesic usage on post operative days 1 and 3 will be recorded. Additional demographic data to include first time to ambulation, surgical complications, and surgical time, infant size, and blood loss will also be examined to determine influence on obtained data.

Progress: Thirty four patients have been entered with no adverse effects. However, during the transfer of several pharmacists to other institutions, the randomization key was misplaced. Since it has not been located, the pharmacy is developing a new key and the study will start over.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/138 **Status:** On-going

Title: Once vs Thrice Daily Gentamicin Dosing in Postpartum Endomyometritis

Start Date: 08/05/94 **Est. Completion Date:**

Department: Obstetrics/Gynecology **Facility:** MAMC

Principal Investigator: CPT Anne B. Shrout, MC

Associate Investigators: MAJ Jerome N. Kopelman, MC
CPT Scott M. Kambiss, MC

Key Words: endomyometritis, gentamicin, dosing

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the once-daily dosing of gentamicin compared to the usual thrice-daily regimen of gentamicin in the treatment of postpartum endomyometritis and in patients with chorioamnionitis that undergo cesarean section.

Technical Approach: Patients will be enrolled from the patient population at Madigan. They must be diagnosed with postpartum endomyometritis or with chorioamnionitis and subsequent cesarean section. Patients will be randomized into two arms. Group 1 will receive the standard gentamycin 1.75 mg/kg every 8 hours IVPB with clindamycin 900 mg every eight hours. Group 2 will receive gentamycin 5.25 mg/kg every 24 hours IVPB and clincamycin 900 mg every eight hours IVPB. Both groups will have frequent drug levels obtained from a heplock in the opposite arm. All patients will remain on antibiotics until afebrile X 48 hours. Clinical response and failure will be determined by chi-square.

Progress: 5 subjects were entered in FY 96, for a total of 13 subjects. Pending further review of a similar study that has been published, this study may be terminated before completion. Dr. Shrout, the original PI, returned in August and took over the protocol from Dr. Kambiss.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PATHOLOGY

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/117 **Status:** Terminated

Title: Investigation of Morphologic Features of Atypical Squamous Cells on PAP Smears with Human Papilloma Virus DNA Probe Correlation

Start Date: 06/16/95 **Est. Completion Date:** Jun 96

Department: Pathology **Facility:** MAMC

Principal Investigator: MAJ Barbara A. Crothers, MC

Associate Investigators: CPT Daniel D. Mais, MC

Key Words: Human papilloma virus, DNA, PAP, morphologic features

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To test the hypothesis that there are defined morphologic features of "Atypical Squamous Cells of Uncertain Significance (ASCUS), suggestive of Low Grade Squamous Intraepithelial Lesion (LGSIL)" which differ significantly from reactive changes on the cervicovaginal PAP smear and can be used to predict the presence of the Human Papilloma Virus (HPV).

Technical Approach: This study will consider a group of 250 female patients, all with PAP smears reported as "atypical squamous cells (ASCUS)" or "reactive changes" from 1 July 1993 to 1 July 1994. The PAP smears will be evaluated independently by the two investigators for the presence or absence of certain predefined morphologic features. These results will be tabulated. All of the PAP smears will then be subjected to DNA probes by *in situ* hybridization (ISH), testing for the presence of HPV types 6, 11, 16, 18, 31 and 33. Cases which reveal viral DNA within the observed atypical cell will be considered positive and all others will be considered negative for LGSIL. The accumulated morphologic data will be subjected to multivariant statistical analysis to determine the significance of each feature in predicting the presence of HPV. The investigators will attempt to establish which features are most useful as criteria for reclassifying ASCUS PAP smears as LGSIL.

Progress: Twenty samples were obtained for a pilot study. The principal investigator was unable to obtain funding to proceed with the study before she was reassigned to another medical center in January 1996.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/085 **Status:** On-going

Title: Parental Assessment of Psychologic Adjustment in Children with Asthma: A Comparison of the Child Behavior Checklist and the Behavior Assessment System for Children

Start Date: 03/17/95 **Est. Completion Date:** Jul 95

Department: Pediatrics **Facility:** MAMC

Principal Investigator: CPT Veronica R. Baechler, MC

Associate Investigators:
MAJ Robert A. Byrne, MS
COL Patrick C. Kelly, MC
MAJ Stephen E. Greefkens, MC

Key Words: Asthma:psychologic adjustment, Child Behavior Checklist, Behavior Assessment System for Children

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To assess the correlation between the Child Behavior Checklist (parent report) and the Behavior Assessment System for Children (parent report) in assessing the social and emotional status of a group of children and adolescents with asthma. 2) To assess the impact of disease severity on the social and emotional status of this population. 3) To assess the impact of moves or service member deployment on the social and emotional status of this population.

Technical Approach: Sixty subjects, ages from 8 to 16 years and including approximately equal number of males and females, who have chronic asthma will be identified through review of Pediatric Pulmonary Clinic files and review of upcoming appointments. After consent has been obtained the mother of these subjects will be asked to fill out both the CBCL and the Parent Report Form of the BASC. In addition, a brief questionnaire inquiring about the subjects health status, recent moves, and service member deployments will be completed by the mother. When data collection is complete, it will be analyzed as follows. Correlation between the various scales of the CBCL and BASC will be analyzed using paired t-tests. ANOVA will be used to study the relationship between disease severity and several scales on the CBCL. An unpaired t-test will be used to study the relationship between recent moves or parent deployment and several scales on the CBCL.

Progress: No new patients were enrolled in FY 96 (30 patients total have been enrolled). New PI has just taken over the protocol and will start enrolling patients again in December 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/052	**Status:** On-going

Title: Intrauterine Growth: Factors That Influence the Relationship Between Gestational Age and Birth Weight, Length, and Head Circumference

Start Date: 03/05/93	**Est. Completion Date:** Mar 96
Department: Pediatrics	**Facility:** MAMC

Principal Investigator: LTC Joanna C. Beachy, MC

Associate Investigators: None

Key Words: intrauterine growth, age, birthweight, length, head circumference

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1000.00	**Periodic Review:** 09/30/96

Study Objective: (1) How does the relationship between gestational age and birth weight, length, and head circumference from data gathered from newborn infants compare with published data? (2) Does the average birth weight, length, head circumference and ponderal index at each gestational age differ from year to year of the study (1981 - 1992)? (3) Do infants from twin/multiple gestation pregnancies in this selected population show the expected growth pattern, that is no alteration in growth until the third trimester? (4) Does the classification of diabetic (gestational versus non-gestational) impact on incidence of large for gestational age infants and on the ponderal index?

Technical Approach: This is a retrospective review of data from > 24,000 infants born over an 11 year period. Infants with diagnosed congenital anomalies, chromosomal abnormalities and hydrops fetalis will be excluded.

Data Analysis: 1) For evaluation of effect of gestational age on birth weight, length, head circumference and ponderal index, all multiple gestation infants and IDMs will be excluded. Data will be analyzed by non-linear regression to generate curve with 95% confidence levels. Alternatively, mean (± 2) standard deviations, third and tenth percentile of birth weight, length and head circumference will be calculated for each gestational age. A smoothed curve will then be generated and compared to previously published curves. 2) Data will also be stratified by year and analyzed in a similar fashion, that is birth weight, length and head circumference will be compared at each gestational age yearly from 1981 - 1992. Statistical significance will be evaluated by regression analysis or ANOVA, controlled for gestational age. 3) The birth weight, length, head circumference and ponderal index from infants of multiple gestations will be evaluated as in (1) and compared with the standard curves generated in (1) and published for twin gestations. Evaluation of the ponderal index may indicate when the placental supply is no longer sufficient. 4) The birth weight, length, head circumference and ponderal index from IDM will be handled in a similar manner. Subdivision of data by White's category of maternal diabetes will be done.

Progress: Data collection is complete on 16,893 births. The PI is still reviewing/editing data set for graphing.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/137 **Status:** On-going

Title: The Relationship of Positive Skin Tests to House Dust Mite, Grass Pollen, and Cat Dander to Asthma in Children Presenting to a Pediatric Pulmonary Clinic

Start Date: 06/16/95 **Est. Completion Date:** Sep 96

Department: Pediatrics **Facility:** MAMC

Principal Investigator: LTC Edward R. Carter, MC

Associate Investigators:
CPT Jeffrey W. Delaney, MC
Troy H. Patience, B.S.
MAJ Evan J. Matheson, MC
COL Donald R. Moffitt, MC

Key Words: asthma, dust mite, grass pollen, cat dander, children

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the following in children who attend the MAMC Pediatric Pulmonary Clinic: (1) the prevalence of positive skin tests to house dust mite (2 species), cat dander, and grass pollen in children with asthma ≥ 4 years old; (2) whether there is positive correlation between severity and chronicity of asthma and positive skin tests, especially to house dust mites; (3) whether there is positive correlation between the age of the child with asthma and the probability of having a positive skin test; (4) whether there is positive correlation between signs/symptoms of allergy and positive skin tests, especially to house dust mites in children with asthma; (5) relationships between total serum IgE, blood eosinophilia, asthma, and allergy in asthmatic patients and to establish the predictive value of these serologic tests for skin test positivity in asthmatics; and (6) to devise an algorithm for deciding which children need an allergy referral, which children should undergo environmental controls without a formal allergy assessment, and which children have such a low risk for allergy that no allergy assessment is necessary.

Technical Approach: A total of 100 to 200 children ≥ 4 years old with asthma presenting to the MAMC Pediatric Pulmonary Clinic for evaluation will be asked to participate in this observational study. Children who meet the diagnostic criteria for asthma will be eligible. Severity of asthma will be categorized as mild, moderate, or severe, based upon test criteria. Asthma will also be categorized as chronic or intermittent based upon the frequency of signs/symptoms. We will make all attempts to include consecutive children to ensure a representative sample. Subjects will complete a questionnaire and a complete history and physical will performed. Blood will be drawn for serum IgE and peripheral blood eosinophil determination. They will receive skin prick tests for sensitivity to house dust mice, grass pollen, cat dander and 2 controls. We will determine the frequency of positive skin tests in this sample and assess the relationships between positive skin tests and patient age, severity and chronicity of asthma, signs/symptoms of allergy, an elevated serum total IgE, and blood eosinophilia. Data analysis methods will include chi-square for presence or absence of an effect on positive skin test for each variable. Multiple regressions will be performed for positive skin tests as a whole and then individually for each of the 3 specific skin tests. These regression analyses will determine which variables or combination of variables that best predicts a positive skin test in these asthmatic children.

Progress: Approximately 100 patients were entered in this study. One patient had arm swelling with the grass pollen test, which improved with antihistamine treatment. All data have been collected and data analysis is progressing on schedule.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/179	**Status:** Terminated
Title: GLAXO Open Label Program for Patients with AIDS		
Start Date: 08/18/95	**Est. Completion Date:** Indef.	
Department: Pediatrics	**Facility:** MAMC	
Principal Investigator: MAJ Mary P. Fairchok, MC		
Associate Investigators: None		
Key Words: HIV, Lamivudine (3TC), Zidovudine		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To make available the therapeutic anti-retroviral agent, 3TC (lamivudine), in combination with zidovudine to patients with progressive, symptomatic Human Immunodeficiency Virus (HIV) disease who are refractory to all other approved therapies and unable to participate in any 3TC controlled clinical trials.

Technical Approach: This open label program offers 3TC (lamivudine) for an expected 2 to 3 pediatric patients with advanced disease (CD4<300) who have been refractory to AZT and DDT. 3TC is a cytosine nucleoside analogue with potent in-vitro inhibitory activity demonstrated against HIV-1. High doses of 3TC have been tolerated over extended durations in toxicology trials providing no evidence to preclude clinical administration. This drug has been extensively studied to date in clinical phase I/II studies involving both pediatric and adult patients demonstrating good tolerance at doses up to 20 mg/kg/day with minimal toxicity. This drug is now available on an open label basis for compassionate use in adult and pediatric patients. The 3TC open label program has been approved and reviewed by the Ethical Review Committee (Kansas). Background demographic data of all patients will be summarized and displayed. Baseline values on study related diagnoses and lab tests will be compared with results obtained during and at the end of the study period. Lab abnormalities will be summarized and displayed by toxicity grade and dose level. Dropout/withdrawal rates and incidences of adverse events and AIDS-defining illnesses will be summarized and displayed by treatment regimen.

Progress: Two subjects were screened for entry into this study. However, the agent was approved and released by the FDA in early November 1995 before the patients were entered on the study. This was a treatment protocol only and was terminated by the sponsor.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/092 **Status:** On-going

Title: Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

Start Date: 07/20/90 **Est. Completion Date:** Sep 91

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Mary P. Fairchok, MC

Associate Investigators:
MAJ Thomas A. Perkins, MC
COL Marvin S. Krober, MC
COL James S. Rawlings, MC
LTC Joanna C. Beachy, MC

Key Words: HIV,diagnostic assays,children

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: 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: One additional child has been entered in this study during FY 96 for a total of four since the study started in 1990.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/060	**Status:** On-going
Title: Single Dose Intramuscular Dexamethasone Acetate vs. Oral Prednisone to Treat Exacerbations of Asthma in Young Children		
Start Date: 02/16/96	**Est. Completion Date:** Apr 97	
Department: Pediatrics	**Facility:** MAMC	
Principal Investigator: CPT Delores M. Gries, MC		
Associate Investigators: COL Donald R. Moffitt, MC	LTC Edward R. Carter, MC Janice Gibbons, M.D.	
Key Words: Asthma, dexamethasone acetate, prednisone, children		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study objective: 1) To determine whether a single intramuscular dose of dexamethasone acetate is as effective as a five-day course of oral prednisone in resolving mild-moderate asthma exacerbations in young children. 2) To determine any differences in tolerance and/or adverse effects between a single dose of IM dexamethasone acetate and a 5-day course of oral prednisone in young children with mild-moderate exacerbations of asthma.

Technical approach: 20 children ages six months to seven years old who present to the MAMC Pediatric Clinic with acute exacerbations of asthma will be eligible to enroll in this prospective, randomized, investigator-blinded study. Patients will be randomized to receive either a single IM dose of dexamethasone or prednisone taken orally each day for five days. Dose will be adjusted for the age of the child. Data to be collected include, a complete physical examination at study entry along with wheeze and cough scores. On days 3 and 7 parent/guardian will be contacted by telephone and wheeze and cough scores, number of doses of albuterol used and tolerance of the treatment will be collected. On days 5 and 14, a complete physical exam will be repeated along with the measures collected on days 3 and 7. In addition an overnight timed urine collection for cortisol determination will be performed. On day 28 a final telephone call will be made to determine the number of patients who suffer a second asthma exacerbation within one month of the study. In addition the following data will be collected, number of treatment failures, time taken for patients to clear the asthma symptoms, number of patients who relapse within one month of the study, number of patients who require emergency department visits and hospitalization for asthma within one month of starting the study, patient satisfaction and complications.

Progress: Four patients have been entered without adverse effects.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/080 **Status:** On-going

Title: $MgSO_4$ Therapy for the Prevention of Intracranial Hemorrhage and Cerebral Palsy in the Very Low Birthweight Infant: Role of Interleukin-6

Start Date: 04/19/96 **Est. Completion Date:** Nov 97

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Roger M. Hinson, MC

Associate Investigators: Robert Mittendorf, M.D., Ph.D.
MAJ Karen M. Nelson, MC

Key Words: hemorrhage:intracranial; cerebral palsy, interleukin-g, magnesium sulfate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether an association exists between the inflammatory cytokine interleukin-6 and intracranial hemorrhage or cerebral palsy and if so, is this relationship altered by antenatal administration of magnesium sulfate.

Technical Approach: This study is designed to test the hypothesis that very low birth weight infants with intracranial hemorrhages and/or cerebral palsy will have elevated interleukin-6 cord blood levels as compared to normal controls and that antenatal administration of magnesium sulfate will alter the cord blood levels of interleukin-6. The cord blood samples will be provided through an ongoing protocol at the University of Chicago investigating whether MgSO4 therapy can prevent intracranial hemorrhage or cerebral palsy in the very low birth weight infant. This protocol is concerned only with the blinded evaluation of the cord interleukin-6 levels. It is anticipated that approximately 200 patients will be enrolled resulting in the same number of samples to be tested. Interleukin-6 bioactivity will be determined by the B9 bioassay and antigenic interleukin-6 will be determined by commercial ELISA. The data will be presented graphically and associations between IL-6, Mg therapy and cord serum level, clinical and histopathologic evidence of chorioamnionitis and outcomes will be evaluated. Differences in IL-6 levels will be tested for statistical significance by t-test. Outcomes will be evaluated by an appropriate non-parametric test such as chi-square.

Progress: Fifty-six cord blood samples have been analyzed for IL-6. Study continues to be blinded as to treatment arms.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/025 **Status:** On-going

Title: Fetal Development: Are Undiagnosed Maternal Inborn Errors of Metabolism Associated With Poor Intrauterine Growth and Congenital Malformations in the Developing Fetus

Start Date: 12/17/93 **Est. Completion Date:** May 95

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Roger M. Hinson, MC

Associate Investigators:
James R. Wright, M.T.
LTC Arthur S. Maslow, MC
CPT Andrew J. Bauer, MC
MAJ Thomas D. Carver, MC
Katherine H. Moore, Ph.D.
MAJ Jerome N. Kopelman, MC
MAJ Katherine S. Foley, MC
MAJ Nathan J. Hoeldtke, MC

Key Words: metabolism, fetal development, malformations, fetal death

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if previously undiagnosed maternal inborn errors of metabolism (amino acidemias or organic acidurias) are a significant cause of fetal growth retardation, fetal malformations and fetal demise.

Technical Approach: In this controlled prospective study, the serum amino acid and urine organic acid contents will be evaluated in 3 groups of pregnant women. Group 1 will consist of women who have had 2 or more spontaneous abortions, a stillbirth, or have delivered a child identified as growth retarded, microcephalic, mentally retarded or with congenital anomalies. Group 2 will be the control group and consist of women who have had no more than 1 spontaneous abortion, or have delivered children with no known anomalies or are pregnant for the first time. Group 3 will consist of women not previously enrolled who are found during the pregnancy to have a fetus which is growth retarded (≤ 3rd percentile on two ultrasounds 3-4 weeks apart), is microcephalic (≤ 3 percentile on 2 ultrasounds 3-4 weeks apart), or has congenital anomalies.

The study questionnaire will be filled out at the time of entrance into the study and will consist of information pertaining to maternal educational and health history.

All samples will be sent to clinical investigation for storage until they can be analyzed. The blood samples will be frozen at -70 C until analyzed for quantitative amino acid content. The urine sample will be analyzed by GD Mass Spectroscopy for organic acid content. If both are normal then no further investigation will be done. If both are abnormal compared to published standards, the appropriate diagnostic work-up will be done to further identify the abnormality. All samples will be collected after an 8-12 hour fast to avoid post-prandial fluctuations in amino-acid concentrations. The study participants will be notified of their individual results (if abnormal) as they become known.

Progress: Dr. Carver PCS'd and MAJ Hinson took over as PI. Fourteen patients have been entered in FY 96 for a total of 217 subjects. Analysis of the amino acid and urine organic acid samples has begun.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/129 **Status:** Terminated

Title: Randomized Trial of Nerbulized vs Instilled Cromolyn Sodijm (Intal) in the Preventin of Airway Inflammation in Ventillated Premature Neonates

Start Date: 07/02/93 **Est. Completion Date:** May 94

Department: Pediatrics **Facility:** MAMC

Principal Investigator: CPT Katherine J. Mizelle, MC

Associate Investigators:
MAJ Margaret G. Richardson, MS
LTC Deborah J. Leander, AN
MAJ Thomas D. Carver, MC
LTC Robington J. O. Woods, MC
MAJ Roger M. Hinson, MC

Key Words: Neonates: airway disease, cromolyn sodium, Intal,

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$4379.00	**Periodic Review:** 10/21/94

Study Objective: To evaluate the efficacy of direct intra-tracheal instillation of Cromolyn Sodium (Intal) vs traditional Cromolyn Sodium nebulization in preventing airway inflammation in a high risk group of intubated premature neonates.

Technical Approach: The study population will consist of premature infants born at 32 weeks gestation and less, who are placed on mechanical ventilation. Those infants for which informed parental consent has been obtained will be randomized to receive either 3 mg Cromolyn via direct intra-tracheal instillation every 6 hours for 16 doses or 20 mg by nebulization every 6 hours for 16 doses. The doses will be started within 12 hours of being placed on a ventilator. At 48, 72, and 96 hours after the first dose is given, the infant will undergo tracheobronchiolar lavage. The lavage fluid will be analyzed for number and type of inflammatory cells as well as for the presence of chemical mediators of inflammation. Analysis of data will be by CHI-square and Student's t-test. Variables that will be considered in the analysis will be use of antenatal steroids, surfactants, antibiotics, indomethacin, diuretics and bronchodilators.

Progress: The original principal investigator has left MAMC. No new patients were enrolled in FY 96. The collected specimens are no longer reliable for comparison. Due to time restraints, the PI was unable to restart this study.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/121	**Status:** Completed
Title: Effectiveness of Spontaneous Labor at Term in Relation to the Hour of Onset		
Start Date: 03/17/95	**Est. Completion Date:** Mar 95	
Department: Pediatrics	**Facility:** MAMC	
Principal Investigator: COL James S. Rawlings, MC		
Associate Investigators:	COL John A. Read II, MC	
Key Words: Labor:spontaneous, labor:hour of onset		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To measure the duration of labor, need for pharmacological augmentation and clinical outcomes of spontaneous labors at term in relation to the hours of onset and hour of delivery.

Technical Approach: Data will be prospectively compiled from all deliveries at MAMC following spontaneous onsets of labor at term (>36 weeks of gestation) during the period of 1 January 1985 through 31 December 1994. The records will be analyzed for duration of labor, need for pharmacological augmentation of labor, and neonatal outcomes in relation to hours of onset of labor and hour of delivery. Neonatal outcome parameters to be compared will be fetal distress, Apgar scores, perinatal mortality, and duration of neonatal hospital stay. Maternal risk factors for poor pregnancy outcome and demographic variables will be considered in the analysis. Data will be analyzed using chi-square analysis or Fischer's Exact-test of discontinuous data, and analysis of variance or the Student's T-test of continuous data.

Progress: Manuscript has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/008 **Status:** On-going

Title: Effect of Short Course High Dose Corticosteroids on the Immune Response to the Influenza Vaccine in a Pediatric Population

Start Date: 10/20/95 **Est. Completion Date:** Oct 96

Department: Pediatrics **Facility:** MAMC

Principal Investigator: CPT Daniel P. Trementozzi, MC

Associate Investigators: MAJ Mary P. Fairchok, MC
LTC Edward R. Carter, MC

Key Words: Influenza, immune response, pediatric, corticosteroids

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To study the effect of short course high dose oral corticosteroids on the immune response to the influenza vaccine in young asthmatics. 2) To increase awareness of the need for annual influenza immunization in a high risk pediatric population.

Technical Approach: One hundred sixty pediatric patients recommended to receive the influenza vaccine will be enrolled. Of these, half will be subjects with asthma who present to the pediatric clinic with a flare of their asthma and who require treatment for a short, 5-day course of high dose oral prednisone. The remaining half will be either healthy siblings of asthmatics or asthmatics who are both asymptomatic at time of enrollment and who have not received oral steroids within three weeks prior to beginning the study. All subjects will receive one dose of the 1995-96 inactivated, split influenza vaccine at a dose of 0.5 cc, given IM. Blood will be drawn just before and 2-3 weeks after vaccination and influenza titers will be determined. Patients will be categorized as responders if they demonstrate a fourfold rise in serum titers to influenza following vaccination.

Progress: Twenty-two patients were entered (15 control and 7 treatment). The initial data analysis, comparing the mean antibody response between the two groups, failed to show a statistically significant difference. Unfortunately, due to the small number of patients in each group, there was insufficient statistical power to reliably exclude a type II (false negative) error, Park, et al, (Pediatrics 1996;98[2]) obtained similar results. However, the authors did not finely discriminate between chronic and acutely treated asthmatics. In light of the above published research, the investigators plan to continue to acquire data for another year in order to confirm and support the results of the above group, using stricter inclusion/exclusion criteria for the prednisone treated group.

DETAIL SHEETS FOR PROTOCOLS

PHARMACY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/055 **Status:** Completed

Title: Evaluation of Antihyperlipidemic Drug Discontinuation at Army Medical Treatment Facilities

Start Date: 02/16/96 **Est. Completion Date:** Jun 96

Department: Pharmacy Service **Facility:** MAMC

Principal Investigator: COL Robert M. Craghead, MS

Associate Investigators: LTC Daniel D. Remund, MS

Key Words: Antihyperlipidemics, drug discontinuation, bile acid sequestrants, statins

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess discontinuation of two types of antihyperlipidemic agents among patients who obtain their medications at Army medical treatment facilities. To compare the cumulative incidence of drug discontinuation for patients who began therapy with a bile acid sequestrant to patients who began therapy with a statin. To determine the proportion of patients in each group who subsequently obtain different antihyperliipidemic drugs after discontinuing the initially-prescribed drug.

Technical Approach: This will be a retrospective multi-center cohort study. The prescription records contained in the Uniformed Services Prescription Database (USPD) will be used to measure the one year cumulative incidence of drug discontinuation for bile acid sequestrants and statins. Telephone interviews with patients will be used to verify patient eligibility, ascertain certain patient factors, and identify patients' perceptions regarding the reasons for discontinuing antihyperlipidemic drug therapy and whether or not the patient decided on his/her own discontinue therapy. The association between the type of antihyperlipidemic drug prescribed and drug discontinuation will be investigated through classical and multivariate analyses. Crude and adjusted drug discontinuation risk differences between the two groups will be calculated. Logistic regression will be used to identify patient, drug regimen, and MTF factors that confound or modify the association between the type of antihyperlipidemic drug prescribed and drug continuation. Logistic regression is an appropriate statistical tool for these analyses because the outcome variable (drug discontinuation) is binary and the period of observation to detect drug discontinuation is the same for all study subjects.

Progress: Discontinuation of antihyperlipidemic drugs was assessed through a review of prescription records from the Uniformed Serviced Prescription Database and telephone interviews with 95 patients. 74% of patients who were initially prescribed a resin type of antihyperlipidemic drug discontinued their medication within one year; 17.8% prescribed with a statin type discontinued within one year; 43.2 % of the resin type subsequently obtained prescriptions for other types of antihyperlipidemic drugs; 25% of those who discontinued the statin type subsequently obtained other types of antihyperlipidemic drugs. A manuscript is being prepared.

DETAIL SHEETS FOR PROTOCOLS

PHYSICAL MEDICINE AND REHABILITATION SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/098 **Status:** On-going

Title: A Randomized Clinical Trial of A Home Program Monitored by a Physical Therapist versus Repeated Outpatient Physical Therapy Visits Combined with Home Program to Treat Stiff Shoulder

Start Date: 04/19/96 **Est. Completion Date:** Jul 97

Department: Physical Medicine & Rehabilitation Svc **Facility:** MAMC

Principal Investigator: Lynn C Burke

Associate Investigators: Kathleen Hummel-Berry

Key Words: Stiff shoulder, home physical therapy, OP physical therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare physical therapy treatment of stiff shoulder using guided home program only, to a protocol of outpatient clinic based physical therapy which includes an identical guided home program of exercises, plus the use of physical agents and passive procedures.

Technical Approach: This will be a prospective randomized clinical trial comparing two forms of physical therapy for stiff shoulder; an individualized home program, and a protocol of physical therapy which combines home program with typical outpatient clinic interventions. One hundred sixty subjects (80 from Madigan Army Medical Center) will be recruited for this multi-center study. Eligible subjects referred to physical therapy will be asked to participate in the study. Therapists providing outpatient care must apply one physical agent (such as ultrasound or heat packs) and one passive technique (such as mobilization or stretching) at each clinic visit, choosing the specific agent and manual technique based on evaluation of the patient's individual needs. The home program of exercises will be the same for both groups, and will address posture correction, range of motion exercises, and education on safe levels of functional activity. Thus, the only difference in the treatment provided to the two groups will be the fact that additional procedures take place in the outpatient therapy visits. Patients will receive treatment for a period of six weeks, or until treatment goals are attained (as judged by the physical therapist), whichever occurs first. Baseline pain level recorded as a value of 1-10, SF-36 and Simple Shoulder Test will be collected at the first physical therapy visit. The same three evaluative tools will be administered as follow-up measures every four weeks thereafter. The measures will be collected at physical therapy visits if patients are still attending physical therapy. They will be handed to the patients by physical therapists, but filled out independently by the patient. When the patient is no longer attending therapy, the measures will be collected by mail. If some patients fail to respond to this mailing, we will collect the SF-36, SST and pain level by telephone.

Progress: Twenty patients have received treatment per the study protocol and regular re-evaluations have been performed with patient completion of follow-up forms per protocol time lines.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/157 **Status:** On-going

Title: The Effect of Pregnancy on the Performance, Health, and Nutritional Status of Postpartum Soldiers

Start Date: 09/21/94 **Est. Completion Date:** Sep 95

Department: Physical Medicine & Rehabilitation Svc **Facility:** MAMC

Principal Investigator: COL Joseph R. Dettori, SP

Associate Investigators:
LTC Kathleen A. Westphal, MC
CPT Anthony Pusateri, MS
COL Paul N. Smith, MC
LTC Alana D. Cline, MS
CPT Teresa M. Vanderlinde, MC

Key Words: female soldiers:pregnancy, health

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To determine the proportion of soldiers who return to their preconception fitness level at their first postpartum APFT, and to compare; (2) distribution, incidence and risk of injury and illness between postpartum soldiers and nonpregnant, non-postpartum soldiers; (3) changes in weight and body composition between soldiers and family members in the postpartum period; (4) bone mineral status between late pregnant and postpartum soldiers and their family members; (5) nutritional status between late pregnant and postpartum soldiers and family members; (6) iron and folate status among late pregnant and postpartum soldiers, late pregnant and postpartum family members, and nonpregnant, non-postpartum soldiers.

Technical Approach: Women in their third trimester of pregnancy will be identified through the OB-GYN clinics at their respective hospitals and asked to volunteer for the study. Non-pregnant soldiers will be solicited through the unit chain of command.

Full-time health personnel hired for the study at each site will measure the dependent variables and collect the data. Study health personnel will be supervised by an Army obstetrician. Study subjects will undergo blood draws to assess iron, folate and calcium status; anthropometric measurements to determine body composition, dual energy x-ray absorptiometry to measure bone mineral density and to validate body fat evaluations. Fitness will be assessed using the last pre-pregnancy Army Physical Fitness Test scores and the first postpartum APFT scores for all soldiers in the study. Medical records of all soldiers will be reviewed monthly to record all injuries and illnesses. Demographics, health habits and diet history, and exercise before, during and following pregnancy will be obtained through questionnaires.

Progress: Blood draws, body fat measurements, flexibility, and DEXA are complete on 125 active duty postpartum soldiers, 125 postpartum family members and 200 non-pregnant, non-postpartum soldiers. Medical records review to determine injury rates is also ongoing, with 50 records reviewed. No data analysis has been performed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/047	**Status:** Completed
Title: The Effects of Caffeine on Strength		
Start Date: 01/19/96	**Est. Completion Date:** Feb 96	
Department: Physical Medicine & Rehabilitation Svc	**Facility:** MAMC	
Principal Investigator: COL Joseph R. Dettori, SP		
Associate Investigators:	Danielle Yancey	
Key Words: Strength, caffeine		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To investigate the effects of caffeine on strength as measured by a hand dynamometer in caffeine-habituated and caffeine-naive subjects.

Technical Approach: Subjects will include 50 - 80 men and women between the ages of 20 and 45. Subjects will be recruited from 864th Engineer Battalion at Fort Lewis, Washington. Subjects will consist of both Officer and Enlisted soldiers and will have varying backgrounds. A health questionnaire will be administered. A Preston JMAR hand dynamometer will be used in this protocol. Caffeine will be supplied in the form of Vivarin and No Doz which are known to contain 100 mg of caffeine and 50 mg of caffeine respectively. The placebo will be supplied in the form of 100 mg of Vitamin C.

Subjects will be asked to abstain from caffeine ingestion for 24 hours prior to the test and not to exercise 24 hours prior to testing and to refrain form tobacco use for 12 hours prior to the test. Day One will include administration of the health questionnaire, measurement of weight and height of the subjects, a familiarity test using the hand dynamometer and answer all questions posed by subjects. Group A, will consist of caffeine-naive subjects (consumption $\leq$150 mg/day). Group B will consist of caffeine-habituated subjects (consumption > 150 mg/day). Subjects of each group will be further separated in a random manner and assigned various doses of caffeine or placebo. The test will be conducted in a single blind fashion. Day Two will include strength pre-testing and post-testing using the hand dynamometer. Day Three will include strength pre-testing and post-testing using the hand dynamometer. In order to determine a 10% change in strength, 15 subjects for each group will need to enroll in this study for a power of 80. A power of 90 would require 21 subjects in each groups. A paired t-test will be used to determine if a difference in strength following caffeine or placebo occurs.

Progress: Thirty-two soldiers completed this study. Caffeine ingestion (in the amounts currently accepted by the International Olympic Committee) was found to increase grip strength in these soldiers. This increase was consistent over strata for soldiers who were caffeine naive and caffeine habituated. A manuscript is being prepared.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/152 **Status:** On-going

Title: Cervical and Lumbar Radiculopathies: How Many Muscles Should Be Studied?

Start Date: 09/20/96 **Est. Completion Date:** Jul 97

Department: Physical Medicine & Rehabilitation Svc **Facility:** MAMC

Principal Investigator: MAJ Tamara D. Lauder, MC

Associate Investigators:
Liliana E. Pezzin, M.D.
LTC Steve S. Shannon, MC
Andrew Gitter, M.D.
Timothy D. Dillingham, M.D.
COL Shashi J. Kumar, MC
Michael Andary, M.D.
Andrew Haig, M.D.

Key Words: Radiculopathy:cervical, Radiculopathy:lumbar

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objective of this study is to determine how many muscles must be studied in order to ensure a high rate of identification of those radiculopathies which can be electrodiagnostically confirmed. This observational, prospective study of consecutive patients will primarily involve data collection and analysis of standard electrodiagnostic studies. The electromyographic screen will be standardized for the upper limb and the lower limb. Two or three additional muscles will be studied beyond what is normally performed in the course of a clinical study.

Technical Approach: A multi-center study will be undertaken to provide approximately 700 subjects. Subjects will include all males and females on whom a cervical radiculopathy (CR) or LSR electrodiagnostic screen is performed. Data will be collected regarding the history, physical examination, and examiner assessment. All patients will have at least one motor and one sensory nerve conduction study. A standardized needle electromyography study will then be done for each extremity studied. A 10 muscle screen will be performed on the upper extremity to look for a CR and an 11 muscle screen will be performed on the lower extremity studied to look for a LSR. Any other additional nerves or muscles may be studied at the discretion of the electrodiagnostician if they are needed to make a clear diagnosis. Data analysis will be carried out similar to previous retrospective studies. In order to determine how many muscles are needed to identify the CR or LSR, various muscle screens will be combined and their identification rates will be analyzed using an SPSS database. The sensitivity of the radiculopathy screens will be evaluated relative to gold standards such as MRI, CT, or myelography on those subjects whom have such studies available. Specificity will not be evaluated as we are not recruiting normal subjects. Analysis of variance will be used to compare which head of the quadriceps and gastrocnemius is more sensitive in identifying a LSR. The relationship between the probability of paraspinal muscle abnormality and the above variables will be determined using a multi-variate probability (PROBIT) analysis. All data analysis will be done at John Hopkins University.

Progress: The protocol has only recently been approved. Seven volunteers have agreed to participate.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/023 **Status:** On-going

Title: Deep Water Running as A Form of Rehabilitation for Ankle Inversuib Sprains: A Look at Maintenance of Land Based Running Performance and Long Term Training Effects

Start Date: 12/15/95 **Est. Completion Date:** Oct 95

Department: Physical Medicine & Rehabilitation Svc **Facility:** MAMC

Principal Investigator: MAJ Tamara D. Lauder, MC

Associate Investigators: COL Shashi J. Kumar, MC

Key Words: Running:deep water

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To provide a total non-weightbearing form of exercise which is more specific for land running and can be performed by a population with injuries that preclude them from weightbearing and/or land running. Specifically, service members with acute ankle sprains will be studied to (1) compare the percentage of subjects in each group which pass the APFT 2-mile run after rehabilitation, (2) compare each individual's post-rehabilitation 2-mile run time to their last pre-injury APFT 2-mile run time within the last year, (3) compare the results of a functional ankle test, consisting of both objective and subjective measures between the experimental group and the control group, and (4) to compare the rate of reinjury and reprofile for injury to the same ankle (requiring medical attention and medical record documentation) at 6 months via a questionnaire.

Technical Approach: The proposed study will look at rehabilitation methods for acute ankle sprains. Approximately 120 active duty male subjects with acute ankle sprains will be evaluated within 72 hours and randomized into a 4 week rehabilitation program of either (1) deepwater running with proprioceptive exercises or (2) the currently used acute ankle rehabilitation program through the Physical Therapy Department. Several outcome measures will be studied as described in the objectives. This data will be used to look for a significant difference among the individuals using the different rehabilitation methods.

Progress: Fifteen subjects have been entered with very poor compliance in the number of times in which they attended the rehabilitation program. Consequently, enrollment is temporarily on hold until, hopefully, a better arrangement can be made to ensure better compliance. An increase in the staff at Physical Therapy which is expected in November 1996 should help to solve this problem.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/006	**Status:** On-going
Title: The Female Athlete Triad: Prevalence in Military Women		
Start Date: 10/20/95	**Est. Completion Date:** Dec 96	
Department: Physical Medicine & Rehabilitation Svc	**Facility:** MAMC	
Principal Investigator: MAJ Tamara D. Lauder, MC		
Associate Investigators: D. D. David	MAJ Marc V. Williams, MC LTC Richard A. Sherman, MS	
Key Words: Female athlete triad, military women, eating disorder, amenorrhea, osteoporosis		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/15/96

Study Objective: To determine the prevalence of the female athlete triad in the female military population at Ft. Lewis, WA. The female athlete triad is the coincidence of 1) pathologic eating behaviors, 2) exercise-induced amenorrhea, and 3) low bone mineral density.

Technical Approach: The Eating Disorder Inventory (EDI, part 1), a questionnaire, will be sent to all active duty females at Ft. Lewis (approximately 3430). Those subjects fitting the criteria for pathogenic eating behavior will be asked to complete the EDI, part 2 and the Scheduled Diagnostic DSMIV for Eating Disorders (SCID) and to come for a clinical interview. Subjects with pathogenic eating behavior and a history of amenorrhea will undergo clinical evaluation and laboratory workup by the gynecology department to determine the cause of amenorrhea. The subset of these women with amenorrhea attributable to exercise will undergo bone densitometry of the vertebral column.

Progress: One hundred thirty four (134) of 222 questionnaires have been returned. A total of 52 of these subjects have qualified for Part 2 and/or part 3 of the study and 40 have completed all parts of the study. To date, subjects have primarily been from MAMC. The investigators are pursuing permission to recruit patients from the field units.

DETAIL SHEETS FOR PROTOCOLS

PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/090	**Status:** Terminated
Title: Clinical Trial to Compare Two Smokeless Tobacco Cessation Programs		
Start Date: 04/01/94	**Est. Completion Date:** Jul 95	
Department: Preventive Medicine	**Facility:** MAMC	
Principal Investigator: LTC Jeffrey D. Gunzenhauser, MC		
Associate Investigators: S. S. VanBeuge	Kathie J. Brendemuhl, RN	
Key Words: smoking cessatioin:smokeless tobacco		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective is to ascertain whether either of two treatment regimens is more effective in assisting individuals in cessation from use of smokeless tobacco products.

Technical Approach: This is a clinical trial which will compare the effectiveness of two regimens on smokeless tobacco cessation rates. Users of smokeless tobacco products in the Fort Lewis and McChord Air Force Base communities will be recruited to participate in a tobacco cessation program designed specifically for smokeless tobacco users. Potential volunteers will be screened through the use of a questionnaire and a limited history and physical examination. After obtaining informed consent, participants will be randomized to receive one of two treatment regimens. Both treatment groups will receive physician advice to quit using tobacco products and will be prescribed nicotine replacement therapy in accordance with the Madigan Army Medical Center (MAMC) prescribing protocol. In addition, the first treatment group (phone counseling) will receive an initial face-to-face counseling session with the study nurse during which time a quit date will be selected, standardized written materials will be provided, and follow-up procedures will be reviewed; subsequently each participant in this treatment group will receive four (4) phone follow-up consultations at 48 hours, 1 week, 3 weeks, and 6 weeks after the preselected quit date. The second treatment group (Freshbreath) will participate in the FRESHBREATH smokeless tobacco behavior change therapy course, a 6-hour course, meeting as a group twice a week (1.5 hours each session) for two weeks. During the course of the trial (1 year), participants in both groups will have access to the study nurse or physician to address specific needs or problems. Cessation rates will be monitored by self-report during phone interviews at 3 months, 6 months, and 1 year. Differences in cessation rates will be assessed through multivariate analysis. Determinants (confounders) of cessation other than treatment group will be included in the analytic model. Statistically significant results will be interpreted at the 0.05 level of significance.

Progress: No funding has been received so the protocol has been terminated.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/011 **Status:** On-going

Title: Comparative Morbidity Study of Active Duty Women Serving in Korea and Ft Lewis by MAJ Jeffrey D. Gunzenhauser, MC

Start Date: 11/04/94 **Est. Completion Date:** Mar 96

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: LTC Jeffrey D. Gunzenhauser, MC

Associate Investigators: CPT Julie A. Pavlin, MC

Key Words: Female soldiers, morbidity, Korea, Ft Lewis

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To describe the out-patient and in-patient morbidity experience of women serving in Korea and compare this to women serving at Ft. Lewis and to men at both locations and to describe behavioral risk factors of women serving in Korea.

Technical Approach: This is an epidemiologic study. Out-patient clinical events which are assessed at military clinics will be categorized into one of 14 specific morbidity categories: orthopedic/injury, respiratory, medical illness, dermatologic, bites/stings, environmental injury, diarrhea/GI, unexplained fever, sexually transmitted disease, ophthalmic, mental health, dental, substance abuse and miscellaneous. Diagnosis will be based on medical record entries (not chief complaints) and will be broken down by gender. Rates of health care usage for men will be estimated by counting all visits registered in clinic logs. One male record will be pulled for each female record pulled (the second male to visit the clinic after the index female visit.

In-patient morbidity experience of women will be studied by analyzing data from the Individual Patient Data System maintained at Ft. Sam Houston, TX. All hospitalization of men and women will be included in the analysis. Each hospitalization at the 121 General Hospital and at Madigan AMC will be classified into one of the 14 morbidity categories to allow broader comparisons with out-patient morbidity data and between genders and locations.

Health surveys will be mailed to a probability sample of female soldiers serving in Korea and at Ft. Lewis. Approximately 1000 women in Korea and 1000 women at Ft. Lewis will be targeted for this survey.

Progress: Over 25,000 clinic visits were coded and over 2,000 questionnaires were entered into databases. Initial analyses of the TMC data and the questionnaire surveys indicate that active duty women in a deployed situation (Korea) have only marginally higher health care utilization rates. For the eight measure of health status studied, women serving in Korea differed significantly from women at Ft Lewis only in the number of reported sick call visits during the preceding 60 days. In contrast, women have higher health care utilization rates than men and more negative self-reports of health status in virtually all eight categories. Data collection far exceeded that projected by the investigators. More detailed analyses are in progress.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/009	**Status:** Completed
Title: Low-Dose Oral Contraceptives and Cardiovascular Disease		
Start Date: 10/02/92	**Est. Completion Date:**	
Department: Preventive Medicine	**Facility:** MAMC	
Principal Investigator: LTC Margot R. Krauss, MC		
Associate Investigators: None		
Key Words: from Christina Hrynio, PAD - review to see if need		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess demographic and behavioral determinants associated with new HIV infections in order to generate information for implementing changes in education strategies currently in use for populations at risk for HIV infection, particularly in terms of potential new risk factors.

Technical Approach: This multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion of antibody to HIV using ELISA with duplicate Western Blot confirmation. There will be one control for each male subject and three controls for each female subject. Controls will be selected at random from the group of all uninfected active duty personnel at the same installation where cases seroconvert and will be matched for age (± 2 years), gender, ethnicity, rank, and length of service. Controls must have tested negative on or after the date their matched case seroconverted. Subjects and controls will be interviewed by trained interviewers from collaborating civilian health agencies who are blinded to the HIV antibody status of study participants. The interview will be conducted from and HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographics, medical history, risk factors of drug use, sexual history, and other risks. The investigators anticipate that 160 to 230 incident cases will be eligible for recruitment each year and feel that the majority of these cases can be recruited. In any multi-risk factor study such as this, the problem of chance statistical considerations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be performed. These methods will include calculation of measures of effect (e.g. matched odds ratios and confidence intervals) for various risk behaviors as well as matched multivariate analyses (e.g. behavioral hazards, conditional logistic regression).

Progress: This was a collaborative study with the University of Washington. Twenty subjects were entered at MAMC. Data has been forwarded to the University of Washington for analysis.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/043	**Status:** Completed
Title: The Importance of Social Support for Successful Tobacco Cessation		
Start Date: 01/19/96	**Est. Completion Date:** May 96	
Department: Preventive Medicine	**Facility:** MAMC	
Principal Investigator: LTC Margot R. Krauss, MC		
Associate Investigators:	CPT Kevin P. Michaels, MC	
Key Words: Tobacco:cessation, social support		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To measure the three components of perceived social support and the social network of participants in the Fort Lewis/Madigan Tobacco Cessation Program related to cessation success. These three components are: (1) affect, (2) affirmation, and (3) aid.

Technical Approach: The NSSQ will be self administered to participants enrolled in the Fort Lewis/Madigan Tobacco Cessation Program. Initial analysis will examine any success with association in demographic variables using the Chi square test. The ordinal data will be grouped into a single population and then assigned ranks to the components of social support to the sample values form smallest to largest, without regard to success of tobacco cessation. A one-sided Wilcoxon test statistic will be calculated from the sum of the ranks. Logistic regression will be utilized to define a model to predict success of tobacco cessation from the components of social support.

Progress: 79% of the participants were contacted at 3 months. 41% had achieved a tobacco free state. The average age was 38 years and subjects were predominantly white, married, active duty males. Everyone had at least a high school eduction. Age, race, marital status, eduction, and beneficiary status were not significant in the analysis. Those participants with a low perceived total function support had a greater frequency of tobacco relapse at three months follow-up. The components of total functional support (affect, affirmation, and aid) were all significant to a p-value less than 0.05.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/041 **Status:** Terminated

Title: Post-Marketing Surveillance of Reactogenicity to Licensed Plague Vaccine Manufactured by Greer Laboratories, Inc

Start Date: 12/15/95 **Est. Completion Date:** Sep 97

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: LTC Margot R. Krauss, MC

Associate Investigators: CPT Dale G. Wallis, MC
COL Kelly T. McKee Jr., MC

Key Words: Plague, Vaccine, reactogenicity, post-marketing surveillance

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To provide post-marketing surveillance on recipients of the Greer plague vaccine. (1) To verify rates of common reactions described in the package insert, observing the vaccine under "field" conditions wherein possible interference and/or additive adverse events may occur with other concurrently administered vaccines. (2) To detect and describe less common, unusual reactions which may occur. (3) To determine the reaction pattern to the third inoculation in the primary series which was not studied in Greer's initial IND.

Technical Approach: Plague vaccine USP, administered according to the schedule outlined in the package insert (1ml at day 0, followed by 0.2ml at about 1 month, and 0.2ml 5-6 months later; boosters to be administered according to mission), is considered a required medical prophylaxis measure for certain military units. Soldiers scheduled to receive plague immunization through normal medical/operational channels will be identified to a research assistant, who will recruit them for participation in the study. Participation in the study will be voluntary, but there will be no signed consent forms obtained. The recipients will be requested to complete Survey Forms at 48 hours, 7 days, and 30 days post-vaccination for the first inoculation. Analysis will address the purpose of the study, which is aimed at identifying if there is a difference in the occurrence of distribution of reactions after each injection dose. Summary data will be compiled to indicate the most common reactions (20% or greater) in rank order with 95% confidence intervals. Medically serious adverse reactions (MSARS) will be tabulated separately with assessment of the projected rate in a large military population using 95% confidence intervals. Comparisons with the Miles/Cutter experience will be performed by cross-tabulating the summary data from this study with published historical rates of the Miles/Cutter vaccine, recognizing that historical data may be limited. All data will be transcribed to a computer database with a double-checked entry system.

Progress: This study was terminated due to an insufficient number of subjects to evaluate.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/159 **Status:** On-going

Title: Relationship of Spouse and Child Abuse in A Military Population

Start Date: 09/20/96 **Est. Completion Date:** Jun 96

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: MAJ Peter D. Rumm, MC

Associate Investigators:
Frederick Rivara, M.D., MPH
LTC Nancy K. Raiha, MS
LTC Margot R. Krauss, MC
Michelle Bell, Ph.D.
Peter Cummings, M.D., MPH

Key Words: Abuse:child, Abuse:spouse, military population

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: For many years there has been a perception that child and spouse abuse has a strong correlation in families. The Military Family Advocacy Program has tracked in a singular data set such abuse in families for seven years in almost 90,000 reported incidents. This study as outlined in the related thesis proposal and Department of the Army Family Advocacy Research Plans is the first documented attempt at looking at the correlation of spouse and child abuse in a large data set.

Technical Approach: The working hypothesis of this study (supported by preliminary data review) is that there is a higher rate of child abuse in families with pre-existing spouse abuse and that particular family characteristics may make some families at increased risk. The data set has been provided through the Family Advocacy Program (FAP) and contains 53 "fields" of information on each case of reported abuse from DA-2436. Additional information will be obtained from the FAP for DEERS data on the number of married couples with children in the Army for use in calculation or relative rates of abuse. The primary goal of the study will be to calculate the incidence of child abuse in families with already documented spouse abuse and compare that rate to the overall Army population of such families. In addition, stratified and logistical analysis of possible subgroups of families, i.e. by ranks, age of abuser, geographical location will be performed to identify groups of families at higher risk for "dual" abuse. There is a strong interest in the Army Family Advocacy Program to have such knowledge to predict families at increased risk.

Progress: Preliminary analysis has demonstrated a strong association between spouse abuse and subsequent child abuse in families. Physical abuse of children has the highest incidence, but other types of abuse also have an elevated incidence. Rank and other demographic factors may help select families at special risk. The PI is in the process of analyzing other variables such as race, age and sex of abuser, age of child, number of children, and rank.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PSYCHIATRY

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/103 **Status:** On-going

Title: Reports, Estimates, and Tests Results of Memory Functioning in Children With and Without ADHD: Concordance Between Self-Report, Parent-Report, Teacher-Report, and Test Results

Start Date: 05/17/96 **Est. Completion Date:** Jun 96

Department: Psychiatry **Facility:** MAMC

Principal Investigator: James R. Masson, MD

Associate Investigators: Kenneth A. Zych
MAJ Robert A. Byrne, MS

Key Words: ADHD, memory, self-report

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To complete a pilot study in two steps in order to ensure that at least Step One, which could be a stand-alone pilot study, gets accomplished. (1) Complete a pilot study (N of at least 15) which yields an initial empirical sense of the concordance between and of the nature and relative reliability of child self-reports, parent-reports, teacher-reports, and test results of memory functioning in children diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD). (2) Once the minimal N of 15 children with ADHD is evaluated and tested to ensure a minimal pilot study, an additional minimal N of 15 children, with only minor medical ailments and no diagnosis of ADHS but some parental concern about memory functioning, will also be evaluated and tested. (3) (optional) Once Step One and Step Two have been ensured with minimal Ns of 15 children each it would be desirable to evaluate and test an additional minimal N of 15 children with only minor medical ailments and no diagnosis of ADHD and no parental concern about memory functioning.

Technical Approach: This study will proceed in two steps. The first step will collect data on memory functioning in a sample of 15 children diagnosed with ADHD, between 6 and 12 years of age, and the second step will repeat the same process in a group of children not diagnosed with ADHD, also between 6 and 12 years of age. Children with estimated IQs below 80 or who are physically unable to complete paper and pencil tests will not be included in the study. The information on memory functioning in each child will be obtained from the self-report of the child, direct memory testing of the child, and from reports by parents and teachers of the child. Measures used with child subjects will be (1) the EDMQ-C, (2) the BASC-SRP-C (for children aged 8-11 years) or the BASC-SRP-A (children of age 12) or BASC-PRS-C, and BASC-TRS-C ratings (for children 6 and 7 years of age), (3) the CVLT-C, (4) the Picture Memory and Design Memory nonverbal memory subtests of the WRAML, and (5) the TONI-2. Measures used with parents will be the EDMQ-P, the BASC-PRS-C (for children aged 6-11 years) or BASC-PRS-A (for children of age 12), and the PNIR-P. Measures used with teachers will be the EDMQ-T, the BASC-TRS-C (for children aged 6-11 years) or BASC-TRS-A (for children of age 12), the APRS, and the PNIR-T. The data analysis will be correlational, using Gorsuch's UniMult, and focused on the concordance between child, parent, and teacher reports of memory functioning in children. Post hoc comparisons will use "protected F or t-tests."

Progress: Thirty-seven children have been administered the test battery. Only two of these subjects were non-ADHD, forcing the study to concentrate only on children with ADHD. Inconsistent responses by some fathers and the complete unavailability of other fathers has resulted in the study focusing on adult ratings from mother and teachers only.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/108	**Status:** On-going
Title: Medical Cost Offset and Clinical Effectiveness of a Behavioral Treatment Program for Medical Resource Overutilizers		
Start Date: 05/06/94	**Est. Completion Date:** Jan 96	
Department: Psychiatry	**Facility:** MAMC	
Principal Investigator: LTC John B. Powell, MS		
Associate Investigators: Carol Ellsworth, MBA	Mary Brencick, MSW Anita Millman-Thorndyke	
Key Words: medical resources, overuse, treatment program		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study will identify patients with few physical findings and whose presenting complaints are produced or aggravated by psychological, rather than organic, factors, and to provide a brief, effective behavioral intervention designed to ameliorate these psychological factors.

Technical Approach: This study will follow 100 patients referred from the Adult Primary Care Center, and compare them to 100 non-treatment controls. Patients will complete a four week behavioral program consisting of four weekly classes and four individual biofeedback sessions. medical usage for the six months prior to treatment (including outpatient visits, inpatient treatment, laboratory procedures, and pharmacy costs) will be compared to usage for the six months post treatment.

Progress: No new subjects were entered in this study in FY 96. Research is on hold pending implementation of a new data collection system. No data were collected during the year.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/013 **Status:** Completed

Title: Effect of Premenstrual Syndrome and Primary Dysmenorrhea on Women's Cognitive Functioning and Job Performance Before and After Biofeedback Treatment

Start Date: 11/04/94 **Est. Completion Date:** Sep 95

Department: Psychiatry **Facility:** MAMC

Principal Investigator: LTC John B. Powell, MS

Associate Investigators:
Jack T. Norris
LTC Milo L. Hibbert, MC
COL Gary D. Davis, MC
Crystal T. Sherman
LTC Richard A. Sherman, MS

Key Words: Premenstrual syndrome, dysmenorrhea, cognitive functioning, job performance, biofeedback

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether PMS and dysmenorrhea: (1) have a significant impact on the job performance of those female soldiers who do and those who do not request treatment for these problems, and; (2) have a significant impact on the cognitive functioning of female soldiers who request treatment, and, if this correlates highly with changes in work performance. Also, to determine whether biofeedback intervention will make a significant impact on the work performance of female soldiers who request treatment by producing about a 50% reduction in pain among about 80% of those requesting treatment. Lastly, to determine whether females given biofeedback training for PMS and dysmenorrhea who do not successfully complete their training will not show a change in the intensity of their symptoms from before to after training.

Technical Approach: We propose to determine the impact of primary PMS and dysmenorrhea on female soldiers's performance of the normal duties and whether treatment with biofeedback alters the impact. Impact will be assessed by having 200 female soldiers form combat service and combat service support units requesting treatment for either PMS or dysmenorrhea deep daily, month long logs of their symptom activity, medication use, and limitations to their performance. One month is the minimum length log acceptable because of the cyclic nature of the problems in relation to the menstrual cycle. Each of these women will also take an hour long, automated cognitive screening evaluation twice. One evaluation will be during the highest level of their symptoms and the other will be at the lowest level. This will permit correlations of changes in cognitive processing with changes in work performance. Two hundred female soldiers not requesting treatment for these problems who are matched with the soldiers requesting treatment for medical history, family life style, and job type will also be asked to keep a log to control for aspects of military life affecting job performance unrelated to PMS and dysmenorrhea. This control group will be large enough to estimate the impact of these problems on job performance among female soldiers since about 15% of young adult civilian women report significant problems with PMS or dysmenorrhea. Participants will be recruited from the appointment lists at MAMC's clinics and the TMCs. The time period between when they make their appointments, through the wait to see a doctor, and the time their first trial medications take effect will permit participants to keep their one month logs before their symptom activity is impacted by any new treatments.

Progress: Twenty-three percent (23%) of the female soldiers surveyed reported significant symptoms of PMS, 8% reported significant dysmenorrhea, and 24% reported both. Subjects were given applications of the Wonderlic Personnel Test, the Million Clinical Multiaxial Inventory, and the Beck Depression Inventory. An Automated Neuropsychological Assessment Metrics presentation was given to 21 subjects at the lowest and highest symptom levels and found no relationship between cognitive functioning and the menstrual cycle. Each participant filled out a month long log of their symptoms before therapy for PMS and dysmenorrhea. Eight of the 21 subjects completed treatment. All reported improvement. There was no difference in cognitive ability between low and high intensities of PMS or dysmenorrhea.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF RADIOLOGY

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/119 **Status:** On-going

Title: Gallbladder Ejection Fractions

Start Date: 06/09/93 **Est. Completion Date:** Dec 94

Department: Radiology **Facility:** MAMC

Principal Investigator: LTC John M. Bauman, MC

Associate Investigators:
MAJ Michael F. Lyons II, MC
MAJ Richard R. Gomez, MC
Jerome Billingsley, M.D.
LTC Clifford L. Simmang, MC

Key Words: gallbladder, ejection fractions

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$6166.00	**Periodic Review:** 09/30/96

Study Objective: To determine the clinical usefulness and reproducibility of gallbladder ejection fractions.

Technical Approach: Fifty volunteers will be studied on two occasions utilizing half of the normal radiopharmaceutical dose. These studies will be separated by no more than 30 days. Subjects will be given an injection of approximately 2.6 millicuries Tc-99m-DISIDA and serial one minute computer acquired images will be obtained for a maximum of 60 minutes. Once maximal gall bladder activity is achieved by visual inspection, 0.01 micrograms/kilo-gram sincalide will be given intravenously for three minutes via infusion pump. Serial one minute computer acquired images will be obtained for 30 minutes following this infusion. The results of the studies will not be used to determine patient care. The patient will be scheduled for cholecystectomy after the second DISIDA scan is completed. The gallbladder will be submitted to pathology for pathologic evaluation. The patient will complete a questionnaire prior to, and at one and six months post cholecystectomy. Mean, range, and standard deviation for each set of data will be calculated. A repeated measures ANOVA will be calculated.

Progress: Eighteen patients have been enrolled. Patient accrual has been slower than expected.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/077	**Status:** On-going

Title: Determination of Normal Regional Myocardial Thallium Distribution and Development of a New Display Technique

Start Date: 05/06/94	**Est. Completion Date:** Jul 94
Department: Radiology	**Facility:** MAMC

Principal Investigator: LTC John M. Bauman, MC

Associate Investigators:	COL Stanton R. Brown, MC
Jerome Billingsley, M.D.	James H. Timmons, MD

Key Words: thallium, myocardial distaribution, new technique

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To determine the normal regional variation in the myocardial distribution of 201T1. (2) To use this information to create a color translation table for semiquantitative analysis of Thallium images. (3) To evaluate the ability of the new translation table to predict the presence or absence of significant coronary artery lesions at cardiac catheterization.

Technical Approach: We intend to pull all Thallium studies and cardiac catheterization data on patients who have had both studies at MAMC since 1 August, 1992. Results of Thallium and catheterization studies will be entered on worksheets and from there into a computerized database.

We will review a minimum of 10 data sets where both the Thallium study and catheterization data are normal. The relative distribution of Thallium on the stress studies will be quantitated using a circumferential image profile on the short axis slices using 8 mid-ventricular slices which demonstrate a complete left ventricular chamber.

Sixty values will be calculated for each of eight central stress slices. The maximum and minimum count values for all slices will give us the range of normal Thallium variation for each patient's stress study. This value, will be expressed as a percent of the maximum uptake. Finally the mean, range and standard deviation for the 10 patients' percent normal variations will be calculated.

The color map will be created using the information from phase I. All images are limited to a maximum of 256 gray levels. We will divide these 156 levels into only 5 colors for our map. As a result, individual pixels will be colored according to their relative count value with respect to the maximum in the image. Break points for color levels will be determined by the mean percent normal variation and standard deviation.

The new color translation will then be used to reinterpret a minimum of 50 Thallium studies for which cardiac catheterization data is available. Studies will be read separately by 2 board certified nuclear medicine physicians without knowledge of the clinical history, previous Thallium result, exercise data or catheterization result. Using only the new color table, results will be annotated as normal or abnormal. If abnormal, location and extent of abnormality will be recorded. Actual colors of defects will be recorded and subsequent data analysis for correlation with the bull's eye plots, prior image interpretations and cardiac cath data will be made for each color level of defect.

Progress: Retrospective analysis to define "normal" is completed. The investigators will commence application of normals to existing images to determine efficacy of the technique.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/038 **Status:** On-going

Title: Digitally Acquired Radiographic Air Contrast Barium Enema vs. Colonoscopy in Polyp Detection, Cancer Detection, and cost in a Federal Tertiary Care Center

Start Date: 12/17/93 **Est. Completion Date:** Jan 95

Department: Radiology **Facility:** MAMC

Principal Investigator: LTC Gregory N. Bender, MC

Associate Investigators:
MAJ Michael F. Lyons II, MC
LTC Amy M. Tsuchida, MC
CPT Thomas P. Peller, MC

Key Words: polyps, barium enema, colonoscopy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if digitally acquired radiographic air contrast barium enema (DAR-ACBE) examinations of the colon might serve as a cost effective surrogate to colonoscopy in the MAMC colon cancer screening program.

Technical Approach: By obtaining DAR-ACBE and colonoscopy on the same patient a test of diagnostic equality for these two examinations will be performed. The diagnostic equality of these examinations will be tested by assessing their ability to find polyps >5mm in size and in finding cancers of any size.

Progress: As a pilot study, the investigators have reviewed more than 1000 charts to determine the basic ability of DAR-ACBE in finding polyps and cancer. Enrollment of patients will begin shortly.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/166	**Status:** Terminated
Title: Cost Effectiveness of Early Technetium 99m Bone Scintigraphy in Traumatic Wrist Injury		
Start Date: 08/18/95	**Est. Completion Date:** Feb 96	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: CPT John D. Crocker, MC		
Associate Investigators: LTC John M. Bauman, MC	Rush A. Youngberg	
Key Words: Wrist, scintigraphy, cost effectiveness		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: One patient was entered in this study. The investigators were unable to obtain a sufficient number of participants, despite the effort of many people. Given the way these injuries are currently managed, further effort in continuing the study was not seen as justified.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/076 **Status:** On-going

Title: Effectiveness of Oral Dolasetron Mesylate (50 mg) versus Prochlorperazine in the Treatment of Nausea and Emesis Due to Fractionated Abdominal Radiotherapy

Start Date: 02/16/96 **Est. Completion Date:**

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Nyun C. Han, MC

Associate Investigators: LTC Steven S. Wilson, MC
LTC Kenneth A. Bertram, MC

Key Words: Nausea, emesis, abdominal radiotherapy, dolasetron mesylate, prochlorperaine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To evaluate the effectiveness of dolasetron mesylate in the treatment of radiation-induced nausea and emesis (RINE) in patients undergoing fractionated abdominal radiotherapy. 2) To evaluate the safety and tolerability of oral dolasetron mesylate in cancer patients receiving radiotherapy. 3) To evaluate the net incremental health care resource utilization, and net incremental work productivity and family/household assistance associated with the use of dolasetron mesylate versus prochlorperazine in the treatment of RINE. 4) To evaluate the use of select quality of life domains in measuring quality of life in patients receiving treatment for RINE.

Technical Approach: This study is a randomized, double-blind, active-controlled, multi-center trial to evaluate the effectiveness and safety of oral dolasetron mesylate in patients exhibiting nausea or emesis after undergoing fractionated abdominal radiotherapy for malignant disease. Patients will be eligible for the study if they experience significant nausea requiring antiemetic medication or have had at least one emetic episode after receiving radiotherapy during the 5 day screening period. Patients will be randomized to receive either oral dolasetron mesylate 50 mg qd or prochlorperazine 10 mig tid. Study medications will be ingested on a tid schedule. Patients randomized to dolasetron mesylate will take one 50 mg dolasetron mesylate capsule (as their first dose) and two matching placebo capsules for a total of three daily doses. The first daily dose of study medications will be ingested within 1 hour prior to the start of radiotherapy. The second and third daily tid scheduled doses of study medication (placebo or prochlorperazine) will be ingested over the remaining 24 hour treatment day. For each day on which no radiotherapy is administered (eg, weekends), study drug is to be administered using the same regimen (1 capsule tid). Radiation treatment will be administered for a minimum of 5 and a maximum of 30 days during the treatment phase. Study drug may be continued for up to 3 days after completion of the last fraction of radiotherapy.

Progress: Five patients have been consented and one was randomized. This patient has since elected to discontinue her radiation therapy and was dropped from the study.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/124	**Status:** Terminated
Title: Measurement Accuracy of Reformatted MR Images in Cardiac Imaging Usign A Pig Cadaveric Model		
Start Date: 06/09/93	**Est. Completion Date:** Jul 93	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	SSG James Adams, NCOIC	
Key Words: MRI, cardiac imaging, pig model,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the accuracy of reformatted images in the measurement of cardiac wall thickness.

Technical Approach: The cadaveric hearts of five pigs will be flushed, filled with and suspended in 10% formalin solution. Vitamin E capsules (visible on MRI) will be attached to the outside of the heart to mark the "long-axis" plane. MRI will then be performed in planes parallel to and oblique to the "long-axis". Reformatted images from obliquely acquired MRI images will be measured for ventricular wall thickness as determined from the "long-axis" view and compared with measurements obtained in the true "long-axis" view. The cadaveric pig hearts, once imaged, will be biplaned and true ventricular wall thicknesses will be measured. The cadaveric measurements will also be compared with those obtained by MRI.

The ventricular wall thickness as determined by (1) direct "long-axis" MR, (2) reformatted "long-axis" views, and (3) actual necropsy measurement of the cadaveric heart will be evaluated for degree of variance and statistical significance.

Progress: Data on four cadaver hearts were obtained. The protocol was terminated because the hardware/software to analyze the data are not available.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/034 **Status:** Terminated

Title: Multicenter, Open-Label Study to Evaluate the Safety, Tolerability, and Efficacy of Optimark (Gadoversetamide Injection) in MRI of the CNS

Start Date: 11/17/95 **Est. Completion Date:** Nov 96

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: LTC Dianna Chooljian, MC
LTC Karl C. Stajduhar, MC

Key Words: MRI, CNS, Optimark

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the safety, tolerability, and efficacy of intravenously administered Optimark as a magnetic resonance imaging (MRI) contrast agent in patients with known or highly suspected CNS pathology.

Technical Approach: A total of 25 patients will be enrolled into the study and routine MRI protocols prior to and following the intravenous administration of 0.1 or 0.3 mmol/kg Optimark will be performed. Patient monitoring will include patient history, physical examination, vital sign and laboratory evaluations and electrocardiograms performed prior to and following Optimark administration. MRI images will also be assessed for lesion conspicuity.

Progress: This protocol was terminated by the sponsor.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/121 **Status:** Terminated

Title: A Multicenter, Randomized, Double-Blind Study to Evaluate the Safety, Toleratility, and Efficacy of Optimark (Gadoversetamide Injection) Compared to Magnevist (Gadopentetate Dimeglumine Injection) ...

Start Date: 05/17/96 **Est. Completion Date:** May 97

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators:
Rush A. Youngberg
LTC Dianna Chooljian, MC
LTC Karl C. Stajduhar, MC

Key Words: MRI, cenral nervous system, contrast agent, gadoversetamide, gadopentetate dimeglumine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the safety, tolerability, and efficacy of intravenously administered Optimark™ (Gadoversetamide Injection) compared to Magnevist® (Gadopentetate Dimeglumine Injection or Gd-DTPA) as an magnetic resonance imaging (MRI) contrast agent in patients with known or highly suspected of having central nervous system pathology.

Technical Approach: This protocol is for inclusion in a multi-center trial into the safety, tolerability and efficacy of the new non-ionic MRI contrast agent, Optimark™, compared to that of Magnevist®. A total of 50 patients will be enrolled into this randomized, double-blind study. Approximately half of the patients will receive 0.1 mmol/kg Optimark™, the investigational contrast agent, and the other half will receive 0.1 mmol/kg Magnevist®, an FDA-approved contrast agent, for their central nervous system MRI examination. Patient monitoring will include patient history, physical examination, vital sign and laboratory evaluations and electrocardiograms performed prior to and following Optimark™ administration. The pre- and post-contrast MRI images will also be assessed for lesion appearance.

Progress: This protocol was terminated due to the departure of the principal investigator. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/037	**Status:** Completed
Title: Arachnoid Granulations: MR Features		
Start Date: 02/05/93	**Est. Completion Date:** Feb 94	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	LTC Miquel J. Rovira, MC	
Key Words: arachnoid granulations:MRI		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The 600 MR studies performed since July 1992 will be reviewed for the presence of arachnoid granulations within the cerebral venous structures.

Technical Approach: All MR studies performed since July 1992 will be reviewed and evaluated for the presence of arachnoid granulations. The diagnosis of arachnoid granulation will be based on the conventional venographic descriptions (MRE angiography or traditional cerebral venography) as interpreted by radiologist. This is a study of description in which statistical analysis will not be necessitated.

Progress: MR venography identified 23 well-circumscribed, round dural nodules (3-10 mm) characteristic for arachnoid granulation in the transverse sinuses of 18 patients. The arachnoid granulations were primarily hypointense (23/23) on T1W images, isointense (19/23) on PW images, and hyperintense (19/23) on T2W images. In the cadaveric series, 8 of 45 patients were found to have arachnoid granulations. Arachnoid granulations of the posterior fossa occur in 18% of the population and are clinically evident on 4% of routine brain MR exams. On MR, arachnoid granulations have a characteristic appearance. Arachnoid granulations of the posterior fossa are common and should be a recognized normal MR variant.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/010	**Status:** Terminated
Title: Magnetic Resonance Venography: A Comprehensive Non-Invasive Tool for the Assessment of Deep Venous Thrombosis		
Start Date: 10/20/95	**Est. Completion Date:** Dec 96	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	Jerzy Szumowksi, Ph.D.	
Key Words: Venography:MR, thrombosis:venous		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To design optimized magnetic resonance venography (MRV) imaging strategies which enable the accurate assessment of the entire deep venous system (from abdomen to calf) within an hour. (2) To investigate the affect of patient positioning on pelvic venous anatomy in female patients. (3) To investigate the use of segmented k-space cine MRI in the evaluation of central venous patency.

Technical Approach: This protocol is an initial investigation into the ability of MRI to supply the anatomic information necessary to evaluate the entire deep venous system within an hour. This protocol will entail (1) the evaluation of a number of black (spin-echo) and =bright blood (gradient-echo, time-of-flight, phase-contrast and cine MRI) techniques with respect to imaging time and quality: (2) the investigation of a new cine technique (FASTCARD) for venous blood flow quantification; (3) the evaluation of female pelvic venous anatomy and the effect of patient positioning (supine and prone); and the (4) development of specialized extremity coils for MR venography.

Progress: This study was terminated as it did not receive funding from USAMRMC. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/064 **Status:** Terminated

Title: A Multicenter, Randomized, Double-Blind Study to Evaluate the Safety, Tolerability, and Efficacy of Optimark (Gadoversetamide Injection) Compared to Magnevist (Gadopentetate Dimeglumine Injection)...

Start Date: 02/16/96 **Est. Completion Date:** Jan 97

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators:
LTC Robert H. Sudduth, MC
MAJ Kazunori Yamamoto, MC
LTC Amy M. Tsuchida, MC
MAJ John G. Carrougher, MC
LTC Karl C. Stajduhar, MC

Key Words: Contrast agent, MRI, Optimark, Magnevist

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the safety , tolerability, and efficacy of intravenously administered Optimark™ (Gadoversetamide Injection) compared to Magnevist® (Gadopentetate Dimeglumine Injection or Gd-DTPA) as an magnetic resonance imaging (MRI) contrast agent in patients highly suspected of liver pathology.

Technical Approach: This protocol is for inclusion in a multicenter-center trial into the safety, tolerability and efficacy of a new non-ionic MRI contrast agent Optimark™ compared to that of Magnevist®. A total of 30 patients will be enrolled into this randomized, double-blind study. Approximately half of the patients will receive 0.1 mmol/kg Optimark™, the investigational contrast agent, and the other half will receive 0.1 mmol/kg Magnevist®, an FDA approved contrast agent, for their liver MRI examination. Patient monitoring will include patient history, physical examination, vital sign and laboratory evaluations and electrocardiograms performed prior to and following Optimark™ administration. The pre- and post-contrast MRI images will also be assessed for lesion conspicuity.

Progress: This protocol was terminated due to the departure of the principal investigator. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/054	**Status:** Terminated
Title: Urologic Stone Conspicuity: Plain Films vs Computed Radiography		
Start Date: 03/05/93	**Est. Completion Date:** Apr 94	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	CPT Robert E. Vaughan, MC	
Key Words: urologic stones:conspicuity		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare conspicuity of urologic stones using conventional plain films vs. computed radiographs.

Technical Approach: Urologic stones sent for chemical/pathologic analysis will be radiographed by both conventional plain film and computed radiography. The stones will be radiographed with a "soft tissue" phantom to simulate normal human soft tissue density. The plain film/computed radiographs will then be independently interpreted for stone location and number by 5 - 10 radiologist/residents. The conspicuity of the stones on plain film will then be compared to that on the computed radiography acquired film. Blind films (i.e. films acquired without stones and only a soft tissue phantom) will be included to "blind" the readers.

Standard ROC curves among readers will be established and Student's t-test analysis for statistical variance in the difference in detected stones between the plain films and computed radiographs will be performed. Stone number and composition will also be considered in the ability to detect stones.

Progress: This protocol was never started secondary to the departure of the associate investigators and that of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/159 **Status:** Completed

Title: Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method

Start Date: 09/21/94 **Est. Completion Date:** Apr 96

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: Rush A. Youngberg
Jerzy Szumowksi, Ph.D.

Key Words: Magnetic Resonance Mammography: fat suppression, Dixon method

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to further refine a promising new MRI technique for fat suppression (phase unwrapping in a 3-point-Dixon method) for application in magnetic resonance mammography (MRM).

Technical Approach: Phase unwrapping in the 3-point-Dixon method is a recently described method for fat suppression which promises to bridge the difficulties encountered with fat signal on post-contrast MRM images. This new fat suppression technique promises to provide the reproducible homogeneous fat suppression necessary for the efficient performance of MRM and the accurate rendering of diagnoses.

This new technique, by increasing the conspicuousness for areas of Gd-enhancement, will dramatically improve the overall accuracy of MRM for breast cancer and make the identification of even very small cancers possible. MR with its reported high sensitivity will potentially identify lesions not otherwise detected by film screen mammography, ultrasound or physical exam at MAMC, MRM has already discovered lesions which were otherwise not detected by these other conventional means. Because the success of any breast imaging modality relies on its ability to diagnose cancer early to effect cure and increase survival, this technique will represent a major advance in breast cancer screening.

Progress: Seventeen females with 18 mammographically suspicious lesions were enrolled, mean age 48.76. Eighteen sets of unilateral 3D SPGR and PU3PD (Phase Unwrapping 3 Point Dixon) images and 11 sets of bilateral FATSAT and PU3PD images were obtained following IV gadolinium contrast media administration. PU3PD was preferred 89% over subtraction 3D SPGR and 73% over FATSAT images for fat elimination and 89% and 55% for lesion characterization. Pathologic confirmation was available for 15/18 lesions. PU3PD afforded improved lesion characterization over 3D SPGR as PU3PD images were not plagued by subtraction artifact. Bilateral FATSAT and PU3PD, performed at the end of each study, both afforded suboptimal lesion/region characterization. Conclusion: PU3PD can provide better fat signal elimination than subtraction 3D SPGR and FATSAT. Lesion morphology on PU3PD images can be superior to subtraction 3D SPGR. PU3PD was developed for a v.5.4. GE Signa 1.5 T MRI scanner.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/018	**Status:** Completed
Title: Comparison of Pre-Admission Computed Tomography With Inpatient Computed Tomography Enteroclysis		
Start Date: 11/17/95	**Est. Completion Date:**	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Richard S. Makuch, MC		
Associate Investigators: James H. Timmons, MD	LTC Gregory N. Bender, MC MAJ Alan D. Pearson, MC	
Key Words: Enteroclycis, computed tomography		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess the ability of CT enteroclysis in detecting partial small bowel obstruction (SBO).

Technical Approach: All films on patients who have had both a pre-admission CT for SBO and an inpatient CT-E will be reviewed. All examinations will be compared to assess if CT-E gives additional diagnostic information not obtained on the admission CT. A significant difference is one that alters the management of the patient. Sensitivity, specificity and positive and negative predictive values will be obtained for the various studies and used to compare the methodologies. Successful outcomes will be analyzed based on length of stay, correct surgical and nonsurgical intervention with cost as a secondary point of interest.

Progress: 40 patients were enrolled. The study found CT-E is beneficial in partial SBO and metastatic disease.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/181	**Status:** Terminated
Title: Optimizing Breath Hold Technique for MR Scanning		
Start Date: 09/15/95	**Est. Completion Date:** Oct 96	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Richard S. Makuch, MC		
Associate Investigators: MAJ Joseph D. Kern, MC	MAJ Vincent B. Ho, MC	
Key Words: MRI, breath holding		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To optimize a patient's ability to hold his/her breath during the performance of an MRI scan and to identify predictors for breath holding capacity prior to scanning.

Technical Approach: This is a prospective study to evaluate an optimize a patient's ability to hold his/her breath during the performance of an MRI scan. any patient obtaining an MRI scan will be eligible. In addition, we will attempt to formulate pre-examination predictors of a patient's breath holding capabilities prior to ME scanning. Up to 500 volunteers will be selected in the following year to participate. A brief questionnaire will be filled out that will provide standard demographic data such as age, sex, social security number, etc. In addition, a quick history will be performed to ascertain the presence of smoking history, congestive heart failure, prior thoracic surgery, COPD or other pulmonary disease. Volunteers will undergo a modified pulmonary function test with a hand-held device to assess peak flow and have their oxygen saturation value recorded with a pulse oximeter. They will then be asked to perform breath hold for as long as possible in the supine-end inspiration and -end expiration and the prone-end inspiration and -end expiration positions with 2 minutes of rest between holds. The volunteers will then be coached to hyperventilate for 15 seconds on 4-6L/min of oxygen and asked to again perform breath hold in the same four positions. Results of breath holding capability will be correlated with initial oxygen saturation peak flow reading as well as demographic data. Data analysis will be accomplished by chi-square method employing the computer software Statview 4 by Abacus Concepts, Inc., Berkeley, CA.

Progress: No patients were entered. The radiologist involved in this protocol resigned from the Army. None of the other radiologists had the time or interest to assist with this study. Therefore, it was terminated.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/081	**Status:** On-going
Title: Pulmonary Manifestations of Gastro-esophageal Reflux Disease: HRCT Findings		
Start Date: 03/15/96	**Est. Completion Date:** Jan 96	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: CPT Manish K. Varma, MC		
Associate Investigators: MAJ Kazunori Yamamoto, MC	MAJ Cristopher A. Meyer, MC	
Key Words: GERD, HRCT, pulmonary		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To investigate the pulmonary high resolution CT findings of patients with GERD. By categorizing HRCT findings in patients with GERD, a distinction may be made between pulmonary manifestations of GERD and other entities which often have similar plain film findings. This would allow clinical decisions regarding therapy, e.g. steroid therapy in UIP versus anti-reflux measurements to be facilitated.

Technical Approach: Gastroesophageal reflux disease is very common in Western Countries and is associated with significant morbidity. Based on symptoms alone, up to 44% of adult Americans experience GERD. The Gastroenterology Department has a proven population of patients with gastroesophageal reflux disease using the gold standard - 24 hour pH probe monitoring. 25 patients will be selected from the patient population after screening out those patients with prior lung disease, smoking, pregnancy, etc. that may interfere with pulmonary findings of GERD. High Resolution Computed Tomography of the lung will be performed in an attempt to categorized findings unique to GERD that are not discernible on plain film examination. CT and CXR findings will be reviewed by a radiologist and radiology resident. A grading system will be devised on the findings of the first five patients which will consist of five normal volunteers with normal pHs and no GERD. These findings will facilitate treatment options, e.g. steroid treatment in UIP verses anti-reflux precautions in GERD, in diseases that have similar plain film findings.

Progress: Three patients have been identified and entered in the study. Two patients have been scanned with one patient showing evidence of lung changes in association with gastroesophageal reflux disease. The third patient has been scheduled for scanning.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/142 **Status:** On-going

Title: Radiologic Guided Aspiration of Intra-articular Ganglia in the Knee

Start Date: 07/19/96 **Est. Completion Date:** Mar 97

Department: Radiology **Facility:** MAMC

Principal Investigator: CPT Manish K. Varma, MC

Associate Investigators: Rush A. Youngberg
LTC John D. Pitcher Jr., MC

Key Words: Knee:ganglion, aspiration

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether radiologic guided aspiration and subsequent injection of 1% Xylocaine of intra-articular ganglia in the knee is a feasible alternative to arthroscopic excision.

Technical Approach: Intra-articular ganglia in the knee are an uncommon cause of knee pain. Patients with intra-articular ganglia in the knee had good or excellent results with arthroscopic excision of the ganglia. However, 50% to 78% of these patients had no associated internal derangement. CT guided aspiration of intra-articular ganglia in the knee has been successful. Ultrasound guided aspiration of ganglion cysts is a potentially cost effective alternative to surgery. We propose to perform radiologic guided aspiration of 15 patients with intra-articular ganglia in the knee. These patients have knee pain and intra-articular ganglia in the knee demonstrated on MRI. All patients will be followed at 3 month and 6 month after the procedure. An MRI will be obtained immediately post-procedure and at 6 months follow up. Failures will be offered operative (arthroscopy) treatment. The standard treatment (arthroscopy) who do not opt for aspiration. We will determine whether the intra-articular ganglia in the knee is the cause of the patients' symptom. Also, we will show whether aspiration and injection of 1% Xylocaine will successfully remove the ganglion cysts.

Progress: From an original list of 15 patients that were identified through the MR clinic with intra-articular ganglions, three have been referred to the orthopedic clinic. One patient passed the clinic exam requirements for the study and underwent ultrasound guided cyst aspiration successfully with obliteration of the cyst by post-MR. The other two are new patients who have not yet been studied.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, CARDIOTHORACIC SURGERY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/156	**Status:** On-going
Title: North American Duraflo II Working Group		
Start Date: 09/21/94	**Est. Completion Date:**	
Department: Surgery, Cardiothoracic Surgery Service	**Facility:** MAMC	
Principal Investigator: LTC Blaine R. Heric, MC		
Associate Investigators:	LTC Maceo Braxton Jr, MC	
Key Words: Duroflo II, heparin, cardiopulmonary bypass circuits		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 03/15/96

Study Objective: To determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcomes indices: (1) homologous transfusion requirements (2) post-op hours until extubation (3) post-op hours until SICU discharge (4) post-op days until hospital discharge.

Technical Approach: The deleterious effects of cardiopulmonary bypass on hematologic parameters have been will established in cardiac surgery. In particular, the systemic inflammatory response is a well recognized entity which occasionally may create severe clinical problems including ARDS (Adult Respiratory Distress Syndrome), neurologic dysfunction, myocardial edema and myocardial dysfunction, and postoperative weight gain.

Heparin coating all blood containing surfaces of the extracorporeal circuit creates a "pseudo endothelium". Early studies, in a relatively small number of patient in Europe, have indicated that platelet function and numbers are preserved. Bleeding is decreased. Levels of complement activation are reduced and, therefore, postoperative pulmonary function is improved. The number of patients studied in a randomized blinded fashion, however, has been very small and, therefore, improved clinical outcome using this new technology has not been documented.

The Duraflo tubing is one of several heparin coated or "biocompatible" surfaces which have been the focus of active research by many of the industries in the past several years. No U.S. center has reported a clinical evaluation of the product, despite the fact that the FDA has approved the majority of the components for use in routine clinical practice. Adding the heparin coating to the tubing increases the expense of open-heart surgery and no study has yet been able to justify its use. This will be the first study to address this question in a scientific fashion.

Progress: Forty patients have been enrolled in this study.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/157	**Status:** On-going
Title: Clinical Investigation of Viewpoint in Image-Assisted Surgery		
Start Date: 08/16/96	**Est. Completion Date:** Sep 97	
Department: Surgery, Otolaryngology Service	**Facility:** MAMC	
Principal Investigator: MAJ Charles V. Edmond Jr., MC		
Associate Investigators: LTC Dianna Chooljian, MC	LTC Richard F. Debo, MC Michael McFarland	
Key Words: Viewpoint, 3-D digitizer, surgery, planning, localization, sinusitis		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study, to be conducted pursuant to this protocol, is to assess the spatial accuracy and reproducibility of fiduciary and anatomic registration in patients who are undergoing functional endoscopic sinus surgery, with the Viewpoint workstation.

Technical Approach: The viewpoint workstation is a computer assisting device designed to aid the surgeon in navigation and localization in 3 dimensions. The overall registration accuracy in representing real time surgical anatomy will be evaluated. Fifteen study patients will be enlisted from the Otolaryngology Clinic who demonstrate a clinical need for sinus surgery. During the patient preparation and operative procedure, the patient will undergo 3 separate measurements using the Viewpoint probe in order to assess fiducial registration accuracy and reproducibility. In addition, anatomic registration accuracy will be assessed and compared with the accuracy of fiducial registration. The data will be evaluated using the average standard deviation with 95% confidence intervals for the registration accuracy over the course of surgery.

Progress: This is a new study that is awaiting MEDCOM approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/177 **Status:** On-going

Title: ENT Surgical Simulator Project

Start Date: 09/02/94 **Est. Completion Date:** Jun 96

Department:
Surgery, Otolaryngology Service

Facility: MAMC

Principal Investigator: MAJ Charles V. Edmond Jr., MC

Associate Investigators:
Doug Sluis, Ph.D.
Bill Winn, Ph.D.
Don Stredney
Gregory J. Wiet, MD
Dale Fawcett
Suzanne Weghorst
Blake Hanaford, Ph.D.
Roni Yagel, Ph.D.
Bill Bolger, MD

Key Words: Simulator:surgical, Simulator:ENT

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To develop and evaluate a minimally invasive prototype surgical simulator to establish real time fidelity requirements for tactile feedback and computer image synthesis.

Technical Approach: This project is a two phase program with the goal of Phase I to construct a simulator prototype to serve as a platform for further enhancement and evaluation. This includes the development of the geometric and virtual database of the human sinus anatomy, the development of a system to track the surgical instruments, and the system software to implement sinuscope camera emulation and tissue dissection. The prototype will provide the novice with the ability to perform a limited sinus surgery procedure on a virtual patient using sinuscope and surgical tools similar to those used in the operating room. Visual recognition skills and psychomotor skills specific to the surgical context are improved through the experience of the simulated surgery.

In Phase II, development will continue by enhancing the simulator to include changes and enhancements suggested by surgeons in the Phase I evaluation. Additional features such as tactile feedback and tissue deformation will be integrated into the prototype as time and budget permit. During Phase II further analysis will determine the simulators training effectiveness in operation.

Progress: The mechanical design and construction of the simulator are approximately 50% complete.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/122 **Status:** Completed

Title: Activation of the Ras Proto-Oncogenes in Adenoid Cystic Carcinoma: A Pilot Study

Start Date: 03/17/95 **Est. Completion Date:** Oct 95

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: CPT Catherine A. Gutfreund, MC

Associate Investigators: MAJ Richard R. Gomez, MC; MAJ Robert M. Tuttle, MC; LTC Richard F. Debo, MC

Key Words: Cancer:adenoid, ras proto-oncogenes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the frequency of activation of the K-ras proto-oncogene in adenoid cystic carcinoma.

Technical Approach: We plan to use the polymerase chain reaction (PCR) to amplify a specific DNA segment of the K-ras proto-oncogene and then examine these PCR products for previously-described oncogenic point mutations. Specimens will be obtained from pathology specimens of histologically proven adenoid cystic carcinoma from 10 patients of any age or sex. The tissue will be recovered from paraffin blocks, prepared for PCR and amplified. The product will then be separated using agarose gel electrophoresis for size and then Southern blotted with K-ras-specific probes. This is a descriptive study and will simply determine the frequency of K-ras mutations seen in adenocystic carcinoma.

Progress: DNA was recovered and the RAS gene amplified on all 8 subjects. The sequencing will be done at WRAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/134	**Status:** On-going
Title: Universal Screening of Hearing Loss Using Transient Evoked Otoacoustic Emissions		
Start Date: 07/19/96	**Est. Completion Date:** Aug 96	
Department: Surgery, Otolaryngology Service	**Facility:** MAMC	
Principal Investigator: CPT Theodore J. Kanne, MC		
Associate Investigators: Lynne A. Schaefer	MAJ Jonathan A. Perkins, MC COL David G. Schall, MC	
Key Words: Hearing loss:newborns, transient evoked otoacoustic emissions		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: First, to review the results of a universal screening program for hearing loss in newborns, which uses Transient Evoked Otoacoustic Emissions (TEOAE's) as a primary screening modality. From this data, hearing loss prevalence in this population will be determined. Secondly, to estimate the sensitivity, specificity, and predictive value of TEOAEs in identifying hearing loss in this study population. Finally, to analyze the cost-effectiveness of hearing screening with TEOAEs as compared to traditional audiometric screening methods.

Technical Approach: In this investigation, we will retrospectively review the outcome of a universal hearing screening program for newborns which includes the use of TEOAEs. The results of TEOAE screenings of 2200 infants born at MAMC since April 1995 will be reviewed. Those subjects who failed on initial TEOAEs and required retesting will be investigated by retrospective review of their medical records and secondary audiologic testing. This data will be used to estimate the incidence of hearing loss in this population as well as help determine its etiology (s). It will assist in the determination of the relative specificity and sensitivity of otoacoustic emissions as compared to the current methods with auditory brainstem response and behavioral audiometry. Our result will be compared to that found in the literature. A thorough cost-analysis profile regarding universal hearing screening with TEOAEs will be generated.

Progress: Approximately 2000 records have been reviewed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/040 **Status:** On-going

Title: The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas

Start Date: 04/21/95 **Est. Completion Date:** Nov 95

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: CPT Glen J. Mesaros, MC

Associate Investigators: MAJ Charles V. Edmond Jr., MC; MAJ Rodger K. Martin, MS; CPT Dale T. Waldner, MC

Key Words: Cancer:head and neck, oncogenes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To identify cases of oral cavity and oropharyngeal Squamous Cell Carcinoma (SCCA) from the Madigan tumor registry with N0,N1 without extracapsular spread, and N1 with extracapsular spread pathology. To utilize PCR technology in the retrospective genomic and gene product examination of oral cavity, oropharyngeal and nasopharyngeal SCCA. To correlate the amplifixcarion and expression of *c-myc* and *int-2* oncogene with the development of extracapsular lympharteic spread of oral caity and oropharyngeal SCCA.

Technical Approach: The goal of this study is to determine whetеher or not an association exists between amplification and/or expression of *c-myc* and *int-2* with the presence of extracapsular spread of tumor outside the involved lymph node. The MAMC tumor registry will be searched for all tumors involving the oral cavity, oral pharynx, and hypopharynx. Specimens will be limited to 1989-1994, formalin fixed and parafin embedded specimens which show nodal neck metastasis. A comparable number of primary tumors showing no nodal metastasis will also be incorporated and matched as to clinical staging parameters with those tumors having evidence of nodal disease. The pathology reports will then be pulled and those tumors showing extracapsular spread of tumor outside the lymphatics wil be sub-categorized. The total of all specimens will be 50. The specimen blocks will be pulled, sectioned and individually reviewed by the Department of Pathology to confirm the diagnosis of SCCA and the presence or absence of extracapsular spread. Primers for mRNA PCR analysis will be derived from sequence analysis of the *c-myc* and *int-2* genes. Since these genes are not normally expressed in differentiated, non-proliferating cells, the demonstration of the expression of these two genes would be consistent with the previous findings in SCCA. If significant correlation is found between presence of the oncogene transcripts (proof of expression) and extracapsular spread, the relationship between extracapsular spread and over- expression of these genes will be explored.

Progress: To date, this research has shown no correlation between the expression of int-2 and c-myc oncogenes, and the histologic finding of extracapsular spread. A serendipitous finding of differential banding of the int-2 primers in several cancer cell lines raises the questions of a previously undescribed variant of int-2. Future analysis will explore this possibility by doing RT-PCR on several cell lines.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/020 **Status:** Completed

Title: Otitis Media Health Status Evaluation: A Pilot Study to Investigate the Use of Clinical Health Assessment, Functional Health Assessment, and Cost Assessment Instruments as Measures of Severity of ....

Start Date: 11/17/95 **Est. Completion Date:** Mar 96

Department:
Surgery, Otolaryngology Service

Facility: MAMC

Principal Investigator: MAJ Jonathan A. Perkins, MC

Associate Investigators:
COL Chung J. Jung, MC
Cay Crowley, Ph.D.
Ramsey Alsarraf, M.D.
George A. Gates, M.D.

Key Words: Otitis media, pediatric, clinical health assessment, functional health assessment, cost assessment

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To test the consistency, reliability, and validity of four clinical and functional health assessment instruments in evaluating otitis media health status in infants and toddlers. These instruments are (a) an Otitis Media Clinical Evaluation, (b) a general Otitis Media Functional Status Questionnaire, (c) a disease-specific Otitis Media Functional Status Questionnaire, and (d) an Otitis Media Diary. (2) To measure indirect costs attributable to such episodes of otitis media via items included in the administered parental questionnaires. (3) To complete (1) and (2) as a pilot study of health and cost assessment instruments to be employed in a large, prospective, randomized clinical trial currently being submitted by the above investigators for an NIH grant application.

Technical Approach: A small group of well children and children suffering from recurrent acute otitis media will be evaluated to determine their otitis media-related health status in two settings. The first, office-based evaluations, consist of a physician-completed clinical evaluation and two parental questionnaires to assess the child's general and disease-specific functional status at enrollment and at two subsequent six week intervals. The second, home-based evaluations, consist of a functional status diary to be completed by the subject's parent or guardian on a daily basis during the twelve week follow-up period. The data obtained in this twelve week period will provide the means by which each instrument may be analyzed for consistency and reliability as an indicator of otitis media-related health status. The validity of the functional status instruments will also be evaluated through correlation with clinical scores of otitis health status and other physician-rated health determinants. In addition, the parental input will be analyzed as a measure of the indirect monetary costs attributable to recurrent acute otitis media, for use in studies on the cost-effectiveness of treatment in the later clinical trial.

Progress: The instruments that were tested in this study proved to be reliable in the assessment of the clinical and functional health status of children with acute otitis media. A manuscript has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/075 **Status:** On-going

Title: Recurrent Acute Otitis Media: Treatment and Outcomes

Start Date: 02/16/96 **Est. Completion Date:** Feb 02

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: MAJ Jonathan A. Perkins, MC

Associate Investigators:
COL Chung J. Jung, MC
Lloyd D. Fisher, Ph.D.
Ramsey Alsarraf, M.D.
George A. Gates, M.D.
COL David G. Schall, MC
Susan Norton, Ph.D.

Key Words: Otitis media, antimicrobial prophylaxis, tympanostomy tube, adenoidectomy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To compare the outcomes of three randomly assigned treatments: a) medical prophylaxis, b) tympanostomy tube (TT) insertion, and c) adenoidectomy (A) plus TT (ATT) in young children with documented, multiple episodes of acute otitis media with effusion (AOME). The comparison will be in terms of a) the number of new episodes of AOME, b) clinical severity of new episodes using a new, disease-specific clinical evaluation scale, c) time with middle ear effusion (MEE), d) time with hearing loss, e) number of re-treatments, and f) number and type of complications of therapy over a three year follow-up period. (2) Compare the outcomes of the three treatments of recurrent AOME above in terms of new scales of functional health status and otitis-specific functionality, resource utilization, cost per unit reduction in otitis episodes, and standard measures of language, cognition, and social development.

Technical Approach: This application proposes a prospective, controlled, partially-blinded randomized clinical trial with three arms: 1) antimicrobial agent, with or without corticosteroid, 2) tympanostomy tubes (TT), and 3) adenoidectomy (A) + TT. Subjects are children from 12-36 months of age with a history of two or more episodes of AOME who are then entered into a pre-study observation phase. Those who experience a total of 4 episodes of AOME in the prior 12 months, at least one of which is documented during the observation period by the study team, will then undergo a complete medical evaluation. If no exclusion conditions are identified and if informed consent is given, the child is enrolled into the clinical trial. Each child is randomly assigned to one of the three groups, receives treatment and is observed at intervals during a three year follow-up phase. At the end, a comprehensive assessment of his or her otologic, audiologic, linguistic, cognitive, and social functional status is made. Follow-up intervals are 6 weeks in the first year, 8 weeks in the second year, and 12 weeks in the third year with intercurrent event visits at any time should symptoms suggestive of otitis media occur.

Progress: This protocol has not been implemented since it is awaiting a decision if funding will be available through an NIH grant.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/044	**Status:** On-going
Title: Pediatric Brochoesophagology Laboratory Using Swine (Sus scrofa)		
Start Date: 01/19/96	**Est. Completion Date:**	
Department: Surgery, Otolaryngology Service	**Facility:** MAMC	
Principal Investigator: MAJ Jonathan A. Perkins, MC		
Associate Investigators:	Andrew Inglis, M.D.	
Key Words: Brochoesophagology, swine model, pediatric, Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To familiarize the junior Otolaryngology residents at MAMC and the UW and the Pediatric surgery fellow at CHMC, with endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children.

Technical Approach: This is a 3-4 hour afternoon laboratory session. During this time, three pigs will be anesthetized under general anesthesia and rigid and flexible bronchoscopy and esophaoscopy will be performed by the course participants under the supervision of an attending endoscopist. Three separate stations will be used so a maximal number of procedures can be performed in the allotted time and the length of anesthesia is shortened. The first station will be for diagnostic flexible and rigid endoscopy. The second will be for tracheobronchial foreign body removal. The third will be for esophageal foreign body removal. A separate station will be used to teach endoscopic lasing techniques on prosected animal tracheal specimens. A morning lecture will be held on pediatric endoscopy prior to the laboratory and a quiz will be given over selected readings in pediatric enoscopy.

Progress: The laboratory successfully enabled the course participants to learn foreign body extraction from both the airway and esophagus. A repeat course is planned for February 1997.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/161 **Status:** Completed

Title: Success of Preoperative Imaging and Unilateral Neck Exploration for Primary Hyperparathyroidism

Start Date: 09/15/95 **Est. Completion Date:** Sep 95

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: CPT Thomas E. Phillips, MC

Associate Investigators: Stephen K. Clark, M.D.; MAJ Charles V. Edmond Jr., MC; David W. Moore, M.D.

Key Words: Hyperparathyroidism, ultrasound, neck exploration

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate that preoperative imaging with high resolution ultrasound and scintigraphy followed by unilateral neck exploration is a valid approach to the management of primary hyperparathyroidism.

Technical Approach: Head and neck surgeons at Swedish Hospital Medical Center, frequently assisted by otolaryngology residents from Madigan Army Medical Center, have performed over 75 neck explorations for hyperparathyroidism over the past 5 years. Their operative approach involves attempts at preoperative localization with ultrasound and nuclear imaging, followed by unilateral neck exploration. This approach is somewhat controversial and not embraced by all surgeons.

Utilizing a retrospective review of all patients' charts who have received parathyroid surgery at Swedish Hospital, with the diagnosis of primary hyperparathyroidism from January 1, 1990 through March 1995 (approximately 75 patients). We will analyze several factors. Most importantly will be long-term success of surgery as measured by maintenance of normocalcemia postoperatively. The sensitivity and specificity of the preoperative imaging as compared to operative findings and histopathology will be determined. An attempt will be made to analyze factors which may have led to treatment failures.

Progress: The medical records of 107 patients surgically treated for hyperparathyroidism at Swedish Medical Center were studied. Inpatient and outpatient records were reviewed in detail, compiling preoperative ultrasound results, preoperative nuclear imaging results, pathology results, operative time, and post-operative calcium levels. Preliminary analysis revels that the cure rate as measured by correction of hypercalcemia for the unilateral neck exploration approach was 93%. Additionally, a significant 45 minute difference was found between the unilateral and bilateral approach ($p<0.0001$). This retrospective study challenges the traditional school of thought espousing bilateral neck exploration and supports unilateral neck exploration guided by preoperative Technetium-99m-sestamibi nuclear scintigraphy.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/050 **Status:** Completed

Title: A Multicenter, Randomized, Parallel Group, Evaluator Blinded, Comparative Study of the Safety and Efficacy of Ofloxacin Otic Solution and Augmentin Oral Suspension in the Treatment of Acute Purulent..

Start Date: 12/16/94 **Est. Completion Date:** Jul 95

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: COL David G. Schall, MC

Associate Investigators: MAJ Ray E. Jensen, MC LTC Richard F. Debo, MC

Key Words: Otorrhea, ofloxacin, augmentin, tympanostomy tubes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/15/95

Study Objective: To compare the safety and efficacy of ofloxacin otic solution to Augmentin oral suspension in the treatment of acute purulent otorrhea in children with tympanostomy tubes.

Technical Approach: This is a multicenter, randomized, parallel group, evaluator blinded study with a comparative therapy control. At least 20 investigative centers will participate. The investigators will collectively enroll approximately 320 subjects to ensure clinically evaluable data from 276 subjects. All subjects will have tympanostomy tube(s) in place and acute purulent otorrhea. Subjects will be treated for 10 days. The ofloxacin otic solution will be instilled twice daily. Augmentin oral suspension wil be administed every 8 hours.Subjects will have baseline pre-therapy qualifying procedures and evaluations performed at Visit 1. All subjects will subsequently return for an evaluation at 4-6 days after initiation of treatment, 1-3 days after completion of treatment, and 7-10 days after completion of treatment. Safety evaluations will be made by assessing adverse events during the course of the study. Safety will also be based on changes in the physical examinations and vital signs performed at baseline, and all return visits. Audiometry will be an additional end point for safety. Efficacy will be based on clinical response during the study by performing outcome assessments at each visit. Bacteriological efficacy will also be evaluated. The primary efficacy parameter will be the presence or absence of otorrhea.

Progress: Thirteen patients were consented and randomized. Eight patients completed the study; two patients did not respond to the study medication and were treated with Augmentin; and three patients were dropped from the study (1 due to Strep, 1 due to an URI, and one due to a drug reaction).

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/051 **Status:** Completed

Title: A Multicenter, Prospective With Historical and Current Practice Control, Open-Label Study to Examine the Safety and Efficacy of Ofloxacin Otic Solution in the Treatment of Purulent Otorrhea...

Start Date: 12/16/94 **Est. Completion Date:** Jul 95

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: COL David G. Schall, MC

Associate Investigators: MAJ Ray E. Jensen, MC; LTC Richard F. Debo, MC

Key Words: Otorrhea, ofloxacin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To demonstrate the safety and efficacy of ofloxacin otic solution in the treatment of chronic suppurative otitis media with otorrhea in adolescents and adults with perforated tympanic membranes.

Technical Approach: This is a multicenter open-label study with an historical control arm (Historical Practice Group) and a current control arm (Current Practice Group). Documented records of Historical Practice at the same institutions for up to the prior four years will serve as the historical control. At least 15 investigative centers will participate. The investigators will collectively enroll approximately 150 subjects to ensure clinically evaluable data from 126 subjects for the ofloxacin group. Subjects will be treated for 14 days. The ofloxacin otic solution will be instilled twice daily. Subjects will be evaluated at baseline, 4-6 days after initiation of treatment, 1-3 days after completion of treatment, and 7-10 days after completion of treatment. Safety evaluations will be made by assessing adverse events during the course of the study. Safety will also be based on changes in the physical examinations and vital signs performed at baseline and all return visits. Efficacy will be based on clinical response during the study by peforming clinical assessments at each evaluation. Bacteriological efficacy will also be evaluated. The primary efficacy parameter will be the presence or absence of otorrhea.

Progress: Three patients were consented and two were given the active drug. Both of these were dropped prior to study completion because of adverse events unrelated to the study medication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/059 **Status:** Completed

Title: The Antimicrobial Activity of Cocaine and Lidocaine with Phenylephrine as Topical Anesthetics on Common Nasal Pathogens

Start Date: 02/16/96 **Est. Completion Date:** Apr 96

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: MAJ Brian M. Sieck, MC

Associate Investigators: MAJ Ray E. Jensen, MC; CPT Wade K. Aldous, MS

Key Words: Pathogens:nasal, cocaine, lidocaine, phenylephrine, anesthetic:topical

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: We intend to determine the antimicrobial activity of 4% cocaine and lidocaine with phenylephrine against common nasal pathogens.

Technical approach: Seven nasal pathogens will all be cultures in the presence of 4% cocaine, 4% lidocaine with 0.5% phenylephrine, 0.5% phenylephrine, methylparaben (the preservative found in lidocaine) or amoxicillin. For each pathogen, two cultures will be done with the substrate. Organisms to be obtained from the microbiology section of the pathology department. The organisms to be used are *Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumonia, Enterobacter sp. Haemophilus influenzae, Moraxella catarrhails* and *Staphylococcus aureus*. Serial dilutions (0.5 ml + 0.5 ml) of 4% cocaine, 4% lidocaine with 0.5% phenylephrine, 0.5% phenylephrine, methylparaben with amoxicillin will be made in typtic soy broth (TSB). These tubes will then be inoculated with a standardized broth culture diluted to 1:200 and incubated overnight. Three controls will be run, a organism control, a broth sterility control and antibiotic sterility control. The tube containing the lowest concentration of anesthetic/amoxicillin and having no growth will be the minimum inhibitory concentration (MIC) for that organism. Subcultures of the tubes with no growth will then be performed. The lowest concentration of anesthetic/amoxicillin permitting survival of no or few organisms on subculture will represent the minimum bactericidal concentration.

Progress: This study looked at the antimicrobial activity of 4% lidocaine with phenylephrine or 4% cocaine in nasal procedures. The pathogens *B. catarrhalis, Enterobacter sp., H. influenzae, K. pneumoniae, P. aeruginosa, S. aureus, and S. pneumoniae* were used. Organisms were tested against two-fold serial dilutions of stock preparations of 4% lidocaine with 0.25% phenylephrine, 0.25% phenylephrine, 0.1% methyl paraben (a preservative found in lidocaine), 250 mg/ml ampicillin, and 4% cocaine. The minimum inhibitory concentration and minimum bactericidal concentration for each of the solutions were obtained. The bacteria studied varied greatly in their susceptibility to lidocaine with phenylephrine and cocaine. Cocaine consistently exhibited greater antimicrobial activity than lidocaine. Phenylephrine and methyl paraben showed slight antimicrobial activity. These topical anesthetics have slight bactericidal activity on nasal specimens which may sometimes lead to false negative results when performing procedures. A paper has been submitted to the Ear, Nose, and Throat Journal for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/040 **Status:** Completed

Title: nm 23 Antimetastatic Gene Product Expression in Head and Neck Squamous Cell Carcinoma

Start Date: 01/19/96 **Est. Completion Date:**

Department: Surgery, Otolaryngology Service **Facility:** MAMC

Principal Investigator: CPT Angie U. Song, MC

Associate Investigators: LTC Richard F. Debo, MC

Key Words: Cancer:head and neck, nm23 gene, antimetastatic

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To examine the relationship of nm23 protein expression in squamous cell carcinomas of the head and neck. To determine the validity for using nm23 expression to predict nodal status, distant metastasis, and overall survival.

Technical Approach: Tissues will be fixed in neutral buffered formalin and embedded in paraffin wax. Three sections will be cut from each tissue sample. One section will be reviewed for diagnosis and the other two sections will be mounted on slides. The primary antibody to nm23-H1 peptide sequence will be applied. The specifically bound antibody to nm23 gene product will be visualized by incubation with a biotinylated secondary antibody followed by a preformed avidin-biotinylated horseradish peroxidase macromolecular complex and substrate. The positive tissue control will be determined using breast adenocarcinoma tissue which has previously been found to give positive nm23 product staining. The negative tissue control will be normal skin epithelium. All tissue samples will also be stained for vimentin to evaluate the protein quality in the sections. Two observers will separately review each case and grade the nm23 product staining. This will be done blind as to the histological diagnosis of each case. The grading system will be from zero to three. Zero will correlate with the negative tissue control, skin epithelium, and grade three will correlate will the positive tissue control, breast adenocarcinoma. Grades one and two will be defined as light and moderate staining respectively. Chi-square analysis will be used to assess the association between nm23 gene product expression and histological difference, positive or negative nodal status, and presence of distant metastasis. These variables are categorical.

Progress: This study examined the expression of the nm23 gene product compared to modal status in 70 patients with squamous cell carcinomas of the head and neck. Reduced immunoreactivity was observed in 88% with positive nodal status. Strong immunoreactivity was observed in 56% with negative nodal status and light immunoreactivity in 33% with negative nodal status. There seems to be a reduced expression of the nm23 gene product when there is positive lymph node metastasis. This is especially demonstrated in the tongue and larynx areas. Grade 0 (weak to none) patients' survival and disease interval was decreased with mortality rate of 58% and survival of 20 months; grade 1 (light to moderate) had a mortality rate of 21% and mean survival of 39 months; and grade 3 had the lowest mortality rate of 17%, yet a mean survival rate of only 16.5 months. The nm23 gene exerts antimetastatic properties and perhaps contributes to the overall patient survival rate.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/105 **Status:** Terminated

Title: Telomerase Activity and Telomere Length in Human Gastric Cancer

Start Date: 06/16/95 **Est. Completion Date:** May 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Tommy A. Brown, MC

Associate Investigators:
LTC William C. Williard, III, MC
MAJ Kenneth W. Westphal, MC
CPT Wade K. Aldous, MS
CPT Raymond S. Lance, MC
Troy H. Patience, B.S.

Key Words: Cancer:gastric, telomerase activity, telomere length

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous gastric 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 gastric cancer.

Technical Approach: Tissue samples will be taken from 40 male and female patients undergoing surgical resection for gastric cancer. Tumors to be investigated include adenocarcinoma, gastric lymphoma, gastric carcinoid, gastric sarcomas and all other malignant and benign tumors. 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 *Rsa*1 and *Hin*f1 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 in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers 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: This study was terminated due to a lack of available tumors.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/106	**Status:** On-going
Title: Telomerase Activity and Telomere Length in Human Breast Cancer		
Start Date: 06/16/95	**Est. Completion Date:** May 96	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: CPT Tommy A. Brown, MC		
Associate Investigators: LTC William C. Williard, III, MC MAJ Kenneth W. Westphal, MC	CPT Wade K. Aldous, MS CPT Raymond S. Lance, MC Troy H. Patience, B.S.	
Key Words: Cancer:breast, telomerase acitivity, telomere length		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous breast 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 breast cancer.

Technical Approach: Tissue samples will be taken from 50 female and male patients undergoing surgical resection for breast cancer. All malignant and benign tumors 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 *Rsa*1 and *Hin*f1 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 in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers 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: Eight samples have been obtained for this study; 6 in FY 96 and 2 in FY 95.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/107 **Status:** Terminated

Title: Telomerase Activity and Telomere Length in Human Pancreatic Cancer

Start Date: 06/16/95 **Est. Completion Date:** May 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Tommy A. Brown, MC

Associate Investigators:
LTC William C. Williard, III, MC
MAJ Kenneth W. Westphal, MC
CPT Wade K. Aldous, MS
CPT Raymond S. Lance, MC
Troy H. Patience, B.S.

Key Words: Cancer:pancreatic, telomerase activity, telomere length

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in pancreatic tumor 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 pancreatic cancer.

Technical Approach: Tissue samples will be taken from 25 male and female patients undergoing surgical resection for pancreatic cancer. All malignant and benign tumors found during pancreatic tumor resection 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 *Rsa*1 and *Hin*f1 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 in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers 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: This protocol was terminated due to a lack of appropriate tumors.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/108	**Status:** On-going
Title: Telomerase Activity and Expression of p53, DCC, and Rb in Human Colorectal Cancer		
Start Date: 06/16/95	**Est. Completion Date:** May 96	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: CPT Tommy A. Brown, MC		
Associate Investigators: LTC William C. Williard, III, MC MAJ Kenneth W. Westphal, MC	CPT Wade K. Aldous, MS CPT Raymond S. Lance, MC Troy H. Patience, B.S.	
Key Words: Cancer: colorectal, telomerase activity, temomere length		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in colorectal tumor 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 colorectal cancer.

Technical Approach: Tissue samples will be taken from 35 male and female patients undergoing surgical resection for colorectal cancer. All malignant and benign tumors of the colon and rectum found 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 *Rsa*1 and *Hinf*1 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 in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers 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: Twenty-five samples have been collected and data analysis has been started.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/009 **Status:** On-going

Title: Postoperative Cisapride Therapy After Colorectal Surgery

Start Date: 10/20/95 **Est. Completion Date:** Oct 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Tommy A. Brown, MC

Associate Investigators:
CPT Jerome M. McDonald, MC
LTC William C. Williard, III, MC
G. Gender

Key Words: Surgery:colorectal, cisapride

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To test the efficacy of cisapride in the postoperative period in relation to bowel motility and length of hospital stay.

Technical Approach: In this double-blind study 66 patients undergoing colorectal surgery will be randomly assigned to one of two groups. The experimental group will receive 20mg cisapride orally four times daily until discharged; the control group will receive placebo. All patients will be given an oral sitz mark radiographic marker on the first postoperative morning to follow bowel motility. A daily portable abdominal x-ray will be taken until 80% of the sitz markers have completely passed through the system. Length of hospital stay, daily progression of radiographic marker, onset of bowel movements, regular diet intake and perioperative complications will be monitored and compared for experimental and control groups.

Progress: Twenty-one patients have been entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/119	**Status:** On-going
Title: C-Reactive Protein in the Diagnosis of Acute Appendicitis		
Start Date: 03/17/95	**Est. Completion Date:** Apr 95	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: CPT Mathew H. Chung, MC		
Associate Investigators: CPT Donald Kim, MC	CPT Brad J. Davis, MC LTC William C. Williard, III, MC	
Key Words: Appendicitis, C-reactive protein		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the negative predictive value of C-reactive protein (CRP) in an attempt to determine if the negative exploratory laparotomy rate (30%) can be significantly reduced. A secondary objective would be to calculate the cost savings of reducing the negative exploratory laparaotomy rate.

Technical Approach: This study will attempt to better define the role, if any, of measuring CRP level in the diagnosis of acute appendicitis. It will determine if a normal CRP is a better negative predictor of appendicitis than normal serial leukocyte counts (WBC) and erythrocyte sedimentation rate (ESR). This study will include 100 subjects, 18 years and older, identified by the general surgery service with suspected appendicitis. Patients will have CRP, ESR and WBC testing during initial evaluation as routine. Those who do not undergo immediate surgery will have CRP, ESR and WBC tested again 12 hours later. The levels of CRP at both of these times and the need for surgery will be collected as data. Those who do not eventually go to surgery will be considered to have no appendicitis for data analysis.

Progress: Twenty patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/045 **Status:** On-going

Title: The Effect of Low-Dose Dopamine on Splanchnic Blood Flow with Intra-abdominal Hypertension in Domestic Yorkshire Swine, Sus scrofa

Start Date: 01/19/96 **Est. Completion Date:**

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Mathew H. Chung, MC

Associate Investigators: LTC Patrick J. Offner, MC

Key Words: Hypertension, blood flow, dopamine, swine,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To investigate the ability of low-dose dopamine to improve visceral blood flow and organ perfusion during induced intro-abdominal hypertension.

Technical Approach: We will use an established porcine model of elevated intra-abdominal pressure. The animals will be anesthetized, mechanicaly ventilated and instrumented. Femoral arterial and venous catheters will be placed and a Swan-Ganz pulmonary atery catherter will be placed via jugular vein. Laparatomy will performed for the placement of Doppler flow probes and gastric and ileal tonometers. Tweo catheters will be placed in the abdominal cavity percutaneously and a urinary catheter will be placed through a cystotomy. Following instrumentation, animals will be randomly assigned to one of four exxperimental groups. Group I is the negative control with no further manipulations. Group II will have elevated intra-abdominal pressure by instillation of saline solution. Group III will have the same elevated (Group II) intra-abdominal pressure established plus low dose dopamine. Group IV will have low-dose dopamine alone. There will be six animals per group. Intra-abdominal presures of 20 and 40 mm Hg will be studied. Measurements will include the following every 20 minutes for two hours during the experiment: (1) renal, hepatic, and superior mesenteric arterial flow and portal vein flow, (2) hepatic and renal perfusion, (3) gastric and terminal ilieum pHi, (4) cardiac hemodynamics, and (5) laboratory values on ABG, mixed venous blood gas and lactate levels.

Progress: The investigators are awaiting funding and purchase of the pigs before the study can begin.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/038	**Status:** On-going
Title: Advanced Trauma Life Support Course Utilizing the Goat (Capra hircus)		
Start Date: 11/18/94	**Est. Completion Date:** Jul 97	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: COL William E. Eggebroten, MC		
Associate Investigators: COL Preston L. Carter, MC LTC Clifford L. Simmang, MC	MAJ Katherine L. Bevill, MC CPT Ronald J. Place, MC LTC Patrick J. Offner, MC	
Key Words: Training protocol:goat, ATLS,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 05/08/96

Study Objective: The objective of this training exercise is to teach physicians one safe method of performing five life-saving procedures for trauma patients.

Technical Approach: This training exercise will MAMC residents in the initial management of trauma patients. The physicians will practice the safe methods of performing the following life-saving procedures in the order listed: venous cut down, dagnostic peritoneal lavage, chest tube insertion, pericardiocentesis and 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 direct basis of psychomotor skills and verbalization of the indications, contraindications and potential complication of each procedure.

Progress: 4 pigs were studied in FY 96, with no unexpected loss of animals. One session was held, training 16 individuals.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/035 **Status:** On-going

Title: Madigan Army Medical Center Institute for Advanced Endoscopic Training Using the Pig (Sus scrofa)

Start Date: 01/23/95 **Est. Completion Date:** Jan 98

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: COL William E. Eggebroten, MC

Associate Investigators:
CPT Donald Kim, MC
MAJ David M. Watts, MC
LTC Clifford L. Simmang, MC
LTC William C. Williard, III, MC
MAJ Clifford A. Porter, MC
LTC Patrick J. Offner, MC
MAJ Timothy F. Deaconson, MC

Key Words: Training:endoscopic, pig,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To familiarize General Surgery residents, staff, and invited surgeons form our local community with techniques in the management of advanced endoscopic-laparoscopic techniques. This would familiarize surgeons with techniques for laparoscopic procedures upon the esophagus and stomach, especially for anti-reflux procedures, and the biliary tract for cholecystectomy and common bile duct exploration and for the small intestine in colon for intestinal resection, appendectomy, and colonic resection.

Technical Approach: This training protocol on laparoscopic and endoscopic surgical procedures will use a total of 10 pigs. Two to four pigs will be used per session with three sessions per year. The animals will be maintained on a nothing-by-mouth status for 12 hours prior to the procedures. General anesthesia will be used. The animals will be intubated, prepped and maintained on inhalant anesthesia. At the completion of the procedures, the pig will be euthanitized. During each procedure, each animal will be used for a single training episode. Maximum teaching benefit will be obtained by repeating the procedures in order that each trainee assigned to the animal may have an opportunity to perform the procedure in rotation. Critique forms will be utilized for the training and will provide evaluation of effectiveness of the course.

Progress: 2 pigs were studied in FY 96, with no unexpected loss of animals. One session was held, training 20 individuals.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/022	**Status:** On-going
Title: The Use of Autologous Fibrin Glue to Prevent Post-operative Seromas in Patients Undergoing modified Radical Mastectomy		
Start Date: 11/18/94	**Est. Completion Date:** Dec 96	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: CPT Bret R. Hansen, MC		
Associate Investigators: CPT Daniel D. Mais, MC	LTC Patrick J. Offner, MC	
Key Words: Mastectomy, seroma, fibrin glue		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if the use of autologously donated fibrin glue can decrease the incidence of post-operative fluid collections in patients undergoing modified radical mastectomy.

Technical Approach: We plan to conduct a prospective, randomized study evaluating the effects of autologously donated fibrin glue on the flaps created during modified radical mastectomy in attempts to increase the adhesion of the flaps to the underlying tissue and prevent post-operative fluid collections. A total of 60 subjects will be recruited and randomized to a study group and a control group. All subjects will donate one unit of autologous blood pre-operatively. This blood will be used to provide the autologous fibrinogen for the study group. Surgeons will be given the fibrin preparation or saline to apply after mastectomy. The surgeons will be blinded as to whether they are applying fibrin glue or control saline. Drainage from the surgical area will be recorded by the subjects and a blinded evaluator will assess fluid accumulation at least weekly after drains are removed. Seroma fluids will be drained as necessary. Rates of seroma formation will be compared using chi-square analysis. The mean total amount of drain output and the mean length of time for the drains to be discontinued will also be analyzed using the Student's T-test or a non-parametric test should the distribution prove to be non-Gaussian.

Progress: No patients have been entered in this study due to rewrites of the consent form and misunderstanding over the approval status of the protocol.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/100 **Status:** Terminated

Title: Gastroschisis in the Newborn Pig (Sus scrofa): Comparing Several Techniques for Conserving Fluid Loss and Maintaining Normothermia

Start Date: 03/24/95 **Est. Completion Date:** Jan 95

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: MAJ Randall M. Holland, MC

Associate Investigators: CPT Edmond Paquette, MC

Key Words: Gastroschisis, fluid loss, normothermia, rabbit,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To examine several methods of conserving fluid loss and maintaining normothermia in new-born pigs with abdominal wall defects. This pilot study is designed for the investigators and the DCI veterinary staff to become familiar with the technical details of intubating, anesthetizing,and operating upon piglets. The data collection methods will also be examined for accuracy and practicality.

Technical Approach: This two-part pilot study will examine and compare several techniques for conserving fluid loss and normothermia in a new-born pig model. In the first part, one 24-48 hour old piglet will receive an intramuscular injection of telazole for sedation, be intubated and given isofluorane gas anesthesia. An incision will be made in the right lower quadrant and, using gentle palpitation, the abdominal contents will be eviscerated to the outside. For the next four hours, various methods of conserving fluid loss and maintaining normothermia will be attempted, including wrapping the abdominal contents in gauze and plastic and in plastic alone. After four hours, the piglet will be euthanitized. Part two is a repeat of part one, except that four piglets will be used and they will be assigned to one of four groups using different methods of conservation. Group one will receive no fluid or heat conservation method. Group two will have the abdominal contents wrapped in moist and then dry gauze. Group three will have the abdominal contents wrapped in gauze and then plastic. Group four will have the entire pig placed into a bowel bag up to its axilla. The temperature and weight of each pig will be taken every 15 minutes and the pigs will be euthanitized after four hours. The intent of the study is to familiarize investigators with intubation, anesthesia, and care and handling of piglets with abdominal wall defects. The values recorded will be used to determine the ranges temperature and fluid loss for a larger study which will follow.

Progress: This animal model was not feasible. Two pigs were used. Other models were deemed to be too expensive and, perhaps, not feasible either, so the protocol was terminated.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/099 **Status:** On-going

Title: Evaluation of Multiple Metastatic Tumor Sources for Mutation of Human Metastasis Suppressor Gene KAI1

Start Date: 04/19/96 **Est. Completion Date:** Sep 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Jerome M. McDonald, MC

Associate Investigators:
LTC William C. Williard, III, MC
CPT Jason L. Blaser, MS
CPT Raymond S. Lance, MC
Katherine H. Moore, Ph.D.

Key Words: Cancer:bladder, Cancer:breast, Cancer:colon, Cancer:kidney, Cancer:lung, Gene KAI1

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective is to demonstrate a loss of expression in the recently localized prostate cancer metastasis suppressor gene, KAI1, in metastatic bladder, breast, colon, kidney, and lung carcinoma.

Technical Approach: The study is designed to determine the presence or absence of the KAI1 metastasis suppressor gene in histologically confirmed metastatic bladder, breast, colon, kidney, and lung carcinoma. KAI1 has been shown to be present in nearly all human tissues to include colon, breast, lung, and kidney by Dong, et al. and is felt to code for an intercellular adhesion molecule. Reverse Transcriptase polymerase chain reaction will be used to amplify the extracted KAI1 RNA from paraffin blocks of histologically confirmed malignant tissue with histologic confirmation of metastasis. Because clinical follow-up is available on all patients in the Tumor registry, patient follow-up can be monitored. The sample population will include any specimen sent to Madigan Army Medical Center's Department of Pathology with histologic confirmation of malignancy by the Madigan Army Medical Center Department of Pathology or an outside institution at pathology's request with histologic confirmation of metastasis. Direct invasion of adjacent tissues by local growth or lymph node involvement does not constitute metastasis for purposes of this study. Sample size will include 10 species for each study organ. All histologic types and grades will be acceptable for analysis.

Progress: Ten paraffin embedded specimens with known metastatic tumors have been located. The Department of Clinical Investigation has proceeded to prove the presence of KAI-1 in normal liver tissue, optimize the extraction of RNA from paraffin embedded specimen, and utilize reverse transcriptase PCR to confirm the presence of KAI-1 expression in normal tissue for the paraffin blocks. Subsequent to this work, microdissection technique was used to separate the tumor tissue from the normal tissue within paraffin blocks of colonic tumor and reparaffinize both specimens. RNA was then extracted from 10 samples, quantified with spectrophotometry, and evaluated for KAI-1 expression with RT-PCR. Unfortunately, all 10 tumor and normal specimens expressed KAI-1 which could represent contamination. In the interim, a group in Japan has developed an antibody to KAI-1 and has confirmed loss of expression of KAI-1 in many tumors with immunohistochemistry. Tumor stage was not discussed with their data. The antibody has been received from their group and the investigators plan to use immunohistochemistry to evaluate stage vs expression.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/142	**Status:** Suspended
Title: Development of An Animal Model for a Simple Bone Cyst in the Goat		
Start Date: 05/26/95	**Est. Completion Date:** Jun 97	
Department: Surgery, General Surgery	**Facility:** MAMC	
Principal Investigator: CPT Richard C. Rooney, MC		
Associate Investigators:	LTC John D. Pitcher Jr., MC	
Key Words: Cyst:bone, goat model,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: Our primary objective is to devise an animal model to observe the developmental course of a simple bone cyst. We will use a goat (Capra hircus) as our model for the human system.

Technical Approach: We propose to develop an animal model and study the developmental course of a simple bone cyst. Since the lining of a simple cyst is similar to the joint lining of synovial tissue, we will test the hypothesis that the intraoperative implantation of synovium will develop into a cyst. Since human bone cysts are often cryptic until a fracture or other symptom occurs, they are not well studied. The development of such a model should facilitate many potential studies of simple bone cysts. Pre-operatively, the goats will undergo a baseline radiographic appraisal of the limbs. Five young animals less than two months old will be used to simulate a fetus when the aberrant synovial implantation of tissues is thought to occur. Under general anesthesia, a partial synovectomy will arthroscopically performed on the hip with implantation made on an adjacent bone. Post-operatively, the goats will be radiographed to appraise maturation of the bone cyst over a twenty three month period. The goats will then be euthanitized and their cyst lining analyzed and compared to that of synovium. Radiographs will be assessed by clinical means to determine development of a unicameral bone cyst. All data will be evaluated for the feasibility of the model.

Progress: Due to other commitments the PI was unable to implement this protocol before being assigned TDY to Alaska. The protocol has been put in a suspended state and will be re-reviewed by the LACUC before the PI can implement it when he returns to MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/141 **Status:** Suspended

Title: Development of a Pig Model to Produce a Growing Fused Limb by Transferring Half of the Open Growth Plate From the Lower End of the Femur to the Upper End of the Tibia When the Tibia's Growth Plate....

Start Date: 05/26/95 **Est. Completion Date:** Jun 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: CPT Richard C. Rooney, MC

Associate Investigators: LTC John D. Pitcher Jr., MC
LCDR Dave Sitler, MC

Key Words: Arthrodesis, hemi-femoral turndown, tibial replacement,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: Our primary objective is to determine the feasibility of maintaining open physeal plates in an autogenous, vascularized bone graft that has been traumatized by operative relocation. We will use a pig as our model for the human system in this pilot study.

Technical Approach: Research has indicated that it is possible to split the lower end of the adult femur (thigh bone), leave its vascular (blood) supply intact, and flip it upside down in order to use it as a replacement for the upper end of the tibia. We intend to develop a similar procedure in skeletally immature pigs to permit the limb to continue its normal growth while in a fused position. The technique is illustrated in the protocol. The total amount to limb growth should be normal because the growth plate is still functional at both ends of the femur. Before the procedure, the pigs will be weighed, have arteriograms and X-rays of limbs taken for status and measurement, establishing a baseline limb length. The some procedures will be performed at one, six and eleven months to assess bone growth. The animal will then be euthanitized and histologically examined. Radiographs, arteriograms, an limb length measurements will be evaluated by standard clinical means. Lengths of limbs will be measured and contralateral joints will be examined and compared to the surgical plates. The operative and non-operative limbs will be compared for parallel slopes.

Progress: Due to other commitments the PI was unable to implement this protocol before being assigned TDY to Alaska. The protocol has been put in a suspended state and will be re-reviewed by the LACUC before the PI can implement it when he returns to MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/184 **Status:** On-going

Title: A Phase II Study to Evaluate LY320052 (rHbl.l) Compared to Standard Allogeneic Blood Transfusion Therapy in Elective Surgery

Start Date: 09/15/95 **Est. Completion Date:** Nov 96

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: MAJ David M. Watts, MC

Associate Investigators:
COL Preston L. Carter, MC
MAJ Clifford A. Porter, MC
COL William E. Eggebroten, MC
LTC William C. Williard, III, MC
LTC Patrick J. Offner, MC
MAJ Timothy F. Deaconson, MC

Key Words: Transfusion therapy, LY320052 (rHbl.l), allogeneic blood therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/18/96

Study Objective: The objective of this study is to examine the efficacy of rHb1.1 (LY320052) as a hemoglobin-based oxygen carrier (HBOC) and colloid volume expander in patients undergoing elective surgery. The primary efficacy objective is to determine whether administration of rHb1.1 reduces the proportion of patients undergoing elective surgery who receive an allogeneic blood transfusion intra-operatively or post-operatively through 7 days post surgery. Another objective is to determine the safety of rHB1.1 compared with standard transfusion therapy.

Technical Approach: This is a multi-center, randomized, double-blind, active-controlled, parallel study of approximately 192 patients. Standard therapy of allogeneic blood transfusion will be used as the active control. Patients between the ages of 18 and 75 who are ASA I, II or III undergoing elective surgery with an anticipated intraoperative blood requirement of 2 to 4 units will be considered for this study. After obtaining consent, patients will be screened with a history, physical examination, and laboratory evaluation. Monitoring and data collection for this study will include pre-, intra-, and post-operative vital signs, and hemodynamic monitoring. Patients will be randomly assigned to receive either standard allogeneic transfusion or rHb1.1. Allogeneic transfusions will be packed red blood cells only, not whole blood. Patients randomized to the standard transfusion group will receive as many allogeneic units as is appropriate and those patients randomized to the rHB1.1 group may receive from 1 to up to 4 units of rHb1.1.1, but anything necessary over 4 will be met with standard therapy. Patients will be followed during and after surgery with examinations and blood tests at days 1,2, 7, and 28 post surgery. Efficacy will be analyzed by measuring the number of allogeneic units after surgery for each group, the average comparative numbers of rHb1.1 units compared to standard therapy. The Lilly Statistical and Mathematic Science Department will perform the statistical analysis presented in the final report.

Progress: This protocol has numerous exclusion criterias making it difficult to qualify patients for the study. No patients have been enrolled at MAMC. Nationwide, with 22 institutions participating, only 7 patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/032	**Status:** On-going

Title: Phase III Population Pharmacokinetic Study for the Determination of Plasma Levels of Synercid (quinupristin/dalfopristin) in Treated Patients (Protocol JRV-135)

Start Date: 11/17/95	**Est. Completion Date:** Jan 97
Department: Surgery, General Surgery	**Facility:** MAMC
Principal Investigator: LTC William C. Williard, III, MC	
Associate Investigators:	LTC Patrick J. Offner, MC
Key Words: Skin:infection, Synercids, plasma levels	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objective: To evaluate Synercid plasma levels obtained in Phase III Synercid study patients in order to develop a population pharmacokinetic/pharmacodynamic model for the drug.

Technical Approach: This is an open-label, Phase III, randomized, comparative, multicenter study of Synercid versus standard therapy in the treatment of complicated gram-positive skin and skin structure infections. An adequate number of study sites will be initiated to enroll a sufficient number of patients for analysis (approximately 450-600 patients to obtain 300 evaluable, 150 per treatment arm). A pathogen isolation rate of at least 70% must be met to ensure that an adequate number of pathogens are identified. After giving informed consent and meeting the Inclusion/Exclusion criteria, patients will be randomly assigned to receive either Synercid iv 7.5 mg/kg every 12 hours, or standard therapy that is based on the clinical presentation of the patient and the susceptibility pattern of the causative pathogen: either Oxacillin iv 2g q 6h or Vancomycin iv 1g q 12h. Patients will be clinically assessed at baseline, on day 4, at the end of study treatment, and test of cure visit (14 to 28 days after treatment discontinuation).

Progress: No patients were enrolled in this study due to the completion of the Synercid protocol prior to the initiation of this pharmacokinetic study. The study will remain open as the investigators anticipate involvement with another Synercid antibiotic protocol within the year.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/004 **Status:** Completed

Title: A Phase Three Randomized Multicenter Comparative Study of Synercid (quinupristin/dalfopristin) vs standard therapy in the treatment of Complicated Gram positive Skin & Skin-structure Infections (#304)

Start Date: 10/21/94 **Est. Completion Date:** Nov 95

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: LTC William C. Williard, III, MC

Associate Investigators:

CPT Peter J. Armstrong, MC
MAJ Brad A. Case, MC
CPT Stefan M. Pettine, MC
CPT Bret R. Hansen, MC
CPT Ronald J. Place, MC
MAJ Katherine L. Bevill, MC
CPT Mathew H. Chung, MC
CPT Thomas K. Curry, MC
CPT Raymond S. Lance, MC

Key Words: infections:skin, synercid, vancomycin, oxacillin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the safety and therapeutic effectiveness of Synercid IV (7.5 mg/kg q 12h) versus standard therapy in the treatment of gram-positive complicated skin and skin-structure infections.

Technical Approach: Patients will be randomly assigned to receive either Synercid IV (7.5 mg/kg every 12 hours), or standard therapy that is based on the clinical presentation of the patient and the susceptibility pattern of the causative pathogen: either Oxacillin IV (2g q 6 hours) or Vancomycin IV (1g q 12 hours). Patients will be clinically assessed at baseline, on day 4, at the end of study treatment, and test of cure visit (14 to 28 days after treatment discontinuation). The primary efficacy parameter will be the Clinical Response determined at the test of cure assessment or when patients discontinue treatment before completing the test of cure assessment. Safety and tolerability of Synercid, oxacillin and vancomycin will be assessed using subjective patient reports, clinical evaluations and laboratory tests.

Progress: This study was closed to patient enrollment, 29 March 1996. Sixteen patients were consented at MAMC and 15 were randomized; one patient did not have the correct organism for treatment. Eleven participants completed the trial through the test of cure visit. One participant completed the treatment phase but did not return for follow-up and test of cure. One patient was dropped due to a reaction to Synercid with the first dose. One patient chose to discontinue because of the inconvenience of home IV therapy. One patient was inadvertently changed to another antibiotic during the treatment phase, which is a protocol violation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/071 **Status:** Completed

Title: Phase III Randomized Multicenter Comparative Study of Synercid (quinupristin/dalfopristin) versus Standard Therapy in the Treatment of Complicated Gram-Positive Skin & Skin-Structure Infections (#305)

Start Date: 02/16/96 **Est. Completion Date:** Apr 97

Department: Surgery, General Surgery **Facility:** MAMC

Principal Investigator: LTC William C. Williard, III, MC

Associate Investigators:
LTC Patrick J. Offner, MC
MAJ Timothy F. Deaconson, MC
COL William E. Eggebroten, MC
MAJ David M. Watts, MC
MAJ Clifford A. Porter, MC
COL Preston L. Carter, MC

Key Words: Infection:skin, Gram-positive, Synercid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objectives are to evaluate the safety and therapeutic effectiveness of Synercid 7.5 mg/kg every 12 hours versus standard therapy in the treatment of Gram-positive complicated skin and skin-structure infections.

Technical Approach: This is an open-label, Phase III, randomized, comparative, multi-center study of Synercid versus standard therapy in the treatment of complicated Gram-positive skin and skin-structure infections. After giving informed consent and meeting the Inclusion/Exclusion criteria, patients will be randomly assigned to receive either Synercid 7.5 mg/kg every 12 hours, or standard therapy that is based on the clinical
presentation of the patient and the susceptibility pattern of the causative pathogen. Vancomycin 1 gm every 12 hours will be the comparison drug of choice used at this institution. Patients will be clinically assessed at baseline, on day 4, at the end of study treatment, and test of cure visit (14 to 28 days after treatment discontinuation). The primary efficacy parameter will be the clinical response determined at the test of cure assessment or when patients discontinue treatment before completing the test of cure assessment. Safety and tolerability of Synercid, cefazolin and vancomycin will be assessed using subjective patient reports, clinical evaluations and laboratory tests.

Progress: This study was closed to enrollment, 25 Jun 96. One patients was consented and randomized at MAMC. She completed the study without problems.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/066 **Status:** Completed

Title: A Parallel, Randomized, Double-Masked, Placebo-Controlled, Multicenter Study of the Effect of Adding 2.0% MK-507 Ophthalmic Solution to 0.5% TIMOPTIC-XE in Patients With Elevated Intraocular Pressure

Start Date: 02/17/95 **Est. Completion Date:** Apr 96

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: COL Kevin J. Chismire, MC

Associate Investigators:
COL David P. George, MC
LTC Rob A. Mazzoli, MC
MAJ Thaddeus J. Krolicki, MC
MAJ Eugene F. May, MC
MAJ Roger K. George, MC
LTC Vernon C. Parmley, MC
MAJ Anthony R. Truxal, MC
LTC Elizabeth A. Hansen, MC
MAJ William R. Raymond IV, MC
CPT Keith Dahlhauser, MC
COL Thomas H. Mader, MC

Key Words: Pressure:intraocular, MK-507 Ophthalmic Solution, TIMOPTIC-XE

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To determine whether 2.0% MK-507 has an additional ocular hypotensive effect when add to 0.5% TIMOPTIC-XE for 3 months in patients who have elevated IOP when on 0.5% TIMOPTIC-XE alone. 2) To collect safety data on 2.0% MK-507 given concomitantly with 0.5% TIMOPTIC-XE.

Technical Approach: 20 subjects will be enrolled in this parallel, randomized, double-masked, placebo-controlled, multicenter protocol. One open-label 2-week run-in period followed by a 12-week masked treatment period. IOP on Day 1 must be either ≥ 24 mmHG in one eye prior to TIMOPTIC-XE at 0900 (fellow eye not less than 20 mmHg) or IOP must be > 22 mmHg in one eye 2 hours following TIMOPTIC-XE at 1100 (fellow eye not less than 18 mmHg). Between group comparison with regard to percent change in IOP from baseline will be made using analysis of variance techniques. The incidence rates for adverse experiences and ocular signs will be compared using Fisher exact-test.

Progress: Twenty patients completed the run-in phase and 15 patients were randomized and completed the study without problems.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/140 **Status:** On-going

Title: A Parallel, Randomized, Double-Masked, Multicenter Study Comparing the Effect of Dorzolamide 2% to Pilocarpine 2% as Adjunctive Therapy to Timolol Maleate Ophthalmic Gel Forming Solution 0.5% in ....

Start Date: 07/19/96 **Est. Completion Date:** Jan 97

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: MAJ Roger K. George, MC

Associate Investigators: COL Kevin J. Chismire, MC

Key Words: Intraocular pressure, Dorzolamide, Pilocarpine, Timolol Maleate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: Primary: To assess the effectiveness of dorzolamide 2% tid added to timolol maleate ophthalmic gel forming solution 0.5% qd compared with pilocarpine 2% qid added to timolol maleate ophthalmic gel forming solution 0.5% qd at morning trough (hour 0). Secondary: To assess the effectiveness of dorzolamide 2% added to timolol maleate ophthalmic gel forming solution 0.5% qd compared with pilocarpine 2% qid added to timolol maleate ophthalmic gel forming solution 0.5% qd at morning peak (hour 2). To collect safety data on dorzolamide 2% given concomitantly with timolol maleate ophthalmic gel forming solution 0.5% qd. To collect safety data on pilocarpine 2% given concomitantly with timolol maleate ophthalmic gel forming solution 0.5%.

Technical Approach: This is a parallel, randomized, double-masked active-controlled study. There is one open-label 3-week run-in period followed by a 12-week double-masked treatment period. The worse eye must be clinically suitable for additional IOP lowering on Day 1. Patient will be randomized at week 3 to one of 2 treatment groups. Intraocular pressure will be measured at 0900 (immediately pre-drop) and 1100 on days 1, 15, 29, 57, and 85. Visual acuity, external ocular examination, slit lamp examination, funduscopic examination, visual field, and ocular symptoms will be evaluated on Days -21, 1, 15, 29, 57 and 85. Between group comparisons with regard to percent change in IOP from baseline will be made using analysis of variance techniques. The incidence rates for adverse experiences and ocular sign will be compared using Fisher exact-test.

Progress: The protocol is awaiting final approval before it can be implemented.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/188 **Status:** Completed

Title: A Parallel, Randomized, Double-Masked Study Comparing the 0.5% Timolol/2.0% MK-0507 Combination Ophthalmic Solution BID to 0.5% Timolol Ophthalmic Solution BID or 2.0% MK-0507 Ophthalmic Solution ...

Start Date: 09/15/95 **Est. Completion Date:** Nov 96

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: MAJ Roger K. George, MC

Associate Investigators:
LTC Vernon C. Parmley, MC
MAJ William R. Raymond IV, MC
COL David P. George, MC
MAJ Eugene F. May, MC
MAJ Anthony R. Truxal, MC
COL Kevin J. Chismire, MC
LTC Rob A. Mazzoli, MC
CPT Gregory S. Witkop, MC
LTC Elizabeth A. Hansen, MC
MAJ Peter G. Torok, MC
CPT R. Kevin Winkle, MC

Key Words: IOP, Timolol, MK-0507

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the intra ocular pressure (IOP)-lowering effect of the 0.5% timolol/2.0% MK-0507 combination to that of 0.5% timolol and to that of 2.0% MK-0507 for up to 3 months. To compare the safety profile of the 0.5% timolol/2.0% MK-0507 combination to that of its components administered as in their usual monotherapy dose regimens over a 3-month period.

Technical Approach: This is a parallel, randomized, double-masked, active-controlled study. A 3-week, open-label timolol run-in period will be followed by a 12-week masked treatment period. Two hundred forty patients with an open-angle glaucoma or ocular hypertension will be entered into the study to obtain at least 200 evaluable patients who complete the 12 week masked period. Patients will be randomized 2:2:1 to receive either the combination b.i.d. + placebo q.d., timolol b.i.d. + placebo q.d., or MK-0507 t.i.d., respectively. It is hypothesized that the test combination and dose of timolol/MK-0507 will have a lowering effect greater than each of its components. The evaluation requires statistical comparisons between the combination and each component. Analysis of variance will be used to evaluate this using the percent change in IOP from the time matched baseline at the Day 90 Hour 0 exam. The ANOVA model will include terms for treatment, clinic and treatment-by-clinic interaction.

Progress: Thirteen patients were enrolled. The study has been closed to enrollment by the sponsor.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/127 **Status:** Completed

Title: Army Aviation Vision Standards Research: The Incidence of Refractive Anomalies in US Army Pilots

Start Date: 05/19/95 **Est. Completion Date:** Sep 95

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: MAJ Steven C. Hadley, MC

Associate Investigators:
COL Thomas H. Mader, MC
LTC Walter J. Hubicki, MC
Troy H. Patience, B.S.

Key Words: Refractive anomalies, Army pilots

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: Our objective is to determine the incidence of refractive anomalies in the US Army pilot population.

Technical Approach: Flight physicals are required annually on all active duty (AD), reserve (Res.) and National Guard (NG) aviators IAW AR 600-105. All flight duty medical exams (FDME) are submitted to the Army Aviation Center at Ft. Rucker, AL for approval and data collection. Fort Rucker maintains copies of all flight physicals. Approximately 20,000 class one (initial entry into aviation service) and class two (annual renewal) FDME are submitted each year. Seven years ago, Ft. Rucker started to electronically store all data from the FDME including visual acuity and refraction. We plan on utilizing the data repository at Ft. Rucker to determine the incidence of refractive anomalies in the AD, Res., and NG pilots in the US Army. Department of the Army civilian and contract aviators will be excluded from the study.

Progress: Twenty-four subjects were entered. A paper was presented at the 1996 ARVO meeting and a manuscript has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/061	**Status:** On-going

Title: The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia

Start Date: 02/16/96	**Est. Completion Date:**
Department: Surg/Opth	**Facility:** MAMC

Principal Investigator: COL Thomas H. Mader, MC

Associate Investigators:
LTC Vernon C. Parmley, MC
Troy H. Patience, B.S.
MAJ J. Wayne Riggins, MC
MAJ Steven C. Hadley, MC
CPT Benjamin N. Gilbert, MC
R. Doyle Stulting, M.D., Ph.D.

Key Words: Myopia, photorefractive keratectomy, military personnel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of the study is to determine if excimer laser photorefractive keratectomy (PRK) is a suitable procedure for use in active duty army personnel for the correction of myopia.

Technical Approach: Approximately fifty personnel in U.S. Army Special Operations, between the ages of 21-50, who meet the inclusion / exclusion criteria will be subjects for the study. Inclusion criteria include cycloplegic refraction between -1.50 and -4.50 diopters, best corrected visual acuity of 20/40 or better in both eyes, and 1 diopter or less of central astigmatism as measured by keratometer. The exclusion criteria include a history of eye surgery or eye infection, corneal neovascularization > 1mm from the corneal/sceral junction, immunocompromised state or systemic corticosteroid medications. Following appropriate preoperative workup, the non-dominant eye of each subject will undergo excimer laser photorefractive keratectomy. Four to six months later, PRK will be performed on the second eye when 20/20 best corrected visual acuity with less than +1 haze has been achieved. Following this procedure, subjects will be followed at specified intervals to monitor the success of the procedure. Subjects will be tested with night vision goggles as well as sighting devices to include those on open rifle sights, rifle scopes, laser range finding devices and target acquisition devices. We will obtain keratometry and cyclopelegic refraction on individuals both at sea level and at altitudes in excess of 10,000 feet.

Progress: No patients have been entered in this study because the unit from which the volunteers were to be recruited has been deployed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/153 **Status:** On-going

Title: Refractive Changes at High Altitude More Than Four Years Following Radial Keratotomy

Start Date: 09/20/96 **Est. Completion Date:** Nov 96

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: COL Thomas H. Mader, MC

Associate Investigators: MAJ Lawrence J. White, MC
Robert Gibson, O.D.

Key Words: Radial keratotomy:refractive changes, high altitude

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: Our objective is to observe changes in corneal shape and visual acuity that may take place in subjects four years or more following radial keratotomy when these individuals are exposed to two weeks at high altitude.

Technical Approach: Our research will be conducted as part of an American medical research project in Nepal in October of 1996. Our subjects will come from members of this research group who will be hiking along a predetermined path of increasing altitude. We will select two study groups for our experiment. The first group will consist of four volunteers who have had radial keratotomies at least four years prior to this study. We will record and examine several ocular parameters on these individuals, both at sea level and following 48 hour exposure to 9,100, 11,350, 14,000 and 15,600 feet. Repeat sea level measurements will be made one week after return to the U.S. These parameters include visual acuity, near point of accommodation, cycloplegic refraction, intraocular pressure, corneal keratometry, and central corneal thickness. Oxygen saturation will also be monitored and recorded using a pulse oximeter. The second study group will consist of 4 normal myopes (nearsighted persons). In these individuals, we will also measure the above listed parameters at the same altitudes as listed above. We will then compare data to see if a significant difference exists between the two groups.

Progress: Plans for travel and shipment of equipment are being coordinated.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/125 **Status:** On-going

Title: Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by Magnetic Resonance (MR) and Computed Tomography (CT) Imaging in the Goat

Start Date: 06/10/94 **Est. Completion Date:** Apr 95

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: LTC Rob A. Mazzoli, MC

Associate Investigators:
COL Thomas H. Mader, MC
COL David P. George, MC
LTC Miquel J. Rovira, MC
CPT Lilia A. Fannin, MC
LTC Vernon C. Parmley, MC
MAJ Vincent B. Ho, MC
LTC William F. Coughlin III, MC

Key Words: Foreign bodies:intraocular, Foreign bodies:intraorbital, Foreign bodies:plastic, MRI, CT scan,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 05/08/96

Study Objective: 1. To determine the efficacy of CT and MR imaging in detecting intraocular or intraorbital plastic foreign bodies in the goat. 2. To determine if intravenous contrast during CT and MR imaging improves the detection of intraocular or intraorbital plastic foreign bodies.

Technical Approach: Twelve goats will be used to evaluate the efficacy of CT and MR imaging in detecting plastic foreign bodies in the eye and around the eye. The goats will be sedated, anesthetized, and intubated prior to the surgical placement of 1 to 6 plastic foreign bodies (sizes ranging from 1/32 - 1/4 inch) in the eye. The wound will not be closed so as to simulate an eye injury. Plain film x-ray, CT and MR images will be obtained. Intravenous dye will be given for the imaging studies. The fellow eye will be the control. After the CT and MR studies are completed, the goats will be sacrificed. Plain films, CT and MR images will be evaluated by four masked physicians (two radiologist and two opthalmologists). These doctors will not know which eye has the plastic foreign bodies. From these evaluations, we will determine if CT or MR are equally effective in detecting the foreign bodies and we will determine if the intravenous dye improved the detection of the plastic foreign bodies.

Progress: All films (plain, CT, MR) have been randomized for the right or left side then reviewed by four investigators in a blinded fashion. Subsequent data has been collected and is currently being analyzed. Films are currently being reviewed again by investigators, analyzing the previously unstudied side.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/178 **Status:** Terminated

Title: Assessment of Post-operative Healing Time and Induced Astigmatism when Penetrating Keratoplasty is Performed Using the Tampa Trephine versus the Traditional Hanna Trephine

Start Date: 09/15/95 **Est. Completion Date:** Oct 97

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: LTC Vernon C. Parmley, MC

Associate Investigators: COL Thomas H. Mader, MC
CPT R. Kevin Winkle, MC

Key Words: Keratoplasty, trephine:Tampa, trephine:Hanna, astigmatism, healing

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To assess post-operative healing time and speed of visual recovery when penetrating keratoplasty (PK) performed by a newly developed corneal trephine (Tampa trephine) is compared with a traditional corneal trephination (Hanna Trephine).

Technical Approach: Sample population for both Tampa and Hanna trephination will be drawn from the cornea clinic of the Ophthalmology Service. For an alpha of 0.05 and a beta of 0.2, a sample size of 10 patient per group will be needed to detect an astigmatic difference of 2.00 diopters with an anticipated S.D. of 1.5 diopters. Patients examined and found eligible for inclusion into the study will receive informed consent and be randomly assigned by the unmasked participant to either the Tampa or Hanna group. Patients meeting the criteria for PK but not wishing to participate in the study will undergo conventional PK with the Hanna trephine. The data will not be included in analysis. After PK, patients in the study will be examined on a scheduled post-operative protocol for the first year after surgery. A nonsurgical (blinded) participant will collect astigmatic and visual acuity data f or comparison. The surgeon examining the patients will know which trephine was used because examination by slit lamp biomicroscopy makes it apparent. Statistical significance tests will be selected according to specific data analyzed, either independent means T-test and confidence intervals for equal time point analysis of quantitative variables, or Fischer's exact-test for equal time point of percentages of qualitative variables.

Progress: No patients were entered. The PI stated that he had not been impressed that patients he has seen from other institutions who have had surgery with the Tampa Trephine do any better than conventional trephines. The Tampa Trephine has limitations of size and increased complexity of use and risk to graft, that without a clearcut benefit caused the PI to terminate the protocol.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/029	**Status:** On-going
Title: A Prospective, Randomied Clinical Trial Comparing Topical Prednisolone 1% to Diclofenac 0.1% in the Treatment of Pseudophakic Cystoid Macular Edema (PCME)		
Start Date: 11/17/95	**Est. Completion Date:** Jun 97	
Department: Surg/Opth	**Facility:** MAMC	
Principal Investigator: MAJ Mark F. Torres, MC		
Associate Investigators:	MAJ Thaddeus J. Krolicki, MC	
Key Words: Macular edema, prednisolone, diclofenac		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To objectively assess the efficacy of topical diclofenac as a treament modality (monotherapy) for PCME. (2) To compare prednislone and diclofenac as treatment for PCME. (3) To assess the safety of long term (potentially up to four months) use of topical diclofenac.

Technical Approach: Patients who are between 6 - 52 weeks post cataract surgery whare found to have PCME will be referred to a vitreoretinal specialist who will confirm the PCME via a contact lens biosmicroscopic examination and serve as a "blind" observer for subsequent follow-up evaluations for that particular patient. If a patient elects to enroll into the study, they will be required to return within 72 hours to have an undilated, best-corrected visual acuity examination using a standardized eye chart from the Early Treatment in Diabetic Retinopathy Study (ETDRS). The patient will the be randomized to received either prednisolone 1% or diclofenac. The investigator/examiner will be blind with respect to which drug each patient is using, making the study a single blind, open label, prospective, randomized clinical trial (multi-center). Follow-up examinations will be performed at 4, 8, 12, and 16 weeks following initiation of drug therapy. At each follow-up, an investigator other than the masked retina specialist will perform the initial portion of the examination, to include completion of the questionnaire and ETDRS visual acuity. During the interval visits the patients will be given a questionnaire asking for subjective rating on their symptoms and any side effects noted when using the drug. The patient will then be examined by the bind retina specialist who will perform an angiogram and grade the PCME as either "present" or "absent". If present, it will be scored as "improve," "unchanged," or "worse." At 8, 12, and 16 weeks, the same evaluation sequence as described at 4 weeks will take place. All angiograms will be reviewed in a masked fashion and independent grades will be compared to those from the original examiner to ensure inter-examiner consistency. The study endpoint will be at the four month follow-up interval. If PCME is still present, it will be left to the investigators to determine any additional therapy. The codes will be broken and the provider will be informed as to which drug was used. In any case, if the patient is willing, investigational follow-up would continue at one month intervals to maximize data received for subgroup analysis.

Progress: Due to strict inclusion and exclusion criteria, no patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/104 **Status:** Completed

Title: Combined Porous Implant and Thin Dermis Fat Graft for Complex Socket Reconstruction

Start Date: 04/15/96 **Est. Completion Date:** Apr 96

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: MAJ Mark F. Torres, MC

Associate Investigators:
LTC Elizabeth A. Hansen, MC
LTC Rob A. Mazzoli, MC
MAJ Darryl J. Ainbinder, MC

Key Words: Socket:reconstruction, porous implant, dermis fat graft

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: A retrospective descriptive study/case series to evaluate the overall clinical outcome of the combined use of porous orbital implants and thin dermis fat grafts in the reconstruction of complex anophthalmic sockets, including those patients undergoing primary enucleation as well as those patients undergoing secondary reconstruction due to primary socket reconstruction failure, in terms of post-operative complications, long term socket viability, and ability to wear a prosthesis.

Technical Approach: We have identified 7 patients, 3 male, 4 female, age range 25-66, over a 5 year period, in need of either primary or secondary socket reconstruction, in which the unique clinical setting of both insufficient orbital volume and insufficient conjunctival surface area co-existed. The patients underwent a combined surgical procedure of porous orbital implantation and thin dermis fat grafting during one surgical event in order to address both deficiencies at once and possibly prevent multiple surgical reconstructive events. The patients have been followed post-operatively over a range of 6 months to 4 years, and evaluated in terms of orbital implant stability, viability of the thin dermis fat graft, and ability to fit, tolerate, and comfortably wear an orbital prosthesis.

Progress: Six patients were studied. None had complications of implant extrusion, implant migration, failure of the dermis fat graft, or socket contraction. Post-operative MRI scans showed viability of the dermis fat graft and vascularization of the porous implant. All 6 patients have been fitted with a prosthesis, which has been worn without complications. The investigators conclude that combined porous implant and thin dermis fat graft is an acceptable surgical procedure for socket reconstruction in which sufficient orbital volume and conjunctival surface area are of primary concern. This procedure can be performed at either primary enucleation or secondary reconstruction, with apparently good post-operative results and little risk of complications. Presented at the annual meeting of the Association of Research and Vision in Ophthalmology.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/163	**Status:** Completed
Title: The Effects of Weight Lifting and Intraocular Pressure		
Start Date: 07/21/95	**Est. Completion Date:**	
Department: Surg/Opth	**Facility:** MAMC	
Principal Investigator: CPT R. Kevin Winkle, MC		
Associate Investigators: CPT Keith Dahlhauser, MC	MAJ Tamara D. Lauder, MC	
Key Words: Intraocular pressure, weight lifting		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To describe changes in intraocular pressure (IOP) that occur while lifting weights with and without performing the valsalva maneuver.

Technical Approach: We will select a single study group of 40 individuals between the ages of 20 to 65 years of age who have no history of ocular disease or major cardiac disease to participate in our study. The evaluation of the patients will take place during two or three sessions. During the first evaluation, the participants will undergo baseline intraocular pressure measurements followed by determination of their one-repetition maximum (ARM), i.e., the highest weight that a subject can lift through the full range of joint motion one time only. At the other sessions, the subjects will lift a series of submaximal weights calculated at different percentages of their previously determined ARM. The submaximal weights lifted will be categorized into four percentages, to make the data more realistic and useful for a real life situation, i.e., 25%, 50%, 75%, and 1008. Also during this session, IOP measurements will be obtained prior, during, and immediately following the exercise, and 10 minutes after the exercise. IOP instillation of topical anesthetic. Changes in IOP will be correlated with the submaximal range of weight lifted that produced the change. The data obtained will then be useful clinically, for postoperative patient instruction.

Progress: Thirty-eight subjects were enrolled. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/164 **Status:** Completed

Title: Refractive Changes Due to Hypoxia Following Radial Keratotomy Surgery

Start Date: 07/21/95 **Est. Completion Date:** Oct 95

Department: Surg/Opth **Facility:** MAMC

Principal Investigator: CPT R. Kevin Winkle, MC

Associate Investigators:
MAJ Lawrence J. White, MC
COL Thomas H. Mader, MC
LTC Vernon C. Parmley, MC

Key Words: Keratotomy, hypoxia

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To observe changes in corneal shape and visual acuity that may take place in subjects one year following radial keratotomy when these individuals' corneas are exposed to a low oxygen tension environment.

Technical Approach: Two study groups will be used for our experiment. The first study group will consist of volunteers who have had radial keratotomies. We will study several ocular parameters on these individuals, both prior to corneas exposure to hypoxia and after one or two hours of corneal exposure to pure nitrogen via a goggle apparatus. These parameters include cycloplegic refraction, intraocular pressure, corneas video keratometry, and central corneas thickness. The second study group will consist of an equal number of myopic military personnel used as controls, in whom the same aforementioned parameters will be monitored both pre and post corneas exposure to a hypoxia environment.

Progress: Twenty subjects were enrolled. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/088	**Status:** Completed
Title: Preoperative Calculation of Safe Glaucoma Implant Sites		
Start Date: 04/19/96	**Est. Completion Date:** Mar 96	
Department: Surg/Opth	**Facility:** MAMC	
Principal Investigator: CPT Gregory S. Witkop, MC		
Associate Investigators: None		
Key Words: Glaucoma, implant, superotemporal quadrant		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To measure the distance from the limbus to the optic nerve in the superonasal and superotemporal quadrants and relate it to the axial length as measured by A scan ultrasonography. This would provide an equation which would allow a surgeon to preoperatively know where to more safely place a glaucoma implant.

Technical Approach: Fifty adult donor eyes, obtained from the Northwest eyebank at no cost to Madigan, will be inflated to physiologic pressure. Superonasal limbus to optic nerve distance (SN-LO) and superotemporal limbus to optic nerve distance (ST-LO) will be obtained. Axial length (anteroposterior [AP] diameter) will be measured by A-scan and pathologic calipers. A multivariate scattergram relating AP to LO distances will determine the coefficient of fit. If appropriate, a linear equation will be derived and then tested with Student's t-test and univariate analysis of AP to compare measured and calculated LO distances. Even if there is not a direct relationship, this study will establish in the literature the normal values for these distances.

Progress: Fifty human cadaver eyeballs were studied. The investigators conclude that a preoperative A-scan can determine the limbus to optic nerve distance. Knowledge of this distance can enable surgeons to choose the implant, quadrant, and placement which will minimize the risk of optic nerve impingement. A paper was presented at the American Academy of Ophthalmology Annual meeting. This was the only paper submitted by a resident that was selected for presentation. A paper was also published in the American Journal of Ophthalmology 117:5, May 15, 1994, p 676.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/135	**Status:** On-going
Title: Anterior Capsular Contraction in Phacoemulsification		
Start Date: 07/19/96	**Est. Completion Date:** Jun 96	
Department: Surg/Opth	**Facility:** MAMC	
Principal Investigator: CPT Keith J. Wroblewski, MC		
Associate Investigators: LTC Vernon C. Parmley, MC	CPT Keith Dahlhauser, MC COL Thomas H. Mader, MC	
Key Words: Cataract, capsular contraction syndrome, phacoemulsificatioin		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To determine risk factors for capsular contraction syndrome after phacoemulsification and posterior chamber intraocular lens placement. We will determine the incidence of capsular contraction syndrome between three different intraocular lenses: silicone, acrylic and polymethylmecrylate performed by one surgeon.

Technical Approach: Our study will retrospectively examine every cataract extraction here at Madigan utilizing three different types of intraocular lenses. We will examine the risk factors for contraction of the anterior lens capsule and study the incidence of lens decentration of the intraocular lens implant. Specifically, is there a relationship between the type and composition of the lens and the incidence of decentration? Is there a relationship between preoperative uveitis, post-operative anterior chamber inflammation and capsular contraction syndrome? We will use chi-square analysis to examine the incidence of contraction syndrome with the type of lens used, capsule contraction with the size of the operative capsulorhexis, and the preoperative history of uveitis with contraction. A logistic regression creating a formula for the different variables could be created and could help determine the risk factors for the different variables.

Progress: Forty-five phacoemulsification procedures with foldable silicone intraocular lens implantation were studied. Nine patients had radial anterior capsulotomy with four relaxing radial incisions. Three of the nine patients complained of decreased visual acuity and glare noted between day 30 and 54 post-operatively. Mean visual acuity of these symptomatic patients was 20/50. Two other patients had chronic anterior chamber inflammation but no symptoms, postoperatively. Their inflammation re-solved abruptly after YAG capsulotomy. Decentration was observed in three patients which also resolved after capsulotomy. The investigators conclude that postoperative inflammation may improve after YAG capsulotomy and that it stabilizes decentration. Early anterior capsule monitoring with appropriate early anterior capsulotomy may prevent serious complications. A paper was presented at the Association for Research and Vision in Ophthalmology in May 1996.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/154	**Status:** On-going
Title: Pulfrich's Phenomenon in Patients with Optic Neuropathy		
Start Date: 09/20/96	**Est. Completion Date:** Dec 96	
Department: Surg/Opth	**Facility:** MAMC	
Principal Investigator: CPT Keith J. Wroblewski, MC		
Associate Investigators: M. B. Brazelo	MAJ Eugene F. May, MC Troy H. Patience, B.S.	
Key Words: Pulfrich's phenomenon, optic neuropathy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: To study the prevalence of Pulfrich's phenomenon in patients with optic neuropathy and see how it correlates to pupillary function, visual field defects, contrast sensitivity and binocular vision.

Technical Approach: Fifty Ophthalmology Clinic patients with a history of optic neuropathy, as evidenced by clinical history and examination, will be recruited for this study. On the same day of each week for three months, we will perform tests on each subject for visual acuity, Humphries Automated Visual Fields, contrast sensitivity, Randot Viewer Stereoacuity, and Pulfrich phenomenon. In addition, one of the associate investigators will perform the swinging flashlight-test in order to grade a relative afferent pupillary defect using neutral density filters. The first portion of data analysis will be determining whether a subject's description of his/her visual experience during testing for Pulfrich's correlates with the laterality of the optic neuropathy. Secondly, correlation analysis will be performed between the density (in log units) of neutral density filter necessary to neutralize each subjects Pulfrich's phenomenon with four other visual parameters. The presence of any correlation between the "amplitude" of Pulfrich's phenomenon and any of the other parameters would support the hypothesis that the presence and extent of Pulfrich's phenomenon in a patient is an objective and quantitative measure of optic nerve dysfunction.

Progress: Twenty-two patients have been studied.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/107	**Status:** On-going
Title: Evaluation of Lateral Ankle Stress Testing With and Without Anesthesia		
Start Date: 05/17/96	**Est. Completion Date:** Jan 98	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: CPT George K. Bal, MC		
Associate Investigators:	LTC William C. Williard, III, MC	
Key Words: Ankle, stress testing, anesthesia		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the significance of pain response/inhibition that occurs during lateral ankle stress testing.

Technical Approach: We will evaluate ankle stress radiographs (using the TELOS Device) without anesthesia, with local anesthetic, and finally with regional/general anesthesia. The sample population will be patients with chronic ankle pain and/or instability seen at Madigan Orthopedic/Podiatry Clinic. Between 50-100 subjects will be studied. The subject will have ankle stress radiographs performed, then repeated with a local anesthetic (intra-articular vs peroneal nerve block). If determined that the patient requires surgery, intra-operative stress radiographs will be performed after induction of regional/general anesthesia. Approximately 20 control subjects will be selected from orthopedic patients requiring surgery. They will have preoperative ankle stress radiographs done, and again after induction of anesthesia for their scheduled surgery. No local anesthetic injections will be used for control subjects. The data collected will be measurements of tibio-talar angle and anterior subluxation from the stress radiographs. These will be evaluated using an independent t-test, and repeated measures analysis.

Progress: The PI has just completed an off-site residency rotation. He is currently working on the final revision to the protocol. No patients have been entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/108	**Status:** On-going
Title: Subtalar Joint Stress Radiography		
Start Date: 05/17/96	**Est. Completion Date:** Jun 97	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: CPT George K. Bal, MC		
Associate Investigators:	LTC William C. Williard, III, MC	
Key Words: Subtalar joint, stress, radiography		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To establish the normal variation of the subtalar joint stress angle. We will also attempt to standardize the method of measurement.

Technical Approach: The normal values of talo-calcaneal angle will be looked at using the TELOS Device and stress radiographs. The sample population will come from patients seen at the Madigan Orthopedic/Podiatry Clinic. We will utilize up to 200 normal subjects with no prior history of ankle injuries. The subjects will have an ankle stress radiograph performed using the TELOS device. After the radiograph is complete, no further participation in the study will be needed. The talo-calcaneal angle will be measured off of the stress radiograph. This data will be evaluated for potential co-variants, and a normal range will be determined with confidence intervals.

Progress: The PI has just completed an off-site residency rotation. He is currently working on the final revision to the protocol. No patients have been entered.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/089	**Status:** Completed

Title: A Randomized Open-label, Parallel Group Comparison of the Safety and Efficacy of Lovenox (Enoxaparin) Injection versus Coumadin (Adjusted Dose Warfarin) in the Prevention of Thromboembolic Disease....

Start Date: 04/01/94	**Est. Completion Date:** Jun 94
Department: Surgery, Orthopedics Svc	**Facility:** MAMC

Principal Investigator: MAJ Barry T. Bickley, MC

Associate Investigators:
LTC John D. Pitcher Jr., MC
LTC Gregg W. Taylor, MC
CPT John T. Steedman, MC

Key Words: thromboembolisis, hip replacement, Lovenox, Coumadin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/18/95

Study Objective: 1) To evaluate the safety and efficacy of Lovenox Injection versus adjusted dose Coumadin in the prevention of clinically significant thromboembolic disease following elective total hip replacement during hospitalization. 2) To determine the medium term incidence (three months post-hospital discharge) of morbidity and mortality resulting from thromboembolic disease following elective total hip replacement surgery in patients treated with Lovenox Injection vs. adjusted dose Coumadin.

Technical Approach: This study is divided into two phases; an inpatient period following surgery, not to exceed 14 days, and an outpatient follow-up period of three months.

This is a randomized, open-label, parallel group, multicenter study conducted in patients 18 years of age or older undergoing elective unilateral primary hip replacement. When the surgeon is satisfied that hemostasis has been achieved, and within 24 hours postoperatively, patients will begin their randomly assigned treatment of either Lovenox Injection 30 mg b.i.d. or adjusted dose Coumadin until hospital discharge, but not to exceed a maximum of fourteen (14) days. (Coumadin may be started up to 48 hours preoperatively at the discretion of the investigator.) Thereafter, all patients will return to the investigator for follow-up examinations at approximately six weeks and twelve weeks post hospital discharge.

The primary efficacy parameter will be the incidence of symptomatic thromboembolic disease during hospitalization and over the subsequent three month period.

Progress: Twenty patients were entered at MAMC in this multicenter study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/176 **Status:** On-going

Title: Computer Assisted Measurement of Scoliosis from Digitized Radiographs versus Traditional Cobb Angle Measurement

Start Date: 12/17/93 **Est. Completion Date:** Sep 93

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: MAJ Clyde T. Carpenter, MC

Associate Investigators:
MAJ Donald V. Smith, MC
LTC Richard W. Kruse, MC
MAJ John W. Dietz, MC

Key Words: scoliosis, computer assisted meaurements

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$500.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to determine the interobserver and intraobserver error and accuracy of measurement in determining Cobb angle measurements of scoliosis and kyphosis using the digitized radiographs and measuring techniques available in the Medical Diagnostic Imaging System (MDIS).

Technical Approach: In the first phase fifty anterior-posterior or posterior-anterior spine radiographs will be collected in the Orthopaedic Clinic by two of the Investigators. These radiographs must demonstrate coronal plane deformity of 10 degrees or more. During this the radiographs will be modified to obscure the patients' names and copy the radiographs into the MDIS system. Each radiograph MDIS image will be assigned a random number. The MDIS image and its corresponding radiograph will have different numbers and a log will be created showing which random numbers have been assigned to corresponding images. The examiners will be blinded to this information.

The images will be measured in random order. All measurements will be made using the Cobb method. A line will be drawn along the superior end plate of the upper vertebra to the inferior end plate of the lower vertebra. Some radiographs will have 2 measurable curves. Only one curve from the thoracic and one from the lumbar area will be measured. Measurements on radiographs will be done with pencil and protractors usually employed in the Orthopaedic Clinic. Measurements on MDIS images will be done by choosing lines along end plates with the mouse and indicator. Actual measurements will be made by each of four observers. Measurements will be recorded on a data sheet.

Progress: All images have been taken and are in the process of being measured.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/110	**Status:** On-going
Title: A Multicenter Study of Treatment of Growth Arrest by Excision of Physeal Bars		
Start Date: 04/21/95	**Est. Completion Date:** Dec 95	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: MAJ Clyde T. Carpenter, MC		
Associate Investigators: None		
Key Words: Growth, physeal bars, excision		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To perform a multi-center, retrospective collection of data on the treatment of deformities arising from growth arrest by the excision of physeal bars bones.

Technical Approach: This preliminary retrospective study will include all patients having had a physeal bar excision and a minimum of two years follow-up. Information collected will include: (1) age, sex, race and body habitus of the patients; (2) etiology, bone involved, placement, age, and size of the bar; and (3) the degree of angular deformity and limb length discrepancy existing prior to excision of the bar. Separate forms will be used to document the specifics of surgical intervention, any subsequent interventions, and to determine results at the end of the follow-up period. Each patient will be analyzed in terms of his/her outcome. The information collected will be used to determine the methods of treatment most often yielding acceptable results in specific situations. Student's t-test, chi-square evaluation of four fold tables, regression analysis or other statistical methods will be utilized as appropriate depending on the nature of the retrospectively collected data.

Progress: Approximately 100 patients have been entered from other institutions. However, there have been no patients at MAMC that met the criteria.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/036 **Status:** Completed

Title: Response to Intra-articular Fractures: Changes in Pressure Distribution and Cartilage Structure After Healing

Start Date: 12/01/95 **Est. Completion Date:**

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: CPT Patrick J. Fernicola, MC

Associate Investigators: Thomas E. Trumbel, M.D.
LTC Delbert E. Casey Jones, MC

Key Words: Fractures:intra-articular, pressure, cartilage,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether or not changes in pressure distribution occur following an intra-articular malunion when an intact joint is studied and if there is remodeling that takes place following fracture union that helps to redistribute the pressure with studies of cartilage structure.

Technical Approach: Transmission electron microscopy will be used to evaluate whether there are structural changes that correlate with the changes in pressure distribution. In order to test the hypothesis the following studies will be performed: 1) Comparison of the intact pressure distribution contact area and centroid to that following the initial fracture malunion. 2) Comparison of the intact pressure parameters to the ones at the time of follow-up. 3) Comparison of the pressure parameters following the initial creation of the fracture malunion to the pressure distribution at the final testing following fracture healing. 4) Evaluation of the control and contralateral articular surfaces for the changes in the collagen structure of the cartilage. 5) Evaluation of the final specimens for correlation of the changes in collagen alignment, cartilage destruction and condracyte survival with biomechanical changes noted.

Progress: Data has been sent to HarborView for analysis. We could not get a hold of Dr. Trumbel to find out the status.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/030	**Status:** Terminated

Title: Randomized Prospective Treatment of Onychomycosis with Undecylenic Acid-Chloroxylenol Solution with a Combination of Surgery and Debridement versus Surgery and Debridement Alone

Start Date: 11/17/95	**Est. Completion Date:** Dec 96
Department: Surgery, Orthopedics Svc	**Facility:** MAMC
Principal Investigator: Randolph Fish, D.P.M.	
Associate Investigators:	CPT Stephen Wilinson, MC
Key Words: Onychomycosis, undecylenic acid-chloroxylenol, debridement	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the effectiveness of Undecylenic Acid-Chloroxylenol Solution for treatment of onychomycosis.

Technical Approach: One hundred consecutive patients treated for onychomycosis (fungal infections of the nails) will be stratified and randomized into groups which are treated with or without Undecylenic Acid-Chloroxylenol Solution (Gordochom*) in addition to the standard treatment. Patients will then be randomized into groups consisting of surgery and medication (active drug or placebo) or surgery alone. (Surgery is defined as mechanical thinning of the nail plate). A positive fungi culture must be present in order to be enrolled in the study. Samples for culture are taken by scraping the nail or by using the slivers of the nail plate and placing them into the culture media. Further descriptive medical data will be collected including the presence of: tinea pedis, tinea capitis, dermatophytosis, etc. Demographic data and associated medical illnesses will be recorded. Prescription medications will be logged. Patients will be seen every two months in the podiatry clinic for regular professional care, and will have a follow up period after treatment of six months. Outcome variables include if the nail is clear, partially clear or unclear. Significance of the difference in the number of patients cured with the standard treatment along with medication versus those patients cured by standard treatment will be calculated using x squared. The test will be repeated every three months using a repeated measurement design.

Progress: This protocol was terminated due to the departure of the principal investigator and the associate investigator. No patients were entered in the protocol.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/082 **Status:** On-going

Title: Comparison of Sterile Isotonic Saline, Purified Water, and Dilute Hypochlorite Solution on the Rates of Infection and Tissue Response in Open Fractures of a Syrian Hamster Model

Start Date: 03/24/95 **Est. Completion Date:** Oct 96

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: CPT Randall K. Hildebrand, MC

Associate Investigators:
MAJ Mark D. Brissette, MC
LTC Frederic L. Johnstone, MC

Key Words: Fractures, saline, purified water, hypocholorite, infection, tissue response,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To compare different irrigating solutions and rates of infection in an open fracture model. 2) To compare the gross and histologic effects in wound healing of an open fracture model after different irrigation solutions.

Technical Approach: A total of 48 syrian hamsters will be used in a 4 groups of 12. There will be 3 treatment groups and one control group. After adequate anesthesia, an incision on a hamster's leg will be made and the thighbone will be broken with a small power saw. The animals will be deliberatly infected, and the treatment group animals will have the wound washed out with one of several kinds of irrigating fluids (sterile isotonic saline, purified water, or dilute hypocholorite solution). The animal will be awaked from anesthesia and returned to a recovery cage to be monitored for pain or infection. Two weeks later it wil be euthanized. The rates of infection will be compared and the tissue around the wound will be examined under a microscope to determine any potentional harmful effects of the infection or irrigation fluid.

Progress: Testing in approximately 40 hamsters was performed in January 1996. A large majority of animals from all four groups were clinically infected at harvest and grew a significant number of bacteria. There were, therefore, no significant differences between the groups and the methods of irrigation. The investigators tentatively plan a relook at the dose response curve of bacterial inoculation and amount of irrigation.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/142	**Status:** On-going
Title: Cost Effectiveness of Screening MRIs of the Shoulder Prior to Neer Acromioplasties		
Start Date: 08/05/94	**Est. Completion Date:**	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: CPT Randall K. Hildebrand, MC		
Associate Investigators:	LTC John D. Pitcher Jr., MC	
Key Words: acromioplasty, MRI, cost effectiveness		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1. To determine the sensitivity (SN), negative predictive value (NPV), and positive predictive value (PPV) and accuracy of shoulder MRIs in predicting rotator cuff tears of the shoulder. 2. To determine whether screening shoulder MRIs in patients with impingement syndrome is helpful and cost effective in the surgical management of preoperative management of those cases that are refractory to non-operative treatment.

Technical Approach: This is a prospective, single-blinded study of MRI vs operative evaluation, comparing their abilities to diagnose rotator cuff tears and other pathology about the shoulder. Patients selected for this study will have met the surgical indications for a modified Neer Acromioplasty for impingement syndrome with or without a suspected rotator cuff tear.

One hundred patients will have an MRI of the affected shoulder within two weeks of the anticipated subacromial decompression. MRI interpretation will be in the form of a radiological report documenting the presence or absence of rotator cuff tears or tendonitis, glenohumeral labral pathology, or other pathology about the shoulder. Intraoperatively the surgeon will record his findings both before and after review of the MRI and the MRI report. However, he will remain blinded to the MRI results until a surgical course has been decided intraoperatively. In other words, the surgery will begin as if no MRI had been performed. After an operative diagnosis and treatment course planned, the MRI and its report will be reviewed. If indicated by the MRI, the planned treatment course will be altered intraoperatively. Any and all treatment alterations based on the MRI will be recorded, and correlations will be made between pathology on surgical observation and those seen on the MRI.

Using open acromioplasty as the gold standard, after 100 surgeries the data will be reviewed to determine the SN, SP, NPV, and PPV, and accuracy of MRI. The need for preoperative MRI will be assessed by determining whether and how many operative plans are affected by the MRI and its interpretation.

Progress: No patients have been entered in this study as discussion between Orthopedics and Radiology regarding the final protocol continuing.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/102 **Status:** On-going

Title: Teaching Program for Practical Microsrugery Using A Rat (Rattus norvegicus, strain HSD) As a Teaching Model

Start Date: 03/24/95 **Est. Completion Date:** Mar 98

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: LTC Frederic L. Johnstone, MC

Associate Investigators: CPT Vermon S. Esplin, MC
LTC Delbert E. Casey Jones, MC

Key Words: Microsurgery:training, rat model,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: This teaching protocol will establish a formal training program in clinical microsurgery for orthopedic residents at MAMC. It will provide microsurgery practice in the repair of small vessels, nerves and tendons of the rat which model those of the hands, face and other body parts of humans.

Technical Approach: One rat will be used per week for 52 weeks for continuous microsurgery training for orthopedic residents. The rats will be placed under general anesthesia, used for numerous practice repairs and then humanely euthanitized at the conclusion of the surgical procedures. Specifically, the femoral artery of the rat serves as an excellent model of small human vessels and will be repeatedly cut and repaired. Residents will be tested after six weeks by oral examination and should be capable of performing extremity revascularizations.

Progress: 5 animals were studied, with no unexpected loss of animals. 5 training sessions were held, with 5 individuals being trained.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/128	**Status:** On-going

Title: Use of Pulsing Electromagnetic Fields to Potentiate Healing of Traumatic Combat and Training Injuries

Start Date: 05/19/95	**Est. Completion Date:** Dec 97
Department: Surgery, Orthopedics Svc	**Facility:** MAMC

Principal Investigator: LTC Delbert E. Casey Jones, MC

Associate Investigators:

MAJ Richard T. Dombroski, MC
Estelle Hamblen, BA, MHA
MAJ Kirk Willard, MC
LTC Richard A. Sherman, MS
Antje F. W. Goeken, Psy.D.
Melissa Wong, BA

Key Words: Pulsing electromagnetic fields, injuries:combat, injuries:training

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The overall objectives of the program are to determine whether pulsing electromagnetic fields (PEMFs) can be useful in potentiating recovery from combat wounds and training injuries when used in conjunction with standard techniques by (1) increasing the rate of healing while reducing swelling after hand, anterior cruciate ligament (ACL), and foot surgery or simple fractures of the long bones faster and further than standard techniques and (2) reduce the recovery time after stress fractures and ACL-related knee pain.

Technical Approach: This project is designed to determine whether exposure to PEMFs can potentiate healing of (a) traumatic combat and (b) training injuries including wounds, stress fractures, sprains, and ACL tears. These are representative of the types of injuries commonly seen in both combat and training. It is part of a program designed to prevent, track, and treat extremity trauma and training injuries among combat soldiers which should result in less loss of time away from the unit. It is the successor to the MRDC-funded project entitled "Use of body surface heat patterns for predicting and evaluating acute lower extremity pain among soldiers" (MRDC #8913004). We intend to study at least 40 subjects of each treatment/injury group. The major variables to be studied are (1) reduction of swelling and (2) increase in the rate of healing. The data will be analyzed separately for hand surgery, foot surgery, ACL repair, and long bone fractures with sub-types co-varied. The pre-surgical baseline measurements of swelling will be compared with daily measurements and the operated extremity will be compared with the intact extremity using a two way, repeated measures analysis of co-variance.

Progress: Six patients have been entered. The study was not funded through USAMRMC; therefore, it is being slowly conducted as funding and personnel time are available.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/160 **Status:** Completed

Title: Use of Pulsing Electromagnetic Fields for the Treatment of Pelvic Stress Fractures and Musculoskeletal Pelvic Pain

Start Date: 09/21/94 **Est. Completion Date:** Sep 95

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: LTC Delbert E. Casey Jones, MC

Associate Investigators:
LTC David J. Magelssen, MC
Antje F. W. Goeken, Psy.D.
LTC Richard A. Sherman, MS
MAJ Arnoldas S. Kungys, MC

Key Words: Stress fractures:pelvic, electromagnetic fields

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether application of Pulsing Electromagnetic Fields (PEMFs) over the stress fracture site, used in conjunction with standard therapeutic approaches, reduces the time to return to full duty in relation to those receiving the standard treatments and placebo PEMFs.

Technical Approach: Subjects diagnosed as having pelvic area stress fractures will receive one hour of PEMF or placebo PEMF therapy five days per week in addition to the standard treatment (sharply reduced activity and minimized walking) from the time the diagnosis is made until return to full duty. Subjects will be randomly assigned to groups and evaluated.

The patient will lay on an exam table with the head of the PEMF generator positioned several millimeters above the stress fracture site. The patient will be exposed to the fields for 15 minutes while on their backs and an additional 15 minutes while on their fronts. Each subject will have a total of 30 exposure to the field every day until they return to duty. The machine makes the same humming sound regardless of whether or not it is generating a field and subjects can not feel the field. Thus, subjects should not be aware of whether they are in the exposure or placebo group. The technician who turns on the device will know which group the subject is in so the machine can be set for either actual or placebo functioning but the technician and physicians doing the evaluations will have no idea which group the patients are in.

Progress: Of 54 sequential female soldiers having the symptoms of pelvic area stress fractures, seven had positive bone scans. Subjects were stratified by stress fracture or musculoskeletal pain and then randomized to placebo or PEMF treatment. Treatment was five days a week until resolution of the problem according to pain ratings, bone scans, and return to duty. Only 12 subjects accepted treatment because it was not possible to do their jobs and come to the hospital every weekday for months. Seven subjects dropped out for the same reason. Although patients with stress fractures receiving a significant number of treatments improved and the three who only received a few treatments did not, the randomized portion of the study did not complete a meaningful number of subjects. None of the subjects with musculoskeletal pain nor those receiving placebo treatment improved. The results indicate that pelvic stress fractures are being over-diagnosed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/155	**Status:** On-going
Title: Establishment of the Natural History/Progression of Pediatric Fingernail Injury Outcomes		
Start Date: 07/21/95	**Est. Completion Date:** May 97	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: LTC Delbert E. Casey Jones, MC		
Associate Investigators: CPT George K. Bal, MC	CPT James T. Vandenberg, MC	
Key Words: Fingernails, pediatric, injuries, natural history		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To establich the natural history of fingernail injury outcomes in children (1-8 years of age) with and without any distal phalanx fractures treated in the MAMC Emergency Department. To determine whether there is a need for follow-up studies on treatment procedures designed to reduce permanent abnormalities in the nails.

Technical Approach: Trauma is a major cause of pediatric fingernail injuries. In children, traums may result in hematoma formation or nail avulsion. When the nail lmatrix and bed are unaffected, the effects are temporary. If the matrix or nail bed is injured, permanent scarring of the nail may result. Among adults, long term effects of trauma may include scaring and dystrophy of the nail if early treatment is not initiated.

Fifty children with fingernail injuries will be studied. Parents of the children meeting the entry criteria will be asked to participate. The child's injury will be assesed and photographed at the time of injury, and at followup visits at six week intervals for six months. A rate of abnormal healing will be determines and associated with cause and severity of the initial injury.

Progress: Thirty-three individuals have been entered. The investigators have had some difficulty with the follow-up phase because parents often do not want to take the time for follow-up for this type of injury.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/111 **Status:** On-going

Title: Economic Evaluation of Scotchcast Plus vs Plaster of Paris for Immobilization of Fracture of the Arm and Leg

Start Date: 05/17/96 **Est. Completion Date:** Oct 96

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: LTC John D. Pitcher Jr., MC

Associate Investigators:
Tim Davies
LTC Delbert E. Casey Jones, MC
Ron Hawkinson

Key Words: Casts, plaster of Paris, Scotchcast Plus

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to determine whether the inhalation of a helium-oxygen mixture (heliox) will improve pulmonary function and respiratory clinical status in adults hospitalized with severe asthma.

Technical Approach: We plan to enroll 15 subjects in this randomized, double blind, prospective, crossover study. Patients between 18-75 years of age admitted to the hospital for treatment of asthma will be asked to participate. The patients will be stabilized, and baseline pulmonary function tests, clinical score, heart rate, and pulsus paradoxus will be recorded. They will then be randomized to inhale either 30% oxygen-70% helium gas mixture or 30% oxygen-70% nitrogen (oxygen enriched air) first. After breathing the first gas via a face mask for 20 minutes, pulmonary function testing, assessment of clinical score, pulsus paradoxus and the other measurements will be repeated again. After a 10 minute period patients will then breath the second gas mixture for 20 minutes, and all the measurements will be repeated. After stopping the second gas mixture patients will rest for another 20 minutes, and all measurements will be measured for a 4th and final time. The patients, their families and all health care professionals with the exception of the respiratory therapist will be blinded to the order of administration of the two treatment regimens. Differences in continuous variables (i.e. FEV_1 and heart rate) will be analyzed with the two sample Student t-test, and difference in clinical scores (mean) will be assessed with the Wilcoxon rank sum test.

Progress: One hundred and thirty four subjects have been enrolled.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/140 **Status:** Terminated

Title: Randomized Prospective Treatment with Low Molecular Weight Heparin in Patients Treated with Plaster Immobilization of the Lower Extremities

Start Date: 05/19/95 **Est. Completion Date:**

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: LTC John D. Pitcher Jr., MC

Associate Investigators:
CPT George K. Bal, MC
CPT Christopher D. Cannon, MC
CPT Randall K. Hildebrand, MC
MAJ Arnoldas S. Kungys, MC
CPT Joseph A. Shrout, MC
LTC David F. J. Tollefson, MC
MAJ Barry T. Bickley, MC
CPT Lori Harriman, MC
CPT Michael E. Kirk, MC
CPT Marc J. Michaud, MC
CPT Mark C. Weston, MC

Key Words: DVT, casts, heparin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine whether treatment with low molecular weight heparin in patients with short and long casts prevents or decreases the incidence of deep venous thrombosis (DDT). To determine the true incidence of DDT in patients treated with lower extremity immobilization for various age groups and risk factor assessment.

Technical Approach: Three hundred consecutive patients treated for orthopedic injuries or with orthopedic surgery who also require lower extremity immobilization will be randomized into groups of patients treated either with and without low molecular weight heparin. (This group of patients will be used to complete the first objective). Categories of patients will include operative and non-operative patients, short and long leg casts, and casts that are weight bearing and non-weight bearing. Prescription medications will be logged. Patients with a high risk for pulmonary embolism will be excluded from the study and treated in the standard fashion with coumadin. For all patients, post treatment sonographic evaluation will be obtained to document the incidence of DVT. Those patients not agreeing to randomization (the number of which ends when the first group's number reaches 300) will be enrolled at their consent to obtain post-casting sonography to aid in determining the incidence for DDT. (This group will be used to complete the second objective). Demographic data and associated medical illnesses will be recorded for all patients. The two groups (randomized patients and those refusing randomization) will be compared to determine if the groups are matched. The rate of thrombosis occurrence in each group will be initially compared using chi-square. A discriminate factor analysis will be used to determine whether any of these categories (or any combination) can predict occurrences of thrombosis.

Progress: This protocol was terminated due to lack of funding. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/092 **Status:** On-going

Title: A Prospectively Randomized Study on the Effectiveness of Post-Operative Knee Bracing for Anterior Cruciate Ligament Reconstruction

Start Date: 04/19/96 **Est. Completion Date:** May 99

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: MAJ Patrick StPierre, MC

Associate Investigators: CPT Michael E. Kirk, MC

Key Words: Anterior cruciate ligament:reconstruction, bracing

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to compare the effect of different post-operative brace patterns on the final outcome of an anterior cruciate ligament reconstruction. This bill be performed by prospectively randomizing patients into two different bracing groups and comparing them with subjective and objective testing during their rehabilitation period.

Technical Approach: In summary, the present knowledge on post-operative bracing for ACL reconstruction is limited. This study is designed to determine if post-operative bracing has an effect on the outcome of an ACL reconstructed patient. A total of 80 patients will participate in the study. After arthroscopically assisted ACL reconstruction patients will be randomized to two study groups. Group A will wear a knee immobilizer for three weeks after surgery followed by no protective bracing for the remainder of their rehabilitation. Group B will wear a Don-Joy IROM brace locked at 0° for three weeks followed by three weeks in the brace with flexion set to 10° less than maximum flexion. At six weeks, the patient will a Don-Joy off-the-shelf functional knee brace daily for six months and for vigorous activities after that for at least the first year. Data collected at one, two, six, twelve, and 24 months will include range-of -motion, Lachman, anterior drawer and pivot shift-tests, as well as thigh circumference measurements. In addition at the six, twelve and 24 month follow-up visits, KT-100, LIDO, Lysholm and IKDC tests will be administered. A significant difference in the stability or functional assessment scores would indicate superiority of one method over the other regardless of cost. If both treatment groups are found to be equivalent, the most cost effective treatment method would be without bracing.

Progress: Eighteen patients are currently enrolled. Data collection has been instituted in Physical Therapy and post-operative evaluations are ongoing.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/086	**Status:** On-going

Title: A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough

Start Date: 03/15/96	**Est. Completion Date:** Apr 99
Department: Surgery, Orthopedics Svc	**Facility:** MAMC
Principal Investigator: MAJ Patrick StPierre, MC	
Associate Investigators:	Hollis Potter, M.D.
Key Words: Rotator cuff, cortical bone, cancellous trough,	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: This study has not received final approval from the Department of Radiology. A joint research committee has been established and hopefully will resolve the issue.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/180 **Status:** Terminated

Title: Lateral Ankle Reconstruction Study

Start Date: 09/02/94 **Est. Completion Date:** Apr 95

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: CPT James D. Swenson, MC

Associate Investigators: LTC John D. Pitcher Jr., MC
CPT Mark C. Weston, MC

Key Words: ankle reconstruction

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: Evaluate functional (subjective) and mechanical (objective) improvement in patients undergoing reconstruction of lateral ankle ligaments.

Technical Approach: Patients found to have unstable lateral ankle ligaments will undergo surgery to reconstruct these ligaments. They will be evaluated before surgery with radiographs and a physical examination of the ankle to determine the amount of pre-operative laxity. Patients will be followed after surgery for at least 6 months at which time repeat radiographs and physical examination of the ankle will be done to determine the amount of post-operative ankle laxity. Patients will also be asked to fill out a questionnaire regarding the functional status of their ankle.

Progress: Thirty patients were enrolled. The study was terminated because a large percentage of the subjects were not available for post-op evaluation.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/087	**Status:** Completed
Title: Structural Bone Allografts in Pediatric Foot Surgery		
Start Date: 12/15/95	**Est. Completion Date:** Nov 95	
Department: Surgery, Orthopedics Svc	**Facility:** MAMC	
Principal Investigator: MAJ Winston J. Warme, MC		
Associate Investigators: Ernest U. Conrad III, M.D.	Vincent S. Mosca, M.D.	
Key Words: Surger:foot, population:pediatric, graft:allograft, graft:autograft		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objectives of this study are to: 1) determine the safety and efficacy of allografts versus autografts with pediatric foot surgery through retrospective review of patient charts and radiographic records; and 2) to make a cost comparison of graft harvest vs allograft use.

Technical Approach: Corticocancellous bone allografts were used to correct deformity in 62 pediatric patients (94 feet) from 1982-1994. Thirty-three autografts were concomitantly used in 25 children. Hospital records and radiographs were reviewed retrospectively to determine safety, efficacy, and time to clinical union. Long-term follow-up (greater than two years) was available on 32 patients (37 allografts and 13 autografts). There were no infections, non-unions, or cases of host rejection in either the short or long-term follow-up groups. Correction was maintained and complete graft incorporation demonstrated in all patients followed long-term. Cost analysis using present costs of allografts and estimated surgical charges for autografts indicate a 10% savings when allografts were used. Our data suggests small structural allografts in the foot are safe, effective and economical in the pediatric population.

Progress: Corticocancellous bone allografts were used to correct deformity in 62 pediatric patients (94 feet). Thirty-three autografts were concomitantly used in 25 children. Hospital records and x-rays were reviewed retrospectively, to determine safety, efficacy, and time to clinical union. Long-term follow-up was available on 32 patients. There were no infections, non-unions, or cases of host rejection. Correction was maintained an complete graft incorporation demonstrated in all patients followed long-term. Cost analysis using present costs of allografts and estimated surgical charges for autografts indicate a 10% savings when allografts were used. The data suggests that small structural allografts in the foot are safe, effective, and economical in the pediatric population. A paper was presented at the 37th Annual Society of Military Orthopaedic Surgeons and a manuscript has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/174 **Status:** On-going

Title: Comparative Effectiveness of (a) Standard Treatment, (b) Standard Treatment Plus Force Measured Orthotic Cutting Methodologies, (c) Standard Treatment Plus Pulsing Electromagnetic Fields, and (d) A ..

Start Date: 07/21/95 **Est. Completion Date:**

Department: Surgery, Orthopedics Svc **Facility:** MAMC

Principal Investigator: MAJ Kirk Willard, MC

Associate Investigators:
LTC Richard A. Sherman, MS
Philip Block, DPM
Kimberly A. Hermann-Do, BS, MHA
Melissa Wong, BA
CPT Stephen Wilkerson, DPM
John Gonzales, CPO
Estelle Hamblen, BA, MHA
Linda Robson, BA

Key Words: Ulcers:lower limbs, ulcers:feet, pulsed electromagnetic fields

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To compare the effectiveness of (a) standard treatment plus placebo pulsing electromagnetic fields (PEMFs), (b) standard treatment plus force measured orthotic cutting methodologies, (c) standard treatment plus PEMFs, and (d) a combination of all three for treatment of stable, open ulcers on the lower limbs nd feet.

Technical Approach: We propose to perform a double-blinded study utilizing metabolically abnormal patients (mostly diabetic) with skin ulcers on their feet and lower legs which have not healed during the previous three months. Participants will be stratified by age, grade of ulcer, diameter of ulcer, and location of ulcer. Patients will then be randomized to one of the four groups described above. During the initial evaluation, all patients will be evaluated for pressure/force patterns and for blood flow to the ulcer. All patients, except those in the orthotics only group, will receive real or placebo PEMF therapy for five days per week for one hour per day until the ulcer heals or sic weeks of treatment. Rate of ulcer healing will be measured by photography and videothermogram. Foot pressure patterns produced while standing still and walking will be measured at each evaluation session using automated pressure sensors set to average the pressure at each square cm of the sole. A power analysis of the pilot results shows that 33 subjects will be needed in each group assuming that we predict the PEMF/orthotic group will do better (one-tailed test) and an 80% chance of finding a difference between the four groups at a 0.05 level of significance. A total of 150 subjects will have to be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

Progress: No patients have been entered. This study will commence as soon as necessary equipment is purchased.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, UROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/104 **Status:** On-going

Title: Telomere Length and Telomerase Activity in Human Testicular Cancer

Start Date: 06/16/95 **Est. Completion Date:** Jul 97

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: CPT Raymond S. Lance, MC

Associate Investigators:
MAJ J. Brantley Thrasher, MC
MAJ Michael J. O'Reilly, MC
CPT Wade K. Aldous, MS
MAJ Kenneth W. Westphal, MC
Troy H. Patience, B.S.

Key Words: Cancer:testicular, telomerase

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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 *Rsa*1 and *Hin*f1 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: This protocol has been slow to mature due to the low numbers of patients with testicular cancer at Madigan. Four patients have been studied. Initial results show a paradoxically decreased telomerase activity compared to control adult testis tissue.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/109	**Status:** On-going
Title: Telomere Activity and Expression of p53 and Rb in Human Transitional Cell Carcinoma		
Start Date: 04/21/95	**Est. Completion Date:** Jul 97	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: CPT Raymond S. Lance, MC		
Associate Investigators: CPT Wade K. Aldous, MS	MAJ J. Brantley Thrasher, MC Troy H. Patience, B.S.	
Key Words: Cancer: bladder, telomere, temomerase		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** 09/30/96

Study Objective: This study encompasses four objectives. To determine the presence or absence of telomerase activity in transitional cell carcinoma 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 human transitional cell carcinoma.

Technical Approach: Tissue samples will be taken from 40 male and female patients undergoing operative resection for bladder cancer. All malignant and benign tumors of the bladder found 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 *Rsa*1 and *Hin*f1 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 in vitro. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers 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: Seventeen solid transitional cell carcinomas have been studied. To date, 100% of these tumors unequivocally express telomerase activity compared to 2 of 10 of the control benign urothelium being positive. Both of the control urothelial specimens were found to have urothelial atypia felt to be a premalignant state. The results of this study were presented at the 72nd annual meeting of the Western Section of the American Urologic Association, 30 Jul 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/158 **Status:** On-going

Title: Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis

Start Date: 08/16/96 **Est. Completion Date:** Oct 02

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: MAJ Henry E. Ruiz, MC

Associate Investigators:
MAJ J. Brantley Thrasher, MC
CPT Douglas W. Soderdahl, MC
CPT John B. Ellsworth, MC
CPT Raymond S. Lance, MC

Key Words: Penile Prosthesis:Ambicor, Inflatable, Safety, Effectiveness

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: No patients have been entered. The investigators are awaiting CIRO approval before implementing the study.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/100	**Status:** On-going
Title: Comparison of Five Second Urinary Home Flow Rates to Formal In-Office Uroflowmetry		
Start Date: 05/17/96	**Est. Completion Date:**	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: CPT Bradley F. Schwartz, MC		
Associate Investigators: MAJ J. Brantley Thrasher, MC	MAJ Henry E. Ruiz, MC	
Key Words: Urinary flow rates, uroflowmetry, home flow rates		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if five second urinary home flow rates correlate with standard in-office uroflowmetry and maximum urinary flow rates. While it is difficult to analyze the costs of procedures performed in our clinic, the medicare reimbursement for in-office uroflows is $78. The specimen cup in the confines of the private household will undoubtedly be less expensive.

Technical Approach: We will attempt to show that home five-second urinary flow rates in the evaluation of bladder outlet obstruction is as accurate and effective as formal in-office uroflowmetry, specifically maximum urinary flow rate (Q_{max}). In addition, home flows will be less expensive and may perhaps be more "physiologic" in the sense that it is obtained in a more natural environment. Fifty five male subjects who seek urologic consultation for signs and symptoms of bladder outlet obstruction will be recruited. Patients will obtain five-second home urinary flow rates using a pre-measured cup, instruction sheet and blank form to document their flows. Flow rates will be obtained once daily for two weeks. They will then have in-office uroflow with uroflowmetry on three separate occasions. A power analysis determined that 55 patients would be required for a 2 cc/sec difference in modalities and 90% power. Data will be analyzed using the paired t-test.

Progress: Thirty subjects have been entered. Preliminary results indicate that both tests are reliable; however, they do not correlate.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/129 **Status:** On-going

Title: Oral Ciprofloxacin for Acute Prostatitis

Start Date: 06/21/96 **Est. Completion Date:** Apr 97

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: CPT Douglas W. Soderdahl, MC

Associate Investigators:
CPT Bradley F. Schwartz, MC
CPT Rayford A. Petroski, MC
MAJ J. Brantley Thrasher, MC

Key Words: Prostatitis, cirpofloxacin, ampicillin, gentamicin, trimethoprim, sulfamethoxasole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To evaluate the efficacy of oral Ciprofloxacin (Cipro) in the treatment of acute prostatitis in comparison to traditional I.V. Ampicillin (Amp) and Gentamicin (Gent).

Technical Approach: The study population will consist of 50 men eligible for MAMC care who present with signs and symptoms consistent with acute prostatitis and meet entry criteria for inpatient treatment with either Cipro or IV Amp/Gent. Patients will be randomized to treatment with Cipro 500mg PO BID for 30 days or IV Amp (1gm q 6hrs)/Gent (5mg/Kg) followed by Trimethoprim/Sulfamethoxazole (Septra DS), one tablet PO BID, for a combined total of 30 days. Efficacy of treatment will be based on length of hospital stay, time to resolution of symptoms, time to defervescence and evaluation of complications. Patients will be followed up in 6-8 weeks after completion of outpatient therapy an will receive exams and laboratory tests according to the Stamey technique. Additional follow-up will be done at 6 and 12 months for recurrence or chronic states. Analysis of data will include chi-square, student t-test and ANOVA.

Progress: An IND was obtained from the FDA for this protocol. So far one patient has been entered. Since accrual has been very slow, Tripler will submit the protocol to their IRB for approval to take part in the study.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/133	**Status:** Completed
Title: Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction		
Start Date: 08/05/94	**Est. Completion Date:**	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: CPT Douglas W. Soderdahl, MC		
Associate Investigators: LTC Kurt L. Hansberry, MC	MAJ J. Brantley Thrasher, MC	
Key Words: erectile dysfunction, self-injection device, external vacuum device		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To directly compare two non-surgical treatments of erectile dysfunction: self-injection vs. external vacuum devices.

Technical Approach: Patients actively undergoing either self-injection pharmacotherapy or external vacuum device (EVD) therapy will be invited to participate in this study. Each patient enrolled will receive a detailed questionnaire which covers satisfaction, effectiveness, and side effect issues of their currently employed treatment modality. The self-injection group will then be given instruction and necessary equipment to employ the EVD. Likewise, the EVD group will receive instructions for injection treatment. After four months, the participants will be asked to complete the same questionnaire to evaluate the alternate modality. The participants will also be asked to comment on their comparison of the two therapies. Sexual partners of the patients will also be asked to attend a follow-up visit and fill out a confidential questionnaire comparing the two different treatments. At the end of the study, the patient and his physician will make an informed decision about which modality to continue with.

Progress: Fifty subjects were studied. Both self-injection and the vacuum device regimens are highly effective and well tolerated treatments for impotence. Younger patients (<60), those with a shorter duration of impotence (<12 months), and those with impotence secondary to radical prostatectomy favored the injection treatments. A paper was presented at the Western Section of the American Urological Association and at the James C. Kimbrough Urological Seminar in FY 96. A manuscript has been submitted to the British Journal of Urology for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/173 **Status:** Completed

Title: The Role of Urine Cytology in the Surveillance of Bladder Cancer

Start Date: 09/15/95 **Est. Completion Date:** Jun 96

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: CPT Douglas W. Soderdahl, MC

Associate Investigators: MAJ J. Brantley Thrasher, MC
LTC Kurt L. Hansberry, MC

Key Words: Cancer:bladder, urine cytology

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the role of urine cytology in the surveillance of bladder cancer.

Technical Approach: The purpose of this study is to determine how urine cytologies can be used in the diagnosis and follow-up of bladder cancer. There are two questions we are trying to answer. We would like to know if urinary cytology has sufficient sensitivity and specificity to potentially eliminate the need for bladder mapping or at least reduce the number of indications for which this is utilized. In addition, we would like to know if urine cytologies might be used confidently in the follow-up of bladder cancer so that the number of surveillance cystoscopies might be reduced. We will involve up to 100 patients with known bladder cancer and those who present with signs and symptoms consistent with bladder cancer. All patients with a positive cytology and/or suspicious visible lesions will undergo random bladder biopsies with or without transurethral resection of bladder tumor. Biopsy results will be used as the gold standard. Bladder barbotage (washing) samples will be obtained by instilling and withdrawing approximately 50cc of normal saline repeatedly to obtain a fresh sample. This cytology sample will be evaluated promptly, since the handling of these samples has been shown to affect the sensitivity of the cytology. We want to then compare these results to that of the biopsy. The sensitivity, specificity, predictive value and negative predictive value will be determined.

Progress: Thirty patients were evaluated. The information gained will not add to the literature.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/113	**Status:** On-going
Title: Relief Strategies for Initiative Bladder Symptoms Associated with Intravesical BCG - A Pilot Study		
Start Date: 05/17/96	**Est. Completion Date:** May 97	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: MAJ J. Brantley Thrasher, MC		
Associate Investigators: William J. Ellis, M.D.	Donna L. Berry, Ph.D., RN	
Key Words: Bladder; oral hydration, dietary supplementation, potassium,sodium citrate, BCG		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this pilot intervention study is to evaluate an oral hydration regimen and dietary supplementation with potassium/sodium citrate as relief strategies for irritative bladder symptoms associated with BCG intravesical therapy.

Technical Approach: This randomized, 2 X 2 pilot study is designed to investigate an oral hydration regimen and urinary alkalinization with potassium/sodium citrate. Forty subjects, experiencing irritative bladder symptoms associated with intravesical bacillus Calmette-Guerin, will be randomized to either an oral hydration regimen, urinary alkalinization with potassium citrate, a combination of the oral hydration regimen and urinary alkalinization with potassium citrate, or usual clinical practices. The intervention will be applied for one week during week 4 of the intravesical treatment course. Urine pH will be monitored and symptoms will be measured using the Irritative Bladder Symptom Inventory. Symptom data will be analyzed using a two-way analysis of variance with a test for interaction.

Progress: Ten patients have been enrolled. Early indications suggest that alkalinization and increased fluid intake may help with the irritative symptoms associated with BCG intravesical therapy.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/002 **Status:** On-going

Title: Measurement of Irritative Bladder Symptoms

Start Date: 10/20/95 **Est. Completion Date:** May 96

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators: Donna L. Berry, Ph.D., RN
LTC Kurt L. Hansberry, MC

Key Words: Cancer:bladder, irritative bladder symptoms

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To test the properties of the Irritative Bladder Symptom Inventory (IBSI) in terms of: a) construct and content validity, b) internal consistency, and c) test-retest reliability in a sample of individuals receiving intravesical therapy for bladder cancer.

Technical Approach: Sixty individuals will be asked to complete the one-page, nine-item IBSI on the first day of intravesical treatment, prior to the instillation, and then each night prior to going to bed for 42 nights. This period includes the duration of intravesical therapy plus 7 days after the final installation. Validity will be examined and internal consistency will be assessed through extensive item and scale analyses. IBSI item analyses will include examination of item descriptive statistics, inter-item measures of association, scale mean, scale variance, and Cronbach's alpha. Test-retest reliability will be conducted at 1- and 2-week intervals. The findings will be used to establish the IBSI as a valid and reliable tool for monitoring irritative bladder symptoms.

Progress: Thirty one patients have been tested and the irritative bladder symptoms score sheet has been proven to be a valid and reliable instrument for irritative bladder symptoms associated with BCG intravesical therapy in men. The instrument must be tested further in women receiving intravesical therapy. Patient enrollment continues.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/164	**Status:** On-going
Title: Prostate Cancer Intervention vs Observation Trial (PIVOT): A Randomized Trial Comparing Radical Prostatectomy vs Palliative Expectant Management for the Treatment of Clinically Localized Prostate ...		
Start Date: 09/21/94	**Est. Completion Date:** Sep 04	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: MAJ J. Brantley Thrasher, MC		
Associate Investigators:	LTC Kurt L. Hansberry, MC	
Key Words: Cancer:prostate, prostatectomy, palliative management		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine which of 2 treatment strategies is superior in reducing all-cause mortality in patients with clinically localized prostate cancer (1) radical prostatectomy and early intervention of subsequent disease persistence or recurrence or (2) expectant management with reservation of therapy for palliative treatment of symptomatic or metastatic disease progression.

Technical Approach: Patients will be randomized to one of the two groups listed (1) will have a radical prostatectomy; (2) will be assigned to Watchful Waiting Management.

Patients in group 1 will have 2 surgical procedures; removal of the lymph nodes from near the prostate gland (pelvic lymph node surgery); and then proceed with the prostatectomy.

Patients in group 2 will not have their cancer removed. Patients will be closely observed; if the cancer causes symptoms, treatment will be aimed at providing relief of these symptoms.

Progress: Patient accrual has been slow across the nation; 244 have been enrolled, mostly at VA medical centers. None have been enrolled at MAMC. The tape has been shown to 38 patients, but none have elected to enter the study. It has been the experience of the investigators that patients are recalcitrant to have management of their clinically localized prostate cancer dictated to them.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/031 **Status:** Terminated

Title: Open-Label, Continuation Study of the Comparative Long-Term Safety and Effectiveness of Two Dosing Regimens of Eulexin in the Treatment of Prostate Cancer

Start Date: 11/17/95 **Est. Completion Date:** Dec 96

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators:
COL John N. Wettlaufer, MC
COL John C. Norbeck, MC
CPT Raymond S. Lance, MC
LTC Kurt L. Hansberry, MC
MAJ Henry E. Ruiz, MC
CPT Douglas W. Soderdahl, MC

Key Words: Cancer:prostate, Eulexin, long term

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To compare the long-term effectiveness of two oral dosing regimens of flutamide, 500mg qd or 250 mg q8h, by measurement of time to disease progression, serum PSA concentrations, quality of life, and patient survival. (2) To compare the long-term safety of these two dosing regimens in this patient population.

Technical Approach: Eligible patients who participated in protocol H95-089-01 will be included in this continuation protocol. Protocol H95-089-01 is expected to enroll 200 patients per arm so the continuation protocol will enroll, at maximum, 200 patients per arm. The Week 12 assessments made in protocol H95-089-01 will be considered the baseline measures (day 0) for the continuation protocol. All analyses will be conducted using two-sided tests of significance.

Progress: This protocol was terminated by the sponsor as it appeared from information gained in the comparative trials (MAMC #95134) that it would render an open label study ineffective.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/134	**Status:** On-going
Title: Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin: 250 mg Q8h vs 500 mg QD		
Start Date: 05/19/95	**Est. Completion Date:** Jul 96	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: MAJ J. Brantley Thrasher, MC		
Associate Investigators: COL John N. Wettlaufer, MC	LTC Kurt L. Hansberry, MC CPT Douglas W. Soderdahl, MC	
Key Words: Cancer:prostate, Eulexin		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To compare the clinical effectiveness of a new dosing regimen (500mg QD) for administering flutamide to the currently indicated dosing regimen of 250 mg Q8H according to (1) the percent of patients normalizing PSA and (2) quality of life differences between the two regimens.

Technical Approach: This phase IV, multi-center, open label, prospective randomization study will include 400 patients (10 from MAMC), ages 40 to 85, with clinically proven and histologically confirmed adenocarcinoma of the prostate gland. The subjects will be randomized to one of two treatment groups, Flutamide 250mg Q8H or Flutimade 500 mg QD, at Time 0. Time 0 is the day of surgical or medical castration. The study treatments will be continued for three months. The two variables to be evaluated are normalized PSA values as determined by standard laboratory PSA test, and quality of life as determined by questionnaire. Laboratory tests will be taken at clinic visits at Time 0, and weeks 4, 8, and 12. PSA normalization will be performed on 12 weeks data after the last patient accrued has reached the 12 week point. In order to achieve the conventional 80% power for showing equivalence, 200 patients per arm will be required based on a threshold criterion of 15%. Evaluation of the Quality of Life modules will involve multivariate analysis of variance for repeated measures for HQL domains and symptoms. Treatment by time interaction effect will be assessed under the repeated measures model to identify HQL domains that are significantly different between the two treatment arms using a two-sided 5% level test.

Progress: Presently 39 institutions are enrolling subjects on this trial; 19 patients have been enrolled at MAMC and 148 study-wide. Study-wide, 16 patients discontinued the protocol due to elevated liver function tests. Preliminary data suggest that both methods are efficacious at lowering the PSA into the normal range. It is too early to comment on toxicity, but the quality-of-life questionnaire would suggest that the 500 mg/day dosing schedule is tolerated and preferred by the patient population. This data has been presented by Dr. Thrasher at multiple institutions under the category of invitational lectureships.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/083	**Status:** On-going
Title: Diet and Prostate Hormones		
Start Date: 03/17/95	**Est. Completion Date:** Jul 95	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: MAJ J. Brantley Thrasher, MC		
Associate Investigators: Stephen R. Plymate, M.D.	Alan R. Kristal, Dr.P.H. Johanna Lampe, Ph.D.	
Key Words: Cancer:prostate, diet, prevention		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1) To better understand the relationships of diet with prostate cancer. 2) To evaluate the potential value of dietary change for the primary prevention or adjuvant therapy of prostate cancer.

Technical Approach: This study will recruit 10 men with newly-diagnosed, localized and histologically well-differentiated prostate cancer who elect to undergo prostatectomy. They will be randomized into two arms: 1) low fat (20%en) and high fruit and vegetable (8+ servings/day) diet for 4-6 weeks before prostatectomy or 2) their usual diet. Dihydrotestosterone and Testosterone concentrations wil be measured in blood, prostate biopsies, and prostate tissue removed at prostatectomy.

Progress: This study has been closed to patient accrual. Seven patients were randomized. The biopsy specimens are now being analyzed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/150	**Status:** On-going
Title: Center for Prostate Disease Research Prostate Cancer Radical Prostatectomy Follow-up Questionnaire		
Start Date: 06/16/95	**Est. Completion Date:** Sep 95	
Department: Surgery, Urology Service	**Facility:** MAMC	
Principal Investigator: MAJ J. Brantley Thrasher, MC		
Associate Investigators:	Judd W. Moul, M.D.	
Key Words: Cancer:prostate, prostatectomy, questionnaire		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The objective of this study is to conduct a comprehensive survey of men who have undergone a radical prostatectomy (RP) for prostate cancer (PC) to assess long-term quality of life (QOL) regarding impotence, incontinence and surgical complications.

Technical Approach: In 1994 there have been over 200,000 new cases of PC diagnosed in the United States, and the use of RP as a treatment modality has increased over 200% since the mid 1980's. With the increasing use of RP, more attention has focused on side effects and complications of the treatment and how they relate to overall QOL in these men. In a multicenter study (WRAMC and MAMC), a QOL questionnaire, regarding impotence, incontinence and surgical complications has been developed. This questionnaire will be mailed to subjects recruited from the database of all RP patients treated at MAMC and WRAMC between 1980-1994. A total of 400 returned questionnaires will be sufficient for data analysis. Most of the results will be descriptive statistics of morbidity percentages. Logistic regression will be used to model long-term quality of life outcome variables.

Progress: One hundred fifty-nine patients have been entered at MAMC and a total of 554 from all three institutions (MAMC, WRAMC, and Keesler AFMC). Preliminary data indicates that despite significant rates of mild incontinence and impotence the vast majority of patients would opt for radical prostatectomy again. Long term problems with stricture are uncommon.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/051 **Status:** On-going

Title: Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer

Start Date: 04/01/94 **Est. Completion Date:** Jan 95

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators:
MAJ Richard R. Gomez, MC
CPT Patrick A. Twomey, MC
Stephen R. Plymate, M.D.
CPT Michael D. Bagg, MC

Key Words: cancer:prostate, IGF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The purpose of this study is to localize IGFBP's -2.-3,-4, and -6 in regions of histologically proven prostate cancer. Additionally, these same techniques will be used to identify these binding proteins in areas of prostatic intraepithelial neoplasia (PIN) and benign prostatic hyperplasia (BPH). The information gleaned from this study will help better understand IGFBP expression in both malignant, premalignant, and benign prostatic tissue.

Technical Approach: Radical prostatectomy specimens will be obtained by the Urology Service and taken to Pathology for histologic sectioning. Prostate adenocarcinoma will be identified in sections (as well as areas of PIN or BPH) with an adjacent section taken for immunohistochemical staining. Immunohistochemical staining will be performed for identification of IGFBP's-4, -2, -3, and -6 in regions of associated neoplasm, PIN or BPH. Approximately 10 patients will be studied with comparisons to be made between neoplastic premalignant, and benign prostatic tissue.

Progress: Data suggest that significant changes in the insulin-like growth factor system occur with the progression of prostate tissue from the benign through the premalignant and into the malignant states. However, present knowledge in this area is in its infancy and the further studies should be done. Therefore, the protocol will be expanded to evaluate insulin-like growth factors 2, 3, 4, 5, and 6 and to evaluate nude mice using an immortalized cell line M12 to look at differences in insulin-like growth factor type 1 receptors and their effect on differentiation and proliferation of these cancer cells.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/144 **Status:** On-going

Title: Evaluation of the Safety and Efficacy of Transurethral Resection of the Prostate Using the Contact Laser System vs Electrosurgery

Start Date: 09/02/94 **Est. Completion Date:**

Department: Surgery, Urology Service **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators: COL John N. Wettlaufer, MC
LTC Kurt L. Hansberry, MC

Key Words: prostate:resection, laser, electrosurgery

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: 1. To evaluate the effectiveness (resection and coagulation) of the Contact Laser System in comparison to that of electrosurgery for transurethral resection of the prostate (TURP). 2. To evaluate the relative cost effectiveness of the Contract Laser in comparison to that of electrosurgery for transurethral resection of the prostate.

Technical Approach: Male patients who have been diagnosed with symptomatic benign prostatic hypertrophy (BPH) will be enrolled into this study once all of the entrance criteria have been fulfilled. After all baseline evaluations have been performed, each patient will undergo TURP using either electrosurgery or the Contact Laser System. All patients will be monitored closely through discharge, and will undergo follow-up evaluation a one and six months, and one year following surgery. Follow-up evaluation will be encouraged (optional) annually for five (5) years thereafter.

Progress: Patient accrual has been closed. Twenty patients were entered at MAMC and 20 patients were entered at WRAMC. Data analysis is in progress.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, VASCULAR SURGERY SERVICE

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/165	**Status:** Completed

Title: A Double-Blind, Pharmacokinetic Comparative Study of Two Concentrations: 1% and 3% Bucladesine Sodium Ointment (DT-5621) in Patients with Venous Stasis Ulcers

Start Date: 07/21/95	**Est. Completion Date:** Sep 96
Department: Surgery, Vascular Surgery	**Facility:** MAMC
Principal Investigator: COL Charles A. Andersen, MC	
Associate Investigators: Edmund Kanar	
Key Words: Ulcer, bucladesine sodium	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: The primary objectives of this study are to determine the extent of potential systemic absorption of 1% and 3% bucladesine sodium ointments (DT-5621) following topical administration, by measuring plasma concentrations of the drug, and to determine the safety of topical 1% and 3% bucladesine sodium ointments (DT-5621) in patients with venous stasis ulcers of the lower limbs. The secondary objectives are to evaluate the efficacy endpoint for the Target Study Ulcer, to evaluate resource use data leading to pharmacoeconomic analysis and modeling, and to evaluate Quality Of Life data.

Technical Approach: This study is designed as a double-blind, randomized trial of 1% and 3% bucladesine sodium Ointments (DT-5621) in patients with venous stasis ulcers. This is a multicenter study that will enroll a total of approximately 80 patients, resulting in approximately 60 evaluable patients. A total of 6 patients will be enrolled at Madigan. Drug will be administered on an outpatient basis. During PK serial drawing days; Day one Week 2, and Day 1 Week 3, patient will stay at the study site for the duration of the blood draws and EKG recordings. Single samples are also drawn for PK (no EKGs) on Day one Week 6, Day one Week 10, and Day one Week 14. The study will be conducted in patients 18 to 85 years of age who are diagnosed as having venous stasis ulcer(s), of the lower limbs; patients with venous stasis ulcer(s) refractory to treatment, may also enter the study. Patients with lesion(s) ranging in size from 2 cm^2 up to 50 cm^2 will be eligible for the study. Each patient will be evaluated for 25 weeks, consisting of a 1-week Run-In Phase, followed by a 12 week Double-Blind Treatment Phase, and finally a 12 week Follow-Up Phase. Each investigator will try to enroll two patients in each of three ulcer size groups; patient with small ulcer(s), (2 cm^2 to 15 cm^2), medium size ulcer(s), (16 cm^2 -35 cm^2) and large ulcer(s), 36 cm^2-50 cm^2). Patients with up to three ulcers with (combined) surface area of 4 cm^2 (for 2 ulcers) or 6 cm^2 (for 3 ulcers) to 50 cm^2 may be entered into the study. However, each ulcer must be at least 2 cm^2. Quality of life and size of the ulcer will be evaluated during the study.

Progress: This study was closed by the sponsor due to nationwide low enrollment. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/163 **Status:** On-going

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

Start Date: 09/20/96 **Est. Completion Date:** Nov 98

Department: Surg, Vascular Surgery Svc **Facility:** MAMC

Principal Investigator: COL Charles A. Andersen, MC

Associate Investigators:
LTC Stephen B. Olsen, MC
George J. Collins
LTC David F. J. Tollefson, MC
Edmund Kanar

Key Words: Carotid endarterectomy, HEMASHIELD

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

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: This study has not been started. The PI is awaiting MEDCOM approval.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/098 **Status:** Terminated

Title: A Prospective Study of Deep Venous Thrombosis (DVT) After Femoral Catheterization

Start Date: 04/21/95 **Est. Completion Date:**

Department: Surgery, Vascular Surgery **Facility:** MAMC

Principal Investigator: LTC David F. J. Tollefson, MC

Associate Investigators:
CPT Peter J. Armstrong, MC
COL Charles A. Andersen, MC
MAJ Lewis L. Low, MC

Key Words: Thrombosis:deep venous, catheterization

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine if femoral venous cannulation places critically ill patients at increased risk for deep venous thrombosis (DVT) despite routine prophylaxis. To determine the time course of this increased risk in relation to duration of femoral venous cannulation.

Technical Approach: A group of one hundred fifty critically ill patients in the Intensive Care Unit (ICU) at MAMC requiring central intravenous access on odd days of the month will be randomized to undergo right or left femoral venous catheterization. All patients will receive DVT prophylaxis consisting of calf pneumatic compression stockings. Patients will undergo serial duplex examinations of the bilateral iliofemoral veins: prior to catheterization; on day 1, 3, 5, and 7 post-catheterization; and, on the intervals thereafter for 4 weeks. The contralateral limb without catheter will be used as the control. The incidence of DVT in the cannulated limb and in the contralateral limb will be compared using a chi-squared analysis with a $p<0.05$ being statistically significant.

Progress: Due to very slow accrual and another study being published on this subject, this project has been terminated.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/097 **Status:** On-going

Title: Abdominal Aortic Aneurysm (AAA) and Chronic Obstructive Pulmonary Disease (COPD); Is There a Relationship

Start Date: 04/21/95 **Est. Completion Date:** Mar 96

Department: Surgery, Vascular Surgery **Facility:** MAMC

Principal Investigator: LTC David F. J. Tollefson, MC

Associate Investigators:
LTC William H. Cragun, MC
CPT Peter J. Armstrong, MC
COL Charles A. Andersen, MC

Key Words: Aneurysm:abdominal aortic, COPD

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: To determine the association, if any, of AAA and COPD as well as potential pathophysiologic explanation

Technical Approach: A comparison will be made between patients with and without COPD and the incidence of AAA. Patients 50 years and older will be selected from those followed in the pulmonary, family practice or adult primary care clinics who have been determined to have COPD by screening history, spirometry and carbon monoxide diffusing capacity (DLCO). Controls will be age/sex matched without COPD. Selected participants will be evaluated by pulmonary function tests (spirometry, DLCO), serum alpha 1 anti-trypsin levels, serum elastase levels, serum cholesterol levels, ankle-brachial indices and abdominal aortic duplex. The incidence in the control and study groups will be compared through Chi-squared analysis and individual variables wills be determined through student T-test. A $p<0.05$ will be determined to be statistically significant. Patients and primary care physicians will be notified of the presence or absence of AAA, abnormal ankle-brachial indices, COPD, or hypercholesterolemia.

Progress: Four patients have been entered in the study.

DETAIL SHEETS FOR PROTOCOLS

SOCIAL WORK SERVICE

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/139 **Status:** On-going

Title: Spouse Abuse Among Active Duty Women Married to Civilian Husbands: An Examination of Interpersonal and Social Factors

Start Date: 08/16/96 **Est. Completion Date:** Aug 98

Department: Social Work Service **Facility:** MAMC

Principal Investigator: LTC Nancy K. Raiha, MS

Associate Investigators:
COL Robert A. Mays, MC
Patricia J. O'Campo, Ph.D.
MAJ Charles D. Magruder, MC
MAJ Gary D. Southwell, MC
Andrea C. Gielen

Key Words: Abuse:spousal, active duty women, civilian husbands

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 09/30/96

Study Objective: (1) To elucidate possible risk factors for domestic violence in the U.S. Army population. (2) To collect information which would facilitate development of more effective spouse abuse prevention programs in the U.S. Army population. (3) To identify military-unique stressors or circumstances which may contribute to the development of an abusive relationship among Active Duty women. (3) To determine if there is a higher prevalence of certain interpersonal relationship patterns among active duty women and civilian men in an abusive situation.

Technical Approach: This study will examine approximately 300 couples who have been identified as substantiated abuse cases by the Family Advocacy Case Management Team. Participants will complete several questionnaires that ask about their life history, current feelings, and how they would describe the relationship between them and their partner. Initial analyses will involve the use of paired-sample t-tests to examine the relationship between husbands and wives on the FES, LISRES, DAS and NEO PI-R's. A chi-square test will be used to examine differences between husbands and wives on the data from the questionnaire. Chi-square Interaction Detector will be used to compare abusive versus control couples. To assess for differences in interrelationships patterns, MANOVA will be used. Canonical correlation will be included in the MANOVA to examine the interrelationship between sets of instrument scores. Once this is accomplished, logistic regression will be done to calculate log-odds ratios of abuse, and nonlinear canonical correlations will be used to examine the relationships between the continuous and categorical sets of variables. Generalized estimating equations will be used as an additional test to assess for the impact of correlation within clusters.

Progress: A research assistant has been hired through the Jackson Foundation and subject recruitment will begin in October 96.

DETAIL SHEETS FOR PROTOCOLS

GYNECOLOGY ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 82/073 **Status:** On-going

Title: GOG 0026A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies

Start Date: 11/20/81 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: malignancy:pelvic

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To implement a master protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment.

Technical Approach: A "rejection" type design will be used with a fixed sample size of 25 eligible patients/disease site/drug or combination studied. The design allows replacement of ineffective regimens by newer agents or combinations. Sections relating to specific agents will be sequentially incorporated into this protocol as these agents are studied. Continuing review will be done for each separate protocol. To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy and a granulocyte count >1500/mm^3, platelet count >100,000/mm^3, BUN <25 mg%, creatinine <1.5 mg%, bilirubin <1.1 mg, SGOT <5 IU. Patients receiving myelosuppressive agents will have adequate bone marrow function as described above. Exception to the general requirement for normal liver function will be secondary to documented metastatic tumor to the liver or as noted in the section dealing with that particular agent. Patients with all primary disease sites of gynecologic malignancies are eligible. Each disease site will be accumulated as a separate study sample. For a particular drug study, the allowable disease site(s) may be further qualified. Ascites and pleural effusion alone are not considered measurable for purposes of the study. A steady rise in the titers of alpha-fetoprotein and beta-HCG will be taken as evidence of disease progression in germ cell tumors of the ovary.

Progress: No new patients entered in FY 96. Protocol 26DD was closed in Apr 96. One patient remains on protocol in this series (26LL).

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 82/007	**Status:** On-going
Title: GOG 0026C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies		
Start Date: 11/20/81	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: COL William L. Benson, MC	COL Roger B. Lee, MC	
Key Words: cancer:pelvic, cisplatinum		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To determine the efficacy of cis-platinum diamminedichloride in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer, who have failed higher priority therapies, will be offered cis-platinum as a Phase II drug to determine its efficacy. The drug is given at 50 mg/m^2 intravenously every three weeks as toxicity permits. Patients who respond or who demonstrate disease will continue to receive the agent until progression has occurred.

Progress: No patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 88/067 **Status:** Completed

Title: GOG 0026DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies

Start Date: 08/19/88 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:pelvic, amonafide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Patients must have normal renal and hepatic function. Patients will be entered as non-randomized cases. Amonafide will be administered as a slow intravenous infusion over an hour at an initial dose of 300 mg/m^2 daily for five days. A serial dose escalation up to 450 mg/m^2 will be used in patient without toxicity after each cycle of therapy until a Grade 1 hematologic toxicity occurs. All patients will receive therapy until disease progression or until adverse effects prohibit further therapy.

Progress: No patients were entered in this study at MAMC. It was closed to patient entry, 12 Apr 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 91/008	**Status:** On-going
Title: GOG 0026II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies		
Start Date: 10/19/90	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: pelvic malignancy, 5-Fluorouracil, leucovorin:high dose		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$8000.00	**Periodic Review:** 02/16/96

Study Objective: To implement a protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment. In this case, the agents are 5-FU and high dose Leucovorin.

Technical Approach: Patients who have received prior 5-FU are ineligible. Leucovorin will be administered in a dose of 200 mg/m^2 daily for 5 days and repeated at four and eight weeks and thereafter every five weeks. 5-FU will be administered in a dose of 370 mg/m^2/day for 5 days, infused immediately after the Leucovorin has been given. An adequate trial will be defined as receiving one course of treatment and living four weeks for additional tumor assessment, provided death is not due to tumor progression. All patients entered on the study will be evaluated for toxicity. Patients will remain on study and continue receiving chemotherapy until disease progression or until toxicity prevents further treatment.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/153 **Status:** On-going

Title: GOG 0026LL: A Phase II Trial of Prolonged Oral Etoposide (VP-16) in Patients With Advanced Pelvic Malignancies

Start Date: 08/06/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:pelvic, etoposide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1. To determine if low dose oral VP-16 given on a daily basis for 21 days out of the month yields significant clinical response in patients who have previously been treated with platinum containing compounds. 2. To evaluate the relative side effects of such low dose therapy.

Technical Approach: Patients with recurrent pelvic malignancies not amenable to curative therapy are eligible. The treatment regimen will consist of oral VP-16 given at 50 mg/m^2/d on the 1st to the 24th of the month. This will be cycled every four weeks until disease progression or adverse effects prohibit further therapy. Patients will be followed by clinical examinations or if applicable chest x-rays prior to the initiation of each cycle.

Progress: This study was mistakenly terminated in FY 95. It has since been re-reviewed and reactivated. Two ptients were entered in FY 94; one is deceased and one is still being followed. The protocol was closed to patient entry, 1 Dec 95.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 81/035	**Status:** On-going
Title: GOG 0041: Surgical Staging of Ovarian Carcinoma		
Start Date: 01/16/81	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: COL William L. Benson, MC	COL Roger B. Lee, MC	
Key Words: cancer:ovarian, surgical staging		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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 was closed to patient entry 12 Feb 87. Thirteen patients were enrolled, 2 have been lost to follow up, 3 have died, and 8 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 81/105 **Status:** On-going

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

Start Date: 08/21/81 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators:
COL Roger B. Lee, MC
COL William L. Benson, MC
LTC Gordon O. Downey, MC

Key Words: Cancer:ovarian, adenocarcinoma, cyclophosphamide, Adriamycin, Platinol

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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 #25.

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 was closed to patient entry, 20 Jul 85. Six patients were entered in the study and one is still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 84/033	**Status:** On-going

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

Start Date: 02/17/84	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators:
COL William L. Benson, MC
COL Roger B. Lee, MC

Key Words: tumor:ovarian, melphalan, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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 or 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 5 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 was closed to patient entry 25 Feb 92. Ten patients were enrolled; 1 has died and 9 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 84/074 **Status:** On-going

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 ...

Start Date: 08/17/84 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: cancer:ovarian, teratoma, tumor:sinus, chemo, bleomycin, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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: Closed to patient entry 10 Feb 92. One patient was enrolled in FY 92 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 86/089	**Status:** On-going

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...

Start Date: 08/15/86	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC
Principal Investigator: LTC Mark E. Potter, MC	
Associate Investigators: COL Roger B. Lee, MC	COL William L. Benson, MC LTC Gordon O. Downey, MC

Key Words: Cancer:cervical, carcinoma, hydroxyurea, 5-FU, Cisplatin, Radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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 protocol was closed to patient entry in December 1990 because it was reported that the two patients entered on the study had died (at a different institution). After further review it was discovered that this was a mistake and the protocol was reopened in Feb 93. Two patients were entered at MAMC and are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/093 **Status:** Completed

Title: GOG 0087G: A Phase II Trial of Paclitaxel (Taxol) in Patients With Advanced or Recurrent Uterine Sarcomas

Start Date: 04/01/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:uterine, sarcoma, Paclitaxel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To compare the efficacy of Paclitaxel (Taxol) in patients with advanced or recurrent uterine sarcomas.

Technical Approach: Patients eligible to participate in this study will be treated with Paclitaxel at 175 mg/m^2 given as a three hour infusion every three weeks. Infusion is administered intravenously after premidication with decadron, and H1 and H2 blockers. Weekly CBC's are monitored and patients will be subseqauently treated with granulocyte-colony stimulator factor (G-CSF) support for prolonged neutropenia or febrile neutropenia. In the event of persistent neutropenia despite G-CSF support, dose reductions will occur. Patients who have received previous pelvic radiation therapy will be treated at a decreased dose of 135 mg/m^2. In the event that tumor measurements are obtainable by either physical examination or routine radiographs, tumor measurement will be obtained every three weeks prior to therpay. If CT or ultrasound imaging is required for tumor measurements, tumor measurements will be obtained every six weeks. Patients will remain on study until disease progression or evidence of significant toxicity.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/013 **Status:** On-going

Title: GOG 0090: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors

Start Date: 10/17/86 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: tumor:germ cell:ovary, cisplatin, etoposide, bleomycin, VAC, vincristine, dactinomycin, cyclophosphamide, BEP

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

Technical Approach: After adequate recovery from surgery (if done) previously untreated patients will be treated by three courses of BEP followed by three courses of VAC. Patients exhibiting disease progression on either phase will be taken off study. Patients who had previous VAC or similar regimens will be treated with four courses of BEP. After recovery from BEP therapy, reassessment laparotomy will be performed in patients with negative markers who are clinically free of disease. Progressing patients will be removed from the study. Patients with no evidence of disease at second look will be followed. Patients with persistent disease at second look will be removed from the study. An adequate trial is defined as receiving two courses of the drug and living at least six weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression of disease.

Progress: No patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/104 **Status:** On-going

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

Start Date: 08/21/87 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators:
COL William L. Benson, MC
COL Roger B. Lee, MC
COL Donald H. Kull, MC

Key Words: cancer:cervix, hysterectomy, lymphadenectomy, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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: Study is closed to patient entry on 18 Sep 1995. One patient was enrolled in FY 88 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 89/036 **Status:** On-going

Title: GOG 0093: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)

Start Date: 03/17/89 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian, chromic phosphate, laparotomy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$2416.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the role of intraperitoneal chromic phosphate (32P) suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy and to evaluate disease free survival, sites and frequency of relapse, and the morbidity from intraperitoneal 32P therapy.

Technical Approach: Patients with primary histologically confirmed epithelial carcinoma of the ovary who are in complete clinical remission, with no persistent or recurrent cancer, and initial FIGO Stage III will be eligible. Patients with distant metastatic disease, previous pelvic or abdominal radiation therapy, previous or concomitant malignancies other than of skin (excluding melanoma), and borderline malignancy of the ovary will be ineligible. Patients will be randomized to one or two regimens. Regimen I will consist of 15 millicuries of intraperitoneal chromic phosphate suspension therapy, preferably within 10 days (but no more than six weeks) after second-look laparotomy. Patients will be randomized before second-look laparotomy and a dialysis catheter will be inserted during second-look laparotomy in those patients randomized to receive 32P. Patients will be rotated every 10 minutes (left side to back to right side) for two hours to facilitate distribution of the 32P. Anterior and lateral scans of the abdominal cavity will be done to evaluate adequate distribution in the peritoneal cavity of the 32P and to confirm that loculation has not occurred. Data collection will continue until disease progression or death.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/028 **Status:** On-going

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

Start Date: 11/21/86 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: cancer:ovarian, cyclophosphamide, cisplatin, P32

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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. 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/m^2 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 protocol was closed to patient entry 14 Mar 94. Five patients have been entered and 1 remains in follow-up.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/091 **Status:** On-going

Title: GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

Start Date: 06/19/87 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: cancer:endometrial, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

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: Closed to patient entry on 3 July 1995. One patient was enrolled at MAMC during FY 95 and two patients were enrolled in previous years. All are being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 89/052 **Status:** On-going

Title: GOG 0108: Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #113891) with or without Cisplatin (NSC #119875) in Patients with Advanced or Recurrent Mixed Mesodermal Tumors of the Uterus

Start Date: 04/21/89 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: tumor:uterus, ifosfamide, cisplatin, uroprotector mesna

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: To determine: whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response; the duration of progression-free interval; and the length of survival as compared to doxorubicin alone.

Technical Approach: Patients will be randomized to either Regimen I or Regimen II. Regimen I: doxorubicin 60 mg/m^2 IV every three weeks to a maximum total dose of no greater than 500 mg/m^2. Regimen II: doxorubicin 60 mg/m^2 IV every three weeks plus cisplatin, 50 mg/m^2 IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m^2. Each regimen will require both dose escalation and dose reduction in accordance with adverse effects observed on the previous course of therapy. Patients who reach maximum doxorubicin dose will undergo a complete re-evaluation. All therapy will then be stopped and the patient followed on no further therapy until progression of disease is documented. Further therapy at that point will be at the discretion of the investigator. Patients on no further treatment will be followed every three months for the first two years, then every six months for three years, and annually thereafter.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/086 **Status:** On-going

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 ...

Start Date: 08/02/91 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix, 5-Fluorouracil, cisplatin, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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 was closed to patient entry 20 May 94. No patients were enrolled at MAMC during FY 96. The one patient enrolled in previous years is still in follow-up.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/064 **Status:** On-going

Title: GOG 0113: An Evaluation of Hydroxyurea, 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative ...

Start Date: 05/03/91 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix, hydroxyurea, 5-Fluorouracil, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the toxicity and feasibility of infusion 5-FU, cisplatin, and hydroxyurea, given concurrent with pelvic radiation therapy in patients with locally advanced cancer of the uterine cervix.

Technical Approach: Multiple studies have confirmed that the presence of metastases to para-aortic lymph nodes is a prognostic factor of greater significance than FIGO Stage. In addition, the pattern of failure in this group is vastly different, with one-half of the recurrences being outside the treated field. Because a major objective of this study is to evaluate local control and survival, this study will be open only to those patients with documented negative para-aortic nodes. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes. Radiation therapy will be given by external beam therapy followed by intracavitary therapy. Cisplatin will be given IV on days 1 and 29 of external radiation therapy; 5-FU will be given IV on days 2, 3, 4, 5, 30, 31, 32, and 33 of external radiation therapy; and hydroxyurea will be given PO four days each week during external radiation therapy. After therapy, patients will be followed every three months for two years and then every six months for three years for progression free interval and survival.

Progress: This study was closed to patient entry, 15 Oct 91. Two patients were enrolled in FY 92 and still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 91/074	**Status:** On-going

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, ...

Start Date: 07/12/91	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: tumor:ovarian stroma, chemo, bleomycin, etoposide, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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, granulosatheca 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: One patient was enrolled in this study in FY 95 and one patient was enrolled in FY 84. One is still being followed and the other was lost to follow-up.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/013 **Status:** On-going

Title: GOG 0116: Evaluation of Adjuvant VP-16 and Carboplatin Therapy in Totally Resected Ovarian Dysgerminoma

Start Date: 10/01/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, VP-16, carboplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the efficacy and toxicity of adjuvant VP-16 and carboplatin in patients with totally resected ovarian dysgerminoma.

Technical Approach: Patients who have had totally resected Stage Ib-III ovarian dysgerminoma will be eligible for this study. Those patients will undergo chemotherapy utilizing VP-16 10 mg/m^2 on days 1-3 carboplatin 400 mg/m^2 on day 1. After completion of the chemotherapy, patients will be evaluated in follow-up every two months for one year, every three months for the second year, then every four to six months thereafter for a total of five years. At the completion of the five year follow-up annual evaluations will then be performed. At the time of each follow-up, physical examination, liver function tests, and tumor markers of Beta-HCG and Alpha-fetoprotein will be obtained.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/061	**Status:** On-going

Title: GOG 0120: A Randomized Comparison of Hydroxyurea vs Hydroxyurea, 5-FU Infusion and Bolus Cisplatin vs Weekly Cisplatin as Adjunct to Radiation Therapy in Patients with Stages IIB, III, IVA Carcinoma

Start Date: 03/05/93	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix, hydroxyurea 5-FU, cisplatin, radiation therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1) To compare the relative efficacy of radiation sensitization of hydroxyurea alone or in combination with 5-Fluorouracil and Cisplatin versus Cisplatin alone in the treatment of Stages II-B through IV-A carcinoma of the cervix. 2) To determine the relative toxicities of these three different radiation sensitization schemes.

Technical Approach: Patients with locally advanced carcinoma of the cervix who have histologically confirmed negative para-aortic lymph nodes will be eligible for this study. Patients who consent will be randomized to three different treatment regimens. All treatment regimens will include the same radiation therapy technique given as standard therapy. Randomization will be between 1) Cisplatin 40 mg/m^2 IV q week X 6, (2) Cisplatin 50 mg/m^2 IV on days 1 & 29 with continuous infusion of 5-FU 1000 mg/m^2 on days 2 - 5 and 30 - 33 and hydroxyurea PO 2 mg/m^2 Mon/Thurs every week during radiation therapy (3) hydroxyurea PO 3 gm/m^2 Mon/Thurs every week during radiation therapy. Following therapy, patients will be monitored every 3 months for first 2 years and then every 6 months for the next 3 years.

To determine the efficacy of cisplatin, the principle parameters to be collected, analyzed and reported are: a) outcome variables (recurrence-free interval and survival) b) tumor characteristics c) host characteristics d) adverse effects (frequency and severity e) therapy administered.

Interim analyses will be conducted at approximately the 2nd, 3rd, 4th and 5th years using a global log-rank test. The goal will be to identify large differences in the recurrence free interval among the three treatment regimens. The interim log-rank test will be adjusted for important prognostic factors.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/014 **Status:** On-going

Title: GOG 0122: Whole Abdominal Radiotherapy Versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

Start Date: 10/01/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, radiotherapy, doxorubicin, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1) To compare the effectiveness of chemotherapy to whole abdominal radiation therapy in patients with advanced endometrial cancer which has been resected to less than 2 cm residual tumor. 2) To compare the relative toxicity of these two treatment strategies.

Technical Approach: Patients who have had surgical intervention for advanced (Stage III or IV) endometrial carcinoma confined to the abdominal cavity will be randomized either to whole abdominal radiation therapy or chemotherapy utilizing Doxorubicin at 60 mg/m^2 and Cisplatin at 50 mg/m^2 given every three weeks for eight cycles. After the completion of therapy patients will be seen and evaluated every three months for two years and six months thereafter for five years after treatment. Nationally 240 patients will be enrolled over 4 years. Patients will be evaluated for length of survival, disease-free survival and toxicity.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/063	**Status:** On-going

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

Start Date: 03/05/93	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix, radiation therapy, cisplatin, hysterectomy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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/m^2 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: One patient was enrolled in this study at MAMC in FY 96, and is in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/064 **Status:** Suspended

Title: GOG 0126C: A Phase II Evaluation of Altretamine (Hexamethylmelamine) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer

Start Date: 01/20/95 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovary, altretamine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the use of altretamine as second-line chemotherapy in patients resistant to platinum containing compounds and taxol.

Technical Approach: Patients with epithelial ovarian cancer refractory to platinum containing compounds and taxol will be eligible for participation in this study. Participants in this study will be treated with altretamine at a dose of 260 mg/m2 daily for 14 days. Treatment cycles will be repeated at 28 day intervals, providing serious side effects or tumor progression do not interfere. During the course of therapy weekly CBC's and liver function tests will be obtained. Should disease progression or severe side effects occur, therapy will be discontinued. Patients will be continued to be followed for life.

Progress: This protocol was suspended by GOG in August 1996 until data could be analyzed to determine if enough patients have been accrued. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/066	**Status:** Suspended

Title: GOG 0126D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer

Start Date: 02/16/96	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, plastinum resistnat, refractory, pyrazoloacridine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the safety and efficacy of Pyrazoloacridine in the treatment of platinum-resistant and refractory epithelial ovarian carcinoma.

Technical Approach: Patients with recurrent epithelial ovarian cancer who are resistant to platinum containing compounds will be eligible for this study. Subjects will be treated with Pyrazoloacridine, administered intravenously over three hours. Treatment cycles will be repeated every three weeks.
During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each course of treatment a history and physical examination will be performed and routine liver function test will be obtained. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination, however, if measured by CT, ultrasound or chest x-ray it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. If complete tumor resolution occurs treatment will continue at least three cycles, but may continue indefinitely at the discretion of the patient and investigator. Patients who develop febrile neutropenia or a granulocyte count less than 500 will have dose reductions as outlined in the protocol. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays may be supported with Granulocyte-Colony Stimulating Factor (G-CSF). Patients entered into this protocol will be followed for life.

Progress: This protocol was suspended in Feb 96 until data could be analyzed to determine if more subjects were needed. No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/115 **Status:** On-going

Title: GOG 0126E: Evaluation of Paclitaxel and SDZ PSC 833 (IND #41232) in Recurrent, Platinum Resistant and Refractory Ovarian Cancer

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, platinum resistant, refractory, paclitaxel, SDZ PSC 833

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the safety and efficacy of combined therapy with paclitaxel and the experimental drug SDZ PSC 833.

Technical Approach: This study will assess the relative effectiveness of SDZ PSC 833 in overcoming drug resistance to paclitaxel in patients with advanced ovarian cancer recalcitrant to standard chemotherapy. Patients with measurable, histologically proven recurrent ovarian cancer are eligible for this study. Participants in this study will be treated with SDZ PSC 833 at 5 mg/kg orally 3 times a day for 12 doses. Doses will be given no closer than 5 hours apart on consecutive days beginning day one of each cycle. Cycles will be repeated every three weeks. On day two, patients will receive paclitaxel at 70 mg/m_2 intravenously over a three hour infusion time. Patients will be treated until disease progression or adverse effect prohibit further therapy. During the course of therapy routine laboratory and radiologic investigations will be obtained.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/071	**Status:** Completed
Title: GOG 0127F: Evaluation of Topotecan (NSC #609699) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix		
Start Date: 01/20/95	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: Cancer:cervix, topotecan		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the safety and efficacy of Topotecan in the treatment of patients with recurrent or metastatic squamous cell carcinoma unresponsive to traditional therapy.

Technical Approach: Approximately two patients with metastatic or recurrent squamous cell carcinoma which have failed traditional therapy are eligible for this protocol. Generally since the GOG has protocols open for the treatment of chemotherapy naive patients, most patients entered into this study will have received previous chemotherapy as well as therapy directed at their primary tumor. Patients entered into this protocol will receive a daily infusion of topotecan administered intravenously for five consecutive days. The administration of the topotecan is delivered over 30 minutes. Toxicity will be monitored and patients continued on study until any cancer progression is noted or severe toxicity limits further treatment. During the course of chemotherapy cycle dosing will be adjusted based on toxicity criteria. If the white blood cell toxicity is the primary toxicity, the initial adjustment would be for a dose reduction. However, if continued dose adjustments are required or febrile neutropenia occurs, G-CSF will be administered. The G-CSF will be administered the day after the Topotecan is finished and continued until day 18 or until the white blood cell count recovers. The principal parameters employed to evaluate the efficacy of each agent are: frequency and duration of objective response, frequency and severity of observed adverse effects, survival time, duration of progression-free interval.

Progress: This study was closed to patient entry on 13 Apr 1995 to review data collection. The study was later reopened and then closed again to patient entry on 29 Apr 96. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/171 **Status:** On-going

Title: GOG 0127H: Evaluation of Prolonged Oral Etoposide (VP-16) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix

Start Date: 07/21/95 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:cervix, squamous cell, etoposide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 07/19/96

Study Objectives: To evaluate the safety and efficacy of prolonged oral VP-16 in the treatment of recurrent or metastatic squamous cell carcinoma of the cervix.

Technical Approach: Patients with historically proven or metastatic squamous cell carcinoma of the cervix will be treated with oral VP-16 for 21 consecutive days out of a 28 day cycle. Treatment will be reviewed on day 29 after a one week break. Patients who have received previous radiation therapy will be started at a lower dose initially. Dose modification with either dose reduction or dose intensification is possible depending on marrow rescue. Clinical management, including physical examination and chest x-ray will be obtained prior to each cycle. If additional imaging studies, such as CT ultrasound or MR are required, tumor measurements will be repeated after every other cycle. Treatment will be discontinued should severe toxicity or tumor progression result. There are no treatment comparisons involved and no known historical controls available. The study design will be primarily based on prior GOG experience in this disease entity. This will insure consistency in evaluation of response. therapy plans demonstrating activity will later be compared and investigated in ensuing phase III studies.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/102 **Status:** On-going

Title: GOG 0128B: Evaluation of Paclitaxel (Taxol) in Persistent or Recurrent Non-Squamous Cell Carcinoma of the Cervix and Vagina

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:cervix, Cancer:vagina, paclitaxel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate efficacy of Paclitaxel (Taxol) in the treatment of patients wil persistent or recurrent non-squamous cell carcinoma of the cervix or vagina.

Technical Approach: Patients with incurable recurrent or persistent non-squamous cell carcinoma of the cervix and vagina are eligible to participate in this study. All patients will receive a 24 hour infusion of Paclitaxel at 170 mg/m^2 everry three weeks. Patients who have received previous radiation therapy to the pelvis will be treated at a dose of 135 mg/m^2 every three weeks. Routine weekly CBCs will be obtained to monitor for significant neutropenia. Should significant neutropenia develop resulting in fever or prolonged neutropenia, dose reduction will occur. If a dose of 110 mg/m^2 still results in significant neutropenia, granulocyte colony stimulating factor (G-CSF) will be used. On subsequent treatment cycles, 5 microgram/kg will be administered subcutaneously starting 24 hours after therapy and continuing until absolute granulocyte count is sufficient. Patients will continue to receive Taxol every three weeks until tumor progression occurs or severe side effects prevent further therapy. Tumor measurements will be obtained prior to every cycle if detectable on physical examination. Measurements determined by x-rays or imaging studies will be obtained every 6 weeks.

Progress: This study was closed to enrollment in Dec 94 to review data collection. It was reactivated in May 95. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/068 **Status:** On-going

Title: GOG 0129E: Evaluation of Dactinomycin (Cosmegen) in the Treatment of Recurrent or Persistent Endometrial Carcinoma

Start Date: 02/16/96 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, dactinomycin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To determine if the Dactinomycin has significant activity with an acceptable level of toxicity in patients with advanced or recurrent endometrial carcinoma who have failed standard therapy.

Technical Approach: This study will assess the relative efficacy as well as toxicity of intravenous Dactinomycin in patients with histologically documented recurrent or advanced endometrial carcinoma with clinically measurable disease who have failed standard therapy and are not curable by surgery or radiation therapy. Dactinomycin will be given intravenously over 15 minutes every four weeks. Treatment will continue until disease progression or significant toxicity precludes further therapy. In the absence of severe toxicity or tumor progression, the patient may remain on therapy indefinitely at the discretion of the investigator.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/027	**Status:** On-going

Title: GOG 0130B, Evaluation of Paclitaxel (Taxol) in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus.

Start Date: 11/18/94	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Mesodermal Tumors of the Uterus

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: To evaluate the efficacy of taxol in the treatment of mixed medsodermal tumors of the uterus.

Technical Approach: Patients with recurrent mixed mesodermal tumors of the uterus sho have failed previous therapy are eligible to particpate in this study. All patients enterd in this study must have clinicaly or radiolicaly measureable tumors. Pateints willbe treated with a 24 hour infusion of paclitaxel at 170 mg/m^2 intravenously. This therapy will be repeated every three weeks until the tumor progresses, side effects intervene, or the patient elects to withdraw from therapy. If the tumor is measureable by physical examination, tumor measurements will be obtained prior to each course of chemotherapy. If, however, radiological investigations are required for determining tumor size, imaging will be performed every 6 weeks. All patinets will be treated wntil disease progression or severe side effects limit subsequent therapy. Annual accrual of approximately 15 partients is expected and approximately 40 are needed for the study.

Progress: This study was closed to patient entry in Feb 96 to review the data. It was reactivated in May 96. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/062	**Status:** On-going

Title: GOG 0131B: Evaluation of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus

Start Date: 02/04/94	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:uterus, leiomyosarcoma, etoposide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To determine if the utilization of semi-continuous low dose oral etoposide has significant activity with an acceptable level of toxicity in patients with advanced or recurrent Leiomysosarcoma of the uterus who have failed standard therpy.

Technical Approach: Patients with histologically confirmed recurrent or metastatic leiomyosarcoma that have failed local therapeutic measures and have adequeate bone marrow, renal, and hepatic function will be invited to participate in this study. Etosposide (VP-16) will be administered at a dosage of 50 mng/m^2/day, day 1-21 every 4 weeks. If side effects are not severe, a patient may remain on the study agent indefinately at the investigator's discretion. Likewise, patients with evidence of progressive disease or those with significant side effects or deterioration of performance status may be removed from study at the investigator's discretion. All patients will be followed until death.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/023	**Status:** Completed
Title: GOG 0132: A Phase III Randomized Study of Cisplatin versus Taxol versus Taxol and Cisplatin in Patients with Suboptimal Stage III and IV Epithelial Ovarian Carcinoma		
Start Date: 11/06/92	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: cancer:ovarian, taxol, cisplatin		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To compare the efficacy of Cisplatin and Taxol alone and together in the treatment of advanced suboptimal Stages III or IV epithelian ovarian carcinoma and to determine which of the three regimens contributes most favorably to progression-free interval and survival.

Technical Approach: Patients with suboptimal Stages III or IV epithelial ovarian carcinoma will be randomized into one of three treatment regimens. Regimen I will be Cisplatin only, Regimen II Taxol only and Regimen III taxol plus Cisplatin. Patients will receive the chemotherapeutic regimen assigned at 21 day intervals for six cycles. Patients with clinical evidence of disease are strongly encouraged to undergo a second look laparotomy to assess response to treatment. Additionally patients will be followed for disease and survival.

The median time to progression for these women treated with a cisplatin-based regimen is 10.4 and 14.4 months with measurable disease and non-measurable disease respectively. The median time to death is 18.5 and 22.5 months respectively. The expected response rate in those women with measurable disease is 60%.

If one of these treatment regimens can increase the median time to progression by 40% (28.6% decrease in the relative failure rate), then this is considered clinically significant. A 30-month accrual period (600 patients) with an additional 12-month follow-up period will provide an 82.5% chance of detecting that one of these regimens provides this magnitude of treatment effect while limiting the type I error to 0.05. The null hypothesis being: the failure rates in each of the three treatment arms are equal.

There is an 80% chance of rejecting the null hypothesis significance if one of these regimens increases the frequency of clinical response by 19% (i.e. 60% to 79%) while limiting the type I error to 0.05.

Progress: This study was closed to patient entry May 94. Study was revised and reopened on 3 Jan 95. The study was closed permanently in Feb 96. No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/139 **Status:** Terminated

Title: GOG 0137: A Randomized Trial of Estrogen Replacement Therapy Versus No Estrogen Replacement in Women With Stage I or II Endometrial Adenocarcinoma

Start Date: 06/09/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:endometrial, estarogen replacement

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To determine if the use of estrogen replacement therapy significantly increased the risk of developing recurrence of endometrial cancer after primary treatment.

Technical Approach: Patients entered into this study will be have endometrial cancer without evidence of metastatic disease beyond the uterus or cervix. Some patients will have been simultaneously entered into a protocol randomizing them to receive radiation or no radiation. Other patients will have received treatment with or without radiation as recommended by their primary physician and/or choice. Patients who are randomized to estrogen replacement therapy will be taking estrogen on a daily basis for the duration of the study. Starting @ .625 mg per day and increasing to a maximum of 1.25 mg per day as needed for hot flashes. Patients who do not receive estrogen replacement therapy will have blood samples obtained every 3 - 6 months for serum estradiol levels to insure the exclusion of an external source of estrogen. All patients will receive yearly mammograms. All other follow up is in a standard fashion.

Progress: This study was terminated by GOG prior to final approval at MAMC. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/087 **Status:** On-going

Title: GOG 0139: A Randomized Study of Doxorubicin Plus Cisplatin versus Circadian-Timed Doxorubicin Plus Cisplatin in Patients with Primary Stages III and IV, Recurrent Endometrial Adenocarcinoma

Start Date: 04/02/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, doxorubicin, cisplatin, ciracadian timed doxorubicin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objective: 1. To evaluate the potential benefit of the administration of Circadian-timed, chemotherapy versus standard administration of chemotherapy utilizing Doxorubicin and Cisplatin. 2. To evaluate the relative toxicities of these two techniques of administration.

Technical Approach: This study will assess the relative benefit either in improved response rate or decreased toxicity by changing the method of delivery of the chemotherapeutic agents from an arbitrarily administered event to a timed delivery method. Patients will be randomized to receive either standard Doxorubicin/Cisplatin infusions given at a dose of Doxorubicin 60 mg per meter squared, IV Push followed by Cisplatin 60 mg per meter squared over 30 minutes immediately following the Doxorubicin in one treatment regimen as opposed to Doxorubicin at the same dose given IV Push over 30 minutes at 6 a.m. with the Cisplatin at 60 mg per meter squared delivered over 30 minutes at 6 p.m. Both chemotherapeutic regimen would be delivered every 3 weeks for a maximum of eight treatments. Dose reduction would occur initially because of advanced age or previous pelvic radiation therapy. Only patients with advanced or recurrent measurable Adenocarcinoma, Adenoacantheoma, Adenosquamous carcinomas, whose potential for cure by radiation therapy or surgery, alone or in combination is very poor. Prior to each cycle of chemotherapy, patients will be evaluated by history, physical examination, and the usual radiologic test required for monitoring tumor response. The treatment will continue for a maximum of eight treatments or until the tumor progresses.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/140 **Status:** Completed

Title: GOG 0140: An Assessment of Age and Other Factors Influencing Protocol Versus Alternative Treatments for Patients With Epithelial Ovarian Cancer Referred to Gynecologic Oncology Group Institutions

Start Date: 06/09/93 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer: ovarian, protocol enrollment

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the reasons for inclusion or exclusion from GOG protocol studies.

Technical Approach: All patients with epithelial ovarian carcinoma, including borderline tumors who are primarily evaluated at MAMC will be eligible for participation in this study. All patients who have signed an informed consent will then have a questionnaire filled out regarding the relevant clinical material as well as selected underlying medical conditions; age, education, race, martial status, gravida and parity. Reasons for exclusion, either medical or other will be listed. Type of initial surgery performed, location of the surgery and types of subsequent therapy will also be entered on this questionnaire. After the completion of this study, which will include 800 subjects nationally, a GOG statistical office will analyze the data. Follow up of these patients is not a requirement of this study.

Progress: This study was closed to patient entry, 5 Feb 96. No patients entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/149	**Status:** Suspended
Title: GOG 0143: Familial and Reproductive Factors in Ovarian Cancer		
Start Date: 08/06/93	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: cancer: ovarian, familial factors, reproductive factors		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1. To further define the epidemiologic pattern of patients with invasive ovarian carcinoma. 2. To store genetic material for comparison should a genetic marker be identified in the future utilizing risk factors for the development of ovarian cancer to target a patient population suitable for screening.

Technical Approach: Patients identified with invasive ovarian carcinoma will be asked to complete a questionnaire. Additionally, two tubes of blood will be obtained and forwarded for storage, for potential DNA analysis. This is an epidemiologic study and requires no follow-up of the patients.

Progress: No patients entered this study at MAMC. Protocol was suspended July 1994, awaiting further instructions from GOG.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/140 **Status:** On-going

Title: GOG 0145: A Randomized Study of Surgery vs Surgery + Vulvar Radiation in the Management of Poor Prognosis Primary Vulvar Cancer and of Radiation vs Radiation & Chemotherapy for Positive Inguinal Node

Start Date: 08/05/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:vulvar, positive inguinal nodes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1. To determine whether he additional radiation therapy to the area of vulvar resection decreases the risk of recurrent cancer in high risk patients. 2. Whether the addition of chemotherapy along with radiation improves the effect of radiation therapy in decreasing the risk of tumor recurrence in the areas treated by radiation therapy. 3. To evaluate the impact of these therapeutic interventions on the overall quality of life both during and subsequent to treatment. 4. To determine if HPV status alters the risk of local recurrence and/or survival.

Technical Approach: Patients with invasive squamous cell carcinoma of the vulva who meet the eligibility criteria will have initial surgery on the vulva and groins. After pathological examination of the specimen, patients will be eligible for randomization to observation or to additional therapy to the vulva. Patients with positive nodes will be randomized to receive radiation alone or radiation and chemotherapy to the inguinal and pelvic nodes. Patient treated with chemotherapy will receive Cisplatin day one, followed by four days of continuous infusion of 5 FU. In addition, patients will complete quality of life questionnaires prior to receiving radiation or chemotherapy, then at three, six, twelve, eighteen, and twenty-four months. All patients will be followed in the OB-GYN Oncology Clinic subsequent to treatment. Initial frequency of follow-up will be at three month intervals for one year, followed by four month intervals for one additional year and then every six months for an additional three years. The patient's disease status will be correlated with the presence or absence of HPV in the tumor and surrounding tissue.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/090	**Status:** On-going
Title: GOG 0146C: Evaluation of Topotecan (SKF 104864-A) (NSC#609699) in Recurrent, Platinum, Sensitive Ovarian Cancer		
Start Date: 03/17/95	**Est. Completion Date:** Indefinite	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: Cancer:ovarian, Topotecan, Platinum-Sensitive		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the safety and efficacy of Topotecan in the treatment of platinum-sensitive epithelial ovarian carcinoma.

Approach: Patients with recurrent epithelial ovarian cancer who have previously responded in a favorable fashion to platinum containing compounds will be eligible for this study. Patients who choose to participate will be treated with Topotecan, administered intravenously over thirty minutes daily for five consecutive days. Treatment cycles will be repeated every three weeks from the first day of chemotherapy. During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each course of treatment a history and physical examination will be preformed and routine liver function test (i.e., PT and PTT) will be obtained. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination or routine chest radiography, however, if measured by CT or ultrasound it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays will be supported with Granulocyte-Colony Stimulating Factor (G-CSF) at 5 mcg/kg/day subcutaneously. G-CSF support-will be administered the day after the last dose of Topotecan and continued through day 18 or until hematopoietic recovery. No G-CSF will be administered when the white blood cell count is greater than or equal to 15,000/mcL. Patients entered into this protocol will be followed for life.

Progress: This study was closed to patient entry, 16 Feb 96, to review the data. It was reactivated, 21 Apr 96. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/065 **Status:** Suspended

Title: GOG 0146D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Sensitive Ovarian Cancer

Start Date: 02/16/96 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, platinum-sensitive, pyrazoloacridine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the safety and efficacy of Pyrazoloacridine in the treatment of platinum-sensitive epithelial ovarian carcinoma.

Technical Approach: Patients with recurrent epithelial ovarian cancer who have previously responded in a favorable fashion to platinum containing compounds will be eligible for this study. Subjects will be treated with Pyrazoloacridine, administered intravenously over three hours. Treatment cycles will be repeated every three weeks.

During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each treatment, a history, physical examination and routine liver function test will be performed. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination, however, if measured by CT, ultrasound or chest x-ray it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. If complete tumor resolution occurs treatment will continue at least three cycles, but may continue indefinitely at the discretion of the patient and investigator. Patients who develop febrile neutropenia or a granulocyte count less than 500 will have dose reductions as outlined in the protocol. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays may be supported with Granulocyte-Colony Stimulating Factor (G-CSF). Patients entered into this protocol will be followed for life.

Progress: This study was suspended, 4 Jun 96, to review the data. No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/094	**Status:** On-going

Title: GOG 0148: The Clinical Utility of Soluable TNF/LT Membrane Receptors in the Serum of Patients With All Stages of Primary Epithelial Ovarian Cancer

Start Date: 04/01/94	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, membrane receptors, tumor necrosis factor, lymphotoxin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To evaluate the clinical utility of TNF/LT membrance receptor levels in the serum of patients with epithelial ovarian cancers as both a screening test and marker of therapeutic effect.

Technical Approach: This investigaton will follow serum TNF/LT membrane receptors in the serum of patients who are undergoing treatment for primary epithelial ovarian cancer under other GOG protocols. Serum will be obtained prior to the first cycle of chemotherapy and then every other cycle thereafter. After the completion of chemotherapy, serum will be obtained every six months for two additional years. In the event that recurrent disease is suspected, serum will be obtained for investigation. The serum samples will be obtained at the time of routine laboratory studies utilized in the monitoring of ovarian cancer patients. No additional phlebotomy is therefore required.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/061 **Status:** On-going

Title: GOG 0150: A Phase III Randomized Study of Acclerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) vs Combination Ifosfamide-Mesna With Cisplatin ... Carcinosarcoma (CS) of the Uterus

Start Date: 02/04/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:uterine, ifosfamide, mesna, cisplatin, abdominal radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: To compasre the use of combination Ifosfamide with Mesna and Cisplatin to hyperfractionated whole abdomen radiation therapy with regard to tolerance and efficacy in patients with carcinosarcomas of the uterus.

Technical Approach: Patients entering this study will have undergone surgical staging, TAH/BSO, and resection of gross intra-abdominal/pelvic disease. They will then be randomized to receive either radiation therapy (given as a hyperfractionated technique) or chemotherapy (utilizing ifosfamide with mesna and cisplatin). The chemotherapy will be administered over a four day period, at three week intervals. Ratients treated with radiation therapy will receive twice a day treatments of 3000 cGy to the whole abdomen with a boost to the pelvis to 5000 cGy. Subsequent to therapy, patients will be seen in the clinic at three month intervals for two years and then six month intervals for the remainder of their follow-up, until completion of their analysis. Routine blood work evaluating renal and hepatic status will be obtained throughout therapy and in post-treatment follow-up.

Progress: One patient was enrolled in this study in FY 96. She is in the follow-up phase. No adverse events reported.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/150 **Status:** On-going

Title: GOG 0152: A Phase III Randomized Study of Cisplatin & Taxol (Paclitaxel) With Interval Secondary Cytoreduction vs Cisplatin and Paclitaxel in Patients with Suboptimal Stage III & V....ovarian carcinom

Start Date: 07/01/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, cisplatin paclitaxel, cytoreduction

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$23500.00	**Periodic Review:** 02/16/96

Study Objective: To determine the impact of interval cytoreductive surgery on the progression free interval, survival and quality of life of patients with subnoptimal debulked Stage III & IV epithelial ovarian cancer.

Technical Approach: All patients will have undergone maximal cytoreductive surgery for their cancer prior to entrance into the study. Subsequently, all patients will receive three treatments at three week intervals of Paclitaxel and Cisplatin by intravenous infusion. After three treatment cycles, patients will be re-evaluated to determine tumor response. Patients with stable disease or tumor response will then be randomized to secondary cytoreductive surgery followed by or three more courses of chemotherapy. Those receiving secondary cytoreductive surgery will receive three more couses of chemotherapy after surgery. Quality of life questionnaire will be completed at intervals during and after therapy.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/149 **Status:** Completed

Title: GOG 0153: A Phase II Study of Recurrent and "Advanced Endometrial Adenocarcinoma Treated With Alternating Courses of Megestrol Acetate (Megace) and Tamoxifen Citrate (Nolvadex)

Start Date: 07/01/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, adenocarcinoma, megestrol acetate, tamoxifen

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the potential up-regulating of progesterone receptors by Tamoxifen to enhance progesterone induced cell kill initiated by Megace therapy for recurrent or advanced endometrial carcinoma.

Technical Approach: Patients eligible for this study will be given megestrol acetate 160 mg/day x 3 weeks followed by tamoxifen citrate 40 mg/day for the next three weeks. This alternate sequence will continue until there is evidence of disease progression or grade 3 or 4 toxicity occurs. Patients will have a physical examination tynir measurements, documentation of major symptoms at six week intervals and HGB, HCT, CBC, Diff, and platelets will be determined every 3 months.

Progress: This study was closed to patient enrollment, 17 Nov 95. No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/028	**Status:** On-going

Title: GOG 0154: Human Immunodeficiency Virus (HIV) Testing in Patients with Invasive Cervical Carcinoma.

Start Date: 11/18/94	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cervical Carcinoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objectives: To determine the frequenxcy of HIV infection in patinets with all stafgew of epithelial cervical carcinoma. To evaluate the impact of HIV infection on the treatment and disease course in patients with cervical carcinoma.

Technical Approach: All patients who have invasive epithelial cervical cancers and who are less than 50 years of age will be eligible for participation. A list of total patients offered the protocol will be maintained without identifying factors along with those sho agree to participate. Patients who agree will be counseled regarding the risks of HIV infection and will vcomplete a questionnaire regarding additional risk factors.All patients who are HIV positive will continue to be followed in this study. They will be followed at six month intervals for one year, then yealry thereafter for he purposes of this study. A clinical summary form will be sumitted at the completion of each visit. The GOG statistical Office will attempt match HIV positive patients wil HIV negative patienrts based on age, tumor grade, stage and other potential confounding factors. Patients in both catagories will be followed for disease progression or the development of secondary tumors as well as the occurance of treatment reltaed toxicity.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/029 **Status:** On-going

Title: GOG 0155, Evaluation of Alpha-Interferon and Isotretinoin With or Without Zidovudine (AZT) in the Treatment of HIV-Infected Women with Invasive Cervical Carcinoma.

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cervical Cancer

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objectives: To evaluate the anti-tumor affect and toxicity and toxicity profile of combination isotretinon and alpha-interferon in HIV positive patients with cervical carcinoma.

Technical Approach: Patients with Bulky stage I and stages II-IV cervical cancer who are HIV positive are eligible for participation. Upon agreeing to participate, further treatment will be determined by the CD4 count. For patients with CD4 counts less than 500, treatment with daily interferon at 6 million units subcutaneously, daily isotretinoin at 1 mg/kg/d orally, and zidovudine (AZT) 100 mg five times per day orally will be initiated. At the end of a four week course, the patients will be re-evaluated. If significant progression of disease, as defined by greater than a 50% increase in tumor volume or the appearance of new lesions, patients will be discontinued for therapy and undergo standard oncologic therapy directed at their cervical cancer. Patients with CD4 counts greater than or equal to 500 will be treated similarly except they will not receive the zidovudine. Weekly CBC's, biweekly liver function tests and lipid profiles will be obtained. At four week intervals, CD4 counts and creatinine levels will also be obtained. After twelve weeks, patients will be evaluated for subsequent tumor-directed therapy. Patients will be followed at three month intervals for 2 1/2 years, at six month intervals for an additional three years and then every year.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/095	**Status:** On-going

Title: GOG 0156: Randomized Trial of Pelvic Radiation versus Doxorubicin Plus Cisplatin in Stage IB, Stage IC, IIA, and IIB EnDometrial Carcinoma

Start Date: 04/21/95	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, radiation, doxorubicin, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: Obiective: To compare radiation therapy versus chemotherapy in an adjuvant setting for high risk, early stage endometrial cancer.

Technical Approach: Patients with high risk Stage IB, IC, IIA, or IIB endometrial cancer is defined in the patient eligibility Section 3.13, page 4 of the protocol will be randomized to receive either post operative radiation therapy or post operative chemotherapy. Radiation therapy will be given in standard pelvic fields to a total dose of 5040 cGy. Patients who are randomized to receive chemotherapy will receive Doxorubicin and Cisplatin therapy given at a dose of 60 mg/m2 and 50 mg/m2 respectively. Chemotherapy will be given at three week intervals for a total of six treatment cycles. While receiving therapy, patients randomized to radiation therapy will have weekly CBCs drawn and patients randomized to chemotherapy will have CBCs, liver function test, and creatine obtained immediately prior to the next cycle of chemotherapy. Subsequent to treatment, all patients will be followed at three to four month intervals for two years. Standard follow-up in the Gyn Oncology Clinic involves six month follow-up thereafter until five years from treatment. However, the protocol requires a less liberal follow-up of yearly evaluations after the two year anniversary date of therapy. Patients will be followed for evidence of progressive disease and survival.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/096 **Status:** On-going

Title: GOG 0157: A Randomized Phase III Trial of Carboplatin (AUG 7.5) and Paclitaxel 175 mg/m2 q 21 Days x 3 Courses versus the Same Regimen x 6 Courses in Patients With Selected Stage IC and II (A,B,C)...

Start Date: 04/21/95 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, carboplatin, paclitaxel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1. To evaluate the role of Taxol in the treatment of early stage high risk epithelial ovarian cancers. 2. To determine the optimal number of treatment cycles for the treatment of high risk early stage epithelial ovarian cancer.

Technical Approach: Patients entered into this study will be treated with intravenous Carboplatin at an area under the curve of 7.5. Taxol at 175 mg/m2 will also be administered. Treatments will be provided intravenously at three week intervals. During the course of chemotherapy, weekly CBCs will be obtained to evaluate toxicity. Prior to each treatment cycle, a history and physical examination will be performed as well as creatine, CA-125 and urinalysis. Other investigative tests will be ordered as needed only. Patients will be randomized prior to the initiation of therapy to receive three or six cycles of chemotherapy. Dose reduction or the addition of G-CSF to reduce myelosuppressive side effects are outlined in the protocol. The primary modality to reduce toxicity will be dose reduction followed by the administration of G-CSF for repeated episodes or for febrile neutropenia. After the completion of therapy, patients will be followed in the GYN Oncology clinic on a monthly basis for six months and then every three months for four follow-up visits. Thereafter, they will be followed on a yearly basis for life.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/072	**Status:** On-going

Title: GOG 0158: A Phase III Randomized Study of A Platinum Compound and Paclitaxel in Optimal Stage III Epithelial Ovarian Carcinoma: Cisplatin vs Carboplatin and 3-Hour vs 96-Hour Infusions of Paclitaxel

Start Date: 01/20/95	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovary, cisplatin, carboplatin, paclitaxel, G-CSF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$56222.00	**Periodic Review:** 02/16/96

Study Objective: To compare the relative efficacy and toxicity of two different platinum compounds when utilized with taxol in two different infusions schemes for the treatment of patients with optimally debulked epithelial ovarian cancer.

Technical Approach: Patients with optimally debulked Stage III epithelial ovarian cancer who agree to participate in this study will be randomized to four different treatment regimens. The treatment reginmens will have two different variables (platinum compound selected - cisplatin or carboplatin and duration of infusion - 3 hours or 96 hours). All patients will be treated at three week intervals. Treatment will consist of six treatments followed by a second-look (reassessment laparotomy). Patients with progressive disease or obviously elevated CA-125's (> 100) will not be required to undergo a second-look laparotomy. After the completion of reassessment laparotomy, patients will be followed at monthly intervals for six months followed by three month intervals for additional 36 months and then every six months thereafter. Physical examinations and CA-125s will be obtained during follow-up.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/067 **Status:** On-going

Title: GOG 0159: A Phase II Study of Goserelin Acetate (Zoladex) in Recurrent or Persistent Endometrial Cancer

Start Date: 02/16/96 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:endometrial, Zoladex

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To evaluate the effectiveness of the gonadotropin releasing hormone analogue Goserelin Acetate in treating patients with recurrent or persistent Endometrial Cancer.

Technical Approach: This study will assess the relative effectiveness of monthly Goserelin Acetate in the treatment of patients with recurrent or persistent endometrial cancer. Patients must have measurable disease with two dimensional measurements of at least 1 cm in each direction if measured by physical examination or chest x-ray, or 2 X 2 cm if measured by other radiologic assessments. Base line observation in tests will be obtained prior to therapy. After initiation of Goserelin Acetate at 3.6 mg subcutaneously every four weeks, follow up physical examination and laboratory evaluation will be obtained as outlined in the protocol. Therapy will continue at least two courses unless there is rapidly progressive disease, and for at least 12 courses if there is no change in disease and if tolerable toxicity is present (Grade 1 and 2). Patients who achieve complete remission will continue on therapy indefinitely. All other patients will continue until progression of disease or if the disease is stable at the discretion of the study chairman. Patients who develop thromboembolic disease will be removed from the study.

Progress: . No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/114	**Status:** On-going

Title: GOG 0162: A Phase III Randomized Trial of Cisplatin with Paclitaxel Administered by Either 24 Hour Infusion or 96 Hour Infusion in Patients with Selected Stage III & Stage IV Epithelial Ovarian Cancer

Start Date: 05/17/96	**Est. Completion Date:** Indefinite
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:ovarian, epithelial, cisplatin, paclitaxel, 24 vs 96 hr infusion

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: To compare the safety and efficacy of 24-hour infusion versus a 96-hour infusion of paclitaxel in the treatment of advanced ovarian cancer. To correlate pharmacokinetics of paclitaxel with clinical outcome.

Technical Approach: This study will assess the relative safety and efficacy of 24-hour versus 96-hour infusion times for the administration of paclitaxel in the treatment of ovarian cancer. Patients with selected Stage III ovarian cancer who are not eligible for other GOG studies may participate in this study. Patients are randomized to receive either of the two study treatments. The 96-hour infusion may be administered as an inpatient or as an outpatient utilizing a standard chemotherapy pump. All patient will receive the administration of paclitaxel followed by cisplatin. Treatment will be administered at three week intervals form the beginning of the previous cycle for a total of six cycles. Grade IV myelosuppression will be modified by dose reduction. GCSF may be utilized for acute febrile episodes. In the event of persistent Grade IV myelosuppression, patients will be removed from the study. Patients with measurable disease will be followed with CT-scans after every other cycle. All patients will have a pre-chemotherapy CT as well as a CT-scan at the completion of therapy. CA-1125 levels will also be followed at regular intervals. Subsequent to treatment, patients will be followed at three month intervals for at least the first year for study and points as well as standard follow-up for ovarian cancer patients. Correlation between pharmacokinetics and clinical outcomes will be made at the conclusion of the study. All patients will receive four samples for pharmacologic studies.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/030 **Status:** On-going

Title: GOG 9303, Cisplatin-DNA Adducts in Ovarian Cancer as a Predictor of Response to Platinum-based Chemotherapy.

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Ovarian Cancer

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objectives: To determine if the level of Platinum-DNA adducts predict responsiveness to the chemotherapeutic regimen of Taxol-Cisplatin in advanced ovarian cancer.

Technical Approach: This investigation is a companion protocol to GOG 152, which investigates the utilization of interval cytoreduction in patients treated with cisplatin and taxol for bulky advanced ovarian cancer. Only patients who are entered in to protocol GOG 152 are eligible for participation in this protocol. Consequently, there are no additional risks for surgery or chemotherapy from participation in this protocol. Subjects will have 40-50 cc of blood drawn 24 hours after administration of the first dose of cisplatin. No additional blood or tissue samples will be obtained. All information regarding tumor response and patient survival will already be provided and available as per protocol 152. The blood levels of DNA products will be analyzed with regard to the response to chemotherapy and overall patient survival.

Progress: No patients have been enrolled at MAMC.

DETAIL SHEETS FOR PROTOCOLS

NATIONAL SURGICAL ADJUVANT BREAST & BOWEL PROJECT

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/147 **Status:** On-going

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

Start Date: 08/06/93 **Est. Completion Date:** Indefinite

Department: NSABP **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: cancer:rectum, 5-FU, leucovorin, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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/m^2 by IV infusion and FU 500 mg/m^2 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/m^2/day and LV 20 mg/m^2/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: No patients have yet been enrolled.

DETAIL SHEETS FOR PROTOCOLS

PEDIATRIC ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/145 **Status:** On-going

Title: POG 0942: A Study of Minimally Invasive Surgery of the Chest in Children with Solid Tumors, A Phase III Intergroup Study

Start Date: 07/19/96 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
MAJ Randall M. Holland, MC

Key Words: Cancer:solid tumors, pediatric, surgery

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To compare the morbidity and mortality rates of open surgical procedures with that of MIS; 2) to compare MIS with conventional surgery in obtaining adequate pathologic material for diagnostic and special biological studies; 3) to compare MIS with conventional open surgery in the assessment of tumor resectability; 4) to assess the impact of MIS and open surgery on short-term quality of life (QOL). Several domains of QOL will be examined including surgery-related pain, physical, social and emotional functioning, and global ratings of health and overall QOL; 5) to compare post-procedure recovery time of MIS with conventional surgical techniques in children with cancer; 6) to evaluate and compare post-procedure pain in MIS with conventional surgical techniques; 7) to compare MIS with standard open surgical techniques in regards to the economic costs; and 8) to provide pilot data on a new instrument for assessing QOL in a pediatric population.

Technical Approach: This study proposes to determine the role of MIS in the management of pediatric cancer. This Phase III randomized study will test whether MIS is as efficacious as standard open surgical operations for the diagnosis and assessment of resectability of pediatric solid tumors, and whether MIS improves recovery and convalescence in addition to decreasing the cost of care for children with cancer. Eligible patients are those who require surgical intervention for diagnosis and staging, evaluation for disease progression or response to therapy, or for supportive or medical management issues during the course of cancer treatment.

Progress: No patients were enrolled in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 93/141	**Status:** On-going
Title: POG 8650: Intergroup National Wilms' Tumor Study - 4		
Start Date: 06/09/93	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: cancer:pediatric, Wilms'		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/21/95

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 was closed to patient entry, 1 Sep 94. One patient enrolled at MAMC in FY93 is being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/052	**Status:** On-going
Title: POG 8930: A Comprehensive Genetic Analysis of Brain Tumors		
Start Date: 12/16/94	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:brain, genetics		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To determine prospectively the clinical significance of abnormalities of cellular DNA content, as measured by flow cytometry in pediatric brain tumors. 2) To determine the clinical implications of cytogenetic abnormalities found in pediatric brain tumors at diagnosis. 3) To determine the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively-acting loci in DNA extracted from pediatric brain tumors. 4) To attempt to derive tumor cell lines and to provide a bank of frozen brain tumor tissue for use in further studies, especially molecular genetic studies.

Technical Approach: This is a non-therapeutic study intented to prospectively collect tissue from newly diagnosed patients with brain tumors. Flow cytometry, cytogenetics, and molecular studies will be used to characterize abnormalities of the DNA and correlate their findings with type of disease/diagnoses, tumor grade, and prognostic indicators.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/018 **Status:** On-going

Title: POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Pediatric Cancer:meduloblastoma, cisplatin, VP-16, radiation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objectives: 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. To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. 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). To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. 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 was closed to patient entry 26 March 96. One patient was enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/164 **Status:** On-going

Title: POG 9047: Neuroblastoma Biology Protocol

Start Date: 09/03/93 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
MAJ Stephen R. Palmer, MC
COL Stephen R. Stephenson, MC
COL Bruce A. Cook, MC

Key Words: cancer:neuroblastoma, biology

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/19/96

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: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/017	**Status:** Completed

Title: POG 9135: Pre-radiation Chemotherpy for Children with Supratentorial Malignant Gliomas and Poorly Differentiated Embryonal Tumors

Start Date: 11/18/94	**Est. Completion Date:** Indefinite
Department: POG	**Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:gliomaa, Cancer:embryonal, radiation, chemotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objectives: To estimate the response of children with supratentorial malignant glioma or poorly-differentiated embryonal tumors (PDETs) to three cycles of either BCNU plus continuous-infusion cisplatin or cyclophosphamide plus continuous-infusion etoposide (VP-16). To determine the acute and sub-acute toxicities of these combination chemotherapies. To estimate prospectively, using neuroimaging studies and CSF cytology, the incidence of neuraxis tumor dissemination at diagnosis in children with measurable residual tumor following initial surgery.

Technical Approach: Patients will be randomized and begin chemotherapy within 4 weeks of diagnostic surgery. One patient per year is expected from MAMC for this study and will randomized to either Treatment A or Treatment B. Patients will be off study after completion of three courses of chemotherapy or upon unequivocal evidence of progress disease. They will then register on POG 9136 for radiation therapy.

Progress: This protocol was closed to patient entry 15 Oct 95. No patients were enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/015 **Status:** On-going

Title: POG 9150/CCSG 6901 - Intergroup Rhabdomyosarcoma Study-IV for Stage I Disease.

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Rhabdomyosarcoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objectives: To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytoxan (VAC vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to: a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CS as a supportive measure for ameliorating hematopoietic toxicity.

Technical Approach: This is a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen for Stage 1 disease, excluding Clinical Group I paratesticular and Groups I and II orbit/eyelid patients, in IRS-IV. The modifications of VAC involve maximizing its intensity: cytoxan is delivered in a single high dose rather than at a lower dose daily x 3, actinomycin-D is delivered more frequently in induction, and VCR more frequently during continuation. The two experimental arms differ from the control in that ifosfamide is substituted for cytoxan in one (VAI) and ifosfamide + VP-16 are substituted for actinomycin-D + cytoxan in the other (VIE). The comparison then, is VAC vs VAI vs VIE. Clinical Group I paratesticular and orbit/eyelid patients will be treated separately with VA alone. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2, and 3 patients with gross residual disease after surgery (clinical group III). Within each stage, except for stage 4 radiotherapy will be randomized or assigned by Clinical Group. Participation in the corresponding tumor study (PO #9153) us required.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/016	**Status:** On-going
Title: POG 9151/CCSG 6902 - Intergroup Rhabdomyosarcoma Study-IV for Stage II and Stage III Diseases.		
Start Date: 11/18/94	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: Rhabdomyosarcoma		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objectives: To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytoxan (VAC) vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

Technical Approach: This study is designed to determine whether an ifosfamide-based combination (VAI) is superior to a cyclophosphamide-based combination (VAC) in previously untreated patients. Therefore, a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen is the study to be undertaken for stages 2 and 3 disease in IRS-IV. The two experimental arms (VAI and VIE) differ from the control arm as follows: ifosfamide is substituted for cyclophosphamide in one cyclophosphamide in the other (VIE). The comparison then, is VAC vs VAI vs VIE in IRS-IV. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2 and 3 patients with gross residual disease after surgery (clinical group III). The goal is to try to improve the local control rate in these Group III patients with Hyperfx-RT, whereas Group II patients in these stages have an acceptable local control rate of 90% with conventional RT and will continue to receive conventional RT in IRS-IV.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/008 **Status:** On-going

Title: POG 9153: Intergroup Rhabdomyosarcoma Study/Laboratory Evaluation of Tumor Tissue

Start Date: 11/04/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Rhabdomyosarcoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 10/20/95

Study Objective: 1) To prospectively correlate clinical features and outcome of newly diagnosed children with rhabdomyosarcoma with cytogenetic abnormalities of their tumors, 2) to measure cellular DNA content by flow cytometry of tumor cells and correlate the DNA index of tumor stem lines with clinical features and treatment response, 3) to determine prospectively the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively acting loci in DNA extrated from pediatric rhamdomyosarcomas, 4) to attempt to derive tumor cell lines and to provide a bank of frozen rhabdomyosarcoma tumor tissue for use in further studies, especially molecular genetic studies, and 5) to determine the degree of specificity of monoclonal antibody probes, 4.2A8, 5.1Hll, and 3.1G11, for childhood rhabdomyosarcoma.

Technical Approach: This is a non-therapeutic study intended to collect tissue from newly-diagnosed rhabdomyosarcoma and undifferentiated sarcoma patients $\leq$ 21 years. Viable tumor tissue, frozen tumor tissue and involved marrow samples will be collected and forwarded to a designated study site.

Progress: One patient enrolled in this study at MAMC in FY 96 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/084	**Status:** On-going
Title: POG 9182: HIV/Malignancy Biology Protocol		
Start Date: 03/17/95	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:lymphoma, HIV		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1) To establish a national registry of pediatric AIDS-associated lymphomas and other malignancies and a repository of well-characterized tumor tissue, cells and sera from affected patients. 2) To conduct prospective Phase I-III clinical trials of anti-cancer and anti-retroviral therapies aimed at improving outcomes and identifying critical determinants of risk. 3) To identify the presence and quantify the viral burden of human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), Human Herpes virus 6 (HHV6), and Herpes Simplex virus (HSV) in the tumor tissue, peripheral blood cells, plasma, and cerebrospinal fluid of pediatric patients with lymphomas and other malignancies; and to characterize the effect of anti-cancer and antiviral chemotherapy with regard to lymphoma stage, disease progression, host response, and toxicity. 4) To conduct the first large-scale molecular epidemiologic study of risk factors related to development of HIV-related NHL in children by means of a case-control analysis of HIV-infection characteristics such as co-infection with EBV, CMV, HHV6, Mycoplasma, the quantitative host viral burden, level of immunodeficiency, and other host characteristics. 5) For HIV+ and HIV- children, to characterize differences in NHL tumor tissue in terms of immuno-phenotype,immunoglobulingenerearrangements and oncogene (c-myc) activation.

Technical Approach: Three groups of children are eligible for this protocol. The first, a "case" group, consists of children with a newly-diagnosed malignancy who are HIV positive. The second, a "malignancy control' group, consists of children with a newly-diagnosed malignancy who do NOT have HIV infection. The third group, a "non-malignancy control" group, consists of children with no evidence of malignancy, but who have a documented HIV infection. A total of 150, 150, and 300 patients, respectively is expected. The subject will be seen in the clinic at least every two months for up to two years, then every 6 months up to 3 years. At each visit blood will be drwn for testing. In addition, a small piece of tumor tissue or other body fluids (including spinal fluid and bone marrow), already obtained as part of routing clinical management bay be examined. We will establish a database as a repository for characteristics of pediatric patients with HIV infection and malignancies. The database will include all appropriate clinical parameters, laboratory measures, and results of molecular and virologic studies. Descriptive analyses of clinical and laboratory data will use various criteria to characterize the study population and to correlate variation in infectious virus and total viral burden with clinical course and other laboratory measurements. Primary endpoints, which may include tumor response, disease-free survival and episodes of grade 3-4 toxicities, will be confined to those specified in POG therapeutic protocols. Contingency tables relating the laboratory variables with stage, age, primary tumor site, histopathology, and clinical response will be produced. Conditional logistic regression will be used to compare biological data for cases to matched controls. Frequency matching will be performed at the Statistics Office at the time of analysis. Kaplan-Meier life tables, log rank tests, and Cox regression will be used to explore the relationship of laboratory variables to outcome.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/056 **Status:** On-going

Title: POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study

Start Date: 12/16/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: leukemia:pediatric, leukemia:lymphoblastic, cytosine arabinoside, leucovorin calcium, hydrocortisone, 6-Mercaptopurine, methotrexate, E. coli asparaginase, Erwinia asparaginase, prednisone, vincritine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: 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: 30 Sep 96 **Protocol No.:** 94/033 **Status:** On-going

Title: POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study

Start Date: 11/05/93 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
MAJ Stephen R. Palmer, MC
COL Stephen R. Stephenson, MC
COL Bruce A. Cook, MC

Key Words: Cancer:non-Hodgkin's, cyclophosphamide, adriamycin, prednisone, methotrexate, 6-mercaptopurine, ARA-C, hydrocortisone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/19/96

Study Objective: 1. To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites. 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/m^2 (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/m^2/day in 3 divided doses x 28 days, Adriamycin 40 mg/m^2/day IV days 1 & 22, and Cyclophosphamide 750 mg/m^2/day IV days 1 & 22. Fluid intake is to be > 3000 ml/m^2 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/m^2 IV, Cyclophosphamide 750 mg/m^2 IV, Vincristine 1.5 mg/m^2 (max 2 mg) IV, and Prednisone 50 mg/m^2 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: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/148 **Status:** On-going

Title: POG 9233/34: A Phase III Randomized Trial of standard vs Dose-Intesntified Chemotherapy for Children Less Than 3 Years of Age With A CNS Malignancy Treated With or Without Radiation Therapy

Start Date: 08/06/93 **Est. Completion Date:**

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
MAJ Stephen R. Palmer, MC
COL Stephen R. Stephenson, MC
COL Bruce A. Cook, MC

Key Words: cancer:CNS, pediatric, chemotherapy, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/19/96

Study Objective: To develop effective methods of treatment for very young children with malignant brain tumors that will minimize late toxicities affecting immature and rapidly developing central nervous systems.

Technical Approach: Patients < 3 yrs of age with a primary intercranial malignancy will be randomized to one of two regimens. Patients assigned to Regimen A will receive six 12-week courses of chemotherapy, given over a total of 72 weeks. Each course consist of 3 drug cycles. Cycle A; vincristine and cyclophosphamide and Mesna will be given on weeks 1, 13, 25, 37, 49 and 61. Vincristine will be repeated on day 8 of this cycle. During Cycle B, patients will receive cisplatin on day 1 and VP-16 on days 3 and 4. Patients on Regimen B will receive eight 9-week courses of chemotherapy. Each course will consist of 2 consecutive cycles of one drug combination (Cycle X) followed by a cycle of another combination (Cycle Y). On Cycle X, vincristine, and Mesna will be given on day 1 of weeks 1, 4, 10, 13, 19, 22, 28, 31, 27, 40, 49, 55, 58, 64, and 67. On day 2 patients will receive cyclophosphamide and Mesna. On days 3-15 patients will receive G-CSF. On Days 8 and 15, vincristine will be given. Cycle Y will be given on weeks 7, 16, 25, 34, 43, 52, 61 and 70. On Day 1 of Cycle Y, cisplatin will be given. VP-16 will be given on days 3 and 4. On days 5-14 G-CSF will be administered.

Patients experiencing progression or recurrence of disease at any time during or within 12 months of chemotherapy will be encouraged to begin radiation therapy immediately. If disease recurs later than 12 months after completing chemotherapy, patients will be discontinued from the study.

Progress: One patient was enrolled in July 94 , completed treatment and was transferred to WRAMC Aug 96. This protocol remains open to patient accrual.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/146	**Status:** Completed

Title: POG 9239: Treatment of Children with Newly-Diagnosed Brain Stem Glioma (BSG) Using Cisplatin as a Radiosensitizer with Either Conventional or Hyperfractionated Radiotherapy. A Phase III Study.

Start Date: 07/01/94	**Est. Completion Date:**Indefinite
Department: POG	**Facility:** MAMC
Principal Investigator: LTC Shirley E. Reddoch, MC	
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC
Key Words: Cancer:glioma, cisplatin, radiotherapy	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: To compare the time to neurologic and/or radiographic progression and overall survival in children with newly-diagnosed brain stem glioma (BSG) who are treated with 100mg/m^2 of infusional cisplatin combined with conventional vs hyperfractionated radiotherapy; and to determine the toxicities of combining 100mg/m^2 of infusional cisplatin as a radiosensitizer with already-tested radiotherapy fractionation regimens.

Technical Approach: This study will evaluate the effectiveness of combining a drug called cisplatin, to be given continuously by vein (IV) over a period of 5 days in combination with either standard radiation treatments given once a day or hyperfractionated (twice daily) radiation treatments. In the first, third, and fifth weeks of radiation therapy, patients will be given a continuous infusion of cisplatin IV over 5 days. The cisplatin infusion will begin at the same time that the radiotherapy begins on that week.

Progress: This protocol closed to patient entry 26 March 96. No patients were enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/172 **Status:** Completed

Title: POG 9262: A Phase II Study of Taxol in Children with Recurrent/Refractory Soft-Tissue Sarcoma, Rhabdomyosarcoma, Osteosarcoma, Ewing's Sarcoma, Neuroblastoma, Germ Cell Tumors, Wilms' Tumor ...

Start Date: 09/02/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:solid tumors, taxol

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: (1) To determine the response rate of recurrent bone and soft tissue sarcomas, neuroblastoma, germ cell tumors, hepatoblastoma, and hepatocellular carcinoma to taxol in a phase II trial. (2) To further define the spectrum of taxol's toxicity in children and adolescents.

Technical Approach: Patients will be premedicated with dexamethasone and diphenhydramine. Taxol will be given intravenously continuously over a 24 hour period. This course will be repeated every 21 days. This treatment may continue for one year, depending on the progression of the disease.

Progress: One patient was enrolled at MAMC (FY94). This patient requested removal from the study to seek surgical procedure and eventually died from the underlying disease. This protocol closed to patient entry 15 January 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/096 **Status:** On-going

Title: POG 9315: A Phase III Study of Large Cell Lymphomas in Children and Adolescents; Compariosn of APO vs. APO + IDMTX/HDARA-C and Continuous vs. Bolus Infusion of Doxorubicin

Start Date: 04/19/96 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC

Key Words: Cancer:lymphomas, chemotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To study whether intermediate-dose methotrexate/high dose ARA-C (ID MTX/HRAra-C), administered during the maintenance phase can improve the event-free survival (EFS) of patients with advanced-stage large cell lymphoma (LCL); 2) to further characterize the immunophenotypic and morphologic correlates of pediatric LCL; and 3) to compare efficacy and cardiotoxicity of doxorubicin given by continuous versus bolus infusion.

Technical Approach: Patients will be randomized at registration to Regimen A or B. Patients who present with CNS disease will go after induction directly to Regimen B. Induction for both regimens will be the same, with additional intrathecals for patients with CNS disease. Maintenance A consists of 8 cycles of ID MTX/HD Ara-C alternating with 5 cycles of VCR/6-MP/ADR/Pred and 2 cycles of VCR/6-MP/MTX/Pred; a total of 15 cycles given at 3 week intervals. Maintenance B consists of 5 cycles of ADR/V/6-MP/Pred followed by 10 cycles of MTX substitution for ADR; a total of 15 cycles will be given at 3 week intervals. Following completion of therapy, examinations will be every month for the first 6 months; thereafter every 3 months until year 2 off therapy and then every 6 months until 5 years off therapy, then annually. Cardiac exams after completion of therapy will be required during first, third and fifty years off treatment.

Progress: No patients were enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/072 **Status:** On-going

Title: POG 9317: Chemotherapy for Children with Advanced Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B Cell ALL

Start Date: 03/04/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:Burkett's lymphoma, ARA-C, cytoxan, Vincristine, Adriamycin, Methotrexate, VP-16, Ifosfamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/19/96

Study Objective: 1) To evaluate the efficacy of adding VP-16/Ifosfamide intensification to the treatment of patients with advanced-stage B-cell malignancies: Stage III & IV DU NHL and B-cell acute lymphoblastic leukemia (B-ALL). 2) To compare the toxicity and efficacy of high-dose Ara-C given by intermittent bolus (q 12 hour x 4) vs bolus/continuous infusion over 48 hours.

Technical Approach: In this groupwide protocol, we propose to add, in a randomized study, two agents active in the treatment of aggressive NHL: Ifosfamide 2.8 g/m^2 with VP-16 100 mg/m^2 qd x 5. All patients in this study will be randomized at diagnosis to receive, throughout therapy, high-dose Ara-C by continuous infusion (CI) or by bolus (actually a 3 hour infusion). The CI Ara-C dose is base on the POG pilot study #9190 with a starting dose of 3.8 g/m^2/48 hours (80 mg/m^2/hr) following 9.5 g/m^2 bolus. The bolus Ara-C dose is taken from POG #8617: 3 g/m^2 q 12 hr X 4 doses. All patients will receive therapy based on POG #8617/8616, with a reduction in duration. After a common induction with fractionated cyclophosphamide, vincristine, Adriamycin, methotrexate by 24-hour infusion, and Ara-C, patients with Stage III disease will receive these drugs without Adriamycin and patients with Stage IV/B-ALLL will receive these 5 drugs including Adriamycin during consolidation. Patients will also be randomized to receive or not to receive VP-16/ifosfamide intensification, except for patients with CNS involvement who will be assigned to receive VP/16 ifosfamide. The study question is being posed in a randomized 2 X 2 factorial design.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/168 **Status:** On-going

Title: POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study

Start Date: 07/21/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:Leukemia, ACML, inteferon, hydroxyurea, Ara-C

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

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). 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: One patient was enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/134 **Status:** Completed

Title: POG 9340/41/42: Treatment of Patients greater than or equal to 365 Day s At Diagnosis With Stage 4 and N-MYC Amplified Stage 2B/3 Neuroblastoma; A Pediatric Oncology Group Phase II Study

Start Date: 07/02/93 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
MAJ Stephen R. Palmer, MC
COL Stephen R. Stephenson, MC
COL Bruce A. Cook, MC

Key Words: neuroblastoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/21/95

Study Objective: 1) 9340 Stage 4 (only) - 1.1) To evaluate the response rate to and toxicity of Phase II single-agent chemotherapy (either continuous infusion Adriamycin, or Taxol) given prior to Phase III therapy to two successive subsets of untreated patients ≥ 365 days of age with INSS Stage 4 neuroblastoma (NB). 2) 9341-2 Stage 5 and N-myc amplified Stage 2B or 3 (Stage C) - 2.1) To measure response rates and toxicity, event-free survival (EFS), survival, and patterns of failure, of patients treated with 6 courses of induction chemotherapy: high dose platinum/VP-16 (HDP/VP), cyclophosphamide/Adriamycin/ vincristine (CAV), ifosfamide/VP (IFOS/VP), CBDCA/VP, HDP/VP, and CAV plus G-CSF, followed by local radiotherapy and autologous bone marrow transplantation (ABMT) (POG #9342). 2.2) To measure response rates, toxicity, EFS, survival, and patterns of failure of patients whose families decline ABMT, and therefore receive an additional 5 courses of therapy (IFOS/VP, CAV, HDP/VP, CAV, CBDCA/VP) plus G-CSF followed by local radiotherapy to the tumor bed. 2.3) To further evaluate the toxicity of autologous bone marrow transplantation (ABMT) using cyclophosphamide/VP/CBDCA ablation plus local radiotherapy.(POG #9342) 2.4) To measure EFS, survival, and patterns of failure of patients who achieve a complete response or partial response or mixed response at the end of induction chemotherapy prior to ABMT. 2.5) To further evaluate the biologic parameters of neuroblastoma as required for POG 9047, and to measure MDR-1 protein (P-glycoprotein) levels, which will be obtained at diagnosis and in marrow purgates and/or available tumor tissue during therapy, with correlation to clinical presentation at diagnosis, clinical course, response to therapy, and survival. To study the activity of four cycles of Adriamycin, bleomycin, vincristine and etoposide (ABVE) followed by 2550 cGy irradiation in clinically or pathologically staged I, II and IIIA, Hodgkin's Disease.

Technical Approach: Patients participating in this study will initially receive two courses of either Adriamycin (IV continuously over 3 days) or taxol (IV continuously over 24 hours). Following initial treatment, intensive therapy with High-dose combinations of 7 drugs will begin. HDP/VP (High-dose cisplatin and VP-16), CAV (Cyclophosphamide, Adriamycin and Vincristine), IFOS/VP (Ifosfamide and VP-16), CBDCA/VP (Carboplatin and VP-16) are the combinations that will be used.

If, after the High-dose therapy, immunofluorescent testing shows < 5% tumor cells the patient will be eligible for autologous bone marrow harvest in preparation for autologous bone marrow transplantation (ABMT). After the marrow is harvested Radiation therapy will be administered to the primary tumor bed. Those refusing ABMT will also receive local radiation therapy and additional courses of the High-dose drug combinations. Also, patients who do not meet eligibility criteria for ABMT will be given additional courses of CAV, HDP/VP, CAV and CBDCA/VP. Patients going on to ABMT will receive ablation therapy beginning 7 to 10 days following radiation therapy. A prescribed course of VP-16, CBDCA, and Cyclophosphamide will be given, careful hydration insured and, when completed, ABMT will be performed. GM-CSF will be given to all patients to enhance rapid bone marrow recovery. Response to ABMT will be evaluated and follow up continued.

Progress: POG 9340 and 9341 closed to patient accrual 9 Dec 95. POG 9342 remains open only for patients presently enrolled on 9341. No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/092 **Status:** On-going

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 .....Osteogenic Sarcoma

Start Date: 04/01/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
COL Bruce A. Cook, MC
MAJ Stephen R. Palmer, MC

Key Words: cancer:pediatric, cancer:sarcoma, doxorubicin, cisplatin, methotrexate, Ifosfamide, MTP-PE

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 04/19/96

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: Two patients were enrolled in this study at MAMC in FY 96 and continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/086 **Status:** On-going

Title: POG 9354: A Randomized Phase III Evaluation of Intensified Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide in the Treatment of Newly-Diagnosed Ewing's Sarcoma or Primitive ....

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone, Cancer:soft tissue; vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1) To compare the event-free survival (EFS) and survival of newly diagnosed patients with Ewing's sarcoma and primitive neuroectodermal tumor (PNET) of boneor soft tissue receiving a 48 week standard regimen of vincristine, cyclophosphamide and doxorubicin alternating with ifosfamide and etoposide with G-CSF to those receiving a 30 week dose intensified regimen of the same chemotherapeutic agents. 2) To assess the diagnostic value and prognostic significance of histologic subtype as defined by routine histology, immunochemistry, electron microscopy, and MIC-2 gene expression. 3) To estimate the frequency of occurrence of serious toxicities and adverse orthopedic outcomes associated with the disease and therapy employed, and to compare them between the regimens. 4) To estimate the occurrence of second malignant tumors in these patients. 5) To determine if event free survival and survival differs between patients with PNET and Ewing's sarcoma, and between PNE and Ewing's sarcoma of bone compared to PNET and Ewing's sarcoma of soft tissue.

Technical Approach: Subjects will be assigned to one of the two regimens. Regimen A will use drugs according to the standard treatment for Ewing's Sarcoma. Regimen B will utilize the same drugs, in higher doses, over a shorter time period. It is not clear at the present time which of the treatment regimens is better. Whether randomized to Regimen A or Regimen B, the drugs listed below will be given as follows: Vincristine will be given IV push (into vein, quickly). Cyclophosphamide will be given by IV infusion over 30 minutes, (Regimen A); or 6 hours (Regimen B). MESNA will be given to prevent bleeding from the bladder which can be caused by ifosfamide or cyclophosphamide. It will be given intravenous infusion simultaneously with the cyclophosphamide or ifosfamide and will continue to be infused for 3 hours following the end of the cyclophosphamide or ifosfamide dose. Three additional doses of MESNA will be administered by IV over 15 minutes at 3, 6 and 9 hours following the end of the cyclophosphamide dose. Doxorubicin will be given by continuous infusion over 2 days. G-CSF will be given subcutaneous (SC, into the skin) or IV over 2 hours. Etoposide (VP-16) will be given IV over 1 hour. Ifosfamide will be given IV over 1-3 hours.

Progress: No patients have been enrolled in this study at MAMC in FY 96, however, one patient was accepted in transfer from WRAMC.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/057	**Status:** Completed

Title: POG 9360: GM-CSF Randomization Plus High-Dose "ICE" in the Treatment of Recurrent/Resistant Malignant Solid Tumors of Childhood, A pediatric Oncology Group, Phase II Study

Start Date: 12/16/94	**Est. Completion Date:** Indefinite
Department: POG	**Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: leukemia:pediatric, solid tumors, carboplatin, GM-CSF, ifosfamide, VP-16

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To determine the antitumor activity and toxicity of the maximum-tolerated dose of ifosfamide and carboplatin plus etoposide (high-dose ICD) against childhood and adolescent malignant solid tumors resistant to conventional chemotherapy. 2) To define the most effective but least toxic dose of GM-CSF to be used to ameliorate the myelosuppression that accompanies ICE therapy.

Technical Approach: This study involves the administration of three drugs; ifosfamide, carboplatin, and etoposide (VP-16) ("ICE" therapy) which have been shown to be active against these tumors, alone or in combination with other drugs. In addition, you (your child) will be given an investigational protein drug, rhu granulocyte-macrophage colony stimulation factor (GM-CSF), in order to decrease side effects of this treatment. You (your child) will be randomized (assigned by chance; such as the flipping of a coin) to one of two doses of GMCSF.

VP-16 will be given intravenously (into the vein) over 60 minutes, followed by ifosfamide (intravenously) over 3 hours every day for three days. Another drug named MESNA will also be given at specified intervals prior to and after ifosfamide. The purpose of MESNA is to help prevent bleeding from the bladder that can occur with ifosfamide. Carboplatin will be given immediately following ifosfamide, intravenously, over 60 minutes, on day 3 only. GM-CSF will be given subcutaneously (just under the skin) on days 4 to 19 or until the blood counts recover. This course may be repeated one or more times depending upon the response and at the discretion of your (child's) physician. You (your child) will no longer receive treatment with these drugs if your (child's) disease worsens or if there has been no response to treatment, or if unacceptable toxicity occurs. Patients on this study will be followed with medical check-ups for approximately two years in order to monitor response to treatment and long-term survival.

Progress: No patients were enrolled in this study at MAMC in FY 96. This protocol closed to patient accrual 26 March 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/087 **Status:** On-going

Title: POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:all types, HIV, Interferon

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

Study Objective: 1) To Estimate the complete response rate for HIV related malignancies treated with interferon (αIFN). 2) The secondary objectives are to estimate the one year disease free survival and to evaluate the toxicity of αIFN 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 αIFN 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 have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/088	**Status:** On-going
Title: POG 9382: Molecular Studies of t(11;22) Translocation in Ewings' Sarcoma and Peripheral PNET of the Bone		
Start Date: 03/17/95	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To determine if the presence of minimal metastatic disease as measured by PCR imparts a poor prognosis in patients with localized disease at diagnosis. 2) To determine the prevalence of minimal residual and metastatic disease in the bone marrow and peripheral blood of patients with Ewing's Sarcoma or PPNET as measured by PCR amplification of the t(11;22) chromosomal translocation. 3) To correlate the presence of minimal residual or metastatic disease at diagnosis with other clinical parameters. 4) To determine the types and frequency of chromosomal breakpoints and fusion transcripts and to identify whether certain chromosomal breakpoints correlate with clinical outcome. 5) To determine at what rate patients with clinically documented metastatic disease (at diagnosis or relapse) have evidence of circulating cells with the t(11;22) translocation in peripheral blood, bone marrow, or other body fluids (e.g. CSF, pleural fluid, etc.).

Technical Approach: For those subjects who are consented, will have their tumor, blood, and bone marrow looked at for residual disease. An additional blood sample will be obtained just prior to the 2nd course of chemotherapy, and at the completion of the study. Molecular studies will then be performed on these items. Statistical inference will be applied to the primary objective (#1), with descriptive measures being utilized to address the remaining objectives, which are viewed as hypothesis generating. Because of the difficulty in obtaining prior information regarding the PCR measurements, no a prior power calculations can be done. Based on POG 8850, accrual of 45 patients/year could potentially be achieved, for a total of 180 In 4 years. To test whether the presence of minimal metastatic disease as measured by PCR defines a poor risk group, we will conduct three one-sided log-rank tests on event-free survival, using a Bonferroni correction (i.e., each test will use $\alpha=0.05/3=0.0167$). The tests will be done at diagnosis, end of cycle 2, and end of therapy, with the two EFS curves at each time point being defined according to whether the PCR is positive or negative.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 95/058	**Status:** On-going
Title: POG 9400: ALinC 16 Classification (C) Protocol		
Start Date: 12/16/94	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators: COL Bruce A. Cook, MC	MAJ Stephen R. Palmer, MC	
Key Words: leukemia:pediatric, laboratory classification		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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.

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: Two patients enrolled in this study at MAMC in FY95 and one patient enrolled in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/144	**Status:** On-going
Title: POG 9404: T-Cell #4 Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced Stage Lymphoblastic Non-Hodgkin's Lymphoma		
Start Date: 07/19/96	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators:	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:lymphoblastic leukemia, T-cell, Cancer:non-Hodgkin's lymphoma		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

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: No patients were enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/059 **Status:** On-going

Title: POG 9405: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

Start Date: 12/16/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: leukemia:peds, leukemia:lymphoblastic, Calcium leucovorin, cytosine arabinoside, E. coli L-asparaginase, Erwinia L-asparaginase, hydrocortisone, 6-mercaptopurine, methotrexate, prednisone, vincristine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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. 4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

Approach: In this research study, the subjectwill 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- asnaraainase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, Icotosine arabinoside (Ara-Cl, 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 subjectwill 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 subjectwill receive the drugs methotrexate and 6- mercaDtoPurine (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 methotresate, 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 subjectwill 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 subjectwill be taken off study in case of relapse in the bone marrow, or any other site, or if the subjectfail to achieve a complete remission during the induction phase of the study.

At the time of bone sarrow 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 2 Dec 95 due to excessive neuro toxicity. One patient enrolled in this study at MAMC in FY95 was taken off study but continues to be followed. Another patient enrolled in FY 96 was transferred to Beaumont Naval Med Ctr.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/060 **Status:** On-going

Title: POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphobnlastic Leukemia (ALL)

Start Date: 12/16/94 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: leukemia:pediatric, calcium leucovorin, ARA-C, E. coli asparaginase, Erwinia asparaginase, PEG asparaginase, hydrocortisone, Daunomycin, 6-mercaptopurine, methotrexate, prednisone, vincristine, VM-26

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To determine the efficacy of a 2.5 gm/m^2 dose versus 1 gm/m^2 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/m^2 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. 4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

Technical Approach: In this research study, a child 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 subjectwill 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: One patient was enrolled in this study in FY 96, however due to an adverse event during induction he was taken off study but continues to be followed. Another patient accepted in transfer from SUNY continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/072	**Status:** On-going
Title: POG 9411: SIMAL 9: Treatment of Relapsed Non-T, Non-B Acute Lymphoblastic Leukemia with Intensive Chemotherapy		
Start Date: 02/16/96	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators:	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:leukemia, pediatric, chemotherapy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To determine the feasibility and toxicity of delivering an intensive reinduction and consolidation chemotherapy regimen for children with acute lymphoblastic leukemia (ALL) following first bone marrow relapse; 2) to compare the induction response rates for patients randomized to weekly PEG versus 3 times a week E. coli asparaginase; 3) to study the induction of blast cell p53, p21 and GADD45 genes in relapsed ALL and correlate with the results of *in vitro* and *in vivo* responses to cytotoxic therapy; 4) to study somatic cell mutations in children with relapsed ALL undergoing intensive chemotherapy; and 5) to compare remission rate, toxicity, and Asparaginase levels in children treated with Peg L-Asparaginase compared to E. Coli Asparaginase during induction and continuation therapy for relapsed ALL.

Technical Approach: Patients will be randomized at registration to PEG-L-Asparaginase (Treatment 01) or E. Coli Asparaginase (Treatment 02) or non-randomly to PEG-L-asparaginase (Treatment 01) if there was prior hypersensitivity to E. Coli Asparaginase. Reinduction therapy will consist of a four drug regimen of doxorubicin, prednisone, vincristine and PEG-L or E. Coli Asparaginase. Intrathecal prophylaxis will be given to patients with or without CNS involvement. Consolidation will consist of non-cross-resistant drug combinations to include Ifosfamide/VP-16/MESNA and Ara-C/Idarubicin. Continuation therapy will include 5 cycles each consisting of four courses of different drug combinations using VP-16/Ifos/MESNA; 6-thioguanine/methotrexate; idarubicin/Ara-C and dexamethasone/vincristine/PEG-L-asparaginase.

Progress: One patient was enrolled in FY 96 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/089 **Status:** On-going

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

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
COL Bruce A. Cook, MC

Key Words: Cancer:AML, ARA-C, Cyclosporine, multidrug resistance

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/16/96

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. 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: No patients were enrolled in this study at MAMC in FY 96, however one patient was accepted in transfer from WRAMC and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/097	**Status:** On-going
Title: POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study		
Start Date: 04/19/96	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators:	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:Wilms, chemotherapy, radiation therapy, biology study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

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: Wilms tumor is the most frequent malignant renal tumor in children. 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 was enrolled in this study at MAMC in FY 96 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/186 **Status:** On-going

Title: POG 9450: Etoposide/Ifosfamide + G-CSF in the Treatment of Newly Diagnosed Metastatic Osteosarcoma or Unresectable Osteosarcoma

Start Date: 09/15/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
MAJ Stephen R. Palmer, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:osteosarcoma, etoposide, ifosfamide, G-CSF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To estimate the response rate to etoposide (VP-16), ifosfamide (IFOS) and G-CSF in patients presenting with newly-diagnosed metastic or unresectable osteosarcoma prior to treatment with other chemotherapeutic agents. 2) To evaluate the toxicity of VP-16/IFOS in newly diagnosed patients. 3) To estimate the duration of survival for patients presenting with newly-diagnosed metastatic osteosarcoma or unresectable osteosarcoma who are treated with a multi-agent chemotherapy regimen preceded by induction therapy with VP-IFOS and G-CSF. 4) To determine the ability of pathologic primary tumor response from 2 courses of pre-surgical chemotherapy to predict outcome as measured by time to disease progression, disease free survival and survival.

Technical Approach: This study involves treatment with the combination of drugs etoposide (VP-16) and ifosfamide (IFOS) at high doses. Granulocytic Colony Stimulating Factor (G-CSF) will be used to help the patient's bone marrow white cells recover faster after each of the first 2 courses of high dose VP-16 and IFOS, and thereafter as necessary. This study will determine the response rate of high dose VP-16/IFOS in the treatment of osteosarcoma and will try to determine whether this high dose combination will improve the overall outcome of this group of high risk patients. Patients will also receive these drugs in standard dosing during continuation therapy in combination with other chemotherapy drugs which are used to treat osteosarcoma. VP-16 will be given intravenously over 60 minutes, followed by intravenous ifosfamiti over 4 hours every day for 5 days. Another drug, MESNA will also be given at specified intervals with and after ifosfamide. The purpose of MESNA is to help prevent bleeding from the bladder which can occur with ifosfamide. G-CSF will be given subcutaneously (injected under the skin) once a day, starting on the day the chemotherapy finishes and continuing until blood counts return to normal. This course will be repeated one more time (approximately 3 weeks later). After 6 weeks, patient will be re-evaluated (x-ray, MRI, CT) to determine the response to this drug combination. If possible, all sites of remaining tumor will then be removed surgically. After surgery, chemotherapy will resume with a combination of drugs (methotrexate. ifosfamide. VP-16 adriamycin and cisplatin) which have been proven to be effective against osteosarcoma. The vitamin Calcium Leucovorin will be given along with the methotrexate. Treatment will then continue for approximately one year.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/039 **Status:** On-going

Title: POG 9457: Intensive Therapy with Growth Factor Support for Patients with Ewing's Tumor Metastatic at Diagnosis

Start Date: 12/15/95 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
MAJ Stephen R. Palmer, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:Pediatric Ewing's, Topotecan, ifosfamide, etoposide, vincristine, adriamycin, cyclophosphamide, G-CSF, interleukin-6

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: (1) To evaluate the response rate, and duration of response in patients with Ewing's tumor, metastatic at diagnosis, treated with maximally intensified therapy. (2) To evaluate the response to new agents utilized in an upfront window. Initially, topotecan will be used as a single agent. When the maximally tolerated dosages of the combination of topotecan and cyclophosphamide are available, the combination will be employed. (3) To assess the role of surgical treatments with regard to local control of primary and metastatic sites and disease course. (4) To determine whether individual variability in ifosfamide and cyclophosphamide metabolism correlated with toxicity and/or response. (5) To evaluate the rise in the absolute neutrophil count following one dose of G-CSF just prior to a chemotherapy cycle as a measure of bone marrow reserve and subsequent myelosuppression.

Technical Approach: In the absence of effective new agents in Ewing's Tumor, attempts to increase the rate of cure have recently centered around increasing dose intensity. Ifosfamide will be used at a dosage level 25% higher than that currently being used, for the first 3 cycles. The dosage will be reduced for the 2 continuation cycles. Cyclophosphamide will also be used in increased dosage with vincristine and adriamycin. This study will encourage the use of surgery for local control, with irradiation of the primary tumor bed, unresectable primary tumors and selected metastatic sties. Topotecan is a camptothecin, a topoisomerase I inhibitor. Initially, this study will use 2 cycles of single agent topotecan 3 weeks apart. At least 14 patients will be registered. When the maximum tolerated dosages of the combination of topotecan and cyclophosphamide are available, subsequent patients will be treated with the combination.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/143 **Status:** On-going

Title: POG 9485: Intergroup Protocol, Assessmentof the Role of Minimal Access Surgery in the Treatment of Childhood Cancer: Intergroup Laparoscopy Protocol

Start Date: 07/19/96 **Est. Completion Date:** Indefinite

Department: POG **Facility:** MAMC

Principal Investigator: LTC Shirley E. Reddoch, MC

Associate Investigators: MAJ Stephen R. Palmer, MC
MAJ Randall M. Holland, MC

Key Words: Cancer:solid tumor, pediatric, laparoscopy, QOL

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To investigate the role of minimal access abdominal surgery (MAS) in terms of the perioperative complication rate and the mortality rate; 2) to compare the impact of MAS and open laparotomy on quality of life (QOL). Several domains of QOL will be examined including surgery-related pain, physical, social and emotional functioning, and global ratings of health and overall QOL; 3) to compare the impact of MAS and open laparotomy on economic costs; 4) to compare the complete tumor resection rate for MAS with open surgery within specific diagnostic groups; 5) to assess the impact of minimal access surgery on compliance with specimen eligibility requirements for therapeutic protocols.

Technical Approach: Pediatric patients less than or equal to 21 years old who require surgery to obtain biopsy material, lymph node sampling for staging, liver biopsies, tumor excisions, organ excision, second-look procedures, etc., will be considered for entry and will be randomized to either open or a minimal access procedure. Protocol eligibility is linked with the requirement to obtain adequate surgical specimens. MAS offers the potential to minimize a potential barrier to enrollment onto protocol therapy. Biologic specimens will be assessed for their adequacy in terms of both the specimen quantity and quality. Demographic data, procedural and overall economic costs, operative time, anesthesia and post-operative analgesia, length of post-operative stay, interval between procedure and subsequent actions, and perioperative morbidity will all be evaluated. Methods of evaluations will include Quality-of-Life assessment, Pain Ratings, Play-Performance/Karnofski assessment, operative and overall mortality, surgery characteristics, radiology review and imaging guidelines.

Progress: No patients have been enrolled in this study at MAMC in FY 96.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/035	**Status:** On-going
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		
Start Date: 11/17/95	**Est. Completion Date:** Indefinite	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Shirley E. Reddoch, MC		
Associate Investigators:	MAJ Stephen R. Palmer, MC	
Key Words: Cancer:pediatric rhabdomyosarcoma, Topotecan		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: (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. (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: One patient was enrolled in this study at MAMC in FY 96 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/120	**Status:** On-going

Title: POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

Start Date: 05/17/96	**Est. Completion Date:** Indefinite
Department: POG	**Facility:** MAMC
Principal Investigator: LTC Shirley E. Reddoch, MC	
Associate Investigators:	MAJ Stephen R. Palmer, MC

Key Words: Cancer:leukemia, lymphoblastic, methotrexate, 6-mercaptopurine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

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; 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: One patient was enrolled in this study at MAMC in FY 96 and one patient was accepted in transfer from SUNY. Both continue to be followed.

DETAIL SHEETS FOR PROTOCOLS

RADIOLOGICAL DIAGNOSTIC ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/136 **Status:** On-going

Title: RDOG(5) 6881: Stereotactic Fine Needle Aspiration Biopsy and Core Needle Biopsy in the Work-up of Lesions Detected by Mammography

Start Date: 06/16/95 **Est. Completion Date:** Indefinite

Department: RDOG **Facility:** MAMC

Principal Investigator: COL Sankaran S. Babu, MC

Associate Investigators:
MAJ Vincent B. Ho, MC
COL Preston L. Carter, MC
CPT Janice C. Stracener, MC
Charlene P. Holt, M.D.
LTC William C. Williard, III, MC
MAJ Barbara A. Crothers, MC

Key Words: Cancer:breast, FNA, Core biopsy, mammography

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objectives: The overall objective of this research protocol is to conduct a randomized clinical trial to study whether stereotactically-guided and/or ultrasound-guided fine needle aspiration (FNA) and/or core needle biopsy (CNB) can replace open surgical biopsy in the diagnostic evaluation of nonpalpable mammographically-detected breast lesions.

Technical Approach: This is a randomized clinical trial to be carried out in mammographic centers nationwide within two consortia. This offers the opportunity to cover the spectrum of experience, equipment and patient populations, all using an agreed protocol to evaluate the use of fine needle and core biopsy used in the work-up of non-palpable breast lesions. The two consortia will enroll a total of 3,600 patients with an expected average MAMC enrollment of two subjects per day for the length of the study. Women having had the appropriate mammographic evaluation and meeting the inclusion criteria will be entered either to stereotactic or ultrasound arms of the study. Those in the stereotactic arm will be randomized to FNA followed by CNB, or CNB alone, both followed by open surgical biopsy or when indicated, 6, 12, and 24 month follow-ups. Those in the ultrasound arm will be randomized to FNA/CNB or CNB. All mammograms will have second readings by experts, and all pathology and cytology will have second readings by reference experts. Data analysis will consist of accuracy determination, agreement analysis, and logistic regression modeling for evaluation of important co-variants on the estimates. In addition, analysis of observer variability, insufficient sample rates, and predictive ability of specific mammographic characteristics will be conducted.

Progress: Study is closed to patient entry. 38 subjects entered at MAMC, following subjects with the last patient finishing in October 1998.

DETAIL SHEETS FOR PROTOCOLS

SOUTHWEST ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 77/054 **Status:** On-going

Title: SWOG 7406: Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III

Start Date: 02/18/77 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
COL Friedrich H. Stutz, MC
LTC H. Irving Pierce, MC
LTC Howard Davidson, MC

Key Words: Cancer: Hodgkin's, MOPP

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy; (2) To evaluate systematic restaging of patients in apparent complete remission; (3) To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging; (4) To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

Technical Approach: All previously untreated patients with Ann Arbor Stages IIIB or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission (PR) is indicated another 4 courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

Progress: Closed to patient entry 31 Aug 78. Two patients where entered in previous years, one patient is still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 77/053	**Status:** On-going

Title: SWOG 7433: Non-Hodgkin's Lymphomas (Stages I, IE, II, and IIE). A Phase III Study.

Start Date: 02/18/77	**Est. Completion Date:** Indefinite
Department: SWOG	**Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:	LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC	LTC Howard Davidson, MC

Key Words: Cancer:Non-Hodgkin's lymphoma, radiotherapy, CHOP

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, I_E, II and II_E treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone or with extended Hydroxyl-daunorubicin (adriamycin), Oncovin (vincristine), and Prednisone.

Technical Approach: Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

Progress: This protocol was closed to patient entry 1 Oct82 and was previously reported as closed. In fact, 2 patients were entered at MAMC, 1 has died and the other is still being followed. The protocol was reactivated in December 1993 in order to allow SWOG to continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 77/024 **Status:** On-going

Title: SWOG 7436: Combined Modality Therapy of Breast Cancer

Start Date: 01/21/77 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC
LTC Howard Davidson, MC

Key Words: Cancer:breast, 5-FU, vincristine, methotrexate, cyclophosphamide, prednisone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

Technical Approach: Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater that six weeks for entry into the study. All therapy will be discontinued after one year.

Progress: This protocol was closed to patient entry in 1 Nov 1979 and was previously reported as closed. In fact, 10 patients were entered at MAMC, 4 have died, and 6 patients are still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 77/018	**Status:** On-going

Title: SWOG 7510: Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel

Start Date: 10/15/76	**Est. Completion Date:** Indefinite
Department: SWOG	**Facility:** MAMC
Principal Investigator: MAJ James S. D. Hu, MC	
Associate Investigators: COL Friedrich H. Stutz, MC	LTC H. Irving Pierce, MC LTC Howard Davidson, MC

Key Words: Cancer:bowel, chemotherapy, BCG immunotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Suerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

Technical Approach: Patients will be randomly assigned to either of the two following regimens; (1) chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would being every eight weeks; (2) chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

Progress: This protocol was closed to patient entry 20 Aug 1980 and was previously reported as closed. 11 patients were entered at MAMC, 8 have died, 3 are still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 78/002 **Status:** On-going

Title: SWOG 7713/14: Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance After Remission Induction

Start Date: 10/21/77 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC

Key Words: Cancer:Non-Hodgkin's lymphoma, CHOP, Levamisole, BCG

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma; (2) For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy; (3) For patients with impaired cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole; (4) To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used; (5) To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases; (6) To establish baseline and serial data on immunologic status in bother chemoimmunotherapy groups.

Technical Approach: Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac disease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or impaired bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

Progress: This protocol was closed to patient entry 1 Oct 1982 and was previously reported as completed. 4 patients were entered at MAMC, 3 have died, one patient is still being followed. The protocol was reactivated in December 1993 do that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 78/047	**Status:** On-going
Title: SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6		
Start Date: 07/31/78	**Est. Completion Date:** Indefinite	
Department: SWOG	**Facility:** MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: LTC H. Irving Pierce, MC	COL Friedrich H. Stutz, MC Suresh B. Katakkar, M.D., DAC	
Key Words: Hodgkin's disease:Stages III & IV, chemotherapy, modality RX		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

Technical Approach: Patients (>15 yrs) must have histologic diagnosis of Hodgkin's disease; no prior chemotherapy. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease will be excluded. Normal marrow patients will receive six cycles of MOP-BAP. Impaired bone marrow patients will receive six cycles of MOP-BAP with dose modifications. Complete Remission (CR) patients with prior radiotherapy will be randomized to Treatment 3 (no treatment) or Treatment 4 (levamisole). CR patients without prior radiotherapy will receive Treatment 5 (radiotherapy). Partial remission (PR) patients without prior radiotherapy or residual bone marrow involvement will receive Treatment 6 (radiotherapy). PR patients with prior radiotherapy or those with residual bone marrow involvement will receive Treatment 7 (4 additional cycles of MOP-BAP); after 10 total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator.

Progress: This study was closed to patient entry 1 Dec 87. Thirteen patients were enrolled in previous years and 5 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 79/096	**Status:** On-going
Title: SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III		
Start Date: 09/21/79	**Est. Completion Date:** Indefinite	
Department: SWOG	**Facility:** MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: Suresh B. Katakkar, M.D., DAC	COL Friedrich H. Stutz, MC COL Irwin B. Dabe, MC	
Key Words: cancer:breast, chemotherapy, modality therapy		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the disease-free interval and recurrence rates in: (1) estrogen receptor positive (ER+) premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) ER+ postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative (ER-) patients with Stage II disease using one vs two years of combination chemotherapy; to compare the effect of adjuvant therapy in Stage II breast cancer using partial mastectomy and radiation vs modified radical or radical mastectomy; to compare the effect of the various adjunctive therapy programs upon survival patterns; and to correlate the estrogen receptor status with disease-free interval and survival.

Technical Approach: Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-FU, vincristine, and prednisone): (1) CMFVP for 1yr pre- or postmenopausal ER patients. (2) CMFVP for 2 yr pre- or postmenopausal ER patients. (3) CMFVP for 1 yr premenopausal ER+ patients. (4) Oophorectomy + CMFVP premenopausal ER+ patients. (5) Tamoxifen alone for 1 yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for 1 yr postmenopausal ER+ patients. Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

Progress: This study was closed to patient entry 15 Aug 89. Thirty-five patients were enrolled at MAMC. Twenty patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 81/064	**Status:** On-going
Title: SWOG 8027: The Natural History of Pathological Stage T(1-2) N(O), M(O) ER+ Breast Cancer		
Start Date: 03/20/81	**Est. Completion Date:** Indefinite	
Department: SWOG	**Facility:** MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: LTC Archie W. Brown, MC	COL Irwin B. Dabe, MC	
Key Words: Cancer:breast, natural history		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative (T_{1-2} N_0 M_0) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

Technical Approach: Patients having undergone radical, modified radical, or adequate local excision with node dissection for histologically proven breast carcinoma whose axillary nodes are negative for tumor and whose estrogen receptor status is positive are eligible. Patients undergoing local adequate excision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days post-operatively as outlined in the protocol. Only patients with pathologic Stage T_{1-2} N_0 M_0 with a primary tumor of ≤5 cm are eligible. The primary tumor must be movable in relationship to the anterior chest wall and may not be involved with extensive skin ulcerations. This protocol involves no randomization or treatment. It consists only of follow-up and documentation of natural history. Patients will be stratified by primary tumor size, <2 cm bs 2 to 5 cm, and by menopausal status. Patients will be followed until relapse or for 10 years, whichever comes sooner.

Progress: Closed to patient entry 1 Oct 82. Five patients were entered; three are still being followed. This protocol was previously reported as completed. In fact, patients are still being followed and the protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 84/018 **Status:** On-going

Title: SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer

Start Date: 11/18/83 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Timothy J. O'Rourke, MC
COL William D. Belville, MC
COL Irwin B. Dabe, MC
MAJ Alfred H. Chan, MC
MAJ Michael D. Stone, MC

Key Words: cancer:bladder, BCG, adriamycin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the effectiveness of intravesical BCG immunotherapy with intravesical Adriamycin in chemotherapy with respect to disease-free interval and two-year recurrence rate; to compare the toxicity of topical immunotherapy and chemotherapy; and to obtain experience regarding disease-free interval and the recurrence rate in patients who develop tumor recurrence and are then crossed over to the alternative treatment arm.

Technical Approach: Following a standard transurethral resection, patients will be stratified by the presence or absence of documented carcinoma in situ and as to prior chemotherapy and then randomized to receive BCG immunotherapy or Adriamycin chemotherapy. Patients who develop tumor recurrence following treatment will be eligible for crossover to the other treatment arm.

Progress: This study was closed to patient entry 20 Dec 85. Three patients were enrolled at MAMC and are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 85/076 **Status:** On-going

Title: SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II

Start Date: 08/23/85 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Michael D. Stone, MC
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
CPT David R. Bryson, MC

Key Words: Cancer:lung, small cell, radiation therapy, adriamycin, cis-platinum, cyclophosphamide, methotrexate, vincristine, VP-16

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To explore the response rate with the concurrent use of radiation therapy plus chemotherapy utilizing cis-platinum, VP-16, and vincristine in limited small cell carcinoma of the lung and to observe the toxicities of this combined modality program.

Technical Approach: Patients will be started on chemotherapy consisting of cis-platinum, VP-16, and vincristine and concurrent radiation therapy to the primary site. After completion of radiation therapy to the chest, prophylactic cranial radiation therapy will be given. After a brief rest period, the patients will be treated with 12 more weeks of conventional chemotherapy consisting of adriamycin, cytoxan, VP-16, vincristine, and methotrexate. Patients who show a complete response will be followed. Patients with less than a complete response will be taken off study and offered alternative therapy.

Progress: This study was closed to patient entry 19 March 86. It was previously reported as completed. In fact, two patients were entered and one is still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 83/056 **Status:** On-going

Title: SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study

Start Date: 03/18/83 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Friedrich H. Stutz, MC
MAJ Timothy J. O'Rourke, MC
MAJ Thomas M. Baker, MC
LTC James E. Congdon, MC
COL Irwin B. Dabe, MC
MAJ Alfred H. Chan, MC

Key Words: cancer:breast, surgery, biological parameters

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/89

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 was closed to patient entry 15 May 88. Twelve patients were enrolled in previous years and nine continue to be followed. Three have expired.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 84/059 **Status:** On-going

Title: SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III

Start Date: 05/18/84 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Michael D. Stone, MC

Key Words: cancer:breast, chemotherapy, emergency room

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare through a randomized prospective study the recurrence rates and disease-free intervals for postoperative axillary node positive estrogen receptor negative breast cancer patients given adjuvant therapy with either short term intense chemotherapy (FAC-M) or one year standard chemotherapy (CMFVP); to compare the effect of these two adjuvant therapies on survival; to compare the relative toxicity of the two therapies; to compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses; and to compare a multiple item questionnaire for assessing quality of life.

Technical Approach: Women who have histologically proven breast cancer with axillary lymph node metastasis and negative estrogen receptors will be entered 14-21 days post-lumpectomy or within 14-42 days post-mastectomy and randomly assigned to receive: Arm I a tapering course of oral prednisone for 6 weeks, weekly IV vincristine for 10 weeks, weekly IV methotrexate, and weekly IV 5-FU plus daily oral cyclophosphamide for a total of one year; or Arm II four cycles of adriamycin (IV day 1), cyclophosphamide (IV day 1), 5-FU (IV days 1 and 8), and methotrexate (IV day 22). Each cycle will be five weeks and total duration of therapy in this arm is approximately 20 weeks. Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy. Added to this protocol will be a sub-study to determine the prognostic significance of circulating human mammary epithelial antigens. This will involve blood tests prior to chemotherapy and then once every three months.

Progress: This study was closed to patient entry 15 Jun 90. Three patients were enrolled, 2 have died and 1 continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 85/009 **Status:** On-going

Title: SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II

Start Date: 11/16/84 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ Michael D. Stone, MC
MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC
MAJ Timothy J. O'Rourke, MC
CPT David R. Bryson, MC

Key Words: Cancer: Non-Hodgkin's lymphoma, m-BACOD

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine an approximate complete remission rate and remission duration for the treatment program of cyclophosphamide, doxorubicin, vincristine, dexamethasone, and bleomycin with intervening moderate dose of methotrexate and leucovorin rescue (m-BACOD) in patients with intermediate and high grade non-Hodgkin's lymphoma and to assess the feasibility of using this regimen in the SWOG with the intent of using m-BACOD in a future Phase III trial.

Technical Approach: Patients will be stratified according to marrow reserve status and creatinine clearance. Treatment will consist of ten 3-week courses. Cytoxan, adriamycin, vincristine, and bleomycin will be given IV on day 1. Dexamethasone will be given by mouth daily for 5 days, and methotrexate will be given on days 8 and 15 at 200 mg/m^2. Leucovorin will be given 10 mg/m^2 by mouth after each methotrexate injection every 6 hours for eight doses. An adequate trial will be defined as the completion of two complete cycles of m-BACOD. Patients with documented progressive disease or less than complete response after an adequate trial will be taken off study. Those with complete response will continue on study with no further chemotherapy.

Progress: This study was closed to patient entry 26 April 1985 and reported as completed. However, two patients had been enrolled in the study and are still being followed. The study was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 86/007 **Status:** On-going

Title: SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III

Start Date: 10/18/85 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
CPT David R. Bryson, MC
COL Irwin B. Dabe, MC
LTC Howard Davidson, MC
MAJ Michael D. Stone, MC

Key Words: leukemia:lymphoblastic, consolidation regimens

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the effects on remission duration and survival of two consolidation regimens: the L-10-M consolidation used in SWOG 8001 versus a regimen employing daunomycin, cytosine, arabinoside, 6-thioguanine and escalating methotrexate/Lasparaginase in patients with adult lymphoblastic leukemia and to compare the toxicities of the two consolidation regimens.

Technical Approach: Patients will begin remission induction with vincristine, prednisone, adriamycin, methotrexate, cyclophosphamide, and adriamycin (36 days), followed by a 14 day rest period. On day 30, patients will have an Ommaya reservoir placed in the frontotemporal area of the skull. Patients failing to achieve an A1 marrow status on induction therapy will go off study. Patients with complete remission will be randomized to one of the following consolidation regimens: ARM I (L-10-M) methotrexate and Ara-c, daily x 5 on days 1, 36, and 71; Ara-c and 6-thioguanine every 12 hr for 12 doses on days 15, 50, and 85; methotrexate days 15, 17, 57, and 59; vincristine and prednisone days 50 and 57; L-asparaginase beginning day 99, three times weekly for a total of 6 doses, and cyclophosphamide day 110 following last dose of L-asparaginase. Arm II: daunomycin days 1-3, Ara-C continuous infusion days 1-5, 6-thioguanine every 12 hr days 15, followed by a 21-28 day rest period. Methotrexate every 10 days from 28-98, L-asparaginase every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 weeks for 36 months or until relapse. An adequate trial will be the completion of remission induction.

Progress: This study closed to patient entry 15 Nov 91. Seven patients were enrolled MAMC. All original patients enrolled at MAMC have died but 1 patient has transferred in (previous FY) and is being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/033 **Status:** On-going

Title: SWOG 8501 (INT 0051): Intraperitoneal Cis-platinum/IV Cyclophosphamide vs IV cis-platinum/IV Cyclophosphamide in Patients with Non-measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III ....

Start Date: 01/16/87 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ David M. Dunning, MC
CPT David R. Bryson, MC
MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC
MAJ Ruben D. Sierra, MC
COL Roger B. Lee, MC

Key Words: cancer:ovarian, chemotherapy, IP, IV cyclophosphamide, cisplatinum

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To perform a Phase III randomized trial of intermediate dose intraperitoneal (IP) cis-platinum and intravenous (IV) cyclophosphamide vs intermediate dose IV cis-platinum and cyclophosphamide for optimal Stage III ovarian cancer; to evaluate the comparative toxicities of the two regimens; and to determine, in the setting of a prospective randomized trial, if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and IP drug administration.

Technical Approach: Only patients with epithelial neoplasms will be eligible. Patients will be stratified by amount of residual disease and performance. They will be randomized to Arm I or Arm II. Arm I: IV cisplatin, 100 mg/m^2 plus IV cyclophosphamide, 600 mg/m^2 every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m^2 plus IV cyclophosphamide, 600 mg/m^2, every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

Progress: This study was closed to patient entry 15 Jul 92. One patient was entered in Dec 86 and refused second look surgery so he was taken off the protocol, but is being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/107 **Status:** On-going

Title: SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III

Start Date: 08/21/87 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL William D. Belville, MC
LTC Lauren K. Colman, MC
MAJ David M. Dunning, MC
CPT Denis Bouvier, MC
COL Irwin B. Dabe, MC
COL Victor J. Kiesling, MC
MAJ Thomas M. Baker, MC
MAJ Ruben D. Sierra, MC

Key Words: cancer:bladder, BCG, immunotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the effectiveness of intravesical and percutaneous BCG immunotherapy given on a maintenance versus no maintenance schedule with respect to disease-free interval and rate of tumor recurrence in patients with transitional cell carcinoma of the bladder; to assess the toxicity of maintenance and no maintenance BCG immunotherapy; and to assess the association of intermediate strength PPD skin test reactivity with disease free status in patients treated with BCG immunotherapy.

Technical Approach: Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG administration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenance or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study.

Progress: This study closed to patient entry 15 Dec 88. Eleven patients were entered in the study and 10 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 86/080 **Status:** On-going

Title: SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma

Start Date: 08/15/86 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ David M. Dunning, MC
MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC
CPT David R. Bryson, MC

Key Words: lymphoma:non-Hodgkin's, chemotherapy, CHOP, m-BACOD, M

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

Technical Approach: Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycles): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV) and prednisone (PO). Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV), bleomycin (IV), dexamethasone (PO), methotrexate (IV), and calcium Leucovorin rescue after each MTX dose. Arm III (Pro-MACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide (IV), doxorubicin (IV), VP-16 (IV), Prednisone(PO), Ara-C (IV), bleomycin (IV), vincristine (IV), methotrexate (IV), calcium leucovorin rescue after each MTX dose, and trimetheprim-sulfamethoxazole (PO). Arm IV (MACOP-B will be given over 12 weeks): methotrexate (IV), calcium leucovorin rescue after each MTX bolus, doxorubicin (IV), cyclophosphamide (IV), vincristine (IV), bleomycin (IV), prednisone (PO), and trimethoprimsulfa (PO). Patients with documented progressive disease may be taken off study at any time; however patients will preferably be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

Progress: This study was closed to patient entry 15 June 1991, and was previously reported as completed. However, two patients were transferred in from another Army medical center and MAMC now follows these patients. It was reactived in December 1993.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 85/073 **Status:** On-going

Title: SWOG 8590: Phase III Study to Determine the Effect of Combining Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of the Head and Neck, Phase III (Intergroup Group.....

Start Date: 06/28/85 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Friedrich H. Stutz, MC
COL William J. Gernon, MC
MAJ Michael D. Stone, MC
LTC Donald B. Blakeslee, MC
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC
CPT David R. Bryson, MC

Key Words: head & neck, surgery, chemotherapy, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

Technical Approach: After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cisplatinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

Progress: This study was closed to patient entry 1 Feb 90. Three patients were entered in previous years and are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 85/064 **Status:** On-going

Title: SWOG 8591: NCI Intergroup #0035, An Evaluation of Levamisole Alone or Levamisole plus 5-Fluorouracil as Surgical Adjuvant Treatment for Resectable Adenocarcinoma of the Colon, Phase III - Intergroup

Start Date: 05/24/85 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Friedrich H. Stutz, MC
MAJ Jens A. Strand, MC
MAJ Michael D. Stone, MC
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC
CPT David R. Bryson, MC

Key Words: cancer:colon, levamisole, 5-Fluorouracil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To assess the effectiveness of levamisole alone and levamisole plus 5-FU as surgical adjuvant regimens for resectable colon cancer; to compare each regimen to untreated controls to determine whether it yields improved survival and if it yields improved time to recurrence, with evaluations conducted independently in patients with Dukes stage B and Dukes stage C lesions.

Technical Approach: Patients with adenocarcinoma arising in the colon who have had a potentially curative section will be eligible. The patients with modified Dukes B2 (serosal penetration) or B3 (invasion of adjacent organs by direct extension) will be randomized to either follow-up without adjuvant therapy or adjuvant therapy with levamisole plus 5-FU. Patients with modified Dukes Stage C (involvement of regional lymph nodes) will be randomized to follow-up without adjuvant therapy, adjuvant therapy with levamisole alone, or adjuvant therapy with levamisole plus 5-FU.

Progress: This study was closed to patient entry 21 Oct 87. Seven patients were enrolled in preveious years and 6 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 87/045 **Status:** On-going

Title: SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia

Start Date: 02/27/87 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ Ruben D. Sierra, MC
COL Irwin B. Dabe, MC
LTC Howard Davidson, MC
MAJ David M. Dunning, MC
CPT David R. Bryson, MC

Key Words: leukemia:non-lymphocytic, Ara-C, daunorubicin, cytosine arabinoside

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high-dose cytosine arabinoside and daunorubicin; to compare the duration of complete remission and of disease-free survival among patients who receive one of the three combinations of induction and consolidation regimens listed below; to determine the comparative toxicities of these three programs, and to determine the feasibility of implementing a predetermined approach to supportive care for these patients in a multi-institutional cooperative group setting.

Technical Approach: Patients will be stratified according to age and institution. Induction therapy will consist of standard dose Ara-C plus daunorubicin (Arm I) or high dose Ara-C + daunorubicin (Arm II). Patients requiring a second cycle of induction will receive the same doses as cycle 1, following the recovery of hematologic toxicities. Consolidation chemotherapy will begin when bone marrow and blood counts have recovered or on day 28 after the last induction cycle. Patients initially randomized to Arm I will be randomized to Arm III (high dose, one cycle only) or Arm IV (standard dose, two cycles). Patients initially randomized to Arm II (high dose) will be assigned to Arm III. Following the completion of consolidation, no further therapy will be given and patients will be followed only. Supportive care will include a predetermined antibiotic regimen determined by the physician.

Progress: This study was closed to patient entry 1 Dec 91. Of the seven patients enrolled at MAMC, 5 have died and 2 are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/039 **Status:** On-going

Title: SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)

Start Date: 02/16/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Rodney C. Davis, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC

Key Words: cancer:bladder, cystectomy, M-VAC

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To study insulin induced hypoglycemia as a model of acute stress and to determine if the change in testosterone seen with acute stress is related to cortisol alone or whether it can also be seen with the stimulation of other adrenal precursor products.

Technical Approach: Ten healthy male volunteers (18-35 years) who are without evidence of current acute or chronic illness will have an insulin tolerance test done with blood samples drawn for cortisol, testosterone, immunoactive LH, bioactive LH, estradiol, and glucose, every 15 minutes for one hour prior to the human insulin bolus to establish baseline values. Blood samples will continue to be drawn every 15 minutes for 180 minutes after injection of the insulin. SHBG will be measured on the first and last sample and endorphin levels will be measured at baseline and at times corresponding to maximal hypoglycemia. A standard multiple dose metyrapone test will be performed one month from the insulin tolerance test. Just before the first dose and four hours after the last dose, serum samples will be obtained for cortisol, estradiol, immunoactive LH, bioactive LH, testosterone, ACTH, SHBG, endorphins, and 11-deoxycortisol. The relationship of bioactive LH to immunoactive LH will be compared using the biologic to immunologic ratio both before and during the acute stress. The data from the metyrapone test will be used to determine if metyrapone can cause a decrease in serum testosterone acutely. Again, the B/I ratio will be compared pre and post-test. Changes in serum concentrations of the measured hormones will be analyzed by repeated measures analysis of variance.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 88/065 **Status:** On-going

Title: SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy

Start Date: 07/15/88 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
CPT Denis Bouvier, MC
MAJ Rahul N. Dewan, MC
COL Irwin B. Dabe, MC
LTC Steven S. Wilson, MC

Key Words: lymphoma:non-Hodgkin's, radiotherapy, CHOP, chemotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate, in a cooperative group setting, the difference in survival, time to treatment failure, and toxicity of two curative approaches to the treatment of patients with localized, intermediate or high grade non-Hodgkin's lymphoma.

Technical Approach: All patients must have biopsy proven non Hodgkin's lymphoma of intermediate or high grade histology except lymphoblastic lymphoma. Patients must have had all visible tumor removed (excisional biopsy) and must have clinically adequate liver and myocardial function to begin treatment at full doses. Patients with known central nervous system disease, previous cancer with a possibility for recurrence which might affect survival or prior chemo or radiotherapy will be ineligible. All patients will be stratified at the time of initial registration by the following: (1) age (<65 years vs >65 years); (2) Stage (I or Ie vs nonbulky II or IIe); (3) histology (diffuse large cell vs other); (4) location of disease (GI involved vs non-GI, abdominal vs non-GI, other); (5) all disease resected vs residual measurable disease. Patients will be randomized to CHOP* (Arm I) or to CHOP plus radiation therapy (Arm II). A complete course of chemotherapy on Arm I will consist of the administration of CHOP every 21 days for eight consecutive cycles unless progressive disease develops. A complete course of chemotherapy for Arm II will consist of the administration of CHOP every 21 days for three consecutive cycles unless progressive disease develops. Radiation therapy will begin immediately after the third cycle of CHOP. Radiation therapy dose, duration, and treatment volume will be determined jointly by the radiation oncologist and the medical oncologist. All patients will be followed at three month intervals until death. CHOP: Cyclophosphamide, 750 mg/m^2 IV, day 1; Doxorubicin, 50 mg/m^2 IV, day 1; Vincristine, 1.4 mg/m^2 IV, day 1; Prednisone, 100 mg/day po, days 1-5.

Progress: This study closed to patient entry 15 June 95. Nine patients have been enrolled at MAMC. Two have expired, so seven continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 88/076 **Status:** On-going

Title: SWOG 8738: Treatment of Extensive Non-small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III

Start Date: 09/16/88 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
LTC Kenneth A. Bertram, MC
COL Irwin B. Dabe, MC
CPT Denis Bouvier, MC

Key Words: cancer:lung:non-small cell, cisplatin, mitomycin-C

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare standard dose cisplatin chemotherapy to high dose cisplatin in hypertonic saline alone to high dose cisplatin/mitomycin-C in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; and to compare the relative toxicities of these three chemotherapy regimens in patients with extensive non-small cell lung cancer.

Technical Approach: Patients will be randomized to one of the following arms: Arm I: standard dose cisplatin (50 mg/m^2, IV) every four weeks for a maximum of eight cycles; ARM II: high dose cisplatin alone (100 mg/m^2, IV) every four weeks for a maximum of four cycles; ARM III: high dose cisplatin (100 mg/m^2 IV) plus mitomycin-C (8 mg/m^2 IV) given every four weeks for a maximum of four cycles. All patients will have an initial assessment of response after two cycles and then reassessment after four cycles of therapy. Patients on Arm I who respond to treatment may receive continued therapy to a maximum of eight cycles. Upon progression of disease, unacceptable toxicity, or patient request, patients will be taken off treatment. All patients will be followed until death.

Progress: This study was closed to patient entry 1 Jun 90. Six patients were enrolled at MAMC in previous years and 1 continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/063 **Status:** On-going

Title: SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors

Start Date: 04/20/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: tumor:germ cell, etoposide, cisplatin, carboplatin, CBDCA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine in a randomized trial the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens; etoposide + cisplatinum and etoposide + carboplatin, for good risk patients with germ cell tumors.

Technical Approach: Patients with active advanced Stage II or Stage III testicular nonseminomatous germ cell tumor with a probability of complete response of >0.5 will be eligible. Patients will be randomized to Treatment Arm A (carboplatin + etoposide, given every 28 days for four cycles) or Treatment Arm B (cisplatin + etoposide every 21 days for four cycles). Following completion of chemotherapy, a complete assessment of all sites of disease will be performed. Following completion of four cycles of chemotherapy and radiographic and marker assessment, surgical resection of all residual masses will be done if deemed necessary by the principal investigator. If no residual malignant tumor or only mature teratoma is completely resected at surgery, no further therapy will be administered. If residual malignant tumor is found but is completely excised, then two more cycles of treatment will be administered. If residual malignant tumor is found but is unresectable, then the patient will receive additional therapy with standard GCT regimens or other therapy as may be indicated at the discretion of the treating physician.

Progress: This study closed to patient entry 15 Dec 90. One patient was enrolled at MAMC and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/119 **Status:** On-going

Title: SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators:
COL John C. Norbeck, MC
CPT Timothy O. Taylor, MC
CPT Bradley F. Schwartz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
COL John N. Wettlaufer, MC
LTC Kurt L. Hansberry, MC
CPT Michael D. Bagg, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC

Key Words: Cancer:prostate, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: One patient was enrolled at MAMC and continues to be followed. Patient accrual continues.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 88/066	**Status:** On-going
Title: SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)		
Start Date: 07/15/88	**Est. Completion Date:** Indefinite	
Department: SWOG	**Facility:** MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: CPT Denis Bouvier, MC	COL Irwin B. Dabe, MC	
Key Words: Hodgkin's Disease, chemotherapy		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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/m^2 IV, days 1 and 8, Vincristine, 1.4 mg/m^2 IV, days 1 and 8, Procarbazine, 100 mg/m^2 PO per day x 14 days, Prednisone 40 mg/m^2 PO per day x 14 days. ABVD: Adriamycin, 25 mg/m^2 IV, days 1 and 15, Bleomycin, 10 units/m^2 IV, days 1 and 15, Vinblastine, 6 mg/m^2 IV days 1 and 15, DTIC, 375 mg/m^2 IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m^2 IV, day 8; bleomycin, 10 units/m^2 IV day 8; and vinblastine, 6 mg/m^2 IV, day 8.

Progress: This study was closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/064 **Status:** On-going

Title: SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas

Start Date: 04/20/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: lymphoma, alpha-interferon, ProMACE-Mopp, chemo

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the disease-free survival of patients with low grade malignant lymphoma who receive alpha-interferon consolidation therapy after intensive induction with chemotherapy, with or without radiation therapy, to those who receive induction therapy alone; to determine the complete response rate, response duration, and survival of low grade lymphoma patients treated with ProMACE-MOPP; and to compare the toxicities of induction and induction plus consolidation therapy in this patient population.

Technical Approach: Patients must have biopsy proven, measurable, Stage III or IV non-Hodgkin's lymphoma of low grade histology. Patients will receive 6 cycles of induction chemotherapy (ProMACEMOPP, days 1-8) unless progressive disease develops during this treatment. At the completion of induction therapy, patients will be restaged to assess response. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete radiographic and laboratory evaluation for evidence of persistent lymphoma approximately one month after completion of chemotherapy. If no evidence of disease is found these patients will be randomized to Alpha IFN or observation. Patients in partial response and whose bone marrow remains positive after 6 cycles of induction chemotherapy will receive 2 additional cycles of chemotherapy and then be reevaluated. If the bone marrow remains involved or the patient has less than a partial response after a total of 8 cycles, the patient will be removed from further protocol therapy. If after 8 cycles, the bone marrow is negative and the patient is in partial response, the patient will receive radiotherapy. Complete responders after induction chemotherapy; complete responders after induction chemotherapy plus radiation therapy; and partial responders after chemotherapy plus radiation therapy will be randomized to consolidation alpha interferon or observation, approximately one month after completion of therapy.

Progress: This study was closed to patient entry 15 Nov 94. Four patients have been entered at MAMC. All patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 89/080 **Status:** On-going

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....

Start Date: 09/15/89 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:breast, chemoendocrine therapy, CAF, tamoxifen

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$8692.00	**Periodic Review:** 11/17/95

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 have been entered in this study at MAMC. One patient expired in FY 96, 6 others are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/020 **Status:** On-going

Title: SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II

Start Date: 12/07/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC

Key Words: mycosis fungoides, retinoic acid, interferon-A

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate the response rate of mycosis fungoides treated with the drug combination of 13-cis retionoic acid (Accutane) plus alpha interferon (Roferon-A) and to assess the qualitative and quantitative toxicities of the regimen in a phase II study.

Technical Approach: Mycosis fungoides is an uncommon lymphoma manifesting initially with skin presentation, but the disease is felt to be incurable. The regimen will be 13-cis retinoic acid, 1.0 mg/kg/day, po in two divided doses (plus vitamin E, 400 IU/day) and alpha interferon, $3x10^6$ microgm/m^2 subcutaneously, three times per week. After eight weeks of treatment, patients with progressive disease will go off treatment. Patients with stable disease or partial or complete remission will be treated for eight more weeks. At this point, patients who have not demonstrated a partial response will be taken off study. Patients who have partial or complete response will be treated for an additional one (complete response) or two years (partial response).

Progress: This study closed to patient entry 3 Jan 93. One patient was enrolled in FY92 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/087 **Status:** On-going

Title: SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954

Start Date: 08/02/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Everardo E. Cobos Jr., MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ James S. D. Hu, MC

Key Words: lymphoma:tissue procurement

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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. One patient expired in FY 96, tissue will be collected on the 2 patients that are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/027 **Status:** On-going

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....

Start Date: 01/19/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:breast, chemotherapy, chemohormonal therapy, premenopausal

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$8200.00	**Periodic Review:** 11/17/95

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 1 Feb 94. Six patients have been enrolled at MAMC in previous years. One patient has been lost to follow-up, five are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/047 **Status:** On-going

Title: SWOG 8854: prognostic Value of Cytometry Measurements of Breast Cancer DNA from Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814

Start Date: 03/16/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: None

Key Words: cancer:breast, DNA, cytometry, postmenopausal

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine if ploidy analysis of breast cancer by routine clinical flow cytometry (CFM) technique can predict response to therapy and survival of patients registered to SWOG 8814 and to determine if ploidy analysis by image processing technique more accurately predicts patient response to therapy and survival than ploidy analysis by flow cytometry.

Technical Approach: Two paraffin blocks, one representing the highest grade region of the primary tumor, the second representing the highest grade regional metastasis in a positive lymph node, will be used. From each of these blocks, two to five sections will be cut and a nuclear suspension prepared. From each suspension, a cytospin preparation will be prepared and stained with Dif-Quik to ensure that the cells present in the H & E slide are represented adequately in the nuclear preparation. A second cytospin preparation will be prepared for staining by the Feulgen technique for image processing DNA analysis. The remainder of the nuclear preparation will be stained with propidium iodide following RNase digestion for FCM DNA analysis. Cox regression modeling will be used to explore the prognostic value of ploidy status as determined by FCM and by image processing, in conjunction with the covariates tumor size, age, ER and PgR levels, and number of nodes.

Progress: This study closed to patient entry 15 Feb 95. This is a companion study using tissue from SWOG 8814. Six samples have been studied, one of the patients has expired in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/067 **Status:** On-going

Title: SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients

Start Date: 06/14/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
LTC Robert B. Ellis, MC

Key Words: cancer:head & neck, cytometry, DNA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: One new patient has entered into this study at MAMC in FY96, total is now 4 patients. Patient accrual continues.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/055 **Status:** On-going

Title: SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III

Start Date: 03/16/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
LTC Kenneth A. Bertram, MC
MAJ Michael R. Morris, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:nasopharyngeal, 5-Fluorouracil, cisplatin, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$3900.00	**Periodic Review:** 11/17/95

Study Objective: To compare radiotherapy with radiotherapy and concurrent cisplatin, followed by three courses of 5-FU + cisplatin for complete response rate, time to treatment failure, overall survival, pattern of recurrence, and qualitative and quantitative toxicities.

Technical Approach: To be eligible, patients must have histologically proven nasopharyngeal carcinoma (excluding adenocarcinoma), Stage III or IV with no evidence of distant metastatic disease, and must not be eligible for higher priority SWOG studies. Patients will be randomized as follows: Arm I: radiation therapy alone for approximately 7 weeks; Arm II: 3 courses of cisplatin (days 1, 22, and 43) concurrent with radiotherapy followed by three courses of 5-FU + cisplatin. Measurable disease must be assessed at least every eight weeks the first year of follow-up. Patients will be seen in follow-up every two months the second year, every three months the third year, and every four months thereafter. A tumor biopsy for flow cytometry will be obtained if tumor recurs.

Progress: This study was closed to patient entry on 1 Dec 95. One patient was enrolled in FY91 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/086 **Status:** Completed

Title: SWOG 8894: (INT-0105, EST-2889): A Comparison of Bilateral Orchiectomy with or without Flutamide for the Treatment of Patients with Histologically Confirmed Stage D2 Cancer

Start Date: 06/15/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:prostate, orchiectomy, flutamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare survival, progression free survival, and qualitative and quantitative toxicities between patients with orchiectomy alone and patients with orchiectomy plus Flutamide.

Technical Approach: Patients must have a histologically proven diagnosis of pathologic stage D2 adenocarcinoma of the prostate with evidence of metastatic disease. Patients must not have had prior hormonal therapy, chemotherapy, or biological response modifiers. Patients will be randomized to bilateral orchiectomy plus placebo po three times a day with meals or to bilateral orchiectomy plus Flutamide po three times a day with meals. Upon disease progression, patient treatment will be unblinded. Patients treated with Flutamide will be taken off protocol. Patients treated with placebo will be offered flutamide given according to the protocol guidelines until the next evidence of progression at which time they will be taken off study.

Progress: This study was closed to patient entry, 15 Sep 94. Three patients were enrolled at MAMC and one patient was accepted in transfer, two patients are deceased and the other two expired in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/029 **Status:** On-going

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...

Start Date: 01/19/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:breast, chemotherapy, endocrine therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$5000.00	**Periodic Review:** 11/17/95

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 was closed to patient entry 1 Feb 93. Nine patients were enrolled in previous years, one expired in FY 96 and the other eight are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 89/021 **Status:** On-going

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...

Start Date: 02/17/89 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
LTC Kenneth A. Bertram, MC
COL Irwin B. Dabe, MC
CPT Denis Bouvier, MC
MAJ Everardo E. Cobos Jr., MC

Key Words: cancer:colon, resection, chemotherapy, leucovorin, levamisole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$50.00	**Periodic Review:** 11/17/95

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/m^2 + 5-FU 425 mg/m^2; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m^2 + 5-FU 600 mg/m^2; 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: Eighteen patients were enrolled at MAMC prior to closure to patient entry on 30 Jul 92. One patient was lost to follow-up, five patients have died from their disease and 12 continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/079 **Status:** Completed

Title: SWOG 8925: Evaluation of Cisplatin + VP-16 Followed by Mitotane at Progression if no Prior Mitotane or Cisplatin + VP-16 Only if Prior Treatment with Mitotane in Patients with Advanced and .....

Start Date: 06/05/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ Paul C. Sowray, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, adrenal, cisplatin, mitotane, VP-16

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate response and response duration of patients with adrenocortical carcinoma treated with combination chemotherapy consisting of cisplatin and etoposide and of patients who receive mitotane after progression on the above chemotherapy (if no prior treatment with mitotane); to evaluate the qualitative and quantitative toxicities of these therapies; and to evaluate and compare tumor morphology of patients with rare tumor.

Technical Approach: Patients will be placed in one of two treatment groups. Patients in Group A will not have received any prior chemotherapy. Patients in Group B will have received prior treatment with Mitotane. Eligible patients in Group A and Group B will be treated with cisplatin plus etoposide every 21 days for a total of 12 months or until progression of disease occurs. Group A patients who develop progressive disease will be treated with Mitotane. Group B patients who progress will be taken off protocol.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/089 **Status:** On-going

Title: SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816

Start Date: 08/02/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Luke M. Stapleton, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ James S. D. Hu, MC

Key Words: lymphoma:serum repository

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 studies. Two specimens have been collected in previous years (0 in FY96).

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/006 **Status:** Completed

Title: SWOG 8952 (INT-0111), (CALG-8952), EST-5487): Treatment of Advanced Hodgkin's Disease - A Randomized Phase III Study Comparing ABVD vs MOPP/ABV Hybrid

Start Date: 10/19/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ William A. Phillips

Associate Investigators:
MAJ Paul C. Sowray, MC
LTC Luke M. Stapleton, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Everardo E. Cobos Jr., MC
LTC Robert B. Ellis, MC

Key Words: Hodgkin's disease, ABVD, MOPP, ABV Hybrid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare ABVD to the MOPP/ABV hybrid as therapy for patients with advanced Hodgkin's disease in terms of complete response rates, disease-free survival, failure-free survival, and both immediate and long term toxicities; to compare the rate of drug delivery of the anti-neoplastic agents, especially the comparative dose rate of ABV in the two treatment groups; and to examine the prognostic importance of time to response, performance status, age, presence of bulky disease, C-reactive protein, erythrocyte sedimentation rate, and prior radiotherapy on survival.

Technical Approach: Until recently, MOPP (nitrogen mustard, vincristine, procarbazine, prednisone) was the standard therapy for advanced Hodgkin's disease. In recent studies, the efficacy of AVBD (doxorubicin, bleomycin, vinblastine, DTIC) containing regimens has been equivalent to or superior to MOPP alone. Eligible patients will be those with histologically documented Hodgkin's disease so advanced that chemotherapy is the treatment of choice. Patients will be randomized to ABVD (all drugs given IV, days 1 and 15) or the MOPP/ABV hybrid (nitrogen mustard and vincristine IV day 1, oral procarbazine days 1-7, oral prednisone days 1-14, and doxorubicin, bleomycin, and vinblastine IV day 8. Cycles will be repeated every 28 days for 6 cycles unless disease progression is documented. At the end of 6 cycles, patients identified to be in complete response will receive an additional two cycles. Patients in partial response will be treated until they reach a complete response and then receive two further cycles for a maximum of 10 cycles.

Progress: This study was closed to patient entry 10 Nov 95. No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/007 **Status:** On-going

Title: SWOG 8957: Feasibility Trial of Post-Operative Radiotherapy Plus Cisplatin Followed by Three Courses of 5-FU Plus Cisplatin in Patients with Resected Head and Neck Cancer, Phase II Pilot

Start Date: 10/19/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
LTC Luke M. Stapleton, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
LTC Robert B. Ellis, MC

Key Words: cancer:head & neck, radiotherapy, cisplatin, 5-Fluorouracil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$9130.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate the feasibility of administering three courses of chemotherapy to resected patients who have received cisplatin and radiation therapy post-operatively and to evaluate the qualitative and quantitative toxicities.

Technical Approach: Patients who have had resected squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx are eligible for the study. Chemotherapy used prior to surgery or radiotherapy in untreated head and neck cancer patients has produced particularly high rates of response. However, previous studies have shown that 20-25% of these patients will refuse further surgery or radiotherapy because of an initial good overall response with chemotherapy alone. To avoid this problem, the chemotherapy in this study will be given after surgery, along with radiation and as maintenance afterwards. Cisplatin, 100 mg/m^2, on days 1, 22, and 43 will be given concomitant with radiation therapy. Three to four weeks post-radiation therapy, maintenance chemotherapy will be started. Maintenance chemotherapy will consist of cisplatin, 100 mg/m^2, day 1 every 21 days for three courses and 5-FU, 1000 mg/m^2, days 1-4, every 21 days for three courses.

Progress: This study closed to patient entry 1 May 92. One patient was enrolled in FY92 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/021 **Status:** On-going

Title: SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver; Surgical Resection of Hepatic Metastases in Combination with Continuous .....

Start Date: 12/07/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ William A. Phillips

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
COL Joseph F. Homann, MC

Key Words: cancer:colorectal, resection, chemotherapy, liver

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To study the effects of long-term continuous infusion of Floxuridine (FUDR)intra-arterially and 5-FU systemically as therapy for liver metastases from colorectal primaries and to study the incidence of recurrence and time to recurrence in patients with 1-3 hepatic metastases treated with resection and continuous infusion of 5-FU into the systemic venous system and FUDR into the hepatic artery.

Technical Approach: This study attempts to combine surgical resection with long term hepatic artery infusion of chemotherapy and continuous infusion 5-FU. Patients with histologic confirmation of colorectal primary carcinoma and evidence of 1-3 liver metastases wither on CAT scan, liver scan or previous laparotomy, with no metastatic disease other than to the liver will be randomized to either surgery plus observation or sugary plus FUDR and 5-FU. FUDR will be given 0.1 mg/kg/day continuously for 14 days via Infusaid pump or arterial subcutaneous device. This cycle will be repeated every 28 days for 4 cycles. 5-FU will be given 200 mg/m^2/day IV continuously for 14 days via permanent IV access device beginning of day 15 of each 28 day cycle and repeated for 4 cycles. When FUDR therapy ends, the IV dosage of 5-FU will be escalated to 300 mg/m^2/day IV continuously for 14 days and repeated every 28 days for eight more cycles.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/131 **Status:** On-going

Title: SWOG 8994: Evaluation of Quality of Life in Patients with Stage C Adenocarcinoma of the Prostate Enrolled on SWOG 8794

Start Date: 08/05/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators: None

Key Words: Cancer:prostate, surgery, radiation therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning

Technical Approach: This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles willb e compared for the two treatment groups at different points in time: baseline, where no differenced are expected six weeks, where the two treatment groups are expected to show maxiumum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key congtinuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurence of specified complications, standard methods of categorical data analysis will be employed.

Progress: One patient was enrolled in FY95 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 90/056 **Status:** On-going

Title: SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide

Start Date: 03/16/90 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
LTC Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
LTC Robert L. Sheffler, MC

Key Words: cancer:testicular, chemotherapy, cisplatin, bleomycin, ifosfamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$12862.00	**Periodic Review:** 11/17/95

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: Prior to closure to patient entry (9 Apr 92) two patients had been enrolled at MAMC. One patient is still being followed (one died Jan 93).

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/056 **Status:** On-going

Title: SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients

Start Date: 03/05/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: Waldenstrom's Macroglobulinemia

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$3352.00	Periodic Review: 11/17/95

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/m^2 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: Two patients were enrolled in FY 93 and are still being followed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 91/094	**Status:** On-going
Title: SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary		
Start Date: 09/06/91	**Est. Completion Date:** Indefinite	
Department: SWOG	**Facility:** MAMC	
Principal Investigator: LTC Kenneth A. Bertram, MC		
Associate Investigators: MAJ Paul C. Sowray, MC MAJ Patrick L. Gomez, MC LTC Robert B. Ellis, MC CPT Jennifer L. Cadiz, MC	LTC Howard Davidson, MC LTC Luke M. Stapleton, MC LTC Robert L. Sheffler, MC MAJ Richard C. Tenglin, MC MAJ James S. D. Hu, MC	
Key Words: cancer:leukemia, cytogenetic studies		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on SWOG protocols and at various times in the course of treatment; to estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients; and to provide quality control for all SWOG cytogenetic data.

Technical Approach: Patients on this study must be registered on one of the following SWOG protocols: 8326, 8600, 8612, 9034, 9108, and all new leukemia protocols approved as of 1990 by SWOG. Patients will receive treatment as directed by the treatment protocols and the treatment protocols will specify when specimens are to be submitted for cytogenetic analysis. Bone marrow samples will be submitted whenever possible, unless the treatment protocol specifies otherwise. However, if the marrow is not aspirable ("dry tap"), a peripheral blood sample will be submitted. A patient may only be registered on this protocol once. Data will be collected by major categories of leukemia: first line AML, first line ALL, relapsed AML, chronic phase CML, CML patients in acceleration or blast crisis; and hairy cell leukemia. The study will be open for accrual of patients for a minimum of five years. The smallest group of patients (CML in acceleration or blast crisis) is expected to have at least 100 patients by that time.

Progress: Five patients were entered in this study at MAMC in previous years. Three are deceased and two are being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/051 **Status:** On-going

Title: SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II

Start Date: 04/03/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Luke M. Stapleton, MC

Associate Investigators:
MAJ Rahul N. Dewan, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, gastric, adenocarcinoma, chemoradiation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate the possible benefit of adjuvant chemoradiation therapy in patients with resected gastric cancer to include: comparison of overall and disease free survival between patients being treated with surgical resection only and those being treated with surgery plus adjuvant therapy; comparison of incidence and patterns of disease failure between surgery and surgery plus adjuvant therapy treated patients; and assessment of patient tolerance of upper abdominal chemoradiation after gastric resection.

Technical Approach: Patients will be randomized to either observation or adjuvant therapy. Adjuvant therapy will consist of one course of 5-FU and Leucovorin given IV. Four weeks later the patient will receive a second course of 5-FU with Leucovorin with concomitant radiation therapy. While receiving radiation therapy, the patient will receive a third course of 5-FU and Leucovorin, which will occur during the fifth week of radiation therapy. After completing radiation therapy, the patient will receive two additional courses of chemotherapy to begin approximately 35 days after completion of radiotherapy.

Progress: One patient was enrolled (FY 94) and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/033 **Status:** On-going

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 ....

Start Date: 02/01/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
COL Joseph F. Homann, MC
MAJ Everardo E. Cobos Jr., MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
COL Daniel G. Cavanaugh, MC

Key Words: cancer:esophagus, chemotheray, surgery, modality therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 was closed to patient entry 31 Dec 95. Three patients have entered this study in previous years. Two are being followed and one died of the disease.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/143 **Status:** On-going

Title: SWOG 9019: A Phase III, Randomized, Prospective Comparison Between Chemotherapy Plus Radiotherapy, and the Same Chemotherapy Plus Radiotherapy Together With Surgery for .... Non-Small Cell Lung Cancer

Start Date: 06/09/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:non-small cell lung

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To assess whether concurrent chemotherapy and radiotherapy, followed by surgical resection, results in a significant improvement in progression-free, overall, and long-term survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2 Positive) and selected IIIB non-small cell lung cancer. (2) To 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 metastasis.

Technical Approach: Patients with regionally advanced non-small cell lung carcinoma will be randomized to one of two arms. Arm I: patients will receive induction radiation therapy to a "tight" field to 4500 cGy. They will receive concurrent cisplatin on days 1 and 8 and on days 29 & 36 with VP-16 days 1-5, repeated on days 29-33 (2 cycles). After completion of induction, patients will be re-evaluated for extent of disease. If there is no progression of the disease, patients will go to exploratory thoracotomy for complete removal of the primary lesion and sampling of nodes.

If the tumor is unresectable or the margins are positive or the mediastinal nodes are positive, an additional 2 cycles of chemotherapy with a radiation boost will be given. Patients who complete the induction phase but have persistent supraclavicular node metastases will also receive 2 more cycles of concurrent chemo-radiotherapy will not go to surgery.

Arm II patients receive "standard" lung field radiation therapy to 4500 cGy and concurrent cisplatin and VP-16 for 2 cycles.

One week prior to completing radiation therapy, patients will be re-evaluated for response. Those patients with no evidence of distant metastases or local progression will continue radiation therapy with no break for an additional 1600 cGy with a boost. They will also receive 2 more cycles of chemotherapy concurrent with radiation.

Any patient who shows local or distant progression after induction chemo-radiation will be taken off protocol..

Progress: Two patients have been enrolled in this study in previous years (1 in FY95). One patient continues to be followed and the other died of the disease.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/052 **Status:** On-going

Title: SWOG 9031: A Double Blind Placebo Controlled Tiral of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Luekemia, Phase III

Start Date: 04/03/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, leukemia, myeloid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the complete response rates and duration of survival in patients 56 or older with acute myeloid leukemia (AML) when treated with standard doses of cytosine arabinoside (Ara-C) and daunorubicin (DNR), with or without recombinant human granulocyte-colony stimulating factor (rhG-CSF); to assess the frequency and severity of toxicities of the two treatment regimens; to compare the duration of neutropenia and thrombocypotenia, the total number of febrile days, the number of days of antibiotic therapy, the number and type of infection episodes, and the number of hospital days in patients treated with or without rhG-CSF; and to correlate biological parameters including cell surface immunophenotype, ploidy, and cytogenetics with clinical response.

Technical Approach: Patients aged 56 and older with AML will be randomized to receive treatment with either Ara-C/DNR plus rhG-CSF or Ara-C/DNR plus placebo (Ara-C days 1-7, C/DNR days 1-3, and blinded drug begins on day 10) Patients who had regrowth of leukemia during this course of treatment will receive a second identical course of treatment except the blinded drug will not be started until the marrow shows <5% blasts. The blinded drug will not be given in the second induction course if the patient has regrowth of leukemia following the first induction course. Following completion of induction therapy, patients who achieve complete remission will be registered to receive two cycles of post-remission therapy, utilizing the same regimen to which they were originally randomized.

Progress: This study closed to patient accrual 1 Jan 95. Two patients have been enrolled in this study in in previous years. One is deceased and one is being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/095 **Status:** On-going

Title: SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia

Start Date: 08/07/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, myelogenous, leukemia

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare the duration of survival in patients with chronic myelogenous leukemia (CML) in blast phase, when treated with either chemotherapy (Ara-C/Daunomycin) alone or chemotherapy plus the resistance modifier, cyclosporine-A (CyA); to estimate the frequency of P-glycoprotein expression and its association with blast lineage and prognosis; and to compare the frequency and severity of toxicity of the two treatment regimens.

Technical Approach: Patients will be randomized to receive treatment with either Ara-C/Daunomycin alone or Ara-C/Daunomycin + CyA. If the day 14 bone marrow shows less than or equal to a 50% reduction in the absolute blast count per 500 cell differential compared with the pretreatment bone marrow, the patient will be considered a treatment failure and removed from the study. If there is more than a 50% reduction in the blast count as stated above, but the patient has not achieved a complete remission or restored chronic phase status, a second course of the original induction regimen will begin on or after day 21. Patients who do not achieve complete remission or restoration of chronic phase after two inductions will be removed from the protocol. Patients who achieve complete remission or restored chronic phase will receive one course of consolidation therapy (same regimen as for induction therapy).

Progress: No patients have been entered at MAMC. Patient accrual continues.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/062 **Status:** On-going

Title: SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III

Start Date: 01/20/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Richard F. Williams, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Cancer:melanoma, immunotherapy, vaccine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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.

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: One patient was enrolled in FY95. Patient accrual continues.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/077 **Status:** Completed

Title: SWOG 9039: Evaluation of Quality of Life in Patients with Stage D2 Cancer of the Prostate Enrolled on SWOG 8894

Start Date: 07/12/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC

Key Words: cancer:prostate, quality of life

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare three primary quality of life endpoints according to treatment assignment: (1) treatment specific symptoms, (2) physical functioning, (3) emotional functioning; and to compare four secondary quality of life variables, according to treatment assignment: (1) general symptoms, (2) role functioning, (3) global perception of quality of life, (4) social functioning.

Technical Approach: This cancer control intervention study measures quality of life in patients with advanced carcinoma of the prostate, specifically SWOG protocol 8894: Treatment of Stage D2 Carcinoma of the Prostate Comparing Orchiectomy +/- Flutamide. The presence or absence of flutamide provides the intervention for this cancer control companion study. Thus, the benefits of randomization, uniform patient selection, and treatment standardization are transferred to the quality of life investigation. The comparison of quality of life measurements between treatment arms will complement the analysis of survival and response data for patients registered to SWOG 8894 and become a critical consideration if no difference is demonstrated in survival between the treatment arms. The Quality of Life Questionnaire will be completed at study entry and at 1, 3, and 6 months after study entry.

Progress: This study closed to patient entry 15 Sept 94. Study is completed with the death of patient (12 Dec 95) who was enrolled FY 93.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/069 **Status:** On-going

Title: SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study

Start Date: 06/14/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Rahul N. Dewan, MC
LTC Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC
LTC Steven S. Wilson, MC
LTC Robert B. Ellis, MC

Key Words: cancer:rectum, 5-Fluorouracil, leucovorin, levamisole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 was closed to patient entry on 22 Nov 92. Three patients were enrolled in previous years and continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/104 **Status:** On-going

Title: SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer: colorectal, chemoprevention, calcium carbonate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: Nine patients have been entered in this study (2 in FY 96), and all continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/032 **Status:** On-going

Title: SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation....Breast Cancer at High Risk of Recurrence

Start Date: 12/04/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:breast, chemotherapy, bone marrow transplantation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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/m^2 PO X 14 days, doxorubuicin 30 mg/m^2 IV days 1 & 8, and flurouracil 500 mg/m^2 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/m^2/96 hr and ThioTEPA 800 mg/m^2/96 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/m^2/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: First patient has entered this study in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 91/096 **Status:** Completed

Title: SWOG 9108 (CALGB-9011, NCIC-CTG CL.1): A Phase III Comparison of Fludarabine Phosphate vs Chlorambucil vs Fludarabine Phosphate Plus Chlorambucil in Previously Untreated B-Cell Chronic Lymphocytic....

Start Date: 09/06/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ James S. D. Hu, MC

Key Words: cancer:leukemia, B-cell, fludarabine phosphate, chlorambucil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To compare in previously untreated CLL patients the response rates and progression free survival with the following three therapeutic regimens: (1) fludarabine phosphate, (2) chlorambucil, and (3) fludarabine phosphate plus chlorambucil; to determine whether the quality of life (need for transfusions, incidence of infections, and performance status) is superior using any of the three regimens; and to determine whether these two drugs are non-cross-resistant by a crossover design for patients failing to respond to the single agent to which they were initially randomized.

Technical Approach: B-cell chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. This study is designed to compare a new drug, fludarabine, (Arm I) to standard therapy, chlorambucil (an alkylating agent, Arm II), and to the combination of fludarabine and chlorambucil (Arm III). The drugs will be administered every four weeks until patients reach a complete remission or maximally beneficial response (up to one year of treatment). Patients with progressive disease on Arm I or II will crossover to the other single agent arm. After completing the prescribed treatment arm, patients may be re-entered if they relapse. Patients will be randomly assigned, with equal probabilities, to one of the three treatment arms. Randomization will be stratified by risk group and duration of disease with treatment allocations being adjusted as necessary t and is still being followed.

Progress: This study closed to patient entry 7 Dec 94. Study is now complete with the death of MAMC's only patient.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/095 **Status:** On-going

Title: SWOG 9109: Neoadjuvant Zoladex and Flutamide in Bulky and Non-Bulky Clinical Stage C Carcinoma of the Prostate, Phase II

Start Date: 04/01/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators:
COL John C. Norbeck, MC
CPT Timothy O. Taylor, MC
CPT Bradley F. Schwartz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
COL John N. Wettlaufer, MC
LTC Kurt L. Hansberry, MC
CPT Michael D. Bagg, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC

Key Words: Cancer:prostate, Zoladex, Flutamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To evaluate the resectability rate following 16 weks of total androgen blockade therapy. 2) To evaluate the likelihood of clinical response to 16 weeks of total androgen blockade therapy. 3) To assess the feasibility of obtaining flow cytometry specimens for the purpose of evaluating the likelihood of an association between ploidy and clinical response or resectability. 4) To evaluate the qualitative and quantitative toxicities from total androgen blockade therapy and the immediate and long-term morbidity associated with radical prostatectomy and pelvic lymph node dissection following neoadjuvant total androgen blockade therapy. 5) To evaluate time to progression.

Technical Approach: Patients with Stage C, D0, and D1 prostate cancer will begin neoadjuvant total androgen blockade within 24 hours of registration. This treatment will consist of Zoladex 3.6 mg S.Q. every 4 weeks X 16 weeks and Flutamide 250 mg P.O. daily X 16 weeks. Patients will be evaluated by digital rectal exam at weeks 5, 9, 13 and 17, and trans-rectal ultrasound at weeks 9 and 17. After 16 weeks of androgen blockade, patients will be re-evaluated to undergo radical prostatectomy with pelvic lymph node dissection. Patients deemed operable will have surgery performed by week 17 or, if the treatment was interrupted, within one week of completing total androgen blockade. Following surgery, all patients, including those that were unresectable or partially resectable, will be followed for subjective/objective evidence of developing toxicities and progression of disease. Following surgery or attempted surgery, no additional therapy is to be given in the absence of progression, at which time patients will go off protocol treatment. Subsequent therapy off protocol treatment is at the discretion of the investigator.

Progress: No patients entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/053 **Status:** On-going

Title: SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II

Start Date: 04/03/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, soft tissue sarcoma, chemotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate, in patients with high grade soft tissue sarcoma of the extremity, the trunk, or the head and neck, the efficacy of primary chemotherapy, wide surgical resection, adjuvant chemotherapy, and radiotherapy on local control, metastasis free survival, and overall survival; To evaluate the utility of tumor response to primary chemotherapy as an indicator of local and systemic disease control in high grade soft tissue sarcoma; and to evaluate the toxicity of primary chemotherapy, surgery, adjuvant chemotherapy, and radiation therapy in this patient population. Secondary objectives include those listed for SWOG 9136, a companion protocol studying biologic parameters.

Technical Approach: Patients with a high grade soft tissue sarcoma of the extremity, trunk, or head and neck area are eligible. Patients will receive chemotherapy using the drugs adriamycin, DTIC, and ifosfamide, given concurrently for three cycles at 21 day intervals. Patients will then undergo wide surgical excision of the primary tumor. Following recovery from surgery, patients with partial or complete response or stable disease will receive another three courses of therapy, followed four weeks after completion of chemotherapy by radiation therapy to the whole area (days 1-5 for 6-8 weeks).

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/088 **Status:** Completed

Title: SWOG 9122: Evaluation of 5-Fluorouracil by Intermittent Infusion in Combination With Alpha-Interferon for Patients with Advanced Renal Cell Carcinoma

Start Date: 04/02/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC

Key Words: Cancer:renal cell, 5-FU, alpha-interferon

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1. To evaluate the response rate of advanced renal cell carcinoma to treatment with 5-FU and Alpha-Interferon. 2. To evaluate the toxicities of 5-FU and Alpha-Interferon in this patient population.

Technical Approach: Patients with histologically proven renal cell carcinoma which is either metastatic and/or recurrent and bi-dimensionally measurable disease and whose measurements have been provided from x-rays, scans, or physical exam obtained within the past 14 days will be invited to participate in this study.

5-Fluorouracil 750 mg/m^2/day IV (continuous infusion) on days 1 - 5 q3 weeks and Alpha Interferon 5X10(6) U/m^2 SC on days 1,3,5 q3 weeks will be given. The first dose of interferon will be given at the beginning of 5-FU infusion. The second and third dose may be given in the evening. Pretreatment with acetaminophen 650 mg 1 hour prior to Interferon and as needed to reduce fever will be given.

The 5-FU treatment may be administered as an outpatient using a portable infusion pump capable of delivering the stipulated dosage of 5-FU at a rate of 2 ml per hour. Patients will be evaluated in the clinic weekly by a physician.

Progress: This study closed to patient entry 15 Oct 93. One patient was enrolled at MAMC in FY93 and died 19 Mar 96, study is complete.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/138 **Status:** Completed

Title: SWOG 9124: Evaluation of Edatrexate (EDX) in Patients With Relapsed or Refractory Germ Cell Tumors, Phase II

Start Date: 07/02/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC

Key Words: cancer:germ cell, edatrexate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To assess the rate and duration of response to Edatrexate; (2) to evaluate the patterns of toxicity (qualitative and quantitative) in patients treated with Edatrexate.

Technical Approach: Adult patients with relapsed or refractory gonadal or extragonadal germ cell carcinomas will be treated with edatrexate 80 mg/m^2 once weekly for 4 weeks by intravenous bolus injection. After a 1 week rest, patients will be re-treated. One course of therapy consists of 2 cycles (10 weeks) of edatrexate. Therapy will continue until disease progression, unacceptable toxicity or patient withdrawal. Standard response criteria will be utilized to judge response.

Progress: Study was closed to patient entry 1 Sep 96. One patient was enrolled in FY95 and expired 14 Apr 95, study is now completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/017 **Status:** On-going

Title: SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma

Start Date: 12/06/91 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
LTC Luke M. Stapleton, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ James S. D. Hu, MC

Key Words: cancer, non-Hodgkin's lymphoma, CVAD, verapamil, quinine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To evaluate the effectiveness of the CVAD chemotherapy regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) when administered in combination with chemosensitizers (verapamil and quinine) which are intended to block the emergence of multidrug resistance in previously untreated patients with intermediate and high grade non-Hodgkin's lymphoma. The effectiveness of CVAD plus verapamil and quinine will be based on the estimate of the complete response rate and the time to treatment failure. (2) To assess the toxicities and side effects associated with the CVAD regimen when combined with verapamil and quinine. Secondary objectives are to further investigate the utility of the proliferative rate (determined by Ki-67 monoclonal antibody), the importance of cell-cell recognition molecules, the role of host response, and the value of detectable levels of p_glycoprotein as prognostic indicators of outcome in conjunction with companion study SWOG 8819; and to further utilize the central serum repository enabling clinicopathologic correlations with the results of studies on the material collected (see companion study SWOG 8947).

Technical Approach: Currently, regardless of the regimen used, 30 to 60% of advanced stage non-Hodgkin's lymphoma patients will relapse and the emergence of clinical drug resistance is a significant problem in these patients. In this study, patients will receive oral verapamil and quinine on days 1-6 as chemosensitizers. They have been shown to reverse the multidrug resistance associated with P-glycoprotein. Starting on day 2, patients will receive a continuous infusion of Adriamycin and vincristine for four days, Cytoxan will be given IV on Day 2 and oral decadron will be given days 2-5. Patients with documented progressive disease at any time will be taken off protocol treatment. Patients with stable disease will receive 2 courses (6 weeks) of chemotherapy. Patients responding to treatment will receive a maximum of 8 courses of chemotherapy. Patients will be restaged upon completion of the treatment program to assess response, with a complete laboratory and radiographic evaluation one month after the completion of therapy. All patients will be followed until death.

Progress: This study was closed to patient entry 15 Feb 93. Two patients were enrolled in previous years and are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/154 **Status:** On-going

Title: SWOG 9126: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in High Risk Acute Myelogenous Leukemia, Phase III

Start Date: 08/06/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: cancer:leukemia, cyclosporine, Ara-C, daunorubicin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1. To compare the complete remission rate and duration of survival in patients with high-risk AML when treated with either chemotherapy (Ara-C /Daunomycin) alone or chemotherapy plus the resistance modifier cyclosporine-A (CyA). 2. To estimate the frequency of p-glycoprotein expression and the correlation with prognosis in patients with relapsed AML, primarily refractory AML, and secondary AML.

Technical Approach: Patients will be randomized to receive either high-dose Ara-C 3 g/m^2/d on days 1-5 and daunorubicin 45 mg/m^2/d on days 6-8, a standard induction regimen for poor-prognosis AML or the same therapy plus cyclosporine A. The cyclosporine A will be given as a loading dose of 6.0 mg/kg IV over 2 hours on day 6 starting 8 hours before the daunorubicin, then 4.0 mg/kg over the next 6 hrs, then 16 mg/kg continuous 24 hr infusion beginning concurrently with the daunorubicin on days 6-8. Bone marrow aspirate and biopsy should be performed on day 14 of induction. Subsequent marrow evaluations should be performed every 7 - 14 days to assess response and recovery period to the next course of chemotherapy.

Patients achieving remission will go on to consolidation. Therapy will consist of the same drugs and dosages except ARA-C will be given on days 1-3 and daunomycin on days 4-6. Cyclosporine A will be given on days 4 - 6 as outlined above. No additional protocol directed treatment will be conducted after consolidation.

Progress: One patient was enrolled in this study at MAMC in FY93 and one patient in FY 94. Both are now deceased.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/097 **Status:** On-going

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

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:Hodgkin's, irradiation, vinblastine, doxorubicin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: Two patients were enrolled in this study, both in FY 94 and continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/056 **Status:** On-going

Title: SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients

Start Date: 04/03/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ George F. Hodeges, MC
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC

Key Words: cancer, soft tissue sarcomas, biologic parameters

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To develop a cooperative group mechanism to study biologic parameters of soft-tissue sarcomas in patients entered onto companion SWOG protocols (see SWOG 9119).;(2) To determine cellular DNA content parameters (DNA CCP) (DNA Ploidy, S-Phase Fraction) of soft tissue sarcomas and to evaluate the effect of these parameters on disease free survival and overall survival. To study the changes in DNA CCP as a result of chemotherapy, and the relationship of these changes to prognosis in patients with soft tissue sarcoma.;(3) To characterize cytogenetic aberrations of soft-tissue sarcomas in the study population. To evaluate the relationship of defined cytogenetic abnormalities to prognosis.;(4) To estimate the level of expression of the multi-drug resistant (MDR) phenotype in untreated soft-tissue sarcoma, and the effect of chemotherapy treatment on the expression of MDR. To evaluate the impact of MDR expression on response to chemotherapy, disease free survival, and overall survival. ;(5) To provide a repository of frozen tissue for future molecular studies in this group of patients.

Technical Approach: As a companion protocol to SWOG 9119 (adjuvant soft-tissue sarcoma trial), DNA CCP, tumor karyotypes, and estimation of the expression of the MDR phenotype of sarcomas entered onto trial will be done.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 92/054 **Status:** On-going

Title: SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II

Start Date: 04/03/92 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
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MAJ James S. D. Hu, MC

Key Words: cancer, osteogenic sarcoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To estimate the time to treatment failure and survival rate of the three drug combination, Adriamycin, cisplatin, and ifosfamide, as an adjunctive treatment of osteosarcoma of the extremity; to evaluate histopathologic tumor necrosis following preoperative therapy with this regimen; to assess the feasibility of determining histopathologic tumor necrosis in a cooperative group setting; to assess the influence of clinical prognostic variables on disease outcome; and to assess the toxicity of this regimen.

Technical Approach: Primary osteosarcoma is an uncommon malignancy but it is associated with only a 20% cure rate, if no more than surgery is used. Chemotherapy increases survival to above 50%, but whether or not this survival could be further increased has to be determined. The current study uses three drugs (Adriamycin, cisplatin, and ifosfamide) in an alternating fashion with the intent of optimizing treatment prior to surgery. Once four cycles of treatment have been completed, surgery will be undertaken. After recovery from surgery, four more cycles of chemotherapy will be given.

Progress: First patient was entered on protocol FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/049 **Status:** Completed

Title: SWOG 9147: Evaluation of Tamoxifen in Desmoid Tumors, Phase II

Start Date: 02/05/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT Diana S. Willadsen, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC

Key Words: cancer:desmoid tumor

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To assess the response rate of fibromatosis to treatment with tamoxifen. To assess the clonality of fibroblasts using a molecular probe for an x-linked enzyme.

Technical Approach: Patients having histologically proven and fully resectable desmoid tumors will be considered for this study. At the time of biopsy, estrogen and progesterone protein assays of the tumor will be done and again at resection. The patient will be placed on Tamoxifen 10 mg PO BID for 6 weeks. At 6 weeks a repeat CT scan or MRI (repeat scan should be the same type as the initial scan) will be done to assess the response. If the objective status at 6 weeks is stable or progressive, surgical excision may proceed. If there is an objective response, treatment will continue another six weeks and after CT scan or MRI excision will proceed. Post-operative or intraoperative radiotherapy will be at the discretion of the treating physician.

Clonality studies will be carried out utilizing restriction fragment length polymorphism techniques with a molecular probe encoding for the enzyme phosphoglycerate kinase. Patients whose tumors would be acceptable for cloning would be "informative females".

If none of the first 20 patients respond to treatment. the study will be closed, and tamoxifen concluded to be inactive. If at least one response is observed, 20 additional patients will be accrued. Five or more responses out of 40 will be considered as evidence warranting further study of tamoxifen.

Progress: Study was closed to patient entry 1 Aug 96. No patients had been enrolled in this study at MAMC. Study is completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/042 **Status:** On-going

Title: SWOG 9152 (EST-4890): Prediction of Recurrence and Therapy Response in Patients with Advanced Germ Cell Tumors by DNA Flow Cytometry

Start Date: 02/05/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Walladsen, MC

Key Words: cancer: germ cell, DNA flow cytometry

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To determine the proliferative activity and presence of aneuploidy within paraffin-embedded histopathologic specimens from patients with advanced disseminated (poor prognosis) GCT; (2) to correlate proliferative activity and aneuploidy with clinical features including response to therapy, relapse-free survival, and overall survival in patients entered on ECOG protocol EST 3887/SWOG 8997/CALGB 8991; Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin plus Etoposide with either Bleomycin or Isosfamide.

Technical Approach: All pathologic materials will be obtained during the routine diagnostic evaluation of patients registered on EST 3887/SWOG 8997 CALGB 8991. Following pathologic analysis of blocks to determine adequacy of tissue, tissue will be prepared for flow cytometry analysis. Three 50 micron sections will be cut, deparaffinized and rehydrated, enzymatically digested, and stained with the DNA intercalcating agent propidium iodide. The florescence of propidium iodide-stained nuclei will be measured on a Coulter 753 tunable dye laser following filtration through a 53 micron nylon mesh. Evaluation of the DNA index (ploidy status) and proliferative activity (cell cycle compartment analysis and proliferative index) will then proceed.

Progress: This study closed to patient entry 1 Feb 95.Two patients were enrolled in FY93. One patient is still be followed and the other died of the disease.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/063 **Status:** Completed

Title: SWOG 9158: A Phase II Evaluation of Trans-Retinoic Acid and Alpha Interferon in Patients with Squamous Cell Carcinoma of the Lung (Stage (IV)

Start Date: 02/04/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:lung, trans-retinoic acid, alpha interferon

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To assess the response rate to trans-Retinoic Acid and Alpha Interferon used in a daily schedule for patients with advanced (TNM Stage IV), well differentiated squamous cell carcinoma of the lung. 2) To further define the qualitative and quantitative toxicities of this regiment administered to this patient population in a Phase II study.

Technical Approach: Patients with a histologically confirmed diagnosis of advanced, well differentiated squamous cell carcinoma of the lung will be invited to participate in this evaluation of trans-Retinoic Acid and Alpha Interferon for the treatment of Stage IV Squamous Cell Carcinoma of the lung. After baseline evaluation, patients will be started on a fixed dose of trans-Retinoic Acid, 150 mg/m^2/d P.O. in divided doses (b.i.d.) with meals and 3 X 10(6) I.U./m^2 of Roferon-A subcutaneously once daily for 5 day/week. Measurable disease will be assessed for response or progression by chest x-ray at least every four weeks and CT scan (if needed) every 8 weeks. Patients will continue to receive therapy until they have stable disease after 16 weeks of therapy, one year after documentation of complete response, two years after documentation of a partial response, disease progression, relapse, or toxicity. All patients will be followed until death. Data will be interpreted by sponsors.

Progress: Study was closed to patient entry 1 May 96. One patient was enrolled in FY95 at MAMC and expired 15 Apr 96. Study is now completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/097 **Status:** On-going

Title: SWOG 9205: Central Prostate Cancer Serum Repository Protocol

Start Date: 05/07/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC

Key Words: Cancer:prostate, serum repository

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator.

Progress: Two patients were enrolled in this serum study, one expired in FY 96. The other continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/115 **Status:** On-going

Title: SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:Hodgkin's, quality of life

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To evaluate prospectively the health status and quality of life (QOL) of early stage Hodgkin's Disease patients receiving either subtotal nodal irradiation or short course chemotherapy plus subtotal nodal irradiation. 2) To describe the short-term, acute effects of two treatments for early stage Hodgkin's Disease patients on patient report of symptoms and on patient QOL. 3) To evaluate the intermediate and long-term effects of two treatments for early stage Hodgkin's Disease patients on patient QOL over five years.

Technical Approach: Patients enrolled in the companion protocol, SWOG-9133, will be asked to complete questionnaires before registration into this study, at 6 months; and annually for seven years. These questionnaires seek to identify and quantitate those differences pertaining to quality of life issues that the added chemotherapy may have in early stage Hodgkin's disease patients.

Progress: No patients have been enrolled in this study.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/107 **Status:** On-going

Title: SWOG 9210: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD-P to VAD-P/Quinine for Induction; (2) Randomization of Prednisone Dose Intensity for ....

Start Date: 05/07/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC

Key Words: Cancer:myeloma, VAD-P, VAD-P, Quinine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To compare the effectiveness of the VAD-P chemotherapy regimen when administered alone or in combination with the chemosensitizer quinine intended to block the emergence of multidrug resistance during remission induction in previously untreated patients with multiple myeloma. 2) To evaluate the chemosensitizing potential of quinine to reverse drug resistance in myeloma patients randomized to VAD-P induction who fail to achieve at least 25% regression with chemotherapy alone. 3) To compare the value of alternate day prednisone 10 mg versus 50 mg for remission maintenance for patients proven to achieve at least 25% regression.

Technical Approach: Patients with proven multiple myeloma (all stages) who have not received prior chemotherapy are eligible for participation in this trial. A dynamic allocation scheme will be used to randomize patients to one of the two induction treatment arms. INDUCTION: ARM I patients will receive Vincristine 0.4 mg IV q.d. on days 1-4, Doxorubicin 9 mg/m^2 q.d. IV on days 1-4, Dexamethasone 40 mg q.d. PO on days 1-4, and Prednisone 50 mg Q.O.D. on days 9, 11, 13, 15, 17, and 19. This cycle will be repeated Q 21 days for a minimum of 6 to 8 cycles (6 months) or a maximum of 17 cycles (12 months). Patients who fail to achieve $\geq$ 25% tumor regression after 12 months of treatment on Arm I (VAD-P) or relapse or progress on Arm I, will be eligible for crossover to VAD-P/Q. ARM II and Crossover schedule patients will receive VAD-P as outlined above on days 2-5 and will also receive Quinine 400 mg t.i.d. on days 1-6 (VAD-P/Q). Patients with $\geq$ 25% tumor regression after 9 to 12 months of induction therapy or patients who achieve $\geq$ 50% tumor regression after 6 months of induction therapy will be randomized to either of two maintenance regimens. If, in the judgement of the physician the patient will continue to benefit from induction therapy, they may continue up to 12 months. MAINTENANCE: ARM III patients will receive Prednisone, 10 mg Q.O.D., until relapse and ARM IV patients will receive Prednisone 50 mg Q.O.D. until relapse.

Progress: One patient has been enrolled (FY 94) and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/090 **Status:** Completed

Title: SWOG 9216: A Randomized Phase III Study of CODE Plus Thoracic Irradiation Versus Alternating CAV and EP for Extensive Stage Small Cell Lung Cancer

Start Date: 04/02/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:lung, cisplatin, adriamycin, vincristine, etoposide, cyclophosphamide, irradiation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine if chemotherapy dose intensification and thoracic irradiation will improve the response rate and overall survival rate in patients with extensive small cell lung cancer.

Technical Approach: Patients with extensive, measurable or evaluable disease will be randomized to 1 of 2 arms. Those randomized to Arm 1 will receive CODE (cisplatin, vincristin, doxorubicin, and etoposide) administered as follows: Cisplatin 25 mg/m^2 IV over 15 minutes weekly; Vincristine 1 mg/m^2 IV over 15 minutes weeks 1, 2, 6, 8; Doxorubicin 40 mg/m^2 IV over at least 10 minutes weeks 1, 3, 5, 7, 9; Etoposide 80 mg/m^2 IV over 20 - 30 minutes day 1 of weeks 1, 3, 5, 7, 9 and Etoposide 80 mg/m^2 PO days 2 & 3 of weeks 1, 3, 5, 7, 9. Those randomized to Arm 2 will receive alternating CAV/EP scheduled as follows: Cyclophosphamide 100 mg/m^2 IV 100 mg every 1 - 2 minutes of weeks 1, 7, 13; Doxorubicin 50 mg/m^2 IV over at least 10 minutes on day 1 of weeks 1, 7, 13; and Vincristine 1.2 mg/m^2 IV over 2 - 3 minutes day 1 of weeks 1, 7, 13 and Etoposide 100 mg/m^2 IV over 20 - 30 minutes days 1, 2 & 3 of weeks 4, 10, 16; Cisplatin 25 mg/m^2 VI over 15 minutes days 1, 2, & 3 of weeks 4, 10, 16. Supportive drugs (corticosteroid, gastroprotective agent, antifungal agent, prophylactic antibiotic Colony-stimulating factor, will be given according to set criteria.

After complete protocol cytotoxic chemotherapy, all patients will be re-staged, with repeat of any investigation that was abnormal prior to entry. If a patients should refuse re-staging, but appears on the available evidence to be in complete response, prophylactic cranial irradiation may be offered at the discretion of the investigator.

Patients on ARM 1 who achieve a complete response or partial response at the primary site with a complete response at all known metastatic sites will receive both thoracic irradiation to the mediastinum and site of the primary and prophylactic cranial irradiation beginning 3 to 4 weeks after completion of systemic therapy. These may be given concurrently and are obligatory.

Patients on Arm II who achieve a complete response will receive at least prophylactic cranial irradiation and this is obligatory. Other radiation therapy for patients in this arm is non-obligatory but may be given at the discretion of the

investigator and should begin 3 to 4 weeks after completion of systemic therapy.

Progression-free survival will be compared between treatment arms. Generalized Wilcoxon and log-rank statistics will be used to compare survival experience between the two arms. A Cox proportional hazards model will be used to assess prognostic factors, and treatment effect will be tested after controlling for important prognostic variables. Response rates and toxicities between the two treatment arms will be compared by Fisher's exact test. Logistic regression will be used to assess and adjust for prognostic factors with respect to complete response.

Some patients responding to the CODE regimen will not be able to continue the weekly chemotherapy because of unacceptable constitutional toxicity or patient refusal. These patients should be offered the standard regimen (alternating CAV and EP) as they may be able to tolerate a chemotherapy program allowing sufficient time between treatments to convalesce from side effects.

Progress: One patient enrolled in FY 95 and expired 17 Jan 96. Protocol is completed due to high frequency of treatment related deaths.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 94/010	**Status:** On-going

Title: SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup

Start Date: 10/01/93	**Est. Completion Date:** Indefinite
Department: SWOG	**Facility:** MAMC

Principal Investigator: MAJ J. Brantley Thrasher, MC

Associate Investigators: None

Key Words: Cancer: prostate, Finasteride

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: 53 patients have been enrolled in this study (27 in FY 96).

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/023 **Status:** On-going

Title: SWOG 9219: A Phase II Evaluation of Interleukin-4 (IL-4) in Patients With Non-Hodgkin's Lymphoma or Hodgkin's Disease

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: Cancer:Hodgkin's, Cancer:Non-Hodgkin's, Interleukin-4

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To assess the response rate of refractory low grade non-Hodgkin's lymphoma, refractory intermediate or high grade non-Hodgkin's lymphoma and refractory Hodgkin's disease treated with interleukin-4, and 2) to assess the qualitative and quantitative toxicities of interleukin-4 administered in a Phase II study.

Technical Approach: Following pretreatment with acetaminophen (650 mg PO) to prevent chills and fever, patients will receive a subcutaneous injection of interleukin-4 (at an initial dose of 3 ug/kg daily for 28 days). Patients must be observed in a medical facility for at least 2 hours after the first 2 daily injections. If no significant side effects occur the patient or family member will be instructed on how to administer subsequent injections at home. Patients will be reevaluated after 28 days with a possible rest period of one or two weeks between 28 day cycles of this treatment.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/136 **Status:** On-going

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

Start Date: 07/02/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
MAJ Timothy P. Rearden, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:non-small cell lung, 13-cis retinoic acid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: Nine patients have been enrolled in this study (4 in FY 96). Two have expired in FY 96, seven continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/108 **Status:** On-going

Title: SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma

Start Date: 05/07/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer: myeloma; topotecan

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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; (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/m^2 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 1 Feb 95. One patient was entered in this study in FY93 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/092 **Status:** On-going

Title: SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease

Start Date: 04/02/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
LTC Robert D. Vallion, MC

Key Words: cancer:lymphoma, tissue procurement

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/110 **Status:** Completed

Title: SWOG 9246: A Phase II Evaluation of Taxol in Patients with Relapsed Non-Hodgkin's Lymphoma or Relapsed Hodgkin's Disease

Start Date: 05/07/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Kenneth A. Bertram, MC
CPT Jennifer L. Cadiz, MC
MAJ James S. D. Hu, MC
LTC Robert D. Vallion, MC
LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Timothy P. Rearden, MC
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MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:Hodgkin's, Cancer:non-Hodgkin's, taxol

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To assess the response rate of relapsed low-grade non-Hodgkin's lymphoma, relapsed intermediate or high-grade non-Hodgkin's lymphoma, and relapsed Hodgkin's disease treated with taxol; (2) To assess the qualitative and quantitative toxicities of taxol administered in a phase II trial.

Technical Approach: All participants of this study must have a biopsy proven diagnosis of low, intermediate or high grade malignant non-Hodgkin's lymphoma or Hodgkin's disease and have received prior therapy. Participants will be stratified by type of disease: low grade lymphoma, intermediate or high grade lymphoma and Hodgkin's Disease. In an effort to avoid acute allergic reactions, all patients will be premedicated with Dexamethasone, Diphenhydramine, and Cimetidine prior to the administration of Taxol. The initial dose of Taxol will be 175 mg/m^2 for all patients except it will be 135 mg/m^2 for those who have received prior radiotherapy to 30% or more of marrow-bearing bone. Therapy will be administered only to inpatients and dosage may be modified for toxicities.

Estimates of response and toxicity will be made for each disease category separately. A response probability of 35% would be of interest, while further testing of this regimen would not be pursued if the response probability was 15% or lower.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/161 **Status:** On-going

Title: SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer

Start Date: 09/21/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: Cancer:colon, resection, chemotherapy:perioperative, 5FU, levamisole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To determine if (1) adjuvant therapy with one week of continuous 5-FU given within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging the disease free interval and increasing survival in patients who are treated with 5-FU/Levamisole only. Endpoints include: treatment failure - as described by recurrence of local/regional or distant metastases - and survival. (2) To establish within ECOG a Central Tissue Repository for paraffin blocks and a frozen tissue bank.

Technical Approach: Patients with primary colon cancer will be randomized to either receive 7 days of continuous intravenous 5-fluorouracil (5-FU) within 24 hours completion of colon surgery or not to receive any perioperative chemotherapy.

The only investigational part of this protocol is the administration of chemotherapy during the period right after subjects colon operation. The operation and the use of 5-FU/levamisole are all standard treatment.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/105 **Status:** On-going

Title: SWOG 9252: Prospective Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II and Stage IIIa Non-small Cell Lung Cancer, Intergroup

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:

LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
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MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:lung, non-small cell, cisplatin, etoposide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in prolonging survival in patients with completely resected Stage II and IIIa non-small cell lung cancer. 2) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in preventing local recurrence in patients with resected Stage II or IIIa non-small cell lung cancer.

Technical Approach: Patients who have undergone a surgery for Stage II or IIIa disease are eligible to participate in this trial. Patients will be stratified for nodal status (N1, N2), histology (squamous, other), weight loss in previous 6 months (< 5%, >= 5%), and lymph node dissection (sampling, complete node resection). After stratification they will be randomized to receive radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) alone or radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) concurrent with Cisplatin (DDP) 60 mg/m^2 IV days 1, 29, 57, 85 and Etoposide (VP-16) 120 mg/m^2 IV days 1, 2, 3; 29, 20, 31; 57, 58, 59; 85, 86, 87. Patients will be followed for 5 years. The statistical analysis will be based mainly on the stratified logrank test for comparison of two treatments. The second endpoint of local recurrence rate will be also analyzed as will the time to recurrence.

Progress: One patient has been enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/073 **Status:** On-going

Title: SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea.... Diagnosed Chornic Myelogenous Leukemia in Chronic Phase

Start Date: 03/04/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
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LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:leukemia, chronic myelogenous, trans-retinoic acid, alpha interferon, hydroxyurea

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$9686.00	**Periodic Review:** 11/17/95

Study Objective: 1). To estimate whether treatment of Chronic Myelogeneous Leukemia (CML), with all-trans retinoic acid in combination with either hydroxyurea or interferon alfa-2a is sufficiently effective based on either hematologic or cytogenetic response, to justify its investigation in phase III trials. 2). To assess the toxicities associated with all-trans retinoic acid plus hydroxyurea or itnerferon alfa-2a in chronic phase CML.

Technical Approach: Patients qualifying for this study will be stratified by age (< 45 vs ≥ 45), splenomegaly (present vs absent), prior hydroxyurea (yes or no), and ANC at diagnosis (<50,000 µl). Patients will then be randomized to one of two treatment arms as follows: Arm I: ATRA and HU or Arm II: ATRA and IFN. This randomization will be dynamically balanced to assure roughly equal numbers of patients within levels of the stratifying factors. All patients in both arms will begin treatment with HU to control or keep the WBC ≤ 20,000/µl and platelets ≤ 800,000/µl. All therapy will include allopurinol. Patients will receive this HUS treatment for a minimum of 21 days and a maximum of 42 days. Patients with WVA ≤ 20,000/µl, platelets ≤ 800,00/µl, and no evidence of progressive splenomegaly after 21 - 42 days of HU will then bergin treatment on their assigned regimens. Patients who do not achieve a WBC ≤ 20,000/µl, platelets ≤ 800,000/µl, and absence of progressive splenonegaly after 42 days will be removed from protocol treatment. Arm I patients will receive ATRA 150/mg/m2/d x 7 days followed by 7 days rest and HU 500 mg qd adjusted to maintain WBC and platelets to predefined levels. Arm II patients will receive acetaminophen 650 mg 1/2 hr before administration of IFN initiated a 3 MIU/m^2/d 5 days/week escalated by 1 MIU/m^2 each week to a maximum of 5 MIU/m^2/day and ATRA 150 mg/m^2/d x 7 days followed by 7 days rest. Treatment regimens will continue until the onset of accelerated or blast phase or relapse from CR or PR. Bone marrow aspiration and biopsy to monitor disease status are required at 3 and 6 months and every 6 months thereafter. Serial blood and urine specimens will be obtained for laboratory analysis.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 93/166 **Status:** On-going

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

Start Date: 09/03/93 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
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LTC Robert B. Ellis, MC
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MAJ John R. Caton, MC

Key Words: cancer:colon, irradiation, levamisole, 5-FU

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 T_4BN_0-2 colon cancer and selected patients with T_3N_1-2 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: One patient has been enrolled in this study at MAMC in FY95 and continues to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/111 **Status:** On-going

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 + ...

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
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Key Words: Cancer:rectal, 5-FU, Leucovorin, Levamisole, radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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/m^2/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: ;a. Arm A: bolus IV injection of 5-FU alone;b. Arm B: protracted venous infusion of 5-FU alone;c. 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: Three patients have been enrolled in this study at MAMC. One patient expired in FY 96, two continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/162 **Status:** Completed

Title: SWOG 9307: Extended Administration of Oral Cyclophosphamide for the Treatment of Poor Prognosis Extensive Disease Small Cell Lung Cancer

Start Date: 09/21/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert D. Vallion, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
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MAJ John R. Caton, MC

Key Words: Cancer:small cell lung, chemotherapy, etoposide, cyclophosphamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: (1) To estimate the response rate of extended oral administration of Etoposide and cyclophosphamide in poor prognosis extensive disease small cell lung cancer; (2) To evaluate the qualitative and quantitative toxicities of this regimen administered in a Phase II study; (3) To investigate possible correlations between peak and trough plasma etoposide levels versus complete response, toxicity, and survival.

Technical Approach: Untreated patients with extensive disease small cell lung cancer have a median survival of approximately 9 weeks. All patients will receive oral Etoposide and cyclophosphamide therapy once a day for 14 days. The dose for both chemotherapy agents will be 50 mg PO QD for the first cycle, with escalation allowed on later cycles. Ease of self administration and good subjective patient tolerance should make this combination of active agents particularly suitable for this patient population

This treatment will continue for at least 6 months unless the patient experiences unacceptable side effects or if the disease becomes worse, at which time the physician will remove their from the study. Cranial Radiation will be given at the beginning of chemotherapy is cancer has already entered the brain.

Progress: This study is closed to patient entry 1 Jun 96. Two patients were enrolled in this study at MAMC in FY95. Both patients died of the disease. Study is now completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/106 **Status:** On-going

Title: SWOG 9308: Randomized Trial Comparing Cisplatin With Cisplatin Plus Intravenous Navelbine in the Treatment of Previously Untreated, Stage IV Non-small Cell Lung Cancer Patients

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
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MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:lung, non-small cell, cisplatin, Navelbine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) Compare the effect of cisplatin alone with that of intravenous Navelbine plus cisplatin on tumor response rate, survival, and time to treatment failure in patients with Stage IV non-small cell lung carcinoma. 2) Compare the toxicity of the two treatment regimens in patients with Stage IV non-small cell lung carcinoma.

Technical Approach: At the time of registration, patients will be stratified by LDH (normal vs abnormal) and classified by the following: a. disease status (measurable vs. evaluable), b. prior surgical resection or RT (yes vs. no), c. histology (squamous cell vs. large cell vs. adenocarcinoma vs. unspecified). They will then be randomized to either of two arms. Arm I patients will receive Cisplatin 100 mg/m^2 over 30 - 60 minuetes every 28 days X 4. Arm II patients will receive Navelbine 25 mg/m^2 repeated weekly X 16 plus Cisplatin 100 mg/m^2 over 30 - 60 minutes every 28 days X 4. Patients will be evaluated every 3 months for the first year, every 6 months the second year, then yearly thereafter.

Progress: This study closed to patient accrual 1 June 95. One patient was enrolled in FY 95 and expired 25 Oct 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/170 **Status:** On-going

Title: SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast.... 0-3 Positive Nodes

Start Date: 09/21/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: cancer:breast, chemotherapy, cyclophosphamide, doxorubicin, positive nodes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: First patient has been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/107 **Status:** On-going

Title: SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phse III

Start Date: 05/06/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:myeloma, BCNU, Cyclophosphamide, Cyclosporine, Dexamethasone, Doxorubicin, G-CSF, Interferon-alpha 2b, Melphalan, Mesna, Methotrexate, Prednisone, Vincristine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To perform a randomzied trial, in newly diagnosed patients with symptomatic multiple myeloma (MM), of standard therapy versus myeloablative therapy, in order to examine whether the greater tumor cytoreduction effected by intensive therapy and manifested by higher incidence of complete remission translates into extended overall survival and progression-free survival. 2) To randomize responding patients with ≥ 75% tumor cytoreduction to interferon-alpha 2b (IFN) versus no maintenance in order to evaluate the role of IFN in MM.

Technical Approach: Symptomatic patients of all stages of multiple myeloma with reasonable performance status will be randomized to high dose chemotherapy with autologous bone marrow transplant or standard VBMCP combination chemotherapy after induction VAD therapy. A required peripheral stem cell harvest will be done for those randomized to the ABMT arm for future high dose therapy if failure occurs. This will be an option for those randomized to the standard arm. Those patients that have an HLA compatible sibling donor will be eligible for allogeneic BMT. A second randomization will be done for those with continued gfreater than 75 percent regression of disease in the ABMT or standared chemotherapy arm while those receiving allo-BMT will be continued on GVHD prophylaxis.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/114 **Status:** On-going

Title: SWOG 9323: Laboratory/Clinical Correlative Studies in Non-Small Cell Lung Cancer: Ancillary Study to SWOG 9252 (INT-0115, E3590, RTOG 91-05, NCCTG 91-24-51)

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:lung, K-ras, p53, antigen, EHF receptor levels, p105, Factor 8

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) To determine the incidence of K-ras and p53 mutations; assess Group A blood antigen and EHF receptor levels; and assess p105 and Factor 8 levels in patients with completely resected Stage II or IIIa SCLC. 2) Correlate these results with patient histology, TNM stage, time to relapse, and survival.

Technical Approach: SWOG 9323 requires that tissue samples of lung cancer resected from each patient enrolled on SWOG 9252 be sent to three central research laboratories. Investigators will study the tissue samples for the tumor markers, K-ras, p-53, and others. Investigators are evaluating these tumor markers to determine if they can predict how patients might respond to treatment for non-small cell lung cancer.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/116 **Status:** On-going

Title: SWOG 9327: Randomized Phase II Pilot Study of Pentoxifylline (Trental) and Placebo in Patients with Metastatic Malignancy and Anorexia/Cachexia Syndrome

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Robert L. Sheffler, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.

Key Words: Cancer:metastatic, anorexia, cachexia syndrome, pentoxifylline, placebo

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To evaluate the effect of pentoxifylline on the quality of life in patients with anorexia/cachexia syndrome related to malignancy; 2) to evaluate the effect of pentoxifylline on the nutritional status of patients with cancer cachexia and on various laboratory measurements of nutritional status; and 3) to assess the feasibility of accruing patients with cancer cachexia in a cooperative group setting.

Technical Approach: The Anorexia/Cachexia Syndrome is a well known entity in patients with metastatic cancer. The mechanism of this entity is felt to be mediated by several factors including cytokine release. Tumor necrosis factor is directly involved in suppressing anabolic enzymes as well as inducing inflammatory and pyrogenic effects by the body. These are all felt to be related to the above syndrome. Pentoxifylline, a TNF inhibitor, has been used in the past for vascular diseases and is well tolerated and will be used in this study to see if any improvement in the anorexia/cachexia syndrome occurs. The end points will be measured by a quality of life questionnaire for both anorexia and fatigue. Nutritional blood parameters will also be used for measurement of nutritional status.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/058 **Status:** On-going

Title: SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary

Start Date: 02/04/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: cancer:breast, histologic grading

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 were enrolled in this study in FY 94 and all are still being followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/147 **Status:** On-going

Title: SWOG 9333: A Randomized Controlled Trial of Mitoxantrone & Etoposide vs Daunomycin & Cytosine Arabinoside as Induction Therapy in Patients Over Age 55 with Previously Untreated Acute Myeloid Leukemia

Start Date: 06/16/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:leukemia, myeloid, mitoxantrone, etoposide, daunomycin, cytosine arabinoside, Age:over 55

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objectives: To compare the complete remission (CR) rate, duration of survival and duration of relapse-free survival (time for CR until relapse or death) for patients aged 56 or older with acute myeloid leukemia (AML) treated with daunomycin (daunorubicin, DNR) and cytosine arabinoside (Ara-C) or with mitoxantrone (Mito) and etoposide. To assess the frequency and severity of toxicities and the durations of neutropenia, thrombocytopenia, and first hospitalization associated with the two induction chemotherapy regimens.

Technical Approach: Acute myelogenous leukemia in the elderly population is usually a fatal disease. Although complete remission rates are about 40-60% with standard chemotherapy induction, relapse rates are high and morbid and sometimes fatal toxicities will occur. This multi-center study aims to improve the remission rate and toxicity profile of induction chemotherapy for AML in the elderly using mitoxantrone and VP-16 and comparing it to standard daunorubicin and Ara-C followed by standard consolidation. Colony stimulating factors with GM-CSF will be given prophylactically as well as prophylactic antibiotics with Fluconazole, Ciprofloxacin, and Acyclovir. We expect 3-4 subjects per year and the entire multi-center recruitment is projected to be 100 per year.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/121 **Status:** On-going

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...

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert D. Vallion, MC

Associate Investigators:
COL Walter G. Graves, MC
LTC Blaine R. Heric, MC
LTC Steven S. Wilson, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
COL Daniel G. Cavanaugh, MC
LTC Maceo Braxton Jr, MC
MAJ Rahul N. Dewan, MC
MAJ Nyun C. Han, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC

Key Words: Cancer:non-small cell lung, chemotherapy, radiotherapy, surgical resection

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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)s 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 obtsain 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/m^2 IVPB days 1, 8, 29, 36 and VP-16 50 mg/m^2 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: Two patients were enrolled in this study (FY 95). Both patients are now deceased.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/122 **Status:** Completed

Title: SWOG 9339: Evaluation of Topotecan in Esophageal Carcinoma, Phase II

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:esophageal, topotecan

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To evaluate the response rate of esophageal carcinoma treated with topotecan; and to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study.

Technical Approach: Patients enrolled in this study will receive Topotecan 1.5 mg/m^2 via continuous infusion IV over 24 hours on days 1, 8, 15, and 22. The retreat interval will be every 42 days (weekly X 4 weeks; 2 week rest period). Patients will continue this treatment schedule as long as they show complete remission, partial remission, or stable disease. Response assessments are to be performed every cycle along with laboratory analysis.

Progress: This study closed to patient entry 1 Dec 94. No patients have been enrolled in this study at MAMC. Study is now completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/091 **Status:** Suspended

Title: SWOG 9340: A Phase III Randomized Study of Radiotherapy With or Without BUdR Plus Procarbazine, CCNU, and Vincristine (PCV) for theTreatment of Anaplastic Astrocytomasma

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT Diana S. Willadsen, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Cancer:astrocytoma, radiotherapy, BUdR, Procarbazine, CCNU, Vincristine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: This study will determine if the experimental drug BUdR given before and during radiation therapy, followed by the chemotherapy drugs procarbazine, CCNU, and vincristine can slow the growth of your tumor. You have been asked to participate in this study because of the type and location of your brain tumor.

Technical Approach: This study involves a random assignment to one of two treatment arms. All patients will receive RT and PCV chemotherapy and half will also receive BUdR. Treatment 1) Subject will be given RTX to the brain five days a week for six to seven weeks. Within two weeks after completing RTX, subject will receive CCNU by mouth for one day (day 1 of each cycle). One week later they will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, they will be given vincristine by vein. Subject will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or at least six but no more than eight times) unless the disease worsens or complications arise. Treatment 2) Subject will be given BUdR by vein continuously for 4 days just before starting the first week of radiation therapy and for four days per week starting on day 4 or 15 of RTX each week during the first five weeks of therapy. BUdR will be given either in the hospital or on an outpatient basis. If hospitalization is required, BUdR will be delivered through a vein in the arm. If not hospitalized, BUdR will be delivered by a portable infusion pump through a vein in the neck and shoulder area. Within two weeks after completing RTX and BUdR therapy, the subject will receive CCNU by mouth for one day (day 1). One week later, the subject will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, the subject will be given vincristine by vein and will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or for at least six but no more than eight times) unless your disease worsens or complications arise. Blood counts and regularly performed physical examinations and laboratory tests will be taken to measure progress and toxicity from these treatments.

Progress: No patients have been enrolled in this study at MAMC. Protocol was suspended 31 Jul 96 to review pathology to determine validity of patients entered.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/092 **Status:** Completed

Title: SWOG 9341: High Dose Ifosfamide (HDI) with Mesna and Granulocyte-Colony Stimulating Factor (rhG-CSF) in Unresectable Malignant Mesothelioma

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT Diana S. Willadsen, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Cancer:mesothelioma, ifosfamide, GCSF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: 1) to assess the activity of high-dose ifosfamide and measna with recombinant human G-CSF (rhG-CSF) in patients with unresectable malignant mesothelioma. 2) To evaluate the toxicity pattern of high-dose ifosfamide/mesna/rhG-CSF given according to this outpatient schedule.

Technical Approach: Subjects will receive ifosfamide and mesna in a solution through the vein. Both drugs will be given daily for 5 days in a row. rhG-CSF will be given by subcutaneous injection, days 6-15. Treatments will be repeated every 21 days as long as disease does not get worse. If disease worsens, subject will be taken off study and offered another treatment. If disease stays the same or improves slightly, subject will continue to receive treatment at the highest tolerable dose for at least two more cycles (one cycle is equal to 21 days) or until disease worsens. If disease completely disappears, subject will receive an additional two cycles of therapy once the disappearance of the disease has been confirmed by laboratory tests necessary to follow disease. At that point, treatment will be stopped and the subject will be followed to see if disease reappears.

Progress: Study was closed to patient entry 15 Sep 96. No patients have entered this study at MAMC. Study is now complete.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/012 **Status:** On-going

Title: SWOG 9347: Phase III Comparison of Tamoxifen versus Tamoxifen with Ovarian Ablation in Premenopausal Women with Axillary Node-Negative Receptor-Positive Breast Cancer < 3cm, Intergroup

Start Date: 10/20/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert L. Sheffler, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC

Key Words: Cancer: breast, Tamoxifen, ovarian ablation, premenopausal

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: 1) To compare the disease-free survival, overall survival, and toxicity of treatment in hormone receptor-positive, premenopausal women with axillary lymph node-negative breast cancer measuring 3 cm or less given adjuvant therapy with tamoxifen alone, or tamoxifen with ovarian ablation. 2) To obtain tumor tissue form these patients for future biologic studies of relevance to this patient population. 3) To compare menopausal symptoms, sexual function and quality of life in patients receiving tamoxifen alone with patients receiving tamoxifen plus ovarian ablation.

Technical Approach: Studies form Scottish trials have shown significant benefit to ovarian ablation for ER receptor positive and lymph node positive breast cancer that are at least as good in terms of overall survival compared to chemotherapy. This study tries to answer this question for patients with less than 3 cm tumors, node negative, ER positive breast cancer patients who are premenopausal. The study has two arms: Tamoxifen vs. Tamoxifen and ovarian ablation. Ovarian ablation will be carried out with either surgical, hormaonal or radiation treatment. End points are disease ferr and overall survival. In addition, tissue will be sent for biologic studies.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/123 **Status:** Completed

Title: SWOG 9348: Evaluation of the Standard DCNU/DTIC/Cisplatin/Tamoxifen Regiment in Disseminated Malignant Melanoma, Phase II

Start Date: 06/03/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:melanoma, BCNU, DTIC, Cisplatin, Tamoxifen

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objective: To esstimate the response rate of the combination of BCNU/DTIC/cisplatin/tamoxifen in patients with disseminated malignant melanoma in order to select the appropriate regimen for combination with alpha-interferon in a future Phase III trial; and to accurately determine the toxicities of this drug combination in order to assess its feasibility in a future Phase III trial.

Technical Approach: Participants in this study must not be receiving or planning to receive concomitant biologic therapy, surgery, radiation therapy, hormonal therapy, or other chemotherapy or other treatment while on this protocol. DTIC, 220 mg/m^2 IV on days 1-3 & 22-24; cisplatin, 25 mg/m^2 IV on days 1-3 & 22-24; BCNU, 150 mg/m^2 IV on day 1; and tamoxifen, 110 mg/m^2 B.I.D. daily will be given throughout treatment. Retreatment interval is 6 weeks. Patients will continue on this regimen until they fulfill one of the defined criteria for removal from treatment. Patients will undergo frequent laboratory evaluations for toxicities. After completion of therapy, patients will be followed every three months for one year, every six months for the next two years, and annually thereafter.

Progress: This study closed to patient accrual 1 Apr 95. One patient was entered in FY 95 and has expired. Study is now completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/024 **Status:** On-going

Title: SWOG 9349: A Randomized Phase II Trial of CHOP with G-CSF Support or ProMACE-CytaBOM With G-CSF Support for Treatment of Non-Hodgkin's Lymphoma

Start Date: 11/18/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: Cancer:Non-Hodgkin's lymphoma, CHOP, ProMACE-CytaBOM, G-CSF

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

Study Objectives: To evaluate the effectiveness of the dose intense CHOP chemotherapy regimen with G-CSF support and the dose intense ProMACE-CytaBOM chemotherapy regimen with G-CSF support in previously untreated patients with intermediate and high grade non-Hodgkin's lymphomas. The effectiveness of the regimens will be based on the estimate of the complete response rate, the time to treatment failure, and ultimately overall survival. To assess the toxicities and side effects associated with the regimens. Also to further utilize the central serum and tissue repositories enabling clinicopathologic correlations with the results of studies on the material collected.

Technical Approach: This study attempts to assess whether dose intense CHOP or Promace-CytaBOM with growth factor support will have any effect on improvement of standard first line therapy in non-Hodgkins lymphoma. Ninety-eight patients will be accrued for each of the two arms. This number of patients will allow for both the complete response rate and probability of treatment failure two years after treatment to be estimated to within at most +/-.10 for each measure. A successful outcome for either regimen is one that has a true probability of 60% or higher of patients being alive without disease at two years. No formal statistical comparisons between arms will be made.

Progress: Three new patients have been enrolled in this study in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/003 **Status:** On-going

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

Start Date: 10/21/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 is closed to patient entry 10 Sep 96. One new patient was enrolled in FY 96.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/093 **Status:** On-going

Title: SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT Diana S. Willadsen, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Cancer:oligodendroglioma, radiotherapy, CCNU, vincristine, procarbazine, vincristine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 94/163 **Status:** On-going

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

Start Date: 09/21/94 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Timothy P. Rearden, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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: Eight patients have been enrolled in this study at MAMC (2 in FY 96). One has expired, seven continue to be followed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/094 **Status:** On-going

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

Start Date: 03/17/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ John R. Caton, MC

Key Words: Cancer:colon, 5-FU, leucovorin, levamisole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/95

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 trial 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: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/151 **Status:** On-going

Title: SWOG 9416: A Phase II Intergroup Trial of Induction Chemoradiotherapy Followed by Surgical Resection for Non-Small Cell Lung Cancer Involving the Superior Sulcus (Pancoast Tumors)

Start Date: 06/16/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:non-small cell lung, radiation, cisplatin, VP-16

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/21/96

Study Objectives: To assess the feasibility and toxicity of treating patients who have pancoast tumors without mediastinal or supraclavicular nodal involvement (T3-4, N0-1) with Cisplatin and VP-16 for two cycle, concurrent with a program of continuous, fractionated chest radiation followed by surgical resection and boost chemotherapy. To assess the objective response rate, resectability rate, and proportion of patients free of microscopic residual disease after such an approach.

Technical Approach: This oncology group protocol is a Phase II chemoradiation induction of superior sulcus (pancoast) tumors, non-small cell lung cancer followed by surgical resection. There are no extraordinary requirements of this study. This study should recruit 4-5 MAMC patients a year, 18 or older, and of either sex with selected Stage IIIa (T3, N0-1) or Stage IIIb (T4, N0-1) tumors involving the superior sulcus. The main goals of this study are to estimate the response, toxicity, and resectability rates following the combined chemoradiotherapy. We plan to accrue a total of 99 patients which will allow for estimation of rates and provide a sufficient number which will undergo resection. The precision of estimation of rates within stage IIIA or IIIb will depend on the breakdown by stage.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/152 **Status:** Completed

Title: SWOG 9424: A Phase II Trial of High Dose Tamoxifen Plus Cisplatin Chemotherapy in Metastatic Non-small Cell Lung Cancer

Start Date: 06/16/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Robert D. Vallion, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:Non-small cell lung, Tamoxifen, Cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** **09/30/96**

Study Objective: 1) To evaluate the efficacy of the protein kinase modulator high-dose tamoxifen in combination with cisplatin in the treatment of men and women with metastatic non-small cell lung cancer (NSCLC). 2) To assess the toxicity of the combination. 3) To estimate the response rate with each gender and to characterize baseline tumor properties such as estrogen/progesterone receptor status, kinase c expression, and mdr-1 glycoprotein expression.

Technical Approach: Patients will receive tamoxifen in tablet form for 28 days, twice a day for seven days. Cisplatin will be given intravenously with two pints of fluid before and after cisplatin. Cisplatin is administered over a period of an hour on days 4 and 11. Routine laboratory test will be done including blood tests, x-rays and scans. After reaching two cycles of treatments, patients will be tested for a response. If a complete response is found, patient will receive an additional two cycles of treatment and then therapy will stop. If after two cycles there is a partial response, patient will receive up to 6 more cycles of treatment. If the disease remains stable of the two cycles, two more cycles will be given. If the disease has not improved, patient will be taken of study.

Progress: This study is closed to patient entry 15 May 96. No patients have been enrolled in this study at MAMC. This study is completed.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/102 **Status:** On-going

Title: SWOG 9445: Prognostic Factor Panel to Predict Preferred Therapy for Node Positive Postmenopausal Breast Cancer Patients (CAF vs Tamoxifen) (A Companion Protocol to SWOG 8814

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.
LTC Robert L. Sheffler, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC

Key Words: Cancer:breast, node positive, prognostic factors, CAF, Tamoxifen

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: Overall objective is to correlate a panel of markers with clinical outcome and responsiveness to adjuvant therapy of node positive post menopausal breast cancer patients who participated in SWOG 8814. Specifically: 1) To evaluate if c-erbB-2 can allow the discrimination of node positive breast cancer patients who markedly benefited from adjuvant therapy with CAF (those with over-expressed c-erbB-2) from patients who did not obtain additional benefit from dose intensive CAF (those with low c-erbB-2 expression); 2) to measure a panel of prognostic factors (histologic and nuclear grade, estrogen and progesterone receptors, c-erbB-2, p53, Ki67, flow cytometrically determined DNA index and S-phase), angiogenesis, hsp27 (heat shock protein 27), nuclear and histologic grading, and immunohistochemically measured estrogen and progesterone receptors on node positive postmenopausal breast cancer patients; 3) to test the association of the factors listed above with biological and clinical features, including recurrence, survival and apparent efficacy of CAF chemotherapy in patients entered on SWOG 8814; and 4) to cut and store additional sections to allow the evaluation of markers that are mechanistically interesting but in the early development stage in breast cancer prognostic work which may be identified within the next 2-3 years, to be analyzed for prognostic significance and impact on the apparent benefit obtained by adjuvant CAF.

Technical Approach: This is a prognostic factor study attempting to find a correlation of several molecular, biochemical, and immunohistochemical, markers with outcomes in node positive breast cancer. It also seeks a correlation of C-erB-2 expression with benefits of adjuvant chemotherapy compared to tamoxifen therapy alone. The paraffin blocks will be submitted for all patients that are registered on SWOG 8814 who have adequate tissue to submit. It will be submitted to University of Texas Health Science Center in San Antonio, Texas.

Progress: One patient was entered in FY 96 at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/094 **Status:** On-going

Title: SWOG 9446: Chemoprevention Trial to Prevent Second Primary Tumors with Low-Dose 13-Cis Retinoic Acid in Head and Neck Cancer

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ John R. Caton, MC

Associate Investigators:
LTC Robert L. Sheffler, MC
LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC
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LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC
MAJ James S. D. Hu, MC
MAJ Richard F. Williams, MC

Key Words: Cancer:head and neck, 13-Cis retinoic Acid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To test the efficacy of prolonged low-dose 13-cRA in reducing the risk of second primary tumors (SPTs) in patients who have had head and neck cancer controlled by surgery and/or radiotherapy; and 2) to evaluate the qualitative and quantitative toxicity of low-dose 13-cRA administered daily for three years.

Technical Approach: Head and neck cancer accounts for 5% of all cancers in the US with 45,000 new cases and 15,000 deaths annually. The standard treatment for early Stage I and II disease is either surgical excision or radiotherapy. However, the major cause of failure in early stage patients is the development of second primary tumors (SPT). The prognosis for patients with SPTs, especially of the lung, is very poor, with a median survival of 5 to 10 months, and less than 10% of patients survive more than 2 years. Toxicity data and the necessity for long-term therapy suggest the need for new chemoprevention approaches to controlling head and neck cancer. Based on recent data showing the greater effectiveness of low dose 13-cRA over B-carotene and mild, tolerable toxicity, we will investigate the efficacy and safety of long-term, low dose 13-cRA for preventing second primary tumors in early stage head and neck cancer.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/117 **Status:** On-going

Title: SWOG 9449: Phase II Study of VIP (Etoposide, Ifosfamide and Cisplatin) in the Treatment of Invasive Thymoma

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
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LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.

Key Words: Cancer:thymoma, etoposide, ifosfamide, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To evaluate the objective response rate in extensive thymoma treated with VIP (etoposide, ifosfamide, cisplatin) plus G-CSF; 2) to evaluate the duration of remission and survival in patients with extensive disease treated with VIP plus G-CSF; and 3) to evaluate the toxicity of the VIP regimen in this population.

Technical Approach: The overall survival for invasive thymoma is 23 to 80 percent at 5 years. For non-invasive thymoma, the 5 year survival is about 4 times greater. Presently the treatment of invasive thymoma is surgical resection with or without radiation therapy to decrease the recurrence rate. Presently there are no large studies in which to make an inference as to what the standard of therapy should be for invasive thymoma. This study is a phase II single arm study evaluating the effect of a chemotherapy regimen traditionally used for germ cell tumors. The chemotherapy will be given prior to any surgery and a response determination will be made. If a complete remission occurs, then no further treatment will be done. For a partial response, surgical resection will be done if resectable and if stable observation until progression. If any patient has limited disease and is a candidate for resection or xrt, then, they will not be eligible for this protocol. The end points are response rate, duration of response, and overall survival.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 95/148 **Status:** Completed

Title: SWOG 9501: A Phase II Trial of Fludarabine and Mitoxantrone (FN) for Treatment of Non-Hodgkin's Lymphoma

Start Date: 06/16/95 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Luke M. Stapleton, MC
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MAJ Richard F. Williams, MC

Key Words: Cancer:Non-Hodgkin's lymphoma, fludarabine, mitoxantrone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: To estimate the two-year progression-free survival rate in patients with previously untreated low-grade non-Hodgkin's lymphoma treated with fludarabine and mitoxantrone. To evaluate the toxicity of fludarabine and mitoxantrone in this group of patients.

Technical Approach: Advanced low grade lymphoma is an incurrable disease. Although high responses are reported, long term, disease-free survival is not common and patients will eventually relapse. Many different chemotherapy modalities have been used and although overall response rates are different, the overall survival is not significantly changed. High dose therapy has been used and is undergoing active investigation. Newer agents have been introduced to attempt to improve the disease free and overall survival of patients with low grade lymphomas. This study attempts to use Fludarabine and Mitoxantrone in combination in newly diagnosed, advanced, low-grade lymphoma patients to see if any efficacy can be achieved in a single arm phase II study. All patients will receive prophylaxis with Septra for pneumocystis. All patients registered for this protocol will be eligible for serum and tissue submission on SWOG protocols 8947 and 8819 respectively.

Progress: This study is closed to patient entry 15 Feb 96. No patients have been enrolled in this study at MAMC. This study is completed.

Detail Summary Sheet

Date: 30 Sep 96	**Protocol No.:** 96/147	**Status:** On-going

Title: SWOG 9509: A Randomized Phase III Trial of Paclitaxel Plus Carboplatin Versus Vinorelbine and Cisplatin in Untreated Advanced Non-Small Cell Lung Cancer

Start Date: 06/21/96	**Est. Completion Date:** Indefinite
Department: SWOG	**Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:	LTC Robert L. Sheffler, MC
LTC Kenneth A. Bertram, MC	LTC Robert B. Ellis, MC
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MAJ John R. Caton, MC	Rakesh Gaur, M.D.

Key Words: Cancer:Non-small cell lung, paclitaxel, carboplatin, vinorelbine, cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objectives: To compare the effect of paclitaxil plus carboplatin to vinorelbine plus cisplatin on overall survival, progression-free survival and tumor response rate in patients with Stage IV and selected Stage IIIB non-small cell lung cancer. To compare the toxicity of the two treatment regimens in patients with Stage IV and selected Stage IIIB non-small cell lung cancer.

Technical Approach: The primary objective of this study is to compare the survival in patients with advanced non-small cell lung cancer treated with cisplatin/vinorelbine with that in comparable patients treated with the combination of carboplatin/paclitaxel. Carboplatin/paclitaxel would be judged superior to the standard regimen of cisplatin/vinorelbine if the true increase in median survival is 50%. Based on the previous Group-wide Phase II study in this disease (SWOG 9308), it is anticipated that 300 total eligible patients per year will be accrued to this study. An accrual period of 16 months should thus result in a study of 200 eligible patients per arm. A median survival of 8 months is anticipated on the cisplatin/vinorelbine. Assuming exponential survival, 16 months of patient accrual, and an additional 12 months of follow-up, a sample size of 200 patients per arm in a study with power 0.94 to detect a 50% increase in median survival in he combination arm, using a one-sided logrank test at level 0.025.

Progress: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/095 **Status:** On-going

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..

Start Date: 04/19/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
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MAJ John R. Caton, MC
LTC Robert L. Sheffler, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.

Key Words: Cancer:breast, lymph nodes, positive receptors, tamoxifen, fenretinide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

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: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/118 **Status:** On-going

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

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
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Key Words: Cancer:head and neck, surgery, radiotherapy, cisplatinum

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

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: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/160 **Status:** On-going

Title: SWOG 9519: Evaluation of Tomudex in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck

Start Date: 09/20/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.
LTC Robert L. Sheffler, MC
LTC Robert B. Ellis, MC
MAJ John R. Caton, MC

Key Words: Cancer:Head and neck, tomudex

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To evaluate the response rate of histologically confirmed recurrent or metastatic squamous cell carcinoma of the head and neck following Tomudex treatment, in order to assess whether Tomudex should be advanced to further studies; and 2) to assess the qualitative and quantitative toxicities of Tomudex.

Technical Approach: Recurrent and metastatic head and neck cancer is incurable. Response rates with chemotherapy have varied, but range from 30 to 75 percent. These response rates are usually not durable and will usually progress within less than 6 months. Chemotherapeutic agents used are cisplatinum and 5 FU alone or in combination, methotrexate, and bleomycin. Tomudex is a new agent that is a specific thymidilate synthetase inhibitor. 5 FU is a TS inhibitor but is non-specific. Tomudex has been used in North America and European trials in colorectal cancer and has shown about a 30 percent response rate. Tomudex will therefore be used to assess its response rate and duration of response in a Phase II trial. The main side effects are diarrhea and cytopenia (especially leukopenia), and reversible liver function test abnormalities.

Progress: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 96/119 **Status:** On-going

Title: SWOG 9520: Controlled Phase II Study of Doxorubicin and Paclitaxel as Frontline Chemotherapy for Women With Metastatic Breast Cancer

Start Date: 05/17/96 **Est. Completion Date:** Indefinite

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ James S. D. Hu, MC

Associate Investigators:
LTC Kenneth A. Bertram, MC
LTC Robert D. Vallion, MC
MAJ John R. Caton, MC
LTC Robert L. Sheffler, MC
LTC Robert B. Ellis, MC
MAJ Richard F. Williams, MC
Rakesh Gaur, M.D.

Key Words: Cancer:breast, doxorubicin, paclitaxel

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review: 09/30/96**

Study Objective: 1) To evaluate the complete remission rate of the doxorubicin plus paclitaxel combination in advanced breast cancer patients with no prior chemotherapy for metastatic disease and either no prior adjuvant chemotherapy or one prior adjuvant chemotherapeutic regimen (non-anthracycline or taxane containing). This evaluation will be made over six cycles of the combination regimen. 2) To test the combination of doxorubicin and paclitaxel for toxicity with particular emphasis on the degree of myelosuppression and the possible cardiac toxicity.

Technical Approach: Metastatic breast cancer is an incurable disease with median survivals of approximately 18 months being reported in many trials. The biologic behavior is very heterogeneous and differences in survival can be seen from study to study. Presently adriamycin-based chemotherapy regimens have shown the most efficacy in terms of response rates, however, long term survivals are the exception. Taxol has shown to have significant activity in metastatic breast cancer and has been combined with adriamycin to treat metastatic breast cancer in single arm trials. Evaluations in this study will be done in conjunction with a concurrently randomized control arm (of doxorubicin and cyclophosphamide) which will be used mainly to assess whether the new regimen has been rested in a patient population with historically expected rates of complete remission and congestive heart failure. This evaluation will be made over six cycles of the combination regimen. Because of the incidence of cardiac toxicity with the Milan regimen, close follow-up of cardiac function will be done in all patients in this trial with maximum doses of Adriamycin to be held well below the threshold of 450 mg/m^2.

Progress: No patients have been entered at MAMC.

DETAIL SHEETS FOR PROTOCOLS

UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 96 **Protocol No.:** 89/013 **Status:** On-going

Title: UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System

Start Date: 01/20/89 **Est. Completion Date:** Nov 92

Department: UWNG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
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MAJ Joseph H. Piatt, MC
COL Irwin B. Dabe, MC
MAJ Mark H. Kozakowski, MC
LTC Kenneth A. Bertram, MC

Key Words: lymphoma:central nervous system, chemoradiotherapy, methotrexate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$328.00	**Periodic Review:** 12/17/93

Study Objective: To evaluate this regimen, the end-points of analysis will be: time to progression of disease from beginning of therapy, response rates and disease stabilization rates, survival time measured from the beginning of therapy, quality of life, and activity level measured by Karnofsky performance status.

Technical Approach: Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver function, and a performance status of >70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m^2, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses, parenterally, on an every 6 hour basis, following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time, the patient will be removed from the protocol and cen be treated with other therapy as indicated. Patients will be followed until death.

Progress: The protocol has been closed to patient entry. One patient was enrolled and is still being followed.

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