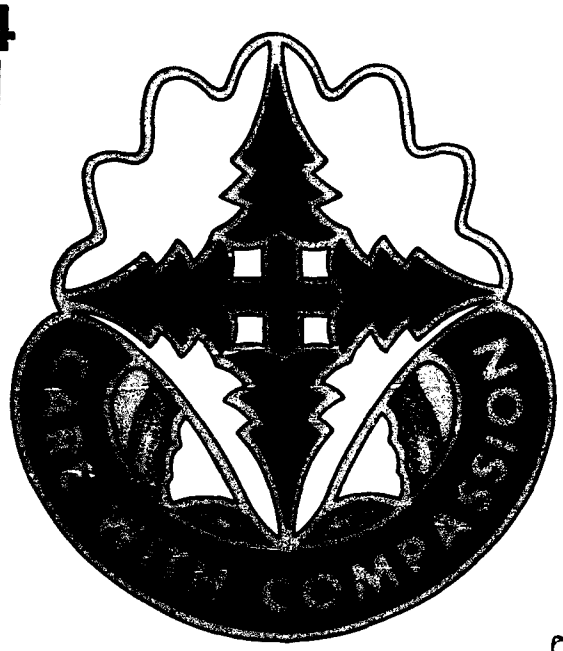
Department of Clinical Investigation

Annual Research Progress Report

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Madigan Army Medical Center

Tacoma, Washington

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13. ABSTRACT *(Maximum 200 words)*

This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 93. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 93. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during this period.

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ANNUAL PROGRESS REPORT

30 SEPTEMBER 1993

DEPARTMENT OF CLINICAL INVESTIGATION
MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431-5000

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ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1993

DEPARTMENT OF CLINICAL INVESTIGATION
MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431-5000

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 Nancy Whitten and Troy Patience for the effort which is obvious in the compilation, preparation, and editing of this publication.

FOREWORD

FY 93 was a busy one for MAMC investigators. DCI processed a record 171 new protocols, representing a 60% increase over the previous year and the historical average. MAMC investigators became more involved with clinical trials, requiring DCI support for 12 ongoing protocols. The basic research thrust continued in the field of molecular biology, particularly in the areas of hormonal aspects of breast cancer, thyroid oncogene expression, and human papilloma virus detection using PCR. A unique dual cotyledon perfusion model of the human placenta was developed, which gave exciting preliminary results. Education efforts continued, with another offering of the "Introduction to Molecular Biology" Short Course taught by CPT Keith Martin and the "Introduction to Clinical Investigation" course taught by members of DCI. Introductory laboratory training was conducted for several local college students. MAMC nurses were again highly successful in obtaining funding, garnering 5 grants.

I wish to acknowledge the support of BG Leslie Burger, Commander, COL Al Buck, DCCS, and COL Charles Mitchell, Director of Education, as well as the commitment to quality and excellence of the DCI staff.

UNIT SUMMARY

1. Objective

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

2. Technical Approach

Description	MANPOWER Rank	MOS
Chief, Clinical Investigation MOORE, Dan C., M.D., COL, MC	06	60P9A
C, Clinical Studies Service JONES, Robert E., M.D., COL, MC	06	61C9A
C, Surg & Animal Care Svc POWELL, Douglas, D.V.M., MAJ, VC (Aug 91 - Aug 93)	04	64C9B
C, Surg & Animal Care Svc CALDWELL, Stephen, D.V.M., CPT, VC (Sep 93 -)	03	64A00
C, Microbiology Svc STEWART, Robert S., Ph.D., MAJ, MS	04	68A9B
C, Bioresearch Svc MARTIN, Keith, Ph.D., CPT, MS	03	68C8Z
NCOIC HANDY, Kevin , SSG (Mar 90 - Dec 92)	E6	92B3M4
NCOIC ROBERTS, Teresa, SFC	E7	91T30R
Vet Animal Spec HEATH, George, SGT (Aug 89 - Aug 93)	E5	91T20
Vet Animal Spec SPAHN, Shelley, SGT (Feb 89 - Dec 92)	E5	91T20
Vet Animal Spec FULK, Terry, CPL	E4	91T20
Vet Animal Spec CARREIRO, Frank, SPC	E4	91T20
Lab Tech CARTAGENA, Edward, SPC	E4	92B
Lab Tech HERNANDEZ, Carlos, SGT	E5	92B

Description	Rank	MOS
C, Biochemistry Svc MOORE, Katherine H., Ph.D.	GS12	0601
Med Tech MATEJ, Louis A., B.S., M.T.	GS9	0644
Med Tech WRIGHT, James R., B.A., M.T.	GS9	0644
Med Tech STYNER, M. J., B.S., M.T.	GS9	0644
Med Tech THOMSON-ARCHER, Kelly, B.S., M.T.	GS9	0644
Statistician Medical PATIENCE, Troy H., B.S.	GS9	0301
Edit Asst/Steno WHITTEN, Nancy J., B.A.	GS7/ GS9	1087
Sec/Steno HOUGH, Eugenia R.	GS6	0318
Maintenance Worker KAEO, Curtis	WG7	4749
Med Tech CRISS-TILLOTSON, Mary "Tilly"* (Dec 92 -)	GS9	0644

* Breast Grant Hire.

Funding FY 93

MEDCASE Equipment	$ 96,561.00
Capital Equipment	50,620.00
Civilian Salaries	280,366.40
Military Salaries	
Consumable Supplies	134,160.00
Contractual Services	6,817.25
TDY - departmental	7,598.00
TDY - presentations	27,638.89
	$596,163.54

EXTRAMURAL FUNDING:

Federal sources:	
USAMRDC	$146,077
NCI	119,900
Other	508,793
Non-federal sources:	
FACT	152,034
HMJ	5,081
	$931,703

3. Progress

During FY 93 there were 394 active protocols that received administrative and/or technical support during the year. Of these, 268 are presently on-going; 5 are in a suspended status, 89 were completed; and 32 were terminated. The principal investigator distribution was as follows: 306 staff protocols, 42 resident protocols, 35 fellow protocols, 2 intern protocols, and 9 other category protocols.

There were 117 publications and there were 120 presentations at regional, national, or international meetings.

4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 26
43 protocols involving 75 residents
123 protocols involving 30 fellows

5. Other training programs supported by DCI:

Training protocols:
(1) Department of Surgery: 3
(2) Department of Emergency Medicine: 2
(3) Department of Pediatrics: 1
(4) Department of OB/GYN: 1
(5) Department of Clinical Investigation: 1

6. Other protocols supported:

43 protocols held by MAMC staff members
161 group oncology protocols
2 Intern protocols
1 Fort Wainwright, AK protocol
1 Letterman MEDDAC protocol
1 USDA protocol
1 I-corps protocol
2 Fort Ord protocols
2 Active duty student protocols
1 Walter Reed Army Medical Center protocol

COMMITTEE MEMBERS

Commander

Madigan Army Medical Center
BG Leslie M. Burger, M.D., MC

Clinical Investigation Committee

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

Chief or delegated representative of:

Department of Clinical Investigation
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
Clinical Psychology Service
Clinical Studies Service, DCI
Microbiology Service, DCI
Biochemistry Service, DCI
Bioresearch Service, DCI
Lab Animal and Surgery Service, DCI
Medical Statistician, DCI

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Deputy Commander of Clinical Services
COL Alfred S. Buck, M.D., MC

Chief or delegated representative of:

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Department of Ministry and Pastoral Care
Pharmacy Service
Social Work Service
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Center Judge Advocate
Non-institutional member

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Animal Use Committee

Chairman
*Deputy Commander of Clinical Services
COL Alfred S. Buck, M.D., MC

Chief or delegated representative of:

Department of Clinical Investigation
Lab Animal & Surgery Service
Department of Nursing
Public Affairs Office
Veterinary Services
Non-institutional member

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 1993:

Comparison of Induction and Recovery From Propofol-Nitrous Oxide Versus Methohexital-Isoflurane-Nitrous Oxide Anesthesia in Ambulatory Oral Surgery Patients by LTC Robert J. Wygonski, DC.

Other nominees were:

Twelve Hour Urine Collections in Comparison to Twenty-Four Hour Urine Collections in Patients with Preeclampsia by CPT Wilma I. Larson, MC.

A Comparison of Sinus X-rays with Computed Tomography in Acute Sinusitis by MAJ Thomas F. Burke, MC.

WERGELAND 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 1993:

The Dual-Perfusion Cotyledon Model: Is a Control Needed? by MAJ Timothy J. Boley, MC.

Other nominees were:

Lead Levels and Their Relationship to Attention Deficit Hyperactivity Disorder and Developmental Delay by CPT Cynthia Kahn, MC.

Do Not Resuscitate: Do Not Provide Care? by CPT Lynn Keenan, MC.

Activation of the PTC Oncogene: A Predictor of Aggressive Behavior in Papillary Thyroid Cancer by CPT R. Michael Tuttle, MC

The Association of Empathy and Specialty Choice In A Sample of Army Interns by CDR William R. Kiser, MC

Estimation of 24 Hour Urinary Nitrogen Excretion From Four and Six Hour Urine Collections in Critically Ill Patients Receiving Nutritional Support by CPT Lynn Keenan, MC.

PUBLICATIONS

FISCAL YEAR 93

DEPARTMENT OF CLINICAL INVESTIGATION

Gerena L, Bass GT, Kyle DE, Oduola AMJ, Milhous WK, Martin RK	Fluoxentine Hydrochloride Enhances in vitro Susceptibility to Chloroquine in Resistant Plasmodium Falciparum. Antimicrob Agents & Chemother 36(12): 2761-2765, 1992.
Stewart RS, Phillips RH, Patience TH	PCR Technology in the Clinical Microbiology Laboratory: Thermal Cycler Idiosyncracies. J Mil Med Lab Science 22(3): 114-119, 1993.

DEPARTMENT OF DENTISTRY

Engibous PJ, Kittle PE, Jones HL, Vance BJ	Latex Allergy in Patients With Spinabifida. Pediataric Dentistry 15(5): 364-466, 1993.
Goho CD	Chemoradiation Therapy: Effect on Dental Development. Pediatric Dentistry 15(1): 6-12, 1993.
Goho CD, Aaron GR	Enhancement of Antimicrobial Properties of Cavity Varnish: A Preliminary Report. J Prosthetic Dentistry 68: 623-25, 1992.
Guzman CM, Aaron GR	Spondylometaphyseal Dysplasia (Kozlowski Type): Case Report. Pediatric Dentistry 15(1): 49-52, 1993.
Meadors LW, Jones HL	Fused Primary Incisors with Succedaneous Supernumerary in the Area of a Cleft Lip: Case Report. Pediatric Dentistry 14(6): 397-99, 1992.
Polk AM	Impaction and Malformation of a Maxillary Central Incisor: Sequelae of Trauma. J Dentistry for Children: 29-32, 1993.
Weber CR, Wygonski RJ, Griffin JM, Boyd BD	Undiagnosed Shrapnel of the Tongue. Military Medicine 158(6): 4427-28, 1993.

DEPARTMENT OF EMERGENCY MEDICINE

Guertler AT	Usefulness of a Diagnostic Test. Annals of Emergency Medicine 21(12): 1516-1517, 1992.

DEPARTMENT OF FAMILY PRACTICE

Forred WA, Brunader REA, Mork TJ, Kugler JP	An Educational Report: The Mechanics of Geriatric Assessment in a Military Community-Based Family Practice Residency. Military Medicine 157(11): 586-590, 1992.
Jerant AF, Arline AD	Babesiosis in California. Western J Med 158(6): 622-625, 1993.
Kiser WR	A Hospital Ethics Committee at War: The Hospital Ship Mercy Experience During Operation Desert Shield and Operation Desert Storm. Cambridge Quart Hlth Care Eth 4: 389-92, 1992.
Kraemer WJ, Dziados JE, et al	Effects of Different Heavy Resistance Exercise Protocols on Plasma B-Endorphin Concentratons. J Appl Physiol 74(1): 450-459, 1993.
Kraemer WJ, Fleck SJ, Dziados JE, et al	Changes in Hormonal Concentrations After Different Heavy Resistance Protocols in Women. J Appl Physiol 75(2): 594-4604, 1993.
Kugler JP	Cardiovascular Problems; IN: Handbook of Sports Medicine, A Symptom Oriented Approach, Lillegard WA and Rucker KS (eds); Andover Medical Publishers, Boston, MA, Chatper 22, 1993.
Kugler JP, Yeash J	The Impact of Sociodemographic, Health Care System, and Family Function Variables on Prenatal Care Utilization in a Military Setting. Jounral of Family Practice 37(2): 143-47, 1993.
Lillegard WAW, Rucker KS	Handbook of Sport Medicine; A symptom Oriented Approach. Andover Medical Publishers, Boston, MA, 1993.

Lillegard WAW, Kruse R	Musculoskeletal Problems in Children, IN: Family Medicine, Principles and Practice, 4th ED, Chapter 16, Springer-Verlag Publishers, 1993.
Nusbaum MRH, Kiser WR, Ellis DD, Runkle GP, Kugler JP	Vitamin B(12) Deficiency. Journal of Family Practice 36(4): 373, 1993.
Runkle GP, Ellis DD, Nusbaum MRH	Psychosocial Support During High Risk Pregnancy. New England Journal of Medicin 328(12): 887, 1993.
Schirner WA	Exercise Induced Bronchospasm; IN: Handbook of Sports Medicine, A Symptom Oriented Approach; Lillegard WA and Rucker KS (eds); Andover Medical Publishers, Boston, MA, Chapter 17, 1993.
Stankus SJ, Johnson NT	Prophylthiouracil-Induced Hypersensitivity Vasculitis Presenting as Respiratory Failure. Chest 102(5): 1595-96, 1992.
Whittaker PE	Quality Assurance Successes: The Highest Quality Sick Call System in the Army. AMEDD Journal, Jul/Aug 1993
Whittaker PE, et al	The Computer-Aided PRP/Nuclear Surety Program. AMEDD Journal; Jun/Jul 1993.
Yetter JF	Cleft Lip and Cleft Palate. American Family Physician 46(4): 1211-1218, 1992.

DEPARTMENT OF MEDICINE

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Cragun WH, Grover B, Dunn T	Acute Respiratory Failure Associated with a Motor Vehicle Accient (Roentgenogram of the Month). Chest 102(5): 1581-1582, 1992.
Douglas DM, Brown JS	Intermittent Throat Tightness in a 37 Year Old Woman. Annals of Allergy 71(2): 100-102, 1993.
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Hnatink O, Pike J, Stoltzfus D, Lane W	Value of Bedside Plating of Semiquantitative Cultures for Diagnosis of Central Venous Catheter-Related Infections in ICU Patients. Chest 103: 896-99, 1993.
Hobbs CJ, Plymate SR, Rosen C, Adler RA	Testosterone Administration Increases Insulin-like Growth Factor-I Levels in Normal Men. J Clin Endocrinol Metab 77: 776-779, 1993.
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May EF, Ling GSF, Geyer CA, Jabbari B	Contrast Agent Overdose Causing Brain Retention of Contrast, Seizures, and Parkinsonism. Neurology 43(4): 836-38, 1993.
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Peele M, et al	TSH Beta Subunit Gene Expression in Human Lymphocytes. Amer J Medical Science 305: 1-7, 1993.
Prewitt K, Laird J, Cambier P, Wortham D	Late Coronary Aneurysm Formation After Directional Atherectomy. American Heart Journal 125: 249-251, 1993.
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DEPARTMENT OF NURSING

Birgenheier PS	Parent and Children, War and Separation. Pediataric Nursing 19(5): 24-28, 1993.
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Adams MM, Read JA, Rawlings JS, Harlass F, Sarno AP, Rhodes PH	Preterm Delivery Among Black and White Enlisted Women in the United States Army. Obstetrics and Gynecology 81(1): 65-71, 1993.

Kopelman JN	Antepartum Diagnosis of Arthrogryposis Associated with Trisomy-18. Military Medicine 158(7): 498-99, 1993.
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PREVENTIVE MEDICINE SERVICE

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Strohm PF, Opheim GS	Mission-Oriented Risk Assessment. J American Society Engineers 38(6): 38-43, 1993.

DEPARTMENT OF PATHOLOGY, BLOOD BANK

Brissette M, Dhru RD	Hodgkin's Disease Presenting as Spontaneous Splenic Rupture. Arch Path Lab Medicine 116(10): 1077-1079, 1992.

DEPARTMENT OF PEDIATRICS

Bass JW, Steele RW, Wittler RR, Weisse ME, Bell V, Heissser AH, Brien JH, Krober MS	Antimicrobial Treatment of Occult Bacteremia - A Multicenter Cooperative Study. Pediatric Infectious Dis J 12(6): 466-73, 1993.
Hinson RM, Schofield TD, French J, Stevenson JG, Stewart D, Kinney JB	Occult Kawasaki Syndrome With Giant Coronary Artery Aneurysms. Western Journal of Medicine 158(2): 188-191, 1993.
Rawlings JS, Smith FR, Garcia J	Expected Duration of Hospital Stay of Low Birth Weight Infants - Graphic Depiction in Relation to Birth Weight and Gestational Age. Journal of Pediatrics 123(2): 307-309, 1993.
Stafford EM	Pelvic Examination - An Essential Skill. Pediatrics 91(3): 682, 1993.
Waecker NJ, Ascjer DP, Robb ML, Moriarty R, Krober M, Rickman WJ, Butzin CA, Fischer GW	Age-Adjusted CD4+ Lymphocyte Parameters in Healthy Children at Risk for Infection With the Human Immunodeficiency Virus. Clinical Infectious Diseases 17(1): 23-125, 1993.

DEPARTMENT OF RADIOLOGY

Bauman JM	Pseudodislocation of the Glenohumeral Joint Diagnosed by Bone Scintigraphy. Clinical Nuclear Medicien 18(2): 147-48, 1993.
Bauman JM	Carotid Occlusion Assessed by 99m-Tc HMPAO SPECT. Imaging Insights Nuc Software 1: 1-3, 1993.
Bender GN, Dodai DD, Briggs LM	Colonic Pseudo-obstruction - Decompression with A Tricomponent Coaxial System Under Fluoroscopic Guidance. Radiology 188(2): 395-98, 1993.
Choi HS, Kim Y, Smith DV, Bender GN	PACS and Its Hospital-wide Implementation: A Case Study at the Madigan Army Medical Center. J Korean Radiol Soc 29: 573-583, 1993.
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Ho VB, Fitz CR, Chuang SH, Geyer CA	Bilateral Basal Ganglia Lesions - Pediatric Differential Considerations. Radiographics 13(2): 269-92, 1993.
Ho VB, Fitz CR, Yoder CC, Geyer CA	Resolving MR Features in Osmotic Myelinolysis (Central Pontine and Extrapontine Myelinolysis). Amer Journal of Neuroradiology 14(1): 163-67, 1993.
Ho VB, Smirniotopoulos JG, Murphy FM, Rushing EJ	Radiologic-Pathologic Correlation: Hemangioblastoma. Amer Journal of Neuroradiology 13: 1343-1352, 1993.
Koo B, Becker LR, Chuang S, Merante F, Robinson BH, MacGregor D, Tein I, Ho VB	Mitochondrial Encephalomyopathy, Lactic Acidosis, Stroke-like Episodes (MELAS): Clinical, Radiological, Pathological, and Genetic Observations. Annals of Neurology 34: 25-32, 1993.
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Schofi Youngbe A	Chest Radiograph Interpretation and Lung Cancer Experience At Madigan Army Medical Center. Military Medicine 158(5): 297-99, 1993.
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DEPARTMENT OF SURGERY

Burgess FW, Anderson DM, Colonna D, Sborov MJ, Cavanaugh DG	Ipsilateral Shoulder Pain Following Thoracic Surgery. Anesthesiology 78(2): 365-68, 1993.
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Carpenter CT, Lester EL	Skeletal Age Determination in Young Children: Analysis of Three Regions of the Hand/Wrist Film. J Pediatric Orthopaedics 13(1): 76-79, 1993.
Cavanaugh DG, Barry MJ, Knight JA, Dearman RM	Diagnosis of Superior Sulcus Tumors - A Further Use of the Thoracoscope. Military Medicine 158(8): 577-578, 1993.
Chandler DW, Grantham DW	Auditory Spatial Resolution in the Horizontal Plane As A Function of Reference Angle: Microstructure of the Azimuth Function.. J of teh Acoustical Society 93(4): 2350-2351, 1993.
Chen JB	Cuboid Stress Fracture, A Case Report. J American Podiatric Med Assoc 83(3): 153-55, 1993.
Frey MAB, Mader TH, Bagian JP, Charles JB, Meehan RT	Cerebral Blood Velocity and Other Cardiovascular Responses to 2 days of Head Down Tilt. Journal of Applied Physiology 74(1): 319-25, 1993.
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Loop SM, Rozanski TA, Ostenson RC	Human Primary Prostate Tumor Cell Line, ALVA-31 - A New Model for Studying the Hormonal Regulation of Prostate Tumor Cell Growth. Prostate 22(2): 93-108, 1993.

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Mader TH, Stulting RD	**Viral Keratitis. Infect Dis Clin North America 6(4): 831-49, 1992.**
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Panje WR, Morris MR	**Oral Cavity and Oropharyngeal Reconstruction; IN Otolaryngology-Head and Nuck Surgery. Mosby Yearbook, St Louis, MO, 2nd Ed, pp 1479-1498, 1992.**
Parmley VC, Stonecipher KG, Rowsey JJ	**Peters Anomaly - A Review of 26 Penetrating Keratoplasties in Infants. Ophthalmic Surgery 24(1): 31-35, 1993.**
Perkins JA, Morris MR	**Treatment of Acute Frontal Sinusitis - A Survey of Current Therapeutic Practices Among Members of the Northwest Academy of Otolaryngology. American Journal of Rhinology 7(2): 67-70, 1993.**
Perkins JA, Smith S, Lyons M	**Bowel Obstruction From Retained Inner Bumper Following Removal of Gastrostomy Tube - A Case Report. Military Medicine 158(2): 120-21, 1993.**
Place R, Velanovich V, Carter P	**Fine-Needle Aspiration in the Clinical Management of Mammary Masses. Surgery Gynecology & Obstet 177(1): 7-11, 1993.**
Roberts JD, Chen TY, Kawai N, Wain J, Dupuy P, Shimouchi A, Block K, Polaner DM	**Inhaled Nitric Oxide Reverses Pulmonary Vasoconstriction in the Hypoxic and Acidotic Newborn Lamb. Circulation Research 72: 246-254, 1993.**
Roberts JD, Polaner DM, Lang P, Zapol WM	**Inhaled Nitric Oxide in Persistent Pulmonary Hypertension of the Newborn. Lancer 340: 818-819, 1992.**
Souliere CR, Kileny PR, Zwolan TA, Kemink JL	**Tinnitus Suppression Following Cochlear Implantation: A Multifactorial Analysis. Archives of Otolaryngology 118: 1291-1297, 1992.**
Thrasher JB, Kreder KJ, Peterson NE, Donatucci CF	**Lidocaine as Topical Anesthesia for Bladder Mappings and Cold-Cup Biopsies. The Journal of Urology 150: 335-36, 1993.**
Travis MT, Cosio MQ	**A Retrospective Review of Orthopedic Patients Returning From Operations Desert Shield and Desert Storm To An Army Medical Center. Military Medicine 158(5): 348-51, 1993.**
Vaccaro JA, Davis R, Hansberry K	**Replacement of Nephrostomy Tube Using Ureteroscopes. Journal of Urology 149(2): 334, 1993.**
Varga JH, Wolf TC, Jensen HG, Parmley VC, Rowsey JJ	**Combined Treatment of Acanthamoeba Keratitis With Propamidine, Neomycin, and Polyhexamethylene Biguanide. Amer Journal of Ophthalmology 115(4): 466-70, 1993.**
Velanovich V	**Causality Concepts in Surgery. Theoretical Surgery 7(4): 197-200, 1992.**
Velanovich V, Kaufmann C	**Two Pitfalls of Laparoscopic Balloon Cholangiography - Recognition and Correction. American Surgeon 59(5): 290-92, 1993.**

Velanovich V, Tapper D	Decision Analysis in Children Wtih Blunt Splenic Trauma - The Effects of Observation, Splenorrhaphy, or Splenectomy on Quality Adjusted Life Expectancy. Journal of Pediatric Surgery 28(2): 179-85, 1993.
Waterhouse W, Enzenauer RW, Parmley VC	Inflammatory Orbital Tumor as an Ocular Sign of a Battered Child. American J Ophthalmology 114(4): 510-12, 1992.
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Wilkinson SV, Jones RO, Sisk LE, Sunshein KF, VanManen JW	Austin Bunionectomy: Postoperative MRI Evaluation for Avascular Necrosis. The Journal of Foot Surgery 31(5): 469-477, 1992.

DEPARTMENT OF RADIOLOGY

Dixon ZR, Burri BJ, Neidlinger TR	Dietary Vitamin A, Retinol-Binding Protein (RBP), and Relative Dose Response (RDR) as Measures of Vitamin A Status. FASEB J 6: A4200, 1992.

U.S. DEPARTMENT OF AGRICULTURE

Burri BJ, Neidlinger TR, Dixon ZR	Methods for Assessing Vitamin A Status in Healthy Adults. FASEB J 6:A4904, 1992.

PRESENTATIONS

FISCAL YEAR 93

DEPARTMENT OF CLINICAL INVESTIGATION

Moore DC	Body Image and Eating Behavior in Adolescents.	33rd Annual Meeting of the American College of Nutrition, San Diego, CA, October 92.
Moore DC	Natural History of Compensated Hypothyroidism Due to Hashimoto's Thyroiditis in Childhood.	NW Pediatric Endocrine Society, Fall Meeting, Seattle, WA, October 92.
Stewart RS	Storage of Human Papillomavirus DNA at Ultralow Temperatures Results in Reduced Polymerase Chain Reaction Amplification.	American Society for Microbiology, 93rd Annual Meeting, Atlanta, GA, May 93.
Stewart RS, Phillips RH	PCR Technology in the Clinical Microbiology Laboratory: Thermal Cycler Idiosyncracies.	Society of Armed Forces Medical Laboratory Scientists, Washington, DC, February 93.
Styner MJ, Moore KH, Matej LA, Archer KT, Plymate SR	Identification of Insulin-Like Growth Factor Binding Proteins in Prostate Cancer Cell Lines.	The Endocrine Society, Las Vegas, NV, June 93.

DEPARTMENT OF EMERGENCY MEDICINE

Burke TF, Buertler AT, Timmons J	A Comparison of Sinus X-rays With Computed Tomography in Acute Sinusitis.	Soceity for Academic Emergency Medicine, San Francisco, CA, May 93.
Guertler AT	A Prospective Study of Benzocaine-Induced Methemoglobinemia in Humans.	Society for Academic Emergency Medicine, San Francisco, CA, May 93.

DEPARTMENT OF FAMILY PRACTICE

Ellis DD	Syncope.	7th MEDCOM Primary Care Conference, Willinger, Germany, October 92.
Ellis DD	ACLS Update.	7th MEDCOM Primary Care Conference, Willingenr, Germany, October 92.
Ellis DD	ADHD.	7th MEDCOM Primary Care Conference, Willingen, Germany, October 92.
Ellis DD	Health Screening.	7th MEDCOM Primary Care Conference, Willingen, Germany, October 92.
Ellis DD	Lightening Injuries.	7th MEDCOM Primary Care Conference, Willingen, Germany, October 92.
Grajcar MS	The Physiologic Toll of the Medical Internship.	Uniformed Services Academy of Family Practice Conference, Corpus Christi, TX, April 93.
Lillegard WA	Back Injuries.	American Academy of Family Physicians Annual Meeting, San Diego, CA, October 92.

ıillegard WA	Elbow, Wrist, and Hand Injuries.	American Academy of Family Physicians Annual Meeting, San Diego, CA, October 92.
ıillegard WA	Should Injuries.	American Academy of Family Physicians Annual Meeting, San Diego, CA, October 92.
'orter SB, Blount BW	Pseudotumor of Infancy and Congenital Muscular Torticollis: A Case Report and Primary Care Perspective.	Uniformed Services Academy of Family Physicians Conference, Corpus Christi, TX, March 93.

DEPARTMENT OF MEDICINE

ıltemus D, Keeling J	Unusual Tattoo Reaction..	Academy of Dermatology Meeting, San Francisco, CA, December 92.
ıltemus D, ſcCalmont T	Eosinophilic Folliculitis: The History Spectrum.	American Academy of Dermatology Meeting, San Francisco, CA, December 92.
;adiz JL, Slicter SJ	Flow Cytometric Assessment of Progressive Platelet Activation in Stored Apheresis Platelets.	Army Chapter of the American College of Physicians, San Francisco, CA, October 92.
;ambier PA	Transcatheter Revascularization of Dysfunctional Dialysis Access: Results and Longterm Follow-up.	Army Chapter, American College of Physicians, San Francisco, CA, November 92.
;hapin BL	Corneal arcus: Its Relationship to Cholesterol Level and Cardiovascular Disease - A Meta Analysis.	Army Chapter of the American College of Physicians, San Francisco, CA, November 92.
;ragun WH, ſeenan LM	*Do Not Resuscitate: Do Not Provide Care?.*	Army Chapter of the American College of Physicians, San Francisco, CA, November 92.
;llis RB, Tuttle RM, ;omez kR	Polymerase Chain Reaction Amplification of B-2 Microglobulin Messinger RNA from Paraffin Embedded Breast Tissue.	Army Regional Meeting of the American College of Physicians, San Francisco, CA, November 92.
;eorgitis W, ;emar H, ſcDermott M	Goitrogenic Effect of Tetraglycine Hydroperiodide Water Purification Tablets.	Army Chapteer of the American College of Physicians, San Francisco, CA, November 92.
;ibson CA, Jones RE, ;unner DL, Lance J, ſoon M, Reed HL	Submaximal Cycloergometry to Determine Changing Metabolic Parameters Following 131-I Therapy for Thyrotoxicosis.	The Endocrine Society, Las Vegas, NV, June 93.
;ibson CA, Reed HL, ſones RE	Use of Basal Thyrotropin (TSH) Concentration to Predict Peak TSH Response to Thyrotropin Releasing Hormone.	U.S. Army Chapter of the American College of Physicians, San Francisco, CA, November 92.
ſhiang SM, ;aruso DR, Tuttle RM, ;omez RR, Peele ME, ſazzaferri EL	Detection of the PTC Chimeric Transcripts in Human Paraffin-Embedded and Frozen Thyroid Tumors.	The Endocrine Society, Las Vegas, NV, June 93.
ſones DL, Jeffers DJ	Physician Generated Practice Guidelines in Reducing Drug Costs - A Prospective Interventional Study.	Society of General Internal Medicine, 16th Annual Meeting, Arlington, VA, April 93.

Keenan LM, Charney PJ, Tuttle M, Snyder RH, Sado A	**Estimation of Twenty Four Hour Urinary Nitrogen Excretion from Four and Six Hour Urine Collections in Critically Ill Patients Receiving Nutritional Support.**	**American College of Chest Physicians, 58th Ann International Scientific Assembly, Chicago, USA, October 92.**
Keenan LM, Ficke RF, Walsh ES, Young-McCaughan SB, Kirk LC, Mueller JP, Cragun WH	**Do Not Resusicitate: Do Not Provide Care?.**	**Army ACP Meeting, San Francisco, CA, October 92.**
Keenan LM, Ricke RFWalsh ES, Walsh ESYoung-McCuag, Young-McCaughan S, Kirk LC, Mueller JP, Cragun WH	**Do Not Resuscitate: Do Not Provide Care?.**	**American College of Chest Physicians International Meeting, October 92.**
Landry FJ, Kroenke K, Lucas C, Reeder J	**Increasing the Use of Advance Directives in Outpatients: A Randomized Trial of a Patient Seminar Versus Written Information.**	**Society of General Internal Medicine, 16th Annual Meeting, Arlington, VA, April 93.**
LeMar HJ, Georgitis WJ, McDermott MT	**Thyroid Adaptation To Use of Tetraglycine Hydroperiodide Water Purification Tablet.**	**The Endocrine Society, Las Vegas, NV, June 93.**
Lyons MF, Gage TP, Tsuchida AM, Schlepp GE, Pearce WA, Peller TP, Walter MH	**The Use of Savary Dilatators in the Management of Colorectal Strictures.**	**American Society for Gastrointestinal Endoscopy, Boston, MA, May 93.**
Lyons MF, Tsuchida AM, Kim GJ, Schlepp GE, Pearce WA	**Colonoscopy Is Not Warranted in Young People Who have Heme Positive Stool By Digital Examination.**	**American College of Gastroenterology, 57th Annual Scientific Meeting, Miami Beach, FL, October 92.**
Lyons MF, Tsuchida AM, Schlepp GE, Pearce WA, Peller TP	**Barrett's Esophagus Is Associated With Colon Cancer Compared To Gastroesophageal Reflux With Stricture.**	**American Gastrointestinal Association/Amer Assoc Study of Liver Diseases, Boston, MA, May 93.**
Pearce WA, Guertler AT, Tsuchida AM, Lyons MF, Peller TP	**Prospective Evaluation of Benzocaine-Induced Methemoglobinemia In Humans.**	**American Society for Gastrointestinal Endoscopy, Boston, MA, May 93.**
Pearce WA, Peller TP, Tsuchida AM, Lyons MF	**Endoscopic Diagnosis and Treatment of Complications of Vertical Banded Gasgrostomy.**	**Army Chapter of the American College of Physicians, San Francisco, CA, November 92.**
Peele ME	**Detection of PTC Oncogene Expression in Fine Needle Thyroid Nodule Aspirates by Reverse PCR.**	**1992 Army Chapter of the American College of Physicians, San Francisco, CA, November 92.**
Peller TP, Lyons MF, Tsuchida AM, Pearce WA, Schlepp GE, Lee SP	**The "Budding" Appendiceal Polyp: A Potentially Overlooked But Treatable Lesion.**	**American Society for Gastrointestinal Endoscopy, Boston, MA, May 93.**
Pike JD	**Development of Respiratory Therapy Consultant Position In A Military Medical Center - A Pilot Study.**	**Army Chapter of the American College of Physicians, San Francisco, CA, October 92.**

Pike JD, Phillips Y, Argyros G	The Use of Bronchodilators by Metered Dose Inhaler Prior to Bronchoscopy.	American College of Chest Physicians, 58th Annual Scientific Assembly, Chicago, IL, October 92.
Sado AS	Use of Indirect Calorimetry in the ICU.	Army Chapter of the American College of Physicians, San Francisco, CA, November 92.
Thompson JW, Irvine T, Grathwohl K, Roth B	Misuse of Metered Dose Inhlaers in Hospitalized Patients.	ACP Washington Regional Meeting, December 92.
Tuttle RM, Gomez RR, Peele ME	Polymerase Chain Reaction Amplification of beta-2-microglobulin Messenger RNA From Paraffin Embedded Thyroid Tissue.	Army Chapter of the American College of Physicians, San Francisco, CA, November 92.
Tuttle RM, Kowalski KR, Smith D, Moore KH, Reed HL	Changes in the Relationship of Circulating Sex Hormone to Sex Hormone Binding Globulin Associated With Winter Military Operations: A Possible Marker of Early Energy Deficits.	The Endocrine Society, Las Vegas, NV, June 93.
Tuttle RM, Peele ME	Thyroid Specimens Obtained by Fine Needle Aspiration of the Thyroid Can serve as Substrate for the Polynerase Chain Reaction.	Army Chapter of the American College of Physicians, San Francisco, CA, November 92.

DEPARTMENT OF NURSING

Birgenheier P	The Physiologic Effects of Positioning Premature Infants in Car Seats.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Campanaro J	Legal Issues for Emergency Nursing.	Tri-Services Conference for Emergency Medicine and Nursing, May 93.
Harwood SJ	Piglet Tracheal Epithelial Regeneration After Suctioning.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Leander D	Interpreting the Language of Neonates.	Pacific Northwest Neonatal Nurses Association Conference, Seattle, WA, March 93.
Loan L	Neonatal Implications of Ventilator Inspired Gas Temperatures.	Western Society of Nursing Research Annual Research Conference, May 93.
Loan L	Endotracheal Suctioning in Neonates.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Loan LA	Neonatal Implications of Ventilator Inspired Gas Temperatures.	Pacific Northwest Neonatal Nurses Association Conference, Seattle, WA, March 93.
McCarthy M	Autonomic, Behavioral, and Self-Reported Assessment of Pain in a Selected Emergency Department Population Before and After Parenteral Analgesia.	Emergency Nurses Scientific Assembly, September 93.
Renaud M	Nursing Case Management.	ANC Advanced Practice Care Conference, Denver, CO, March 93.

Renaud M	**Hyperbilirubinemia: One Thousand Points of Light.**	**Pacific Northwest Neonatal Nurses Association Conference, Seattle, WA, March 93.**
Renaud M	The Effects of A Modified Care Environment on the Growth and Development of High Risk Infants.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Turner BS	Jump Starting A Research Project.	Second Annual Nursing Research Conference, Durham, NC, December 92.
Turner BS	Team Approach to Research.	Second Annual Nursing Research Conference, Durham, NC, December 92.
Webb SB	Physiologic Responses to Exogenous Surfactant.	Washington State Nurses Association, Spokane, WA, August 93.
Williams D	Implications and Evaluation of Clinical Information Systems.	American Nurses Association International Conference, Rome, Italy, January 93.
Wilson S	Weaning: The Transition of the Preterm Infant to an Open Crib.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Yackel EE	A View on Nurses Smoking and Its Influence on Patient Health Practices.	Washington State Nurses Association Annual Meeting, Spokane, WA, June 93.
Young-McCaughan SB	Sexual Functioning in Women with Breast Cancer Comparing Women Treated with Systemic Adjuvant Therapy to Women Treated Without Pharmacological Manipulation.	Annual Meeting of AMSUS

NUTRITION CARE DIVISION

Grediagin A	The Effect of Exercise Intensity on Body Composition Change in Untrained Moderately Overfat Women.	Sport and Cardiovascular Nutrition Meeting, San Diego, CA, April 93.

DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Armstrong AY	Hyperactivation in Cryopreserved Spermatozoa: Effects of Progesterone and Various Membrane-Active Agents.	Armed Forces District of the American College of Obstetricians/Gynecologists, Norfolk, VA, November 92.
Larsen WI, Brady WK, Kopelman JN	Twelve Hour Urine Collections in Comparison to Twenty Four Hour Urine Collections in Patients with Preeclampsia.	Armed Forces District of the American College of Obstetricians/Gynecologists, Norfolk, VA, November 92.
Macedonia CR, Rasband W	Three Dimensional Imaging of the Fetal Head Using A Continuous Running Acquisition Process.	American Institute of Ultrasound and Medicine, HI, March 93.
Markenson GR	The Effects of Estradiol and Progesterone on Vasoactive Substances in the Dually Perfused Cotyledon Model	Armed Forces District of the American College of Obstetricians/Gynecologists, Norfolk, VA, November 92.
Yanko CA, Kopelman JN, Read JA	Quantitative Evaluation of Blood Loss in Parturients With and Without Clinical Chorioamnionitis.	Western Society for Clinical Research, February 93.

DEPARTMENT OF PATHOLOGY, BLOOD BANK

Hodges GF, Lenhardt TM, Cotelingam JD	Bone Marrow Involvement in Large Cell Lymphoma - Prognostic Significance of Discordant Disease.	Canadian/American Association of Pathologists, New Orleans, LA, March 93.

DEPARTMENT OF PEDIATRICS

Carter ER	Use of the Interrupter Technique in Assessing Airways Obstruction.	Regional Cystic Fibrosis Conference, Seattle, WA, May 93.
Carter ER	Use of Heliox in Obstructive Airways Disease.	Annual Meeting of the Washington Thoracic Society, January 93.
Carter ER, Stecenko A, Pollock B, Jaeger M	Update on Theophyline Use in Pediatric Asthma.	Pediatric Respiratory Disorder Conference, March 93.
Guevara JP, Clark J, Keplar B, Athya B	Prevalence of Cardiac Abnormalities in Children With SLE.	Uniformed Services Pediatric Society, San Antonio, TX, March 93.
Rawlings JS, Read JA	Effectiveness of Spontaneous Labor in Relation to the Hour of Onset.	Uniformed Services Pediatric Society, San Antonio, TX, March 93.
Vahn CA, Stephan MJ, Culbertson G	The Association of Mullerian Aplasia With the Oculoauriculovertebral (OAV) Spectrum.	David W. Smith International Conference on Morphogenesis and Malformations, Tremblant, Canada, August 93.

DEPARTMENT OF RADIOLOGY

Bauman J, Budd S, Katts N, et al	A Conceptual Plan to Link A Nuclear Medicine Department to the Medical Diagnostic Imaging Support System (MDIS) PACS Configuration.	Society of Photo-Optical and Instrumentation Engineers, Newport Beach, CA, February 93.
Ho VB	Bone Scintigraphy in Sports Medicine.	Radiological Society of North America, 78th Annual Scientific Assembly, Chicago, IL, November 92.
Ho VB	Pineal Region Masses: Differential Diagnosis.	Radiological Society of North America, 78th Annual Meeting, Chicago, IL, December 92.
Ho VB	Scintigraphic Artifacts: A Systematic Approach.	Radiological Sodiety of North America, 78th Annual Meeting, Chicago, IL, November 92.
Ho VB, Chuang HS, Rovira MJ, Koo B	Juvenile Huntington Disease: CT and MR Features.	American Society of Neuroradiology, Vancouver, Canada, May 93.
Ho VB, Smirniotopoulos JG	Pineal Region Masses: Differential Diagnosis.	American Society of Neuroradiology, Vancouver, Canada, May 93.
Ho VB, Smirniotopoulos JG	Pineal Region Masses: Differential Diagnosis.	Radiology Society of North American Annual Meeting, Chicago, IL, November 92.
Kransdorf MJ, Buetow PC, Meyer CA	Soft Tissue Tumors in the First Year of Life: A Review fo 587 Cases..	American Roentgen Ray Society, 93rd Annual Meeting, San Francisco, CA, April 93.

Leckie RG, Goeringer F, Smith DV, Smith S, Choi HS, Bender G, Haynor DR, Kim Y	An Early Evaluation of MDIS Workstations at the Madigan Army Medical Center.	Society of Photo-Optical and Instrumentation Engineers, Newport Beach, CA, February 93.
Leckie RG, Smith CS, Smith DV, Donnelly J, Cawthon MA, Weiser J, Willis CE, Goeringer F	The Medical Diagnostic Imaging Support (MDIS) System: A Large PACS and Teleradiology Project.	7th International Symposium and Exhibition for Computer Assisted Radiology, Berlin, Germany, June 93.
Leckie RG, Smith DV, Smith S, Cawthon MA, Weiser J, Donnelly J, Goeringer F	Computed Radiography: Successess and Concerns After Implementation of a Completely Digital Imaging System at a Large Medical Center.	American Roentgen Ray Society, 93rd Annual Meeting, San Francisco, CA, April 93.
Parker JES, Pestaner JC, Meyer CA, Babu SS	Nipple to Lesion Distance Discrepancy on Craniocaudal and Mediolateral Oblique Views.	American Roentgen Ray Society, San Francisco, CA, April 93.
Peller PJ, Ho VB	Scintigraphic Artifacts: A Systemic Approach.	Radiology Society of North America, Chicago, IL, November 92.
Rovira MJ, Ho VB	MRI and MRV of the Posterior Fossa Dural Sinuses: Normal Anatomy and Variants.	American Society of Neuroradiology, Vancouver, Canada, May 93.
Smith DV, Cawthon MA, Leckie RG, Mun SK	Medical Diagnostic Imaging Support (MDIS) System Implementation at Madigan Army Medical Center as a Model for Installing a Large Scale Picture Archiving and Communications System.	Third PACS-RIS School, Washington, DC, April 93.
Smith DV, Mun SK	Specifications and Future Directions for Large Scale Picture Archiving and Communications Systems (PACS).	Third PACS-RIS School Proceedings, Washington, DC, April 93.
Smith S, Leckie RG, Smith DV, Donnelly J, Cawthon MA, Sauls F, Romlein J, Willis CE	MDIS: A Large PACS and Teleradiology Project for the Military - An Overview of the First Year of Operation.	American Roentgen Ray Society, 93rd Annual Meeting, San Francisco, CA, April 93.

DEPARTMENT OF SURGERY

Anderson EE, Perez LM, Amling CL, Thrasher JB, Newman GE, JoynerRE	Palliative Urinary Diversion for Ureteral Obstruction As A Consequence of Metastatic Prostate Cancer.	American Urological Association, 88th Annual Meeting, San Antonio, TX, May 93.
Burgess FW	Anticoagulant Effect of Magnesium Sulphate as Measured by Thromboelastography.	Eighteenth Annual Meeting of the American Society of Regional Anesthesia, Seattle, WA, May 93.
Burgess FW, Colonna D, Anderson DM, Sborov MJ	Postoperative Referred Pain Following Thoracotomy.	American Society of Anesthesiologists, October 92.
Burgess FW, Snodgrass G, Helman JD, Sborov MJ	Combined Epidural/General Anesthesia and the Hemodynamic Response to Hemorrhage.	American Society of Anesthesiologists, October 92.

PRESENTATIONS - MAMC - FY 93

Carpenter CT, Cosio MQ	The Role of Arthrography in Ulnar Collateral Ligament Injuries of the Thumb.	American Orthopaedic Association Meeting, Seattle, WA, March 93.
Carter PL	Experience with Biliopancreatic Diversion in Reoperative Bariatric Surgery.	American College of Surgeons, October 92.
Chandler DW, Grantham DW	Auditory Spatial Resolution in the Horizontal Plane As a Function of Reference Angle: Microstructure of the Azimuth Function.	Acoustical Society of America, Norfolk, VA, April 93.
Chandler DW, Souliere CR, Edmond CV	Effects of Blast Overpressure on the Ear: A Case Study.	American Academy of Audiology, Phoenix, AZ, April 93.
Cox H, Jones RO, Sunshein KF	Direct Extension Osteomylitis Secondary To Onychocryptosis: A Review of Literature and 3 Case Reports.	American College of Foot and Ankle Surgeons, San Diego, CA, February 93.
Gee BT, Parmley VC, Fannin LA, Mader TH, Truxal AR, Varga JA, Kannen KA, Hansen CN	Safety of Intraocular Administration of E5 Gram-Negative Endotoxin Monoclonal Antibody in Rabbit Eyes.	Association for Research in Vision and Ophthalmology, Saratoga, FL, May 93.
Gingrich JR, Thrasher JB, Paulson DF	Radical Nephrectomy for Renal Cell Carcinoma: A Contemporary Review of Presentation, Complications, and Outcome of 356 Cases.	American Urological Association, 88th Annual Meeting, San Antonio, TX, May 93.
Grace TS, Jones RO, Sunshein KF, Harkless LB	Metatarsus Proximus and Digital Divergence: Its Association with Intermetatarsal Neuroma.	American College of Foot and Ankle Surgeons, San Diego, CA, February 93.
Knight RW, Hansberry KL, Bagg MD	Impotence Following Transurethral Resection of the Prostate (TURP). *First place for a resident paper.*	Kimbrough Urologic Seminar, November 92.
Mader TH, Aragonas, Fox, Stein	Ocular Injuries of Operation Desert Shield/Desert Storm.	American Academy of Ophthalmology, Dallas, TX, November 92.
Mancuso JJ	Epidural Analgesia in an Army Medical Center: Impact on Cesarean and Instrumental Vaginal Deliveries.	Society for Obstetric Anesthesia and Perinatology, 25th Annaul Meeting, Indian Wells, CA, May 93.
Neary MT, Jones RO, Sunshein K, VanManen W, Youngberg R	Avascular Necrosis of the First Metatarsal Head Following Austin Osteotomy: A Follow-Up Study.	American College of Foot and Ankle Surgeons, San Diego, CA, February 93.
Neary MT, Jones RO, Sunshein K, VanManen W, Youngberg R	Avascular Necrosis of the First Metatarsal head Following Austin Osteotomy: A Follow-up Study..	American College of Foot and Ankle Surgeons Annual Meeting, San Diego, CA, February 93.
Ng JD	Comparison of Three Corneal Trephines for Penetrating Keratoplasties to Treat Larg Central Corneal Perforations	"Keratorefracture Surgery in the Military" National Meeting, Washington, DC.
Perez LM, Thrasher JB, Robertson JE, Paulson DF	Is Radical Prostatectomy Appropriate in Elderly Men?.	American Urological Association, 88th Annual Meeting, San Antonio, TX, May 93.

Reno JP	**Individual Preparedness As A Measure of Effectiveness of Hearing Conservation Programs.**	**Military Audiology Meeting, Norfolk, VA, 0.**
St Pierre P, Staheli LT, Green NE, Smith JB	**Femoral Neck Stress Fractures in Children and Adolescents.**	**American Orthopaedic Association, Seattle, WA, March 93.**
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Sunshein KF, Wilkinson SV, Jones RO, Sisk LD, VanManen JW	**Evaluation of the Rate of Avascular Necrosis Formation Following Austin Bunionectomy.**	**American College of Foot and Ankle Surgeons, San Diego, CA, February 93.**

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DETAIL SHEETS FOR PROTOCOLS

ACTIVE DUTY STUDENT DETACHMENT, HSC

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/126 **Status:** On-going

Title: The Effect of Body Position on Ventricular Arrhythmias in the Coronary Artery Disease Patient in the CCU

Start Date: 08/06/93 **Est. Completion Date:** Mar 94

Department: Student Detachment, HSC **Facility:** MAMC

Principal Investigator: MAJ Cheryl A. Creel, AN

Associate Investigators: None

Key Words: ventricular arrhythmias,body position

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

Study Objective: 1. To determine if there is a difference in the onset of silent ischemia as evidenced by an ST segment shift (elevation or depression) and/or ventricular ectopy when the coronary artery diseased (CAD) patient is repositioned to the right or left lateral position from the supine position within the first 72 hours of admission to the Coronary Care Unit (CCU). 2. To determine if repositioning from the right or left lateral position to the supine will reduce the ST segment shift and/or ventricular ectopy. 3. To identify personal or illness-related factors that are associated with the onset of silent ischemic changes after repositioning.

Technical Approach: A convenience sample of the first 33 patients admitted to the CCU who meet the criteria and consent to participate will be chosen. The investigator will compare rhythm strips with 12 lead EKGs for basic rhythm and PR and ST segment baselines. The patient positioning protocol will be conducted on the following day. Patients will be placed on a cardiac monitor and 3 leads which best indicate potential areas of ischemia will be utilized. These areas will be identified either by the most recently documented heart catheterization results or by 12 lead EKGs which show ischemic changes in specific leads. If neither of these is available, the patient will be monitored in leads V1, V5, and AVF. Cardiac rhythm strips, B/P and SaO_2 values will be taken immediately after repositioning and then again at 5 minutes. After baseline data are obtained he patient will be repositioned 3 times and data collected.

A paired t-test will be used to determine whether there is an increase in silent ischemia after repositioning from supine to lateral and from lateral to supine. A Cramer Coefficient C will be the nonparametric analysis to measure the degree of association between personal and illness factors and the presence or absence of myocardial ischemia on the right or left lateral position.

Progress: This protocol is in the process of IRB review at the University of Washington. The project will begin when that approval is received.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/011 **Status:** Completed

Title: Sensitivity of Transiently-Evoked Otoacoustic Emissions in Monitoring Adult Cis-platin Patients

Start Date: 10/02/92 **Est. Completion Date:** Nov 92

Department: Student Detach, HSC **Facility:** MAMC

Principal Investigator: MAJ John E. Ribera, MC

Associate Investigators: George Haskell, Ph.D.

Key Words: cancer,otoacoustic emissions,cisplatin

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To evaluate the sensitivity of transiently-evoked otacoustic emissions (TEOAEs) in monitoring ototoxicity in Cis-platin recipients. The questions being asked are: 1. How sensitive are TEOAEs in relation to the standard test (behavioral audiometry to include extended high frequencies) in early identification of hearing loss in patients receiving Cisplatin treatment? 2. Which of two transient stimuli (clicks or tone bursts) is more sensitive to change in cochlear function due to Cisplatin-induced ototoxicity?

Technical Approach: The sample population will be comprised of approximately 30 adult male and female subjects (40 years of age or older) from MAMC and Seattle VA Medical Center (SVAMC). Subjects will be placed in either the control group (those not receiving Cisplatin treatment) or the experimental group (Cisplatin recipients). Subjects will be screened via an intake history, middle ear test and audiogram. Once criteria for inclusion in the study have been met, subjects in both groups will be tested using the IL088 Otoacoustic Analyzer. The screening tests and emissions analysis will comprise the "baseline test" which will be administered to both groups with the experimental group being evaluated just prior to Cisplatin treatment. Both groups will be tested approximately 1-2 weeks (a.k.a. post-test #1) and subsequently 3-4 weeks post-baseline (a.k.a. post-test #2). The test protocol during each of the post-tests will be identical to the baseline test. This is a repeated measures design and will be analyzed using a repeated measures ANOVA to identify possible treatment effects. Other descriptive statistics will also be used as deemed appropriate. Results will be used to develop a clinical protocol for ototoxicity monitoring at MAMC and SVAMC.

Progress: No patients were enrolled at MAMC. Data analysis is being completed on patients that were enrolled at SVAMC. A dissertation will be written from that information.

DETAIL SHEETS FOR PROTOCOLS

BEHAVIORAL SCIENCES DIVISION, CLINICAL PSYCHOLOGY

Detail Summary Sheet

Date: 30 Sep 93	**Protocol No.:** 93/025	**Status:** On-going
Title: Sexual Harassment: Attitudes and Actions		
Start Date: 12/04/92	**Est. Completion Date:** Mar 93	
Department: BSD/Clinical Psychology	**Facility:** MAMC	
Principal Investigator: CPT Mary G. Lambie, MC		
Associate Investigators: None		
Key Words: Sexual Harassment,attitudes,actions		

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

Study Objective: To assess the effects of gender, status, race and attitudes towards sexual harassment on perceptions of the seriousness of sexual harassment incidents, in determining what actions should be taken in sexual harassment cases and on perceptions of organizational response to harassment.

Technical Approach: Ranks E-1 to E-4, E-6 to E-8, O1 to O3, and O4 to O6, with O1 to O6 having been in leadership positions will participate in this study. Each subject will be asked to complete a personal data sheet. They will also be asked to complete a Sexual Harassment Attitude Scale (SHAS) developed by Mazer and Percival that has been modified somewhat to focus only on the work place (i.e. phrases such as in class, at school etc., were deleted).

They will then be given written narratives of sexual harassment incidents. After reading the narratives, they will be required to 1) determine the seriousness of the incident on a Likert-type scale 2) recommend what type of action (from a provided list) should be taken in each scenario and 3) select which action from the list they feel their command is most likely to take for each scenario.

Analysis of Variance will be performed for each dependent variable (perceived seriousness of sexual harassment incidents, rater's perceived seriousness of sexual harassment incidents, rater's actions for sexual harassment incidents, perceived organizational actions for sexual harassment incidents, and difference scored between rater's actions and perceived organizational actions). The SHAS will be treated as a continuous variable, and therefore will need to be analyzed using bivariate regression analysis for the dependent variables of seriousness of the incident and personal actions taken.

Progress: Data was collected from 408 active duty soldiers attending sexual harassment training. At this time no further data will be collected. Data analysis and final interpretation are in progress.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 87/100	**Status:** On-going
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: Enrollment into the study continues (n=265). No data analysis has occurred.

Detail Summary Sheet

Date: 30 Sep 92 **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 Factor (Deslorelin)

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:** 07/02/93

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 and post 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: Treatment continues on 2 patients and data continues to be collected.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/092	**Status:** On-going
Title: Characterization of LH Isoforms in Treated and Untreated Precocious Puberty		
Start Date: 09/06/91	**Est. Completion Date:** Jun 92	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: MAJ Jim Hansen, MC	CPT Katherine H. Moore, MS	
Key Words: precocious puberty,LH:isoforms		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $1843.00	**Periodic Review:** / /

Study Objective: To determine the luteinizing hormone (LH) isoform pattern in precocious puberty and demonstrate whether there is a change in isoform pattern during therapy with gonadotropin-releasing hormone (GnRH) analogue (leuprolide) and to confirm whether changes in LH bioactivity correlate with parallel changes in LH isoform pattern during therapy.

Technical Approach: This is a collaborative study using serum obtained from subjects in the University of Iowa protocol entitled "New Treatments to Improve the Final Height of Children with Central Precocious Puberty". Paired frozen sera from 12 subjects, will be processed as follows: 1 ml of serum will be dialyzed against two changes of 2 liters of 0.025 M Tris (pH=9.3) for 2 hours and then applied to a 1.0 x 20 cm Mono P HR 5/20 column (4 ml column volume), which has been equilibrated with 15 column volumes of 0.025 M Tris (pH=9.3). The sample is eluted with 50 ml Polybuffer 96 (diluted 1:10 with water, pH=6.0) at 1 ml/min and collected in 2 ml fractions. To study LH isoforms which are present between pH 7 and 4, similar procedures will be used, substituting Polybuffer 74 and Tris protein precipitation with 0.5 ml of 1% BSA and 2.8 g of powdered ammonium sulfate. After thorough mixing and incubating at 20 deg C for 2 hr. the fractions are centrifuged at 1500 g for 30 minutes. Supernatant is discarded and precipitates are washed once with saturated ammonium sulfate and then reconstituted in 0.5 ml of assay buffer for LH RIA and bioassay. Aliquots of fractions which contain LH activity will be pooled for each chromatofocusing peak and analyzed for LH immunoactivity and bioactivity. Changes in bioactivity correlating with changes in chromatofocusing pattern will be sought in pre and post treatment sera.

Progress: Chromatofocusing of trough and peak, pre and post treatment samples was completed and initial work on the LH bioassay was begun. Initial analysis of LH RIA on chromatofocusing samples showed that Lupron treatment tended to reduce the basic:acidic (B:A) ratio of LH isoforms at the time of an LH peak.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/048 **Status:** On-going

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: MAJ Robert A. Newman, MC

Key Words: delayed maturation and growth,boys,oxandrin

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

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 is a treatment protocol with very strict criteria. We have had no patients to date that met the criteria.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/060	**Status:** Completed
Title: Thyroid Volume in Adolescents as Determined by Ultrasound		
Start Date: 05/03/91	**Est. Completion Date:** May 92	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: CPT Janice C. Stracener, MC	MAJ James H. Timmons, MC LTC Thomas R. Babonis, MC	
Key Words: thyroid volume,ultrasound,adolescents		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To determine normal size (volume) of the thyroid gland in adolescence and to correlate it with clinical surface measurements, as well as other clinically important variables such as body weight or body mass index, height, and pubertal stage.

Technical Approach: Ten subjects of each sex at each age, between 12 and 18 years, with normal health and normal size thyroid gland will be studied. Height, weight, and Tanner stage will be recorded and the thyroid gland will be measured using standard surface measurement techniques. Subsets of 20 patients each will be examined by two examiners to determine inter-observer variability of measurement techniques and by the same examiner on two separate occasions to determine intra-observer variability of measurement. Thyroid volume will then be determined by ultrasound, on an Acuson 128 with a 5MHz short-focus linear array transducer. One set of 20 subjects, selected randomly, will undergo a second examination by the original examiner within one week of the initial examination to determine if measurements are reproducible. A second set of 20 subjects will have additional measurements performed with 5MHz and 7.5 MHz linear array transducers using a GE3600RT instrument at the time of the initial measurement to insure reproducibility of the measurements between instruments and at different frequencies of ultrasound. All measurements will be performed twice by each of two separate investigators to determine both intra-observer and inter-observer variability in the measurements. Method of Data Analysis: description of volume change by sex, age, pubertal stage, and body mass index comparison of sex and age differences by linear regression stepwise linear regression to determine best fit for influence on changing volume correlation coefficient to validate surface measurement versus volume determination.

Progress: Of the 28 patients who completed the study, it is hoped that 20 will have useful data. Data analysis is being delayed and will be combined with results of protocol 87/100.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/058 **Status:** On-going

Title: Is Sex Hormone Binding Globulin Locally Produced in Breast Cancer Tissue?

Start Date: 05/01/92 **Est. Completion Date:** Jun 94

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: CPT Katherine H. Moore, MS

Associate Investigators: MAJ Kenneth A. Bertram, MC
Louis A. Matej, B.S.

Key Words: SHBG, breast cancer

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

Study Objective: To gain insight into the regulation of breast cancer growth and development and to correlate the estrogen and progesterone receptor status of breast cancer biopsy tissue with the presence of sex hormone binding globulin (SHBG) mRNA.

Technical Approach: SHBG is a high affinity binding protein for androgens and estrogens. This protein is normally produced in the liver, released into the blood and functions to regulate the amount of free androgen or estrogen available for action at target organs. Recently, receptors for SHBG have been identified on prostate carcinoma cells. Prostate cancer, like breast cancer, is generally considered to be modulated by steroids. One proposed consequence of the SHBG receptor on cancer cells is the additional targeting of steroid to the cells. SHBG may have a role independent of steroid action and may be a growth factor itself. One of the oncogenes that is important in breast cancer development is p53. It has been found recently that changes in p53 and SHBG may be linked. Both of these genes are on the short arm of chromosome 17 near an area prone to rearrangement and mutation. Breast cancer cell lines (MCF-7 and ZR75-1, initially) will be examined for the presence of SHBG and mRNA and for factors that regulate transcription. In addition, the investigators will probe for SHBG mRNA in primary breast cancer tissue obtained at biopsy and surgery. Cancer cell membranes and primary tissue will be assayed for the presence of SHBG receptors. Techniques used will include Northern analysis, RIA of the conditioned media for expressed SHBG, and western analysis to determine the form of p53 expressed in the cells (wild type vs mutant). This study will thus characterize a potentially new oncogene for breast cancer and lead to a greater understanding of the mechanisms of cancer formation.

Progress: Recently, receptors for SHBG have been identified on steroid responsive tissues, including prostate carcinoma and endometrium. The goal of this series of experiments was to determine if mRNA for SHBG is expressed in breast cancer call lines and tumor tissue. Two estrogen receptor positive cell lines were used, the ZR-75-1 cells, but no detectable message from the MCF-7 cells. The ZR-75-1 cells were used for studies investigating the transcriptional regulation of SHBG mRNA, which indicated that thyroxine may increase levels of SHBG mRNA, and estrogen and insulin may reduce levels. When MCF-7 cells were re-examined for SHBG RNA using PCR, specific message could be detected. Also, evidence of alternative splicing of the SHBG mRNA in breast cancer cells was found. Finally, amplification of RNA extracted from breast tumor tissue by PCR revealed the presence of SHBG mRNA in estrogen receptor positive tumors.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/043 **Status:** Completed

Title: Sex Hormone Binding Globulin (SHBG) Carbohydrate Function and Characterization

Start Date: 03/01/91 **Est. Completion Date:** May 92

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: CPT Katherine H. Moore, MS

Associate Investigators:
MAJ John E. van Hamont, MS
Louis A. Matej, B.S.
Philip H. Petra, Ph.D.
CPT Robert M. Tuttle, MC

Key Words: SHBG:carbohydrate function, SHBG:characterization, Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To determine if the carbohydrate composition of sex hormone binding globulin (SHBG) varies with physiological status between pregnant females and normal males and to determine the role of the carbohydrates covalently attached to SHBG in the biological functions of this glycoprotein.

Technical Approach: Each monomer of human SHBG contains three carbohydrate chains. Two are attached to asaparagine residues (N linked) and one to a threonine (O linked). The N linked carbohydrates will be enzymatically removed with N-Glycanase and O linked carbohydrates will be removed with neuraminidase followed by O-Gylcanase. The affinity and specificity of the modified proteins for dihydrotestosterone, testosterone, and estradiol will be determined using the DEAE-cellulose filter assay. Also the ability of the modified proteins to compete for prostate membrane receptors will be determined. Native SHBG will be labeled with ^{125}I Bolton-Hunter reagent, purified by chromatography on G-75, followed by Con-A chromatography. The ability of the deglycosylated SHBG to compete with the labeled SHBG will be determined and affinity calculated by scatchard analysis. SHBG was purified from pregnancy serum and normal male serum to determine if physiological condition affected the carbohydrate composition of SHBG. Normal serum levels of SHBG are 10 fold greater in pregnant women than normal men. One possible reason for the differences in levels could be serum half-life due to carbohydrate composition. The carbohydrate composition of the SHBG will be determined with an electrochemical detector after hydrolysis in trifluroacetic acid. Serum half-life will be determined using rats as the experimental model. As rats do not possess a serum SHBG, natural protein can be injected (no ^{125}I label) and the clearance measured by IRMA. The animals will have chronically implanted cannulas, allowing repeated sampling from individual animals. Samples will be collected for 6 days.

Progress: Sex hormone binding-globulin is a homo-dimeric glycoprotein which functions as a steroid transport protein in serum. One interest in investigating the functional importance of the oligosaccharides is the investigation of their importance in steroid binding. SHBG was purified from human serum and asparagine and threonine linked oligosaccharides removed enzymatically. The efficacy of enzyme cleavage of sugars from the protein was confirmed with mass spectrometry and lectin blots. The affinity of steroids for SHBG was not affected by removal of the sugars. A second objective was to study SHBG produced under different physiological states to determine if the

sugar content of the protein was under hormonal control. SHBG was also purified from normal male serum and serum collected from pregnant women and purified to homogeneity. Neutral sugar and sialic acid content was analyzed by HPLC, using pulsed ampermetric detection under alkalike conditions. Oligosaccharide content was similar between both sources of SHBG. To further investigate the influence of source of SHBG (i.e., male vs pregnant female), the metabolic clearance of SHBG also was investigated using rat models as they do not have a circulating SHBG, allowing the injected material to be directly measured by immunoassay. The clearance of SHBG also was compared between pregnant female rats and normal female rats to determine if pregnancy itself affected the serum half-life of SHBG. The clearance of male SHBG was not different from pregnant female sHBG, confirming the implication of the similarity of sialic acid content, that serum half-life should be similar. Also, the clearance of SHBG was similar in non-pregnant and pregnant animals, indicating that pregnancy did not influence the metabolic clearance of this carrier protein.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/109 **Status:** Completed

Title: Characterization of Equine Inhibin Sequence Analysis and Carbohydrate Composition

Start Date: 09/21/90 **Est. Completion Date:** Oct 92

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: CPT Katherine H. Moore, MS

Associate Investigators: Kristine M. Wiren, Ph.D.

Key Words: equine inhibin,sequence,carbohydrate composition,animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$8870.00	**Periodic Review:** 06/07/93

Study Objective: To purify equine inhibin from foll[illegible]d, to compare specific activity and carbohydrate chemistry to inhibin from other species, and to determine the sequence of equine inhibin and determine its homology to other known sequences.

Technical Approach: Inhibin, a heterodimeric protein, is a member of the transforming growth factor (TGF) family of proteins. These proteins have a variety of functions, including tissue regeneration and tumor growth. The structure of this family of proteins is remarkably conserved across species and through different protein members of the family, including such diverse proteins as xenopus vg-1 protein to inhibin. The classical function of inhibin is in the regulation of follicle stimulating hormone (FSH) release, but the mRNA for inhibin is found in many tissues, indicating a multifunctional role for this protein. The comparison of the amino acid sequence of inhibin from different species identifies important regions of the protein in its biological functions. The functions of horse inhibin will be tested both immunologically and with the in vitro biological assay, using cultured rat pituitary cells. The protein will be purified and the carbohydrate content determined. The sequence of the protein will be deduced from a cDNA library established from horse gonadal tissue. This comparison of a naturally occurring analogue will advance our understanding of the relationship of the protein structure to its many functions.

Progress: A manuscript was written and accepted by the Journal of the Society for the Study of Reproduction. A paper was presented at the Endocrine Society meeting in FY 92.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/005 **Status:** On-going

Title: Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine, Goat, Rabbit, Ferret, Rat, Mouse)

Start Date: 12/06/91 **Est. Completion Date:**

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: MAJ Douglas A. Powell, VC

Associate Investigators: None

Key Words: cancer, alimentary tract,nasogastric tissue sampling,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$125.00	**Periodic Review:** 06/07/93

Study Objective: (1) To help the Department of Clinical Investigation (DCI) technical staff 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 manipulation (3) to teach DCI technical staff basic surgical skills that will enable them to better assist investigators.

Technical Approach: Training sessions on handling animals, anesthesia, soft tissue surgery, blood withdrawal, injections, and necropsy techniques will be periodically held at the Department of Clinical Investigation. Swine, goats, rabbits, ferrets, mice, and rats will be used in these training sessions. All animals will be appropriately anesthetized except for injection techniques and IV blood withdrawal. All animals will be handled and utilized in accordance with The Guide for the Care and Use of Laboratory Animals (US Department of Health and Human Services), AR 70-18, and other applicable regulations.

Progress: Eight animals, used in other protocols, were utilized in the training of veterinary support personnel. Training included intubation and anesthesia procedures, venous and arterial access.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/074	**Status:** On-going

Title: Microbiological Analysis of Male NGU Specimens by Polymerase Chain Reaction: A Retrospective Study

Start Date: 06/05/92	**Est. Completion Date:** Aug 92
Department: Clinical Investigation	**Facility:** MAMC
Principal Investigator: MAJ Robert S. Stewart, MS	
Associate Investigators:	MAJ Margot R. Krauss, MC
Key Words: urethritis,polymerase chain reaction	

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

Study Objective: To perfect new PCR assays and to determine the prevalence rates by PCR in male NGU samples collected February through April 1989 for human papillomavirus (HPV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), Chlamydia trachomatis, Trichomonas vaginalis, and Mycoplasma genitalium and to compare prevalence rates from both culture and PCR methods for Chlamydia trachomatis.

Technical Approach: Approximately 200 male NGU urethral specimens were collected during the months of February through April 1989 for MAMC Protocol #89/19 "Urinalysis As A Screening Exam for NGU in Males Attending an STD Clinic." These samples were cultured for Chlamydia trachomatis and Ureaplasma urealyticum and the remaining fraction was stored frozen at -20 degrees Centigrade. These stored samples will be thawed, processed for DNA extration, and analyzed by PCR for organisms not previously suspected, including HPV, HSV, HIV, C. trachomatis, T. vaginalis, and M. genitalium.

Progress: PCR assay for Chlamydia trachomatis is in development. We are currently optimizing the sensitivity level with a goal of being able to detect 10-50 elementary bodies. The HPV assay is fully developed and has a sensitivity level of 30 viral gnomes. The assay for Ureaplasma urealyticum will not be run because those samples were completely consumed in the original study in 1988.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/075 **Status:** On-going

Title: Precise Tissue Distribution of DNA and Hormone Receptors in Breast Biopsies as Clinical Prognosticators: A Retrospective Study

Start Date: 06/05/92 **Est. Completion Date:** Jun 93

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: MAJ Robert S. Stewart, MS

Associate Investigators: Troy H. Patience, B.S.

Key Words: breast biopsy,DNA,hormone receptors

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

Study Objective: To develop a computerized laser confocal microscope-based image analysis system which would provide more clinically significant information for breast cancer diagnosis than is currently available.

Technical Approach: A scanning laser confocal fluorescent microscope will be used to optically section breast tumor biopsies stained with DNA specific compounds and fluorochrome conjugated monoclonal antibodies. Nuclei flagged for further consideration by the computer will be analyzed by newly developed software which will contain tissue sensitive algorithms. Proximity relationships between aneuploid and hormone receptor deficient nuclei will be compared to normal nuclei within the same and adjacent fields. These proximity relationships, expressed as calculated values, will provide improved prognostic information when compared to the currently employed aneuploid (DNA indices) and proliferation (S-phase indices) determinations. Tissue sensitive proximity values for hormone receptors will also improve current prognostic correlations.

Progress: This project is pending MRDC funding. The grant is under review.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/073	**Status:** On-going
Title: Molecular Microbiology Assay Development		
Start Date: 06/05/92	**Est. Completion Date:** Indef.	
Department: Clinical Investigation	**Facility:** MAMC	
Principal Investigator: MAJ Robert S. Stewart, MS		
Associate Investigators:	M. J. Styner, B.S.	
Key Words: molecular microbiology assay		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To develop and improve assays required for other new and ongoing protocols.

Technical Approach: The scientific literature will be searched continually for reports of new assays, techniques, and methods dealing with molecular biology as it applies to microbiological diagnostics. These improved techniques will be tested in the lab at the Department of Clinical Investigation and assays developed as needed for application in other protocols. These assays will be evaluated with cultured organisms and discarded medical samples and tissues to insure that the methods developed have clinical value and function properly with both controls and clinical materials.

Progress: The genotyping of HPV method utilizing the direct incorporation of dig-d-UTP is in development. Preliminary data leads us to expect a 10 to 100 fold increase in sensitivity over conventional electrophoretic detection of PCR product.

The assay for Mycoplasma genitarium is in development. Enhanced primers of Mycoplasma sp. are being synthesized for improved detection in tissue cultures.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/034 **Status:** On-going

Title: Insulin-Like Growth Factor Binding Proteins in Prostate Carcinoma Cell-Lines

Start Date: 01/03/92 **Est. Completion Date:**

Department: Clinical Investigation **Facility:** MAMC

Principal Investigator: M. J. Styner, B.S.

Associate Investigators:
CPT Katherine H. Moore, MS
James R. Wright, M.T.
COL Stephen R. Plymate, MC
Louis A. Matej, B.S.
Kelly L. Thomsen-Archer, B.S.

Key Words: protein,growth factor,prostate carcinoma

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

Study Objective: (1) To determine if insulin-like growth factor binding proteins (IGF-BP's, IBP's) are present in prostate cancer cell lines and to find which of the five IGF-BP's are expressed (2) to determine if different insulin and IGF levels affect the expression of IGF-binding proteins in the prostate cancer cell lines and (3) to see if there is an association between insulin and IGF levels and the expression of IGF-BP and SHBG in the prostate cancer cell lines.

Technical Approach: Northern analysis will be performed on total and messenger RNA extracted from prostate cancer cells using IGF-BP probes to detect the presence of an RNA message for the IGF-binding proteins and to get an idea of their relative sizes. Southern analysis will also be performed on total genomic DNA extracted from prostate cancer cell lines to further establish the presence of the genes for these binding proteins. Insulin will be administered to the prostate cancer cells in serum free media to determine if it is a regulatory factor of the IGF-BPs and analysis of its effect will be done by Western blot and Northern blot. IGF-I will also be used in cell treatments to determine its effects on the production of the IGF-BP's. SHBG probes will also be used on these blots to determine any correlation between the expression of IGF and SHBG binding proteins in these cells and their response to insulin and IGF levels.

Progress: Total RNA was extracted from prostate cancer cell lines DU 145, ALVA-41, ALVA-101 and a liver cancer cell line HEPG2 used for comparison using guanidinium/phenol extraction methods. Total RNA was size fractionated on a horizontal 6% formaldehyde agarose gel and transferred to a nylon membrane for hybridization. cDNA for hIGFBPs 1-5 was used for generating radio-labelled probes and hybridized to the Northern blots for analysis. Autoradiography reveals bands for IGFBP-1, 2, 3, 4 and 5 in the four cell lines studies.

Ligand blot analysis was performed on conditioned media from ALVA-101 and ALVA-41 cell lines using radio-labelled IGF-I. Autoradiography identified IGFBP bands binding at 25kDa and 30 kDa in both cell lines.

In summary: 1) expression of mRNA for IGFBP 1-5 is present in these cell lines and 2) IGF binding protein mRNA is translated into functional protein in the prostate cancer cell lines used.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF DENTISTRY

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/059 **Status:** Completed

Title: The Influence of Prophylactic Administration of Intravenous Ondansetron on Post Operative Nausea and Vomiting and Length of Stay in the Post Anesthesia Care Unit

Start Date: 05/03/91 **Est. Completion Date:** May 92

Department: Dentistry **Facility:** MAMC

Principal Investigator: MAJ Cecil R. Dorsett, DC

Associate Investigators:
COL Jerre M. Griffin, DE
Mark J. Bergin-Sperry, RN
MAJ Frederick W. Burgess, MC
MAJ Charles R. Weber, DC

Key Words: postoperative nausea,vomiting,ondansetron

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 05/01/92

Study Objective: To determine if routine prophylaxis with intravenous ondansetron decreases the incidence of postoperative emetic episodes in patients undergoing oral and maxillofacial surgery procedures and to determine the relationship between prophylactic intravenous ondansetron and length of stay in the post anesthesia care unit.

Technical Approach: Eighty patients presenting for elective oral surgery, over the age of 18 years, who are scheduled for general anesthesia will be studied. All patients will receive the same anesthetic care program and will be randomized to receive either ondansetron IV at the beginning of the surgical phase of treatment or a saline placebo. Postoperative evaluation will include emetic episodes, time to awakening, time to orientation, and time to discharge. Antiemetic rescue will be provided if subjects experience three episodes of emesis in one hour or if the intensity of nausea and emesis requires immediate treatment. The administration of a rescue antiemetic will be considered to indicate insufficient efficacy of the antiemetic treatment. Subjects will be evaluated 18-24 hours postoperatively and again at a follow-up appointment within 4-7 days from surgery. Data analysis will be primarily focused on the difference in the incidence of vomiting occurring between the placebo and ondansetron treatment groups using chi-square analysis. Times to discharge from the postanesthesia care unit will be assessed for significance with the unpaired t test.

Progress: Fifty patients were studied (12 in FY 93). Data are being interpreted and a paper will be written..

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/062	**Status:** Completed
Title: Postoperative Complications in Operating Room Dentistry for Children		
Start Date: 05/01/92	**Est. Completion Date:**	
Department: Dentistry	**Facility:** MAMC	
Principal Investigator: MAJ Paul J. Engibous, DE		
Associate Investigators:	LTC Herschel L. Jones, DE	
Key Words: dentistry,children,postoperative complications		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To record the incidence and type of postoperative complications in operating room dentistry for children and to evaluate the possible effects of age, sex, anesthetic agent used, length of anesthesia, and total fluid deficit on the incidence of postoperative complications of pediatric dental patients treated in the operating room.

Technical Approach: Approximately 50 subjects, ages 1-12, will be studied. The operating room dentist will complete a questionnaire after the patient has been discharged following dental rehabilitation. The dentist will be asked to report on past history of motion sickness, postoperative nausea and/or vomiting, and fever and provide information on the age, sex, anesthetic agents used, time of anesthesia, length of time NPO, fluid replacement during surgery, and patient temperature. The patients will have a postoperative examination approximately two weeks after surgery as is currently required for standard practice. Association of procedural factors with complications and without complications will be tested. Discrete variables will be tested using a chi-square analysis. Continuous variables will be analyzed with a t-test.

Progress: A paper was written and accepted by the Education Committee of the Pediatric Dentistry Residency program.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/068 **Status:** Completed

Title: Parental Recall of Informed Consent for General Anesthesia Dental Procedures

Start Date: 04/20/90 **Est. Completion Date:** Feb 91

Department: Dentistry **Facility:** MAMC

Principal Investigator: LTC Paul E. Kittle Jr., DE

Associate Investigators: COL Gerald R. Aaron, DC
LTC Herschel L. Jones, DE

Key Words: informed consent,dental

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 05/03/91

Study Objective: To evaluate if, and to what level, parental recall of the aspects of informed consent for dental operating room procedures exists to evaluate whether selective listening (blocking out of disconcerting information) exists and to evaluate whether parental recall of the aspects of informed consent is better when the risks are presented in written or oral format.

Technical Approach: Parents of children 18 months through 6 years of age schedule for dental rehabilitation in the operating room due to the patient's young age, uncontrollable behavior, situational anxiety, and/or extent of dental care needed will be studied. An overview of the study will be explained to the parent(s) prior to the operating room interview. They will then be asked to fill out an intake questionnaire which will obtain information on the child's age, number of siblings, dental and medical history, the parent's educational level, and how the parent thinks the child will react to dentistry in general. With the parent, patient, and attending staff member present, the resident will proceed to give specific informed consent in either an oral and specific written format or in an oral and nonspecific written format. Following completion of the operating room case, a follow-up visit will be scheduled at either two weeks or two months at which time questionnaires will be administered to test the parents' recall of the specific procedures they were told might be accomplished. Data analysis will include descriptive (background variables and postoperative data) comparisons (contingency table using chi-square statistics) of background information versus postoperative questionnaire data at two weeks and again at two months and comparison of the postoperative questionnaire data at two weeks versus two months.

Progress: An abstract has been submitted for presentation. Thirty-eight patients were enrolled in the study and no adverse outcomes were experienced.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/098 **Status:** Completed

Title: Waste Anesthetic GAS (WAG) Exposure of Pediatric Dentists During Operating Room Dental Procedures

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

Department: Dentistry **Facility:** MAMC

Principal Investigator: LTC Paul E. Kittle Jr., DE

Associate Investigators: MAJ Curtis D. Goho, DC

Key Words: waste anesthetic gas,pediatric dentists

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

Study Objective: To ascertain the waste anesthetic gas (WAG) exposure level of pediatric dentists during operating room dental rehabilitation cases in which uncuffed nasal intubation is used; and to compare these levels with published data on WAG exposure for other operating room personnel during cases that routinely use cuffed endotracheal tubes.

Technical Approach: Fifty dentist exposed to WAG while performing dental procedures of at least one hour duration and utilizing an uncuffed endotracheal tube will be studied. Monitors will be attached to either the face mask or the collar of the dentist and halogenated anesthetic agents and nitrous oxide will be monitored. Background monitoring will be done utilizing the Miran infrared spectrophotometer monitor system and the 3M WAG monitoring system. Historical records for WAG exposure will be used as much as possible. Age of the dentist, anesthetic agent used, endotracheal tube size, and pressure at which leak around the tube was noted will be recorded. Pediatric dentist exposure levels will be compared to historical WAG exposure levels for the study site operating rooms as well as general published data on acceptable WAG exposure levels. Exposure levels will also be compared to simultaneous background WAG monitoring. Chi square will be used to evaluate the data, utilizing the SPSS computer statistical package.

Progress: An abstract has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/063 **Status:** Completed

Title: Common Behavior Management Techniques Used in Pediatric Dentistry: Why Parents Accept or Object to Them

Start Date: 05/01/92 **Est. Completion Date:**

Department: Dentistry **Facility:** MAMC

Principal Investigator: MAJ Michael G. Page, DE

Associate Investigators: LTC Paul E. Kittle Jr., DE

Key Words: pediatric dentistry,behavior

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

Study Objective: To determine, as specifically as possible, why parents like or dislike various common behavior management techniques used in pediatric dentistry and to catalogue their feelings.

Technical Approach: The parents of pediatric dental patients being treated in the Pediatric Dentistry Residency Program will be shown 2-3 minute video vignettes of patients being treated using common behavior management techniques. The techniques that will be investigated will be voice control, tell-show-do, hand-over-mouth, active restraint by parent, active restraint by dental personnel, passive restraint (Papoose Board), nitrous oxide sedation, oral premedication and nitrous oxide, and general anesthesia. The viewers will have control of the video unit so that they will be able to view and respond at their own pace. There will be a short taped introduction explaining the purpose of the study and what behavior management techniques are. Each technique will be clearly identified on the tape and instructions for completing the questionnaire will also be provided on the tape. The parents will be told that the patient on the video is to undergo a routine operative procedure (stainless steel crown) and extraction of an abscessed tooth and that the procedure was successfully completed. The parents will be asked to respond to survey questions based on the video to elicit their attitudes toward the techniques presented. The subjects will also be asked to state their specific likes and dislikes of the techniques. After filling out the survey, they will be asked if their answers would have been different if the procedure the children underwent were only a simple filling as opposed to something more serious. The surveys will be tabulated and the likes and dislikes will be categorized.

Progress: A paper was written and accepted by the Education Committee of the Pediatric Dentistry Residency program.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/061 **Status:** Completed

Title: Comparison of Induction and Recovery From Propofol-Nitrous Oxide versus Methohexital-Isoflurane-Nitrous Oxide Anesthesia in Ambulatory Oral Surgery Patients

Start Date: 06/14/91 **Est. Completion Date:** Apr 92

Department: Dentistry **Facility:** MAMC

Principal Investigator: MAJ Robert J. Wygonski, DC

Associate Investigators:
COL Douglas B. Boyd, DC
MAJ Frederick W. Burgess, MC
COL Jerre M. Griffin, DE

Key Words: anesthesia,induction,propofol-nitrous oxide,methohexital-isoflurane-nitrous oxide

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

Study Objective: To determine if propofol-nitrous oxide anesthetic offers better induction, maintenance, and early recovery of general anesthesia and a significant difference in psychomotor and qualitative response during the intermediate recovery phase than methohexital-isoflurane-nitrous oxide anesthesia for ambulatory oral surgery patients.

Technical Approach: Subjects will undergo preoperative testing of recovery assessment tests (Trieger Test and Continuous Performance Test) on the day of surgery to establish individual baseline scores. All patients will receive 3 mg d-turbocurarine and 0.2 mg glycopyrrolate prior to induction. After preoxygenation, anesthesia will be induced in Group I with propofol 2.5 mg/kg and in Group II with methohexital 1.5 mg/kg. Maintenance of anesthesia will be as follows: Group I - continuous infusion of propofol starting at 9 mg/kg/hr and titrated to effect Group II, isoflurane 0.0% to 2.0% titrated to effect. All other surgical/anesthesia procedures will be per standard protocol. Time from induction to termination of anesthesia, agent, end of procedure, and eye opening will be recorded as early recovery time. On arrival in the recovery room each patient will be given a subjective recovery score by the recovery room nurse. Each patient will receive a postanesthesia recovery score (PARRS) on arrival in the recovery room and every 15 minutes thereafter. Patients will repeat the Trieger Test and the Continuous Performance Test at 20, 40, and 60 minutes post extubation. These measurements will be recorded as intermediate time. Patients will fill out a questionnaire 24 to 36 hours after anesthesia. This will be recorded as late recovery time. Data analysis will focus on the difference between the groups in reference to induction and recovery characteristics. Analysis of post anesthesia observations will be carried out by a chi-square analysis. The Treiger and Continuous Performance tests data will be analyzed by repeated measures ANOVA.

Progress: Psychomotor testing revealed no significant difference between the two groups. Postanesthetic adverse outcomes were significantly higher in Group II (nausea, vomiting and headache) than Group I. Both techniques provide safe and effective outpatient anesthesia.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/100 **Status:** On-going

Title: The Randomized Use of Helium-Oxygen Mixture for the Administration of Bronchodilator Therapy in the Treatment of Bronchial Asthma

Start Date: 09/04/92 **Est. Completion Date:** Jul 93

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Richard D. Brantner, MC

Associate Investigators:
CPT David A. Della-Giustina, MC
MAJ William T. Hurley, MC
MAJ Linda M. Brantner, MC

Key Words: asthma,helium-oxygen mixture,bronchodilator

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$315.00	**Periodic Review:** / /

Study Objective: To determine the therapeutic role of Heliox in the administration of bronchodilator therapy for the treatment of acute exacerbations of bronchial asthma.

Technical Approach: Each patient (n=150) will be evaluated using peak flow rates and given supplemental oxygen. Patients with peak flow rates <180 L/m will be given prednisone, 60 mg, by mouth. Patients will then be randomized to a nebulized albuterol treatment administered either by the air driven method or by Heliox at a rate of 8 L/min. Albuterol treatment will continue as above every 30 minutes for a total of four treatments. Patients will be on continuous pulse oximetry monitoring. Repeat evaluations will consist of vital signs and physical examination to include respiratory rate and lung auscultation every 30 minutes. Peak flow/FEV_1 measurements will be obtained at entry and at 10 minutes after each nebulized bronchodilator treatment. A final peak flow/FEV_1 will be obtained 20 minutes after the last nebulizer treatment. Patients will be asked to respond to a questionnaire indicating the severity of presenting symptoms, the time to feeling improvement in respiratory effort, and the decrease in objective wheezing. Patients will be contacted by phone 48 hours after discharge to repeat the questionnaire. Groups will be compared for age, sex, history of severity of disease, initial pulse oximetry, and respiratory rate, using the t-test. Initial FEV_1 will be determined and percent predicted will be determined using the patient's age, sex, height, and weight, and groups compared as to severity using the t-test. Subjective rate of improvement in symptoms will be analyzed using the Mann-Whitney U Test. Both peak flow and FEV_1 measurements will be plotted and percentage of improvement from baseline determined. The percentage improvement in FEV_1 will be compared between the two groups using the t-test.

Progress: Study is ongoing. Interim data analysis will be performed at 50 patients.

Detail Summary Sheet

Date: 30 Sep 92 **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
CPT Bernard J. Roth, MC
CPT James W. Thompson, MC
CPT Timothy R. Murray, MC

Key Words: COPD,helium,oxygen

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

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: Study was delayed because of the need to obtain oxygen equipment/adapters. Enrollment is now underway.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/051 **Status:** On-going

Title: The Use of Intravenous Morphine for Early Pain Relief in Patients With Acute Abdominal Pain

Start Date: 02/05/93 **Est. Completion Date:** Mar 94

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Thomas F. Burke, MC

Associate Investigators:
CPT Sarah R. Mack, MC
COL Preston L. Carter, MC
Steven A. Pace, MD
CPT Ronald J. Place, MC

Key Words: abdominal pain, morphine

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

Study Objective: To determine if treating patients with acute abdominal pain with intravenous morphine affects patient evaluation (both in ease and accuracy), outcome, and satisfaction with pain control.

Technical Approach: One hundred adult patients with abdominal pain sufficiently severe to warrant opiate analgesia and pain duration of < 48 hours will be asked to enter the study. Patients will undergo double blind randomization to either a morphine or saline arm early in the evaluation. After an examination and completing a patient self administered visual analog pain score (VAS), the patient will undergo intravenous access, placement of a cardiac monitor and continuous pulse oximetry. After morphine or saline is titrated to effect, further patient evaluation and care is no different than usual. Physician titration of "study drug" is by administering a 0.01 cc/kg (morphine = 10 mg/cc) initial bolus at a rate of 0.1 cc/minute followed by 0.2 cc every 5 - 10 minutes until one of the following endpoints is reached. 1) Reduction of pain such that the patient is comfortable and, upon being offered, requests no further analgesia. 2) Any respiratory or central nervous system depression. 3) Maximum dose of 2 cc (saline or 20 mg morphine) is given. 4) Any other unwanted effects. A repeat examination will be performed and self administered patient VAS 15 - 30 minutes after titration is completed. Patients will be questioned by phone one week after discharge and continue each week until such time that a definitive diagnosis is reached.

Method of data analysis: 1) Analysis of variance to compare the change in visual analog pain. 2) Compare the age (T-test) and sex distribution (Chi Square) between two groups. 3) Use Kappa or Chi Square to compare the following variables between the two groups: a) Concordance of the presumptive diagnosis and eventual diagnosis. b) Determine if study drug administration improved evaluation. c) Determine patient satisfaction.

Progress: Seventy-six patients have been entered into the study and followed closely to gain clinical outcome data. There have been no cases of study drug reaction and no cases of unexpected 72 hour returns. The study should be completed within the next 12 weeks.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/039 **Status:** On-going

Title: Treatment of Corneal Abrasions: Is Eye Patching Necessary?

Start Date: 02/07/92 **Est. Completion Date:**

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT James M. Nold, MC

Associate Investigators:
CPT Lee E. Payne, MC, USAF
CPT Jack K. Handley, MC
MAJ Andrew T. Guertler, MC
CPT Jan Vanderlinde, MC

Key Words: corneal abrasion,patching

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

Study Objective: To determine if eye patching results in faster healing or provides pain relief in patients with uncomplicated traumatic corneal abrasions.

Technical Approach: Approximately 300 patients diagnosed with a corneal abrasion will be randomized to either a patch or no patch. Patients with evidence of ocular pathology in addition to the corneal abrasion will be excluded from the study. The group with the patch will have bacitracin ophthalmic ointment instilled and the eye patched. Patients who are assigned to the no patch group will have bacitracin ointment placed in the eye and no patch. All patients will be reevaluated at 24 hour intervals. Persistent abrasions will be quantified and treatment will continue identical to initial treatment (single instillation of bacitracin). Follow-up at 24 hour intervals will continue until the abrasion is no longer evident on slit lamp examination. Specific quantification of the corneal abrasion, using the measuring reticule on the slit lamp, will be done at the initial evaluation and all subsequent evaluations. Patients will be given medication for pain control to be used every 4-6 hours as needed. Pain scores will be determined using a visual analog scale prior to leaving the emergency room and at 8 hour intervals until the abrasion has healed. Patients will be instructed to record time, type, and amount of analgesic used. Summary descriptive statistics will be used to assess basic data. Specific parameters to be compared between groups include time to healing and pain scores. Comparison of healing time between groups will be accomplished using the Mann Whitney test. Comparison of pain scores will be accomplished by analysis of variance of a single repeated measure.

Progress: Enrollment stands at 90 and continues. Interim analysis indicates no difference in groups but statistical analysis of significance/power is pending.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/043 **Status:** Completed

Title: Utility of Sinus Tenderness as a Diagnostic Sign in Sinusitis

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

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Greer E. Noonberg, MC

Associate Investigators:
CPT Thomas F. Burke, MC
MAJ Danny M. Douglas, MC
MAJ James H. Timmons, MC
COL James S. Brown, MC
CPT Jonathan A. Perkins, MC
MAJ Roderick D. Moe, MC
COL W. Pierre Andrade
MAJ Kevin L. Quinn, MC
CPT Diana S. Willadsen, MC

Key Words: sinusitis,diagnosis,tenderness

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

Study Objective: To determine the predictive value of sinus tenderness in the diagnosis of acute sinusitis.

Technical Approach: Patients over 18 years of age with no prior history of documented sinusitis with symptoms within two weeks of onset of either headache or facial pain and purulent nasal discharge or nasal congestion will be evaluated. A routine physical examination including teeth inspection will be performed. In addition, percussion for sinus tenderness will be performed using a standard reflex hammer and measurement of sinus tenderness using a dolorimeter to measure pressure/pain threshold over the frontal and maxillary sinus areas of the face. The dolorimeter is a spring-loaded gauge with a range of 0 to 9 kgs with a protective rubber stopper attached to a plunger. The dolorimeter will be placed directly each area to be studied and force applied slowly and steadily from 0 to 9 kg in 5 seconds. The patient will be asked to identify when the pain begins (pain threshold) and the test will be stopped. A standard sinus CAT scan will be performed within 48 hours. Nasal endoscopy will be performed in all patients within 24-48 hours of enrollment. Middle meatus cultures will be taken by endoscopy. A 30 degree Hopkins Telescope will be used to examine the nasal cavity after anesthetizing the nose with particular attention given to the middle meatus region. Chi square analysis will be used to compare CAT scan to dolorimeter values.

Progress: Complaints of sinus pain had CT documented findings of sinusitis. Sinus tenderness has high sensitivity and poor specificity in diagnosing sinusitis and is therefore not a useful diagnostic test in assessing sinusitis.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/019 **Status:** Completed

Title: The Effect of Calcium Administration on Albuterol's Ability to Lower Serum K+ in a Hyperkalemic Swine Model

Start Date: 11/06/92 **Est. Completion Date:** Jun 93

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Michael W. Peterson, MC, USAF

Associate Investigators: LTC Blake P. Gendron, MC

Key Words: hyperkalemia,calcium,albuterol,potassium,animal model,animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To demonstrate that calcium administration does not interfere with the use of albuterol for hyperkalemia in an intact organism applicable to normal humans.

Technical Approach: This blinded, randomized, placebo controlled four armed study using nine swine will use the animals as their own controls. Two indwelling lines will be placed under anesthesia and the sites allowed to heal. The animals will be anesthetized for the experimental runs to alleviate any pain or anxiety. The animals will be intubated and nebulization will be given by fitting a small volume nebulizer in the inhalation circuit. Each animal will undergo four runs, one in each treatment arm. These will be separated by at least 5 days. The animals will be randomized to a latin square design to account for any gross changes in K+ physiology that order may induce. Hyperkalemia will be produced by the infusion of 2 meq/kg of KCL over 1 hour (the prestudy trial will determine the optimal K+ dose). The control runs will receive nebulized saline and a saline injection. Those on an albuterol run will have 0.4 mg/kg albuterol nebs and saline. Those on the albuterol and calcium run get albuterol nebs and an I.V. injection of calcium gluconate 0.15 ml/kg or 10% solution. When on the calcium run they get a saline neb and the calcium injection. The nebulization will be given by fitting small volume nebulizers into the inspiratory circuit. The animal will be on a Marquet EKG monitor throughout the experiment and rhythm along with heart rate will be recorded at pretreatment, every 4 min. during KCL infusion and at sample times. Blood specimens for K+ and venous pHs, will be obtained at designated times and analyzed on a Kodak Ectachem 700 device to determine that albuterol does indeed lower K+ in this new hyperkalemia model.

Progress: Due to the number of animals studied and some missing data, the results of the study were inconclusive.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 82/025 **Status:** On-going

Title: Emergency Room Procedure Training

Start Date: 02/19/82 **Est. Completion Date:** Feb 87

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: LTC Matthew M. Rice, MC

Associate Investigators:
MAJ Steven C. Dronen, MC
MAJ Mel D. Robinson, MC
MAJ Stanley P. Liebenberg, VC
LTC Cloyd B. Gatrell, MC
COL Frederick Burkle, MC
LTC Samuel T. Coleridge, MC

Key Words: emergency room,training protocol,animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1360.00	**Periodic Review:** 06/07/93

Study Objective: To provide training to acquire the necessary manipulative skills in performing invasive, life-saving procedures for the Emergency Medicine Residency Program.

Technical Approach: The procedures listed below will be performed in two separate parts 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. Part I consists of: 1. Femoral vein cutdown, 2. Peritoneal lavage, 3. Tube thoracostomy, 4. Thoracotomy, 5. Aortic cross-clamping, 6. Control of pulmonary hemorrhage, 7. Cardiac wound repair, 8. Endotracheal intubation, 9. Percutaneous transtracheal ventilation, 10. Cricothyroidotomy. Part II consists of: 1. Tissue pressure monitoring, 2. Arterial pressure monitoring, 3. Swan-Ganz catheter placement, 4. Transvenous ventricular pacemaker placement, 5. Transthoracic ventricular pacemaker placement, 6. Pericardiocentesis, 7. Segstaken-Blakemore tube placement, 8. Auto transfusion from hemothorax, 9. Twist drill decompression, 10. Skull trephination.

Progress: Four animals were used for training Emergency Medicine residents.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/016 **Status:** On-going

Title: Pediatric Intubation Training Utilizing the Ferret Model

Start Date: 01/19/90 **Est. Completion Date:** Indef.

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: LTC Matthew M. Rice, MC

Associate Investigators: LTC Cloyd B. Gatrell, MC
LTC Patrick C. Kelly, MC

Key Words: training protocol,pediatrics,intubation,ferret,animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$400.00	**Periodic Review:** 06/07/93

Study Objective: To enhance the clinical skills of health care providers in managing pediatric airways, specifically intubations. This protocol will be used to support the Pediatric Advanced Life Support Course. The participants in this course are members of the Army, the Air Force, the Navy, and the Public Health Service.

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: Five animals were utilized (1 session) to facilitate intubation training.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/169 **Status:** On-going

Title: The Relationship of Intraocular Pressure and Symptoms of Acute Mountain Sickness at Moderate Altitude

Start Date: 09/03/93 **Est. Completion Date:** Oct 93

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT Ian S. Wedmore, MC

Associate Investigators: None

Key Words: intraocular pressure,mountain sickness

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

Study Objective: To determine if a relationship exists between intraocular pressure (IOP) and symptoms of acute mountain sickness (AMS) during acute exposure to moderate altitude (up to 14,000 feet).

Technical Approach: Members of an organized climb of Mount Rainier agreeing to participate in this study will have ocular pressures measured at 4 altitudes up to 4300 M. To facilitate measurement, 2 drops of proparicaine will be placed in each measured eye. Subjects will simultaneously complete a questionnaire commonly used for altitude research to look for symptomatology of AMS. Climbers who use no chemical AMS prophylaxis as well as those who use dexamethasone for AMS prophylaxis will be included in the study.

Results of IOP will be compared to AMS symptoms to determine if any correlation exists utilizing Pearson coefficient. A T test will be applied to baseline and higher altitude IOPs to determine if any significant change in IOP with altitude occurs.

Progress: The principal investigator is TDY; therefore a report is not available. The protocol will be reviewed for continuation when the PI returns to MAMC..

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/078 **Status:** Completed

Title: Oral Versus Intravenous Steroid: A Prospective Study in Acute Asthma

Start Date: 06/15/90 **Est. Completion Date:** Feb 92

Department: Emergency Medicine **Facility:** MAMC

Principal Investigator: CPT David C. White, MC

Associate Investigators:
LCDR Richard S. Perren
MAJ Kirin M. Russell, MC
LCDR Kyle D. Holmes, MC

Key Words: asthma:acute,steroids:oral,steroids:IV

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To compare the efficacy of oral prednisone and intravenous methylpredisone in the treatment of adults with an acute asthma exacerbation by comparing FEV_1, patient's subjective index, and physician evaluation of clinical course.

Technical Approach: The patient sample will be 100 patients, ages 18-45 years, presenting to the Emergency Room with exacerbation of asthma, unrelieved by the usual home treatment. Each patient will be evaluated by the physician and tested with a portable spirometer. Oxygen saturations will be recorded per pulse oximetry. Arterial blood gases may be used in place of pulse oximetry if the clinical situation dictates. The patient will then be randomized in a double blind fashion to receive either IV methylprednisolone and oral grape Tang or oral prednisolone mixed with grape Tang and normal saline IV. All patients will receive oxygen and a beta-agonist as per emergency room protocol, three treatments, 20 minutes apart. Patients will be evaluated with spirometry for FEV_1 on arrival and every hour for three hours. Patients will be discharged or admitted as clinical circumstances warrant. Discharge steroid dosing will be left to the discretion of the treating physician. Follow-up evaluation will consist of repeat vital signs (every 30 minutes), physician examination (after every treatment), patient symptom scale of 1 to 10 (every hour), and spirometry (every hour). Patients who are discharged will be contacted the following day for evaluation of subjective complaints and will be asked to rate themselves on the patient symptom scale. FEV_1 and FVC will be analyzed with repeated measures analysis of variance. Analog scaled variables like physician exam and subjective index will be analyzed with appropriate non-parametric methods.

Progress: Results show a selection bias of unclear etiology in which healthier individuals tended to be grouped in the placebo group. This resulted in a tendency for placebo-treated patients to do better than either oral or I.V. treated patients, as all patients improved. Secondary analysis of degree of improvement show statistically greater relative improvement in the I.V. treated group relative to presenting severity. This is arguably because of having greater "room for improvement". The study is terminated because it is felt that it would be unlikely to eliminate this bias with less than 120 patients (2.5 X current enrollment) which is an unattainable goal.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/097	**Status:** Terminated
Title: Pediatric Pain Assessment Survey		
Start Date: 08/07/92	**Est. Completion Date:**	
Department: Emergency Medicine	**Facility:** MAMC	
Principal Investigator: CPT David C. White, MC		
Associate Investigators: MAJ Kerry R. Johnson, MC	Cami Tier, AN	
Key Words: pediatric pain,acute injuries,parental preferences		

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

Study Objective: To correlate the amount of pain from an acute injury as assessed by pediatric patients, their parents, and the treating physician; to determine whether pediatric patients are more fearful of needles/IV's and their perceived pain when compared to acute pain; to determine if pediatric patients and parents think children feel pain more, less, or the same as adults; to determine if pediatric patients and/or parents prefer for the parents to be present or absent during treatment of acute painful injuries; and to assess parents opinions as to method of administering pain control for acute injuries to pediatric patients.

Technical Approach: Subjects will be children between 3 and 15 years of age who present to the Madigan emergency room with acute painful injuries. The child and parent will each complete a questionnaire regarding how they perceive pain and how it should be treated. The child will rate the pain using the facial pain scale and/or the visual analog scale at the time of presentation to the emergency room and at discharge. The parent and the physician will rate the pain on a visual analog scale at the time of presentation, at discharge, and during the procedure. The questionnaires will be compiled and the results analyzed using ANOVA with repeated measures for the pre- and post-treatment responses. Student's t test will be utilized to analyze data between the three groups. Chi-square analysis will be used to compare whether children or parents feel that kids feel pain more, less, or the same as adults and also to compare the parents rating of methods to provide pain relief.

Progress: The initiating PI (Dr. Johnson) was reassigned and was to re-write the questionnaire. The study was then to be conducted at both sites. Dr. Johnson has not contacted Dr. White regarding the study. Since he has failed to do this, Dr. White has decided that he will terminate the protocol at MAMC.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF FAMILY PRACTICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/076 **Status:** On-going

Title: Comparison of Family Practice (FP) In-Training Exam Scores Between Residents Who Have Done A General Medical Officer Tour of Duty After A FP Internship & Residents....Continuous 3 Year FP Residency

Start Date: 04/02/93 **Est. Completion Date:** Jul 94

Department: Family Practice **Facility:** MAMC

Principal Investigator: MAJ David D. Ellis, MC

Associate Investigators:
MAJ Steve Reissman, MC
MAJ George Wakeman, MC
LTC Ron Jones, MC
LTC Wayne A. Schirner, MC
COL Earl Lorenzen, MC
LTC Wayne Blount, MC

Key Words: residents,ITE

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

Study Objective: To compare Family Practice In-training Exam Scores (ITE) between residents who have completed a General Medical Officer tour of duty after a Family Practice Internship and Residents who have had a continuous three year Family Practice Residency.

Technical Approach: Data on those graduating from six Army FP residency programs will be requested from each program director. The program director will collect the data and send it to the investigator without information that identifies the respondents. The information provided will have personal, biographical, and educational information, plus military experience and ITE scores. The data will be arranged with follow-up retrieval as needed.

Data analysis will be done using a 2 tailed t-test to attempt to identify either a positive or negative difference in these two groups. Due to the "real world experience" of GMO residents, their ITE scores may actually be better than the CFP residents. On the other hand, if being away from a training environment for a period of time has caused a deterioration of scholastic level, we would hope to identify this as well.

Progress: Investigators have reviewed 200 academic records from 10 residency programs. After completion of data entry and determination of results, the study will be submitted to either Military Medicine or Family Medicine for publication.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/013 **Status:** On-going

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 Brain C. Harrington, 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

Key Words: preeclampsia,exercise,heart rate

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

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: Having tested almost half of our needed total of subjects, we have developed a smooth reproducible testing system. Because of the lag time until delivery we do not have complete databases of all those tested. New research has been published on Aspirin use in pregnancy, adding to the information base for our study. The most significant problem so far has been time constraints for testing. Because of our full schedules we have had to add several month to our timetable.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/077	**Status:** Completed
Title: The Effect of Internship on Empathy		
Start Date: 04/02/93	**Est. Completion Date:** Jun 93	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: CDR W. R. Kiser, MC		
Associate Investigators: MAJ David MacDonald, MC	CPT Kim A. Dugger, MC MAJ Bruce M. LeClair, MC	
Key Words: empathy,internship		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: The purpose of this study is to determine the effect of the internship experience on the empathic construct of physicians-in-training.

Technical Approach: Interns at three military hospitals (MAMC, TAMC, DDEAMC) who both took part in a pre-internship Interpersonal Reactivity Index (IRI), a self reporting empathy measure, and provided their social security numbers will be individually and confidentially contacted by the investigators and requested to participate in this study. Those voluntarily agreeing to take part will be asked to again complete the IRI, to again provide their social security number, and to return the materials to the responsible associate investigator in a sealed envelope. The collected materials will be forwarded to the principal investigator for analysis.

The IRI yields interval level data and consists of 4 subscales, each examining one dimension of empathy. The data in each subscale, previously collected from pre-internship IRIs, will be compared to the post-internship data via the use of paired t-tests, to test the hypothesis that empathy, as measured by any of the subscales of the IRI, is significantly affected ($p \leq 0.05$ 2-tailed) by the internship experience.

Depending on the mix of the obtained sample, the group may be divided and the data examined along demographic lines as well (i.e. gender, specialty choice, professional degree etc.) to determine if these variables have an impact on the change in empathy over the period of internship.

Progress: Significant differences in empathic concern were found among female allopaths and in perspective taking among male osteopaths, with higher levels of empathy found in those interns entering primary care. A thesis was prepared and accepted for M.A. in Social Science at Pacific Lutheran University. A paper was also submitted for the Steiger award competition.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/083 **Status:** Terminated

Title: The Effect of Internship on Moral Reasoning

Start Date: 07/02/92 **Est. Completion Date:** Jun 93

Department: Family Practice **Facility:** MAMC

Principal Investigator: CDR W. R. Kiser, MC

Associate Investigators: Donnie J. Self, Ph.D.
LTC John P. Kugler, MC

Key Words: moral reasoning,internship

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

Study Objective: To determine if moral reasoning ability is affected by the experience of internship.

Technical Approach: The well publicized instances of dishonesty in biomedical research over the past several years stress the need to refocus attention to the ethical components of the medical profession and to ensure that the educational processes foster, rather than hinder, moral development. As a preliminary step toward this goal, it is important to discover what effect the components of the present medical education system have on moral reasoning. This study will examine the effect of the internship year as one component of the medical education system. Interns agreeing to take part in the study will be administered the Defining Issues Test (DIT) in the first month of internship and again in the month prior to the completion of the internship. The DIT is a questionnaire to help determine how people feel about social problems. This is done by having the individuals being tested read stories regarding social problems and then answer questions regarding their opinions on these problems. Demographic information important to describe the sample and to identify potential confounders will be obtained. The DIT yields interval level data. The dependent variable is the change in DIT scores pre and post internship and a t-test will be used to compare these differences. Comparisons will also be made between the pre and post internship DIT scores and the demographic information using chi-square analysis, t-test, and regression analysis where appropriate.

Progress: The number of subjects who returned the questionnaire was inadequate. Attempts are being made to use the data to begin a pilot study at Naval Station Jacksonville.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/058 **Status:** Completed

Title: An Analysis of Selected Elements of Family Function and Related Variable in Adolescent Pregnancy

Start Date: 04/05/91 **Est. Completion Date:**

Department: Family Practice **Facility:** MAMC

Principal Investigator: LCDR Euelya L. Lewis

Associate Investigators: None

Key Words: pregnancy:adolescent,family function,adolescent:female,parent participation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 08/07/92

Study Objective: To compare family function (as measured by FACES III) family satisfaction and parent/adolescent communication of pregnant vs nonpregnant teens and observe the effect on teen pregnancy rate.

Technical Approach: Subjects will be contacted as they are identified through the organizations and schools who are participating, a total of 400 subjects is the target sample. In the instance where there are groups of subjects, a presentation will be made about the protocol. Prior to receiving the questionnaires, subjects will be given a consent form for themselves and a parent or guardian. Once parents/guardians who wish to participate are identified, they may be accessed in one of three ways: 1) personally contacted by PI, 2) brought home by the subject, 3) mailed to parent/guardian. The latter two are followed up by a phone call to reinforce and encourage participation and packet completion. Data will be analyzed using the chi-square method looking at the frequency distribution in the balanced mid-range and extreme family types of pregnant and nonpregnant teens. The data will also be used to compare balanced families vs those non-balanced families in the remaing four quadrants. The third method of analysis will employ a score called Distance from Center of Circumplex (DFC). This is a linear score used for correlational analysis and is an indication of the distance of an individual's cohesion and adaptability score from the center of the model. And finally, discriminant function analysis will be used to predict group membership or status on a categorical or nominal level variable on the basis of two or more independent variables.

Progress: No further work was done in FY 93. A thesis was written as a requirement for the degree of Master of Arts in Social Science.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/084 **Status:** On-going

Title: Back Pain in Aviators: A Descriptive Study of the Type of Care Received/Sought and Implications for Flight Status - Part Two

Start Date: 07/02/92 **Est. Completion Date:** Mar 93

Department: Family Practice **Facility:** MAMC

Principal Investigator: LCDR Danell E. Lovins

Associate Investigators: LTC John P. Kugler, MC
MAJ Daniel Fitzpatrick, MC

Key Words: back pain,aviators

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

Study Objective: (1) To determine if a difference exists in the type of health care behavior/preference between pilots with more flight hours (experience) and pilots with fewer hours (student pilots) and (2) to determine if a difference exists in the type of health care behavior/preference between those aviators who experience no pain, pain that does not interfere with lifestyle, and pain that interferes with lifestyle.

Technical Approach: Six hundred surveys will be distributed to initial phase, advanced phase, and instructor pilots (200 per group). The questionnaire will address affect on performance of duties, types of professional help sought, medications taken, if medication has been taken while flying, back injuries, back surgery, help sought outside the military health care system, avoidance of health care for fear of being taken off flying status, type of pain and how it was resolved, and if the subject had ever been grounded because of back pain. Data from both aviators who have experienced back pain and those who have not will be analyzed in this study. Analysis of variance (ANOVA) will be used to test for differences in flight hours by degree of back pain/discomfort. A post-hoc test will be used to isolate any differences noted in the ANOVA. An unpaired T test will be used to test for differences in the type of health care and amount of flying experience. ANOVA will be used to test for significance in differences in health care versus pain. Descriptive statistics will be used to describe the sample in this study.

Progress: Questionnaires have been mailed. No other report is available.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/093 **Status:** Completed

Title: The Prevalence of Sexual Concerns in a Population of Women Who Have Sought Routine Gynecological Care & What Barriers Exist for the Discussion of Sexual Concerns With Physicians/Health Care Providers

Start Date: 04/02/93 **Est. Completion Date:** Apr 93

Department: Family Practice **Facility:** MAMC

Principal Investigator: MAJ Margaret R. Nusbaum, MC

Associate Investigators: None

Key Words: sexual concerns,prevalence,barriers,discussion

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

Study Objective: To determine both the prevalence of sexual concerns, and the barriers to the discussion of sexual concerns by women with their physicians.

Technical Approach: Women who have had a pap smear at MAMC will be mailed an anonymous survey instrument. A follow up letter will be sent approximately two weeks after the initial mailing as a reminder and thank you for participation.

No names will be used other than for mailing purposes. A coding system will be used to identify the clinic and number of the survey mailed out. These codes will be maintained after mailing. No identifiers will be linkable to individual responders. All mailing information on the subjects will be destroyed upon return of surveys and completion of the study.

Descriptive statistics will be used. Correlations, regression techniques, and multivariate analysis will be used, based on descriptive statistic findings.

Progress: The results of the study suggest that women may have sexual concerns at the time of routine exams and health care providers should be a resource for addressing these concerns. Particular issues have greater concern for different age groups, supporting the need to address sexuality in a biopsychosocial or systems approach. Sexuality should be considered an integral part of health, quality of life, and general well being.

Detail Summary Sheet

te: 30 Sep 92 **Protocol No.: 92/085** **Status:** Terminated

le: Diagnoses Which Stimulate Physician Initiated Discussions About Advance Directives: A Survey of Practicing Physicians

rt Date: 07/02/92 **Est. Completion Date:** Aug 92

partment: Family Practice **Facility:** MAMC

incipal Investigator: CPT Jefferey Johnson, MC

sociate Investigators: CPT Cliff A. Robertson, MC

y Words: advance directives,power of attorney,CPR

cumulative		**Est. Accumulative**		**Periodic Review:**
EDCASE Cost:	$0.00	**OMA Cost:**	$150.00	/ /

udy Objective: To define which diagnoses prompt physicians to discuss terminal care ues such as advance directives, medical power of attorney, and cardiopulmonary suscitation.

chnical Approach: A survey will be distributed to the medical and surgical staff signed to Madigan (excluding the pediatric, pathology, and administrative partments). The survey will determine demographic data, the estimated frequency of tients with advance directives as well as the frequency of terminal care discussions tween the physician and patient in the previous month. The pilot survey will ask the spondents to write in diagnosis which they feel would justify a discussion about lvance directives or DNR orders. Results of the pilot survey will be used to formulate a t which will then be submitted in survey form to practicing physicians in Pierce unty who are listed with the Washington State Medical Society. The results will be assified using simple descriptive statistics. A percent of those responding for each ven specialty will be calculated by coding the mailed surveys. A comparison of advance rective utilization will be made between and among specialties. Diagnoses will be ouped and frequencies will be described and compared between specialties as well as mpared by setting (outpatient vs inpatient). A list will be compiled of the 15 most mmon listed diagnoses from the initial MAMC survey which will be confirmed by the ysicians in the county.

ogress: This was a pilot project with 23 physician respondents at MAMC. The iginal PI (CPT Robertson) left MAMC and the individual assigned to take over the otocol (CPT Johnson) was not aware that he was supposed to work on the project. herefore, no further work has been done on the study and it has been terminated due to e departure this year of Dr. Johnson.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/123	**Status:** On-going
Title: Vasectomy Reversal: A Heuristic Investigation of the Experience		
Start Date: 06/09/93	**Est. Completion Date:** Apr 94	
Department: Family Practice	**Facility:** MAMC	
Principal Investigator: MAJ Guy P. Runkle, MC		
Associate Investigators:	CDR W. R. Kiser, MC	
Key Words: vasectomy:reversal		

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

Study Objective: To explore the experience of vasectomy reversal through heuristic methodology.

Technical Approach: Potential volunteers will be identified from the log of patients who have undergone vasectomy reversal will be contacted and the nature of the research design and purpose will be explained. Those who express interest in participating will be given a written description of the study to include time commitments and consent will be obtained.

Data collection with take place through extended interviews between the principal investigator and the research participants. The interview, to be recorded, will be unstructured and the goal will be to allow the participant to tell his story to a point of natural closing. After the interview, the tape will be transcribed and an individual portrait of the research subject's experience will be prepared. The participant will be provided a copy of the profile for his review and a second interview will be scheduled for feedback. The participant may elect to delete or correct information that he feel compromising or inaccurate in reflecting his experience. This will result in reiteration until the accuracy of the portrait is confirmed by the research participant.

This research will be submitted as the thesis requirement for an M.A. degree.

Progress: Data collection is in progress. Six subjects have been interviewed, and an additional six subjects have been identified as potential study participants. Initial analysis of the first five cases has been performed.

A tentative conceptual model has been developed from analysis of the first cases, and appears to have been highly salient in the interviews of subsequent participants. This model involves identification of goals, influences, alternatives and barriers to initial sterilization and other life circumstances changes following vasectomy sterilization reversal. Influences, alternatives and barriers to sterilization reversal are explored as well as stages of the sterilization process, consequences of sterilization reversal and changes following sterilization reversal.

DETAIL SHEETS FOR PROTOCOLS

I CORP SURGEON, FORT LEWIS, WA

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/047	**Status:** On-going

Title: Implementation of a Voluntary Fitness Program and Pilot Project and the Consequent Evaluation of Physical Fitness Levels of Pregnant Soldiers Before, During and After Pregnancy to Substantiate ....

Start Date: 02/05/93	**Est. Completion Date:** Dec 93
Department: I Corp Surgeon	**Facility:** MAMC

Principal Investigator: SPC Wendy M. Urich

Associate Investigators: CPT Anne Grediagin, RD
Ann Lancaster, CHN

Key Words: pregnancy:specialized fitness regime

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

Study Objective: To evaluate the benefits of a specialized exercise program for pregnant soldiers and to submit the findings to the U.S. Army Physical Fitness School for evaluation.

Technical Approach: Each pregnant soldier will be required to fill out a series of questionnaires regarding pre-pregnancy and current fitness levels, work conditions, and lifestyle habits. In addition, both project groups (the exercise group and the control group) will be asked to fill out additional questionnaires which will evoke subjective answers concerning the subjects's feelings about her current exercise regimen, the proposed exercise regimen, and her self esteem. Unit commanders will be asked to fill out a subjective questionnaire concerning their feelings of current pregnancy P.T. prescriptions and of the program in which their soldiers are currently involved. Each soldier will undergo a fitness evaluation which involves measures of: resting heart rate and blood pressure, body weight, subcutaneous skin fold, and cardiorespiratory fitness. An individualized program will be developed for soldiers of the Exercising Group. Health information classes covering various topics in pregnancy will be given twice weekly. The Unit-exercise groups will engage in unit-directed P.T., which follows usual prescription and current standards of exercise for pregnant soldiers. Fitness evaluations of both groups will be conducted at the end of the second trimester, mid-way of the third, and again postpartum. Subjective questionnaires will be completed again at the end of the second trimester. Within the 28th week of gestation, all participating individuals will undergo an ultrasound to determine fetal growth. The investigative staff will obtain postpartum information. Unit Commanders will be asked to assess subjects physical readiness through a standard Diagnostic P.T. Test to be administered within the 8th week after delivery. Physical data as per Army Regulation levels will be evaluated with a T-test to compare means between the exercise group and control group. Nominal data will be compared using a chi-square method of analysis. Use of either the chi-Square or T-test will be utilized depending on how the data is interpreted.

Progress: Thirty-two first trimester subjects, with uncomplicated pregnancies, were randomly assigned to one of two groups. Initial fitness assessments were completed. The exercise group subjects exercise three days per week, and control groups subjects exercise with their units following current Army training guidance.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, ALLERGY/IMMUNOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/055 **Status:** Terminated

Title: Multicenter Clinical Evaluation of Penicillin Skin Testing

Start Date: 05/19/89 **Est. Completion Date:** Jun 90

Department: Medicine/Allergy **Facility:** MAMC

Principal Investigator: COL James S. Brown, MC

Associate Investigators:
COL Bernard Branch, MC
MAJ Marcia L. Muggelberg, MC
COL William F. Tuer, MC
COL Michael Martin, MC
CAPT David Moyer, MC
COL W. Pierre Andrade
COL Richard W. Weber, MC
MAJ Allen F. Kossoy, MC
Robert A. Ledoux
CPT William L. Ebbeling, MC
CAPT Fang L. Lin, MC

Key Words: penicillin skin testing

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To determine if there is a difference in the incidence of skin test positivity to the different skin testing reagents prepared by different methods in patients with a history of penicillin allergy as well as in subjects with no previous history of an adverse reaction to a penicillin-like drug.

Technical Approach: Allergists in the Army, Air Force, and Navy will participate in this multicenter study. Adult (>21 years) subjects (n=200) requiring penicillin skin testing will be questioned for prior exposure to beta lactam antibiotics and will receive prick skin testing, followed by intradermal skin testing for each reagent to which there is no significant prick skin test reaction, to PPL, fresh pen G, penicilloate (MDM-A), penicilloate (TS-Sullivan), and penilloate (MDM-B), in the usual concentrations, as well as routine histamine and diluent controls. The two penicilloates and the penilloate are not commercially available and will be prepared in a single batch at FAMC. MDM-A and MDM-B will be prepared following Saxon's clarification of Levine's method. Penicilloate TS will be made by Sullivan's method. A blood sample will be drawn from subjects with positive skin test reactions and frozen for use in a future in vitro study of comparative potency of the testing reagents. It is hoped that at least 200 subjects without history of adverse penicillin reaction will be tested and that at least 30 skin test positive patients will complete the comparative potency phase of the study. The number of history positive patients and the number of history-negative subjects in whom one or more skin test results are positive will be reported as a percentage of the total number of patients and subjects tested for each reagent. In the comparative potency evaluation, the Kruskall-Wallis test will be used to discern if there is a difference in the wheal size for penicilloate A vs penicilloate B vs MDM. If a difference is detected at the α=0.05 level, multiple comparisons will be made also at the α=0.05 level using a nonparametric modification of the Newman-Keuls method. Comparison of end point skin test reactivity for fresh and aged preparations for each reagent will be made at the α=0.05 level by means of the Mann-Whitney test.

Progress: No patients have been entered at MAMC since FY 90. Dr. Brown, who took over the protocol, has been unable to restart the study.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, CRITICAL CARE MEDICINE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/159	**Status:** On-going
Title: Randomized Trial of E5 Antiendoxin Monoclonal Antibody in Patients With Severe Sepsis		
Start Date: 08/06/93	**Est. Completion Date:** Nov 94	
Department: Medicine/Crit Care Med	**Facility:** MAMC	
Principal Investigator: LTC Anthony S. Sado, MC		
Associate Investigators:	MAJ Kathleen M. Sheehan, MC	
Key Words: sepsis,monoclonal antibody		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To determine whether the administration of E5 enhances survival in patients with severe sepsis due to documented gram-negative infection when compared to placebo.

Technical Approach: Hospitalized patients > 18 years who have a documented serious gram negative infection within 2 calendar days prior to entry will be screened for clinical signs of sepsis. Patients will be randomized to receive standard antibiotic therapy and E5 (monoclonal antibody) versus standard antibiotic therapy. E5 will be given over 1 hour on days one and two and the patients will be monitored for any adverse effects. All patients will be followed for survival at days 14 and 28.

Progress: Medication has not been received to initiate the study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/131 **Status:** On-going

Title: Pilot Study - Thromboelastograph Assessment of Suspected Acute M.I./Unstable Angina Patients Pre- and Post- I.V. Magnesium Administration

Start Date: 07/02/93 **Est. Completion Date:** Jan 94

Department: Medicine/Crit Care Med **Facility:** MAMC

Principal Investigator: MAJ Kathleen M. Sheehan, MC

Associate Investigators: MAJ Doreen Saltiel, MC

Key Words: myocardial infarction,magnesium,thromboelastograph

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$53.33	Periodic Review: / /

Study Objective: To determine the extent of anticoagulant effect of I.V. magnesium sulfate in patients admitted with suspected acute myocardial infarction or unstable angina.

Technical Approach: Acute myocardial infarction patients ordered to receive I.V. magnesium sulfate (2 gm bolus) will be entered into this pilot study to evaluate possible anticoagulant effects of magnesium. A sample of venous blood will be withdrawn with admission laboratories prior to magnesium level, and standard measures of coagulation (PT/PTT, thrombin time, and fibrinogen) will be performed. Approximately 15 minutes into the infusion, repeat coagulation studies will be obtained and repeat thrombo-elastograph will be available in approximately 60 minutes. Statistical method to be employed is paired t-test.

Progress: Five subjects have been entered, no significant differences have been noted..

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/074 **Status:** On-going

Title: Transcatheter Closure of the Patent Ductus Arteriosus Using a Retrievabler Coil Occlusion System in the Newborn Lamb Model

Start Date: 04/01/93 **Est. Completion Date:** Aug 93

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

Principal Investigator: MAJ Patrick A. Cambier, MC

Associate Investigators: MAJ Karl C. Stajduhar, MC
MAJ Richard R. Gomez, MC

Key Words: Patent ductus arteriosus:Newborn lamb model,retrievable coil occlusion system,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1662.00	**Periodic Review:** 06/07/93

Study Objective: The trial outlined in this protocol is designed to evaluate the efficacy of a prototype wire coil device to occlude arteriovenous flow in the patent ductus arteriosus (PDA); establish the safety regarding deployment and retrievability of the system over a range of PDA internal diameters; and to assess the long-term histologic vascular sequelae of coil implantation.

Technical Approach: Animals will be kept NPO for 4 hours prior to the procedure. Intravenous access will be obtained via a catheter placed in the external jugular vein. After surface electrodes for cardiac monitoring are in place, appropriate anesthesia will be initiated and the animal will be intubated. Femoral artery and vein cutdowns will be completed and aortography of the transverse aortic arch will be performed to identify the patent ductus arteriosus (PDA). In the event a PDA is not noted via the aortagram, a limited main pulmonary arteriogram will be carried out to visualize the pulmonic diverticulum, and the PDA traversed via the pulmonic ostia. A guiding catheter will be used to engage the aortic ostium of the PDA. Although the majority of newborn lambs will have sufficiently large PDAs for deployment of the coil device, a small percentage of the PDAs may require pre-dilation using standard angioplasty techniques. In the event that the PDA is visualized via the pulmonary circuit, a guide wire will be inserted into the aorta via the PDA pulmonic diverticulum and advanced through the previously placed femoral arterial sheath. Over this wire, the guiding catheter will be advanced via the ascending aorta, engaging the PDA diverticulum at which time the coil device will be deployed into the PDA, and occlusion of flow documented by angiography. The coil will then be retrieved. The coil device will then be permanently deployed in the ductus arteriosus. In the event the PDA cannot be traversed, the coil will be placed into a collateralized end-artery (i.e. internal carotid), to permit testing of the flow occluding nature and retrievability of the device. After completion of this process the catheters will be removed and the animal recovered and maintained. At the end of the routine 3 week follow-up time period (in 2 - 3 animals, as long as 3 - 4 months), the animal will be euthanized. Necropsy will be performed to determine gross and histological appearance of the coil, specifically at the pulmonary and aorta ostia to determine intimal aortic injury or presence of thrombus.

Progress: Successful testing and deployment of 11 of the planned 12 retrievable coil occlusion devices has occurred. Successful results have provided further incentive to continue investigation of a second generation device. FDA testing is now underway.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/151 **Status:** On-going

Title: Cardiac Safety of Sexual Intercourse Following Myocardial Infarction As Assessed by High Resolution Holter Monitoring

Start Date: 08/06/93 **Est. Completion Date:** Jul 94

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

Principal Investigator: CPT Cynthia L. Clagett, MC

Associate Investigators: MAJ Patrick A. Cambier, MC

Key Words: intercourse,myocardial infarction,Holter monitoring

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

Study Objective: (1) To determine the cardiac safety of sexual intercourse following myocardial infarction (MI) by directly assessing for the presence of ischemia and dysrhythmia using high resolution Holter monitor. (2) Determine if post myocardial infarction pre-discharge exercise tests predict who will be at risk for ischemia or dysrhythmia during sexual intercourse.

Technical Approach: Patients who have suffered an acute MI within the preceding month and have a stable sexual relationship as determined by the patient will be eligible for this study. After clinical evaluation, chart review and review of other tests deemed appropriate by the primary physician; the patients will undergo 24 hour outpatient Holter monitoring within 1 month after MI. During the monitor period, they will be asked to engage in their normal activity and to engage in sexual intercourse during this time. Patients will be asked to document any symptoms and record time of activities, specifically sexual intercourse, in a patient diary. If for any reason patients do not have intercourse or find the device inconvenient, they may choose to reschedule another monitoring period or to discontinue the study. A blinded investigator will review the monitor tapes. The number, duration, and time of onset and offset of ischemic episodes will be recorded. A period including sexual intercourse will be specifically analyzed. The presence of ischemia or dysrhythmia during the sex period will be compared to the remaining 24 hour period and to the findings on exercise testing.

The incidence of ischemia and dysrhythmia will be calculated with 95% confidence intervals for the proportions.

Progress: Eighteen (18) patients have been enrolled.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/018 **Status:** On-going

Title: Cardiac Dimensions in Female Athletes

Start Date: 11/06/92 **Est. Completion Date:** Jun 93

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

Principal Investigator: MAJ Alice M. Mascette, MC

Associate Investigators: MAJ Patrick A. Cambier, MC
MAJ Karl C. Stajduhar, MC

Key Words: cardiac dimensions,female athletes

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

Study Objective: To non-invasively obtain cardiac dimensions in women engaged in regular vigorous aerobic and power training.

Technical Approach: Twenty volunteer female athletes engaged in regular vigorous aerobic activity and twenty volunteer female athletes engaged in regular power sports will undergo standard two dimensional echocardiography. Standard measurements of left ventricular wall thickness (septum and posterior well) and cavity dimensions will be measured on-a-line from the parasternal long axis view at the time of study. The technical staff will be blinded as to the exercise interview conducted at the time of recruitment. The echocardiograms will be overread by two staff cardiologists and measurements recorded. Differences will be resolved by averaging results. A cohort of age, height, and weight-matched controls will be recruited and mean dimensions from their studies statistically compared with the athletes using the ANOVA test.

Progress: Forty-five subjects have been enrolled to date but attempts are still being made to enroll more weight lifters. The study has shown significantly increased left ventricular (LV) dimensions in aerobic and anaerobic athletes, increased maximum wall thickness in anaerobic athletes, and conflicting results on LV mass and mass index.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/103 **Status:** On-going

Title: A Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of RheothRx Injection (Polaxamer 188) in Patients with Suspected Acute Myocardial Infarction

Start Date: 05/07/93 **Est. Completion Date:** May 94

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

Principal Investigator: COL Joseph A. Paris, MC

Associate Investigators:
COL Roger F. Chamusco, MC
MAJ Doreen Saltiel, MC
MAJ James C. Mullin, MC
MAJ Mark E. Peele, MC
CPT Scott A. Sample, MC
LTC John M. Bauman, MC
MAJ Alice M. Mascette, MC
MAJ Karl C. Stajduhar, MC
MAJ Patrick A. Cambier, MC
CPT Michael A. Rave, MC

Key Words: myocardial infarction,RheothRx

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

Study Objective: (1) To evaluate the effect of RheothRx Injection, if any, on resultant myocardial infarct size, compared to placebo, when given to patients with suspected AMI who are not treated acutely with thrombolytic therapy or direct percutaneous transluminal coronary angioplasty (PTCA). (2) To assess the safety of RheothRx Injection in this patient population.

Technical Approach: This is a multicenter, randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of RheothRx Injection in patients with suspected acute myocardial infarction who are not eligible to receive thrombolytic therapy or acute, direct PTCA. Such patients presenting with ongoing symptoms suspicious of AMI of at least 30 minutes in duration but within 6 hours since onset will be considered for enrollment in the study. Two hundred and fifty (250) patients will be enrolled at approximately ten to fifteen centers. Eligible patients will receive a 48 hour intravenous infusion of either RheothRx injection or placebo. All patients will receive aspirin throughout the hospitalization. Randomization to RheothRx injection or placebo will be stratified by the initial type of EKG abnormality (ST elevation or ST depression/ T wave inversion/ bundle branch block/ non-specific intraventricular conduction delay present at the time of enrollment and by the enrolling center. The safety of RheothRx will be evaluated using periodic laboratory tests, assessments of vital signs, physical examination, collection of adverse experiences, bleeding complications, and disease-related events. Efficacy will be assessed by measures of myocardial infarct size, left ventricular ejection fraction, and clinical outcome. Infarct size will be measured on days 5 - 10 by single photon emission computer tomography using technetium 99m sestamibi. Ejection fraction will be measured on days 5 - 10 by radionuclide ventriculography. Clinical outcome will be assessed by monitoring the occurrence of prospectively specified clinical events during the six-month period following randomization. Two composite scores of efficacy will be computed from the recorded events.

Progress: Thirteen patients have been enrolled in this randomized trial. Efforts to recruit study participants are ongoing.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/027 **Status:** On-going

Title: Comparison of Intravenous Adenosine With Exercise in Thallium-201 SPECT in Patients With Left Bundle Branch Block

Start Date: 12/04/92 **Est. Completion Date:** Jun 94

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

Principal Investigator: CPT Michael A. Rave, MC

Associate Investigators:
COL Roger F. Chamusco, MC
LTC John M. Bauman, MC
MAJ Doreen Saltiel, MC
MAJ Stephen E. Budd, MC

Key Words: left bundle branch block:adenosine and exercise

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$3000.00	Periodic Review:	/ /

Study Objective: To determine if the diagnostic value of adenosine in conjunction with thallium-201 SPECT imaging is improved over standard thallium exercise testing in patients with left bundle branch block.

Technical Approach: Patients referred for ischemic heart disease will receive pharmacologic stress with adenosine at 0.14 mg/kg and an exercise thallium-201 SPECT imaging (using a symptom limited Bruce exercise protocol) approximately one week apart. A cardiac catheterization will be performed within four weeks of the scans. All thallium SPECT images will be evaluated by two experienced observers blinded to the clinical history and angiography results. The radio nuclide studies will not be matched for the same patient until all studies have been read. The cineangiograms will be reviewed by a single reviewer blinded to the results of the thallium imaging. At the end of enrollment the results of the imaging studies and cardiac cath lab evaluations will be paired up and analyzed.

Progress: Five patients have completed all three phases of the study to include exercise thallium, adenosine thallium, and cardiac catheterization. Thallium data is to this date still blinded. We feel that we have captured all patients meeting criteria and have at least offered them participation in the study; none have declined enrollment. Recruitment for the remaining participants is active.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

Detail Summary Sheet

ate: 30 Sep 92 **Protocol No.:** 92/020 **Status:** Completed

itle: Evaluation of the Efficacy and Safety of Glimepiride versus Glyburide in Subjects with Noninsulin-Dependent Diabetes Mellitus (NIDDM)

tart Date: 01/03/92 **Est. Completion Date:**

)epartment: Medicine/Endocrinology **Facility:** MAMC

'rincipal Investigator: COL David L. Bunner, MC

ssociate Investigators:
LTC H. Lester Reed, MC
CPT Robert M. Tuttle, MC
LTC (P) Robert E. Jones, MS
LTC Daniel H. Knodel, MC
CPT Carl A. Gibson, MC

Key Words: diabetes,noninsulin-dependent,glimepiride,glyburide

ccumulative		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

Study Objective: To evaluate the efficacy of Glimepiride and Glyburide as oral ypoglycemic agents over the dosing ranges tested in the treatment of subjects with non-nsulin dependent diabetes mellitus and to compare the safety of Glimepiride and Glyburide in these subjects.

Technical Approach: This is a multicenter, double-blind, randomized, parallel design tudy. Patients will be entered in a four week washout period, utilizing placebo tablets. At the end of the four-week washout period, subjects will be stratified into two groups ccording to the fasting plasma glucose on Day 12: Group 1: low fasting plasma glucose = 160-240 mg/dl, and Group 2: high fasting plasma glucose = 240-300 mg/dl. Patients will hen be randomized to receive either Glimepiride or Glyburide for a 12 week titration eriod and then for a 40 week maintenance period. Patients will have an eye xamination and an electrocardiogram prior to randomization. The eye exam will be epeated at months 6 and 12 and the EKG will be repeated at month 12. Efficacy will be valuated using fasting plasma glucose (each visit), and glycosolated hemoglobin (weeks) and 16 and months 6, 10, and 12) as the primary variables. Fasting insulin and C-eptide as well as two hour postprandial glucose, insulin, and C-peptide (week 0 and nonths 6 and 12) will be evaluated as secondary variables. Baseline demographic and ackground variables will be summarized by treatment group to assess the omparability of each group at the beginning of the randomization phase. Means and ategories will be compared for between group homogeneity using either analysis of ariance or Mantel-Haenszel tests. Safety data, including laboratory assessments and dverse events, will be tabulated and displayed for clinical review. Important changes rom baseline in laboratory values will be summarized and adverse events will be abulated according to body system.

Progress: Fourteen patients were entered. Two were dropped from the protocol for trictly technical reasons. Twelve completed the protocol. Data has been forwarded to he sponsor.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/101	**Status:** On-going
Title: Androgen Effects on Glucose Metabolism in Men		
Start Date: 05/07/93	**Est. Completion Date:** May 94	
Department: Medicine/Endocrinology	**Facility:** MAMC	
Principal Investigator: CPT Barrett L. Chapin, MC		
Associate Investigators: COL Stephen R. Plymate, MC	LTC (P) Robert E. Jones, MS	
Key Words: metabolism,androgen		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: 1. To demonstrate that androgen administration to young men will result in enhancement of glucose metabolism via non-insulin mediated glucose uptake (NIMGU). 2. To demonstrate that the administration of androgen in this study will not result in adverse effects on the prostate, serum lipids, or blood pressure.

Technical Approach: Androgen will be administered to 20 healthy, young men. A companion study of 20 healthy, elderly men will be conducted at American Lake Veterans Hospital. The androgen will be administered to subjects as testosterone enanthate (TE), an androgen that can be aromatized to an estrogen, and testosterone deconate (TD), an androgen that is not aromatized to a potent estrogen, at 100 mg I.M. q week for 12 weeks in a cross-over design with a 10 week washout period. Ten subjects will receive the TD first and ten subjects with receive the TE first.

The major clinical tool used to study glucose and insulin metabolism will be the frequently sampled intravenous glucose tolerance test (FSIVGTT). In addition to the FSIVGTT, IGF-I, IGF-BPs, GH, lipids, strength, body composition, prostate studies (including PSA), digital examination, and ultrasound for residual urine volume and prostate size in each of the four time periods in which FSIVGTT is performed will be done (at baseline, during the first 12 week androgen treatment period, during the washout period, and during the second androgen treatment period).

Data will be expressed as the mean ± standard error (SE). Tests will be done to determine whether the order in which the treatments are given affected the outcome (sequence effect) or whether the response seen in the first treatment period differed from that seen during the second treatment period (period effect). Data for which no sequence or period effect can be detected will be analyzed to establish (1) if the effect of androgen therapy on any measured variable differs depending upon whether TE or TD was used (a between-treatment analysis), and (2) if a given variable changed over time due to androgen therapy (within-treatment analysis). If no sequence or period effects are noted, the study will be analyzed as a crossover design. Paired data will be analyzed using a Student's t-test. An unpaired t-test will be used to test differences between groups.

Progress: No patients have been entered because the nurse instrumental in data collection was reassigned. With the arrival of a new nurse to assist with data collection the study will be restarted.

Detail Summary Sheet

te: 30 Sep 92 **Protocol No.: 93/102** **Status:** On-going

tle: Evaluation of Calcium Metabolism After Biliopancreatic Bypass Surgery

art Date: 05/07/93 **Est. Completion Date:** Oct 93

partment: Medicine/Endocrinology **Facility:** MAMC

incipal Investigator: CPT Barrett L. Chapin, MC

sociate Investigators:
LTC Daniel H. Knodel, MC
MAJ John D. Ng, MC
LTC Homer J. Lemar Jr., MC
COL Preston L. Carter, MC

y Words: metabolism,calcium,biliopancreatic bypass

cumulative		**Est. Accumulative**		**Periodic Review:**
EDCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

udy Objective: To determine if there are changes in calcium metabolism after liopancreatic bypass surgery, and if so, to characterize the biochemical profile of those anges.

chnical Approach: Patients who have had biliopancreatic bypass surgery within the evious three years will be invited to participate in this study. The control will be an ual number of patients who have had a different surgical procedure for obesity called rtical banded gastroplasty. These populations will be matched for age, sex, and nount of weight loss. It is assumed that the surgery of vertical banded gastroplasty es not cause calcium abnormalities. If the control group population has significant normalities in the biochemical evaluation of calcium metabolism, the protocol will be vised to add an additional control group. That group would consist of an equal mber of age and sex matched people without any evidence of disease or obesity.

Evaluation of serum and urine markers of metabolic bone disease will be rformed in each group. Tests performed to evaluate calcium metabolism will be rum calcium, albumin, alkaline phosphatase (a marker for bone turnover), agnesium, phosphorus, parathyroid hormone, 25-hydroxy vitamin D, 1.25-dihydroxy tamin D, and a 24 hour urine collection for calcium and hydroxyproline (a marker for ne turnover). Evaluation of other fat soluble vitamins will be performed by checking othrombin time (vitamin K) and serum carotene (vitamin A). Confirmation of normal ver function will be obtained with serum gamma glutamic aminotransferase. nfirmation of normal renal function will be obtained with serum creatinine and 24 ur urine creatinine.

If the serum carotene level is below normal, the patient will be referred to the phthalmology Service for formal testing for night blindness.

Statistical analysis between the study and control group will be performed with an paired T test or by ANOVA if a second control group is added.

rogress: Six study subjects and 5 controls have been entered.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/069	**Status:** On-going
Title: Phospholipid Composition of Human Epididymal and Ejaculated Spermatozoa		
Start Date: 06/05/92	**Est. Completion Date:** Jun 94	
Department: Medicine/Endocrinology	**Facility:** MAMC	
Principal Investigator: COL Robert E. Jones, MC		
Associate Investigators: None		
Key Words: spermatozoa,phospholipid,epididymus		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: (1) To determine the quantitative changes in sperm plasma membrane phospholipids and phospholipid-bound fatty acids as they traverse the epididymis and (2) to compare these results to the values obtained from ejaculated sperm.

Technical Approach: Thirty fertile volunteers undergoing elective vasectomy will be asked to provide two semen samples prior to surgery. During the surgical procedure, sperm will be obtained by milking the proximal end of the vas deferens and epididymis. The samples will be washed in a calcium free buffer, and the phospholipids will be extracted using chloroform and methanol. The extracted phospholipids will be kept under a nitrogen atmosphere at -70 degrees centigrade until they are assayed. Pooling of samples may be necessary to ensure adequate detection of minor phospholipds and fatty acids. The position and bonding of fatty acids will be determined through a combination of enzymatic and chemical hydrolysis. Quantification of fatty acids will be performed using gas chromatography, and either high performance liquid chromatography or quantitative thin layer chromatography to identify phospholipids. Results will be expressed by normalizing values to sperm number, to phospholipid phosphorous, or as a percentage of total sperm lipids of a similar class. The data will be handled using descriptive statistics, and the statistical analysis will employ an unpaired t test or an ANOVA when appropriate.

Progress: No further work was performed on this project during this fiscal year.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/023 **Status:** On-going

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

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

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

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

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: The complex regulatory kinetics of long chain fatty acid:CoASH ligase (AMP) have been lucidated and the manuscript has been published.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/038 **Status:** On-going

Title: Detailed Studies Into Membrane Lipid Synthesis in Human Sperm

Start Date: 02/16/90 **Est. Completion Date:** Feb 99

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators: COL Stephen R. Plymate, MC
CPT Brenda K. Bell, MC

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: Preliminary kinetic data on acyl transferase have been obtained suggesting that the enzyme has an acidic pH optimum, a K_m of 7-12 μM and a V_{max} of 0.16 μmoles/10^7 sperm/hour.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 83/081 **Status:** On-going

Title: Studies on Fatty Acid Activation in Spermatozoa: Kinetics and Localization

Start Date: 09/16/83 **Est. Completion Date:** Sep 84

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators: COL Stephen R. Plymate, MC
COL Bruce L. Fariss, MC

Key Words: spermatozoa,fatty acid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$785.00	**Periodic Review:** 04/05/91

Study Objective: To define the kinetic characteristics and cellular localization of the enzyme system responsible for the initiation of saturated fatty acid metabolism in spermatozoa.

Technical Approach: Normal human semen samples will be used to establish a ligase assay. Ligase activity will be measured using a sensitive radioligand/millipore filter procedure that utilizes (3H)-coenzyme A as the radioactive trace. Approximately 0.2 m C of (3H) will be present in each individual assay. The samples will be centrifuged at 2800g for 10 minutes at room temperature, the seminal plasma supernatant will be discarded, and the sperm pellet will be resuspended in an isotonic buffer. This sperm mixture will be recentrifuged and washed twice prior to use. After the final centrifugation, the pellet will be diluted in a potassium enriched buffer to achieve a sperm density of $2x10^8$/ml. The assay mixture will contain palmitic acid, ATP, Mg++ and CoASH and will be initiated by the addition of the washed sperm preparation. Time and protein dependency curves will be run to determine the length of incubation needed to achieve first order kinetics in the measurement of initial velocities. Both Lineweaver-Burk plots and hyperbolic best-fit will be used to calculate approximate Km values for each substrate. Temperature, pH curves, and rates with alternate substrates will also be run. Enzyme location/latency will be determined by assaying separate cell fractions prepared by sonication and differential centrifugation of the isolated sperm. The effects of sulfhydryl reagents, albumin, and detergents will be studied to assist in estimation of latency.

Progress: There has been no further progress on this project during this fiscal year.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/026 **Status:** On-going

Title: Neutral and Polar Lipid Synthesis in Human Spermatozoa: A Correlation with Morphology and Function

Start Date: 01/15/88 **Est. Completion Date:** Jun 89

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators:
COL Stephen R. Plymate, MC
MAJ Karl E. Friedl, MC
MAJ Charles J. Hannan, MC

Key Words: spermatozoa,lipids,morphology

Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
$40,000	$2000.00	04/05/91

Study Objective: To compare the rates of fatty acid activation to acyl CoA and subsequent disposal into neutral or polar lipids with sperm morphology or an assessment of sperm motility.

Technical Approach: The incorporation of palmitic (16:0) and docosahexaenoic acids (22:6) into neutral or phospholipids will be measured by incubating whole, fresh sperm with 3H-16:0 and 14C-22:6. Total lipids will be extracted using the method of Bligh and Dyer. The chloroform phase will be taken to dryness under N2 at 42C C and subsequently reconstituted in a minimal volume of chloroform. The chloroform mixture will be applied to a silicic acid column and subsequentially eluted with 20 ml chloroform followed by 20 ml of methanol. The chloroform fractions containing neutral lipids will be combined, evaporated, and repeatedly extracted to remove the free fatty acids. Both the methanol and chloroform elutes will be counted, and an aliquot of each will be chromatographed on silica gel G to ensure complete separation. Incorporation rates will be expressed as nmoles fatty acid incorporated/106 sperm or nmoles phospholipid P/hour. After extracting the sperm with 0.1% Triton X100, ligase activity will be measured. Both 16:0 and 22:6 will be used as substrates in the incubations. Ligase activity will be expressed as nmoles acyl CoA formed/min/mg protein. The seminal plasma concentrations of these compounds will be measured using an enzymatic spectrophotometric technique. These parameters will be considered separately in relationship to ligase activity and lipid synthesis. Semen samples will be handled and analyzed according to the current WHO guidelines. Morphology will be assessed on fixed smears, and motility will be objectively quantified with an automated semen analyzer. With the exception of the sperm density, the semen quality will be blinded to the person performing the biochemical analyses. Incorporation rates and the distribution of the fatty acid labels and ligase activity will be correlated with sperm morphology and motility of the semen sample using either linear regression or chi-square analyses.

Progress: No further progress has occurred on this study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/070 **Status:** Completed

Title: Characterization of Serovar-Specific Ureaplasmal Antigens by Analysis with Monoclonal Antibodies

Start Date: 08/19/88 **Est. Completion Date:**

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: COL Robert E. Jones, MC

Associate Investigators: MAJ John E. van Hamont, MS

Key Words: antigens,ureaplasma,monoclonal antibodies,Animal Study

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$3700.00	Periodic Review: 06/07/93

Study Objective: To identify and define antigenic determinants specifically associated with the 14 serovars of Ureaplasma urealyticum.

Technical Approach: Mice will be immunized with ureaplasma serovar antigens by either intrasplenic injection of aqueous antigen or subcutaneous injection of antigen with adjuvant followed by an IV booster of aqueous antigen. The spleen cells from the immunized mice will then be fused with P.653 myeloma cells. The cell culture supernatants from the resulting hybridoma clones will then be screened for antibody reactive with homologous ureaplasmal antigens as well as with growth medium components. The investigator will then characterize reactive monoclonals for serovar and subgroup specificity via the growth inhibition assay, metabolic inhibition assay, mycoplasmacidal assay, and direct fluorescent assay. The monoclonals identified as having type specificity will be used in the analysis of colloidal gold labeling procedures for localization of type-specific antigen by electron microscopy and for affinity column chromatography purification of type specific antigen from ureaplasma cell lysates. The monoclonals and antigens thus characterized will be used in the development of assays for future identification of clinical isolates of Ureaplasma and analysis of host serological responses.

Progress: No further work has been undertaken on this protocol in FY 93. Results suggest that, in a susceptible host, colonization with Ureaplasm urealyticum could induce antisperm antibodies capable of inhibiting spermatozoal mobility.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/068 **Status:** On-going

Title: The Time Course for Metabolic Responses to Thyroid Hormone: Specific Contributions of Muscle Efficiency and Resting Oxygen Utilization

Start Date: 06/05/92 **Est. Completion Date:** Jan 94

Department: Medicine/Endocrinology **Facility:** MAMC

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

Associate Investigators:
LTC (P) Robert E. Jones, MS
LTC H. Lester Reed, MC
COL David L. Bunner, MC
CPT Carl A. Gibson, MC

Key Words: thyroid hormone,muscle efficiency,oxyten utilization

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

Study Objective: To determine the relationship between serum thyrotropin (TSH) concentrations and the efficiency of skeletal muscle during a changing thyroid status; to identify if these measures of pituitary and peripheral thyroid hormone action covary with the same time constant in transition from hyperthyroidism to euthyroidism; and to assess the specific contribution of a changing muscle work efficiency to the increased oxygen utilization associated with excess states of thyroid hormone.

Technical Approach: Oxygen utilization will be measured with four submaximal bicycle ergometer workloads in 15 hyperthyroid patients undergoing treatment and 15 euthyroid control subjects. These workloads will support a linear regression analysis to determine muscle efficiency and resting oxygen use. This measure will be carried out before and biweekly during treatment for hyperthyroidism in order to determine the time course of tissue responses during normalization of serum thyroid hormones. Specifically, serum thyrotropin (TSH) will be simultaneously measured and the time course of normalizing sensitive assays of serum TSH and exercise kinetics will be contrasted as two tissue responses to this changing thyroid hormone status. Euthyroid controls will establish normal ranges and the test variability, while allowing comparisons between themselves and the hyperthyroid and hypothyroid subjects. The study population will include hyperthyroid patients who have elected radioactive iodine therapy for their disease and a control group of normal euthyroid patients who are taking a stable and fixed replacement dose of thyroid hormone.

Progress: Enrollment has been completed and only one subject remains active in the protocol. Preliminary data analysis reveals a clear correllation of thyroid function with oxygen consumption at submaximal levels of exercise. Thyroxine levels more closely parallel changes in oxygen consumption than do TSH levels which lag behind. Bicycle ergometry at submaximal stress is able to show changes in oxygen utilization assocciated with changing trhyroid function.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/097 **Status:** Completed

Title: The Use of Thyroid Tissue Obtained by Fine Needle Aspiration (FNA) as Substrate for Polymerase Chain Reaction (PCR) Amplification of Thyroglobulin and the Papillary Thyroid Cancer (PTC) Oncogene

Start Date: 10/04/91 **Est. Completion Date:** Apr 92

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: MAJ Mark E. Peele, MC

Associate Investigators: CPT Robert M. Tuttle, MC

Key Words: cancer:thyroid,PCR,thyroglobulin,FNA,PTC oncogene

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$1250.00	Periodic Review:	/ /

Study Objective: 1. To show that thyroid tissue obtained by routing fine needle aspiration (FNA) can be used for the polymerase chain reaction (PCR) amplification of thyroidal genomic DNA and messenger RNA transcripts. 2. Utilize PCR to amplify DNA sequences unique to the RET and PTC (papillary thyroid cancer) oncogens. The presence of PTC in FNA samples of thyroid nodules may represent a marker for papillary thyroid cancer. 3. Utilize reverse PCR to amplify specific thyroidal messenger RNA transcripts of the RET and PTC oncogenes. Reverse PCR amplification of thyroglobulin messenger RNA transcripts will serve as an internal control. 4. Develop a protocol for routine PCR amplification of FNA samples allowing timely study of oncogenes present in thyroid nodules with the ultimate goal of developing prognostic tests for primary thyroid neoplasms.

Technical Approach: Twenty patients undergoing fine needle aspiration of the thyroid for clinically indicated evaluation of thyroid nodules or masses will be offered participation in this study. Four to six aspirations will be performed as per the clinic routine. The aspiration needle will be rinsed into a centrifuge tube containing RPMI cell culture media. The adequacy of aspirated material present on slides prepared in the clinic for cytologic interpretation will be determined according to accepted guidelines. The purpose of the FNA is to provide adequate material for the cytologic evaluation. Clinical material present in excess of this standard will be considered for use in this protocol. Excess aspiration material will be collected by needle rinses into 1000 ul of either RPMI cell culture media or phosphate buffered saline (PBS). Cells will be rapidly pelleted by centrifugation after the rinse to remove excess plasma proteins. The cell pellet will be resuspended in 25 ul DEPC treated water and rapidly chilled to -70 deg C. This material will then be stored until laboratory study begins. PCR will be used to amplify thyroidal genomic and mRNA. The material collected from the FNA will be heated to 65 deg C in the presence of RNasin and hypotonic DEPC treated water to linearize the nucleic acids. The mRNA and DNA will serve as the templates for the PCR amplification. Three sets of PCR primers and oligomers will be synthesized. All the primer sets have an engineered span containing a restriction enzyme site (HINDIII) on the 5' portion to allow insertion of the amplified material into a sequencing vector. Thyroglobulin will be amplified as the positive control, the oncogenes PTC1 and RET will be amplified from aliquots of the same material. The first step in the amplification of the mRNA will be the synthesis of first strand complementary DNA. The cDNA and linearized DNA will be amplified as per standard PCR protocols for 35 cycles. The amplified products are separated on an agar gel and blotted onto a nylon membrane, the

blot will be probed with the specifically engineered oligonucleotide probes to determine the molecular identity of the amplified PCR products. Amplified fragments of interest will be cloned into an expression vector and sequenced using Taq polymerase and conventional dideoxynucleotide chain elongation termination.

Progress: FNA of thyroid cancer provides adequate material for successful amplification of normally expressed genes (Tg) and activated oncogenes (PTC).

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/081 **Status:** Completed

Title: The Effect of Thyroid Hormone Suppression on Thyroid Nodules Found to be Indeterminate by Fine Needle Aspiration

Start Date: 08/02/91 **Est. Completion Date:**

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: CPT Robert M. Tuttle, MC

Associate Investigators:
MAJ John P. Kushner, MC
MAJ Arnold A. Asp, MC
COL Robert E. Jones, MC
COL Ernest L. Mazzaferri, MC
MAJ James H. Timmons, MC

Key Words: thyroid nodules,thyroid hormone suppression,needle aspiration

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To differentiate benign from malignant thyroid nodules in a subgroup of patients with indeterminate fine-needle thyroid biopsy cytology using thyroid hormone suppression by serially determining the volume of thyroid nodules using ultrasonography and by serially following thyroglobulin measurements during thyroid hormone suppression and to establish ultrasonographic criteria to define adequate thyroid hormone suppression.

Technical Approach: This is a multicenter study originating at MAMC in which 150 patients will be enrolled. Patients being evaluated for a solitary thyroid nodule or a dominant nodule in a multinodular thyroid who are found to have indeterminate cytology on a fine needle aspiration will be offered enrollment. The baseline evaluation will include thyroid function tests, thyroglobulin, and a thyroid ultrasound. The volume of the nodule will be determined using a digitizer pad and Sigma Scan software. The patient will be placed on a suppressive dose of L-thyroxine (as defined by an undetectable ultra sensitive TSH) and followed at 3 month intervals using repeat ultrasound examinations. The duration of the study is 6 months. At the end of the study, all patients will have their nodules removed unless, at the end of study, the nodule is <0.5 cm or has decreased to less than 75% of the original volume. The degree of suppression in nodule volume, if any, will be correlated with the final pathology of the nodule.

Progress: Ten patients were studied. Suppressive doses of levothyroxine were given to ten patients with a FNA diagnosis of follicular neoplasm. Thyroid ultrasounds were done at baseline and at three and six months. One patient had a malignant diagnosis at surgery while nine patients had benign histology. Change in nodule size did not correlate with final histology diagnosis. Other clinical parameters likewise failed to differentiate benign from malignant nodules.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/127 **Status:** On-going

Title: Oncogene Activation in Neoplastic Thyroid Tissue Occurring After Exposure To A Nuclear Blast: The Marshall Island Experience

Start Date: 06/09/93 **Est. Completion Date:** Jun 94

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: CPT Robert M. Tuttle, MC

Associate Investigators:
Sissy S. Jhiang, Ph.D.
CPT Rodger K. Martin, MS
Michael Bourneman, MC
Jean Howard, M.D.
COL Ernest L. Mazzaferri, MC
MAJ Robert B. Ellis, MC
MAJ Richard R. Gomez, MC
Larry Sakas, MC
Goerge Begus, M.D.

Key Words: thyroid,nuclear blast,ongogene activation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$3174.00	**Periodic Review:** / /

Study Objective: 1. To determine the frequency of activation of the Papillary Thyroid Cancer (PCT/retTPC) oncogene in neoplastic thyroid tissue that developed after exposure to a nuclear blast. 2. To determine the frequency of K-ras point mutations in neoplastic thyroid tissue that developed after exposure to a nuclear blast. 3. To correlate the clinical course of these radiation induced thyroid cancers with the activation of each oncogene.

Technical Approach: Approximately 30 samples of paraffin embedded thyroidectomy samples from individuals with a documented presence in the Marshall Islands in 1954 and with a diagnosis of papillary thyroid cancer, follicular thyroid cancer, or other non-malignant neoplasia and any normal thyroid tissue available will be used to recover DNA and mRNA using techniques that have proven successful in our laboratory. These samples will be compared with samples from (1) Marshall Islanders not exposed to fallout that developed thyroid neoplasia (2) non-radiation induced thyroid neoplasia collected at Ohio State University (OSU) and Madigan Army Medical Center (MAMC). The paraffin blocks will be sectioned on a microtome using sterile technique and a new microtome blade for each block. A new histology slide will be prepared and reviewed to verify that thyroid tissue is present in the block and to re-confirm the diagnosis. The paraffin sections will be placed into a sterile 1.5 ml sterile microcentrifuge tube and sealed. A sample from each paraffin block will be blindly evaluated by both the laboratory at OSU and MAMC. The DNA and messenger RNA extracted from the paraffin embedded tissue will be examined to determine quality and quantity of extracts. Optical densities (OD 260/280) and agarose mini-gel electrophoresis will be done on sample extracts. Beta-2 microglobulin and the TSH receptor will be amplified with PCR to document integrity of the nucleic acids recovered. Samples in which the consituitively expressed messenger RNA's can be amplified with PCR will be used for oncogene amplification. The mRNA extract will serve as substrate for cDNA synthesis using the specific PTC downstream primer. The cDNA will then serve as substrate for PCR. After PCR, the mixture of amplified products generated from a specific primer set will be separated by size using standard agarose gel electrophoresis. Appropriate size markers will be used to provide size parameters of amplified products. Additional characterization of the PCR amplified product includes Southern hybridization studies with specific DNA oligomer probes. The oligonucleotide probes will be 3 prime tailing

with digoxigenin dUTP or 5 prime labelled with ^{32}P. Chemilluminescent detection will be done using the Genius/Lumiphos detection method. This method has been used successfully in our lab to detect picomolar amounts of target DNA.

Statistically, the rates of activation of each oncogene in each subgroup will be compared using chi square testing. Unpaired t test and Fischer's exact test will be used to determine if oncogene activation is more frequent in metastatic disease versus non-metastatic disease and to compare baseline measurements between groups. Logistic regression analysis of those clinical variables shown to be significant by chi square will be used to determine which single or combination of variables correlate with oncogene activation. Finally, to determine whether the activation of the oncogene is a significant prognostic factor, univariate and multivariate Cox regression will be used defining failure as first recurrence or never disease free and assuming the oncogene activation was present at diagnosis.

Progress: Approximately 100 papillary thyroid cancers have been examined for the presence of the activated PTC/ret oncogene. PTC/ret activated oncogene was found in approximately 6% of localized papillary thyroid cancers and up to 30% of widely matastatic papillary thyroid cancers. This suggests that the activation of PTC/ret may be an important molecular marker that may be used to predict clinical behavior.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/080 **Status:** On-going

Title: A Prospective Evaluation of Gonadal Damage in Thyroid Cancer Patients Treated with Radioactive Iodine

Start Date: 09/06/91 **Est. Completion Date:**

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: CPT Robert M. Tuttle, MC

Associate Investigators:
COL Stephen R. Plymate, MC
COL Robert E. Jones, MC
MAJ Arnold A. Asp, MC
William Bremner, MD, Ph.D.
COL Ernest L. Mazzaferri, MC
David Gardner, MD
Christina Wang, MD
MAJ Charles J. Hannan, MC

Key Words: cancer:thyroid,gonads,radioactive iodine

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

Study Objective: To determine whether radioactive iodine therapy given as treatment for thyroid cancer is associated with gonadal dysfunction in men by examining the effect of radiation exposure on serial semen analysis, serum follicle stimulating hormone (FSH) levels, serum inhibin levels, FSH response to gonadotropin releasing hormone (GnRH), and inhibin response to clomiphene stimulation.

Technical Approach: All euthyroid men undergoing thyroid surgery at the six participating institutions will be screened for entry into this protocol. This group will include at least 20 men with known thyroid cancer in whom RAI therapy may or may not be planned as was men undergoing non-cancer related thyroid surgeries. Those patients determined to be candidates for RAI ablation post-operatively by their primary physicians will constitute the study group. Those men who do not receive RAI post-operatively will constitute the control group. Both the control group and the study group will follow identical protocols. Initial entry labs will be drawn before surgery. Subsequent labs (testosterone, TSH, LH, semen samples, etc.) will be obtained just before RAI is administered and at 2, 4, 6, and 8 months after RAI administration. The control group will have identical samples obtained at 1, 3, 5, 7, and 9 months after surgery. Since 4-6 weeks is required post-operatively for the TSH to rise high enough to allow administration of RAI, this sample schedule will allow both groups to be sampled at the same time. In addition, GnRH and clomiphene stimulation will be done at months 5 and 9 after surgery in both groups. Semen analysis will be started with an estimation of motility using the World Health Organization graded scale of 1 - 4+. A portion of the sample will be frozen and a slide prepared for final interpretation at MAMC-DCI. This final interpretation will evaluate the specimen for sperm count and morphology. In this way all sperm counts can be done by a single investigator, minimizing or eliminating inter-observer variation. Repeated-measures ANOVA will be performed on the lab values taken over time to determine differences in control vs study groups.

Progress: No subjects have been entered due to a lack of patients who meet the criteria.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/033 **Status:** Completed

Title: Papillary Thyroid Cancer Oncogene: Prevalence, Specificity, and Clinical Significance

Start Date: 02/05/93 **Est. Completion Date:** Dec 92

Department: Medicine/Endocrinology **Facility:** MAMC

Principal Investigator: CPT Robert M. Tuttle, MC

Associate Investigators:
CPT Rodger K. Martin, MS
D. Caruso
CPT Katherine H. Moore, MS
MAJ Richard R. Gomez, MC
COL Ernest L. Mazzaferri, MC

Key Words: oncogene:papillary thyroid

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$2234.00	Periodic Review:	/ /

Study Objective: 1. To develop a technique that allows polymerase chain reaction amplification of thyroid genosmic DNA and messenger RNA sequences from paraffin embedded thyroid tissue. 2. To retrospectively examine all paraffin embedded thyroid cancer tissues available at Madigan Army Medical Center for the presence of the newly described papillary thyroid cancer oncogene (PTC) and its messenger RNA. 3. To correlate the clinical course of these thyroid cancers with the presence or absence of the PTC oncogene by retrospective chart review of files in the tumor registry. 4. To examine other abnormal but non-malignant thyroid tissue for the presence of the PTC oncogene. 5. To prospectively obtain fresh samples of all thyroid tissue surgically removed at MAMC for subsequent molecular analysis. 6. To design a rapid diagnostic test for the presence of the PTC gene.

Technical Approach: Recently a new oncogene (PTC) has been characterized that appears to be specific for papillary thyroid cancer. Furthermore, the presence of the PTC transforming gene may identify patients who are more likely to have aggressive thyroid malignancies. Studies of the prevalence and clinical significance of PTC have been hindered by the lack of fresh papillary thyroid cancer tissue and the need for long term follow-up. Both of these obstacles can be overcome at MAMC. The pathology archives at MAMC hold approximately 60 paraffin embedded thyroid cancer blocks as well as hundreds of non-malignant thyroid tissue blocks. The messenger RNA from these blocks will be recovered and subsequently amplified using standard PCR technology. Furthermore, the clinical case histories corresponding to these tissue blocks have been tracked on a yearly basis by the tumor registry. Ten year follow-up on many of these patients is available. By correlating the presence of the PTC transforming gene with numerous clinical characteristics, the role of PTC as a prognostic factor can be defined.

Determining the presence of the PTC transforming gene is too cumbersome and time consuming to be performed in a clinical laboratory. Therefore, a screening test for the PTC transforming gene needs to be developed that is more rapid and easier to perform.

In addition to examining paraffin embedded tissue, a library of freshly collected and frozen thyroid tissue will be assembled. A sample of all thyroids removed surgically at MAMC will be recovered and stored in the Department of Clinical Investigation. The tissue recovered would normally be discarded by the pathologist. In this way, a library of thyroid tissue of various pathologies can be assembled and used as an abundant source

of RNA and DNA for this and future studies.

Progress: This work demonstrates the mRNA recovered from routinely prepared, paraffin embedded neoplastic thyroid tissue can be amplified with RT-PCR and therefore be used to study mRNA expression in numerous paraffin blocks stored in pathology archives. Our data are consistent with the low rate of PTC activation reported by other groups and also suggest that activation of the PTC oncogene is more common in patients with metastatic papillary thyroid cancer than in those with localized disease. Because long term survival rates are poor in metastatic papillary thyroid cancer, activation of the PTC may be an important molecular marker for prognosis. Activation of the PTC oncogene is the first molecular abnormality reported in papillary thyroid cancer that is associated with a definite clinical outcome.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, GASTROENTEROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 90/098	**Status:** Completed
Title: Does Laparoscopy Add to the Diagnosis of Nonfocal Liver Disease?		
Start Date: 08/17/90	**Est. Completion Date:** Apr 92	
Department: Medicine/Gastroenterology	**Facility:** MAMC	
Principal Investigator: MAJ Michael F. Lyons II, MC		
Associate Investigators: MAJ Amy M. Tsuchida, MC	CPT Robert J. Lodato, MC MAJ Gregory E. Schlepp, MC	
Key Words: liver disease,laparoscopy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To determine the diagnostic utility of laparoscopy in the evaluation of nonfocal liver disease and to compare the diagnostic accuracy (in the evaluation of diffuse liver disease) of a pinch biopsy to that of a core biopsy, both via laparoscopy.

Technical Approach: Fifty adult patients with elevated liver enzymes for >3 months and no prior liver disease or biopsies will be studied. Before entry patients will have a standard laboratory workup, abdominal CT and/or ultrasound and liver spleen scan. A detailed history and family history will be obtained. Laboratory testing to include liver function tests, total protein and albumin, glucose, iron, ferritin, TIBC, SPEP, HBV, AMA, ANA, HIV serology, CBC PT/PTT, and serum bile acids will be obtained and recorded. Two or more non-invasive imaging studies (LSS, U/S, or CT) will be done. Immediately prior to laparoscopy, one or more of the associate investigators will assess the non-invasive work-up and form a prelaparoscopy diagnosis for four groups: cirrhosis, chronic hepatitis, normal, and fatty change. Laparoscopy with biopsies will be done, using standard technique. During the laparoscopy (before biopsy results are known), the associate investigators will make a diagnosis based on the non-invasive workup and laparoscopic findings. The two diagnoses pre and post-laparoscopy will then be compared with the histologic diagnosis. The core biopsy histologic diagnosis will be compared to the pinch biopsy result. Four fold tables for chi square analysis will be used to compare the sensitivity, specificity, and positive and negative predictive values of the pre and post-laparoscopic diagnoses. Chi square analysis will be used to compare the accuracy of the pinch biopsy to that of the core biopsy.

Progress: Fifty subjects were entered which completed data collection. A paper was presented to American College of Gastroenterology, 56th Annual Scientific Meeting.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/051 **Status:** Terminated

Title: A Long-Term Screening Project for the Prevention of Adenocarcinoma of the Esophagus in Patients with Barrett's Esophagus, Intestinal Metaplasia of the Stomach and Partial Gastrectomy for Peptic .....

Start Date: 05/03/91 **Est. Completion Date:** Indef.

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

Principal Investigator: MAJ Michael F. Lyons II, MC

Associate Investigators:
MAJ Gregory E. Schlepp, MC
MAJ Mark D. Brissette, MC
MAJ Amy M. Tsuchida, MC
COL Michael J. Carlon, MC

Key Words: cancer:esophagus,Barrett's,stomach

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 07/02/92

Study Objective: To prospectively follow patients with Barrett's Esophagus, intestinal metaplasia of the stomach, and post partial gastrectomy in an attempt to identify precancerous or early cancerous changes in tissues utilizing histology, flow cytometry, immunochemistry, and cytogenetics.

Technical Approach: Approximately 200 subjects with a diagnosis of Barrett's esophagus, gastric intestinal metaplasia by prior upper endoscopic biopsy or by history of partial gastrectomy for 10 or more years will be studied. After visualizing the esophagus, stomach, and duodenum, biopsies will be obtained from these areas as dictated by the subject's diagnosis. One half of the biopsy specimen will be processed for histology, classified according to the type of mucosa present, and designated negative, indefinite, or positive for dysplasia. Specimens forwarded for flow cytometry will be processed in the routine fashion. Data will be gathered and analyzed by an on-line computer. Cell cycle parameters will be analyzed using a first order polynomial S phase. By this nonlinear least squares curve-fitting technique, the G1/G0 (2N) and G2/M peaks (4N) are fit using normal distributions and the region between these two peaks is allotted to cells in DNA synthesis (S phase). Aneuploid peaks will be fit by inclusion of additional Gausian peaks in the least squares analysis. If patients are identified as having indefinite or definite dysplasia or if they have increased S or G2/M flow cytometry fractions (S>7%, G2>6%) they will be contacted to undergo repeat endoscopy at three to six month intervals for closer surveillance. Otherwise, patients will undergo annual evaluation as outlined above. At the time of endoscopy, subjects will have serum drawn for analysis of mucin core protein and p53 antigen antibody production by immunochemical methods. Patient histology, immunochemistry, cytogenetics, and flow cytometry data will be followed over time. These data will be compared to determine if there is a correlation using Student's unpaired t-test to predict dysplasia or malignancy.

Progress: The study was never implemented because of lack of funding for flow cytometry.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/004 **Status:** Terminated

Title: A Multicenter, Randomized, Double-Blind, Placebo Controlled, Evaluation of Healing & Relapse Rate Following Oral GR122311X Compared With GR885202X, Ranitidine & Placebo in Patients With Duodenal Ulcer

Start Date: 10/02/92 **Est. Completion Date:** Jun 93

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

Principal Investigator: MAJ Michael F. Lyons II, MC

Associate Investigators:
MAJ Gregory E. Schlepp, MC
MAJ Amy M. Tsuchida, MC
MAJ William A. Pearce, MC

Key Words: duodenal ulcer,ranitidine bismuth citrate

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

Study Objective: To compare overall success rates of GR122311X 400 mg bid, GR88502X 240 mg bid, Ranitidine 150 mg bid, and placebo.

Technical Approach: Patients must be 18 to 80 years of age, have one endoscopically diagnosed duodenal ulcer measuring at least 0.5 cm but less than or equal to 2.0 cm in the largest diameter, and be an ambulatory outpatient.

The study will be conducted in two parts. Part 1 will be a four or eight week treatment phase, with assessments at baseline, Week 2, Week 4 and if required Week 8. Part 2 will be a 24 week post-treatment observation phase with assessments at 4, 8, 12, and 24 weeks after treatment ends.

Part 1 All patients will receive 4 weeks of treatment. At week four, patients will have an endoscopic examination. Unhealed patients will continue in the study for an additional four weeks of treatment and then return to the clinic for a Week 8 evaluation including endoscopy. Patients unhealed after 8 weeks of treatment will be withdrawn from the study.

Part 2 Patients with healed ulcers at Week 4 or Week 8 will enter the post-treatment phase. Patients will not be administered any study drug during this period but return for endoscopic examination and safety visits at 4, 8, 12 and 24 weeks after the end of treatment.

All patients will receive Maalox antacid tablets for pain relief, as needed, during Part 1 of the study and for persistent pain during Part 2.

Progress: The study was closed by the sponsor before HSC approval was obtained.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/005 **Status:** Terminated

Title: A Multicenter, Randomized, Double Blind, Placebo Controlled Evaluation of Healing & Relapse Rates Following Oral GR122311X Compared With GR88502X, Ranitidine & Placebo in Patients with Benign...

Start Date: 10/02/92 **Est. Completion Date:** Jun 93

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

Principal Investigator: MAJ Amy M. Tsuchida, MC

Associate Investigators:
MAJ Gregory E. Schlepp, MC
MAJ Michael F. Lyons II, MC
MAJ William A. Pearce, MC

Key Words: gastric ulcer,ranitidine,bismuth,citrate

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

Study Objective: To evaluate healing and relapse rates in patients with benign gastric ulcers following eight weeks treatment with either GR122311X 400 mg bid, GR88502X 240 mg bid, Ranitidine 150 mg bid, or placebo.

Technical Approach: This is a randomized, double-blind, placebo-controlled, parallel group study. Patients included will be 18 to 80 years of age with one gastric ulcer of at least 0.5 cm but less than or equal to 2.0 cm in the longest diameter.

The study will be conducted in two parts. Part 1 will be an eight week treatment phase with assessment at baseline, Week 4 and Week 8. During the treatment phase the patients will be randomized to receive one of the study medications, returning for evaluation and endoscopy at Week 4 and Week 8. Patients unhealed after 8 weeks of treatment will be withdrawn from the study.

Part 2 will be a 24 week post-treatment observation phase with assessments at 4, 8, 12, and 24 weeks after treatment ends. Patients developing an ulcer will be discharged from the study at the time of the corresponding endoscopy.

All patients will receive Maalox antacid tablets for pain relief, as needed, during Part 1 of the study and for relief of persistent pain during Part 2.

Progress: The sponsor closed the study to patient entry before HSC approval was obtained.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/100 **Status:** On-going

Title: A Long Term Safety Evaluation of Kapanol and MS Contin in Patients With Moderate to Severe Cancer Pain

Start Date: 05/07/93 **Est. Completion Date:** Jun 94

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

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
LTC Howard Davidson, MC
MAJ Mark E. Robson, MC
CPT James S. D. Hu, MC
MAJ Richard C. Tenglin, MC
MAJ Luke M. Stapleton, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:pain relief,Kapanol,MS Contin

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

Study Objective: The purpose of this open-label extension study is to compare the long-term safety and efficacy of Kapanol (sustained-release morphine sulfate) capsules to MS Contin (controlled release morphine sulfate) tablets in patients with moderate to severe cancer pain. The primary parameters will be a comparison of morphine-related side effects, laboratory values, adverse events, and pain control.

Technical Approach: Ambulatory inpatients or outpatients with moderate to severe chronic pain due to disseminated or locally invasive cancer who were randomized into study CDD-14556 entitled "A Randomized, Double-Blind, Parallel Groups Study Comparing the Efficacy and Safety of Kapanol to MS Contin in the Management of Patients with Moderate to Severe Cancer Pain" are suitable for entry into this trial.

The final visit procedure results for CDD-14556 will be used for the initial visit for this extension trial. After providing written informed consent, each patient will be randomized to one of the following three treatment groups for initial treatment in this trial: A. Kapanol capsules - once every 12 hours (investigators may consolidate the total daily dose into one dose taken every 24 hours at their discretion if clinically appropriate); B. Kapanol capsules - once every 24 hours (investigators may divide this total daily dose into two q12h doses if clinically appropriate; C. MS Contin tablets - once every 12 hours

The dose of morphine selected at the initial visit will be based on the total daily dose of morphine (scheduled dose plus rescue) required during CDD-14556. Dose adjustments will be allowed during the trial. IRMS oral tablets will be available as rescue medication during this trial as needed without protocol restriction for all study patients.

Blood and urine specimens for laboratory analysis will be collected at intervals throughout the trial to insure patient safety.

The patient and the investigator will provide assessments of the patient's pain control at the time of each clinic visit.

Progress: The study has just started. There have been no significant findings.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/099 **Status:** On-going

Title: A Randomized, Double-Blind, Parallel Group Study Comparing the Efficacy and Safety of Kapanol to MS Contin in the Management of Patients With Moderate to Severe Cancer Pain

Start Date: 05/07/93 **Est. Completion Date:** Dec 93

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

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
LTC Howard Davidson, MC
MAJ Mark E. Robson, MC
CPT James S. D. Hu, MC
MAJ Richard C. Tenglin, MC
MAJ Luke M. Stapleton, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:pain relief,severe,Kapanol,MS Contin

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

Study Objective: The objectives of this trial are to compare the safety and efficacy of Kapanol sustained-release morphine sulfate capsules given every 12 hours and every 24 hours, to those of MS Contin controlled-release morphine sulfate tablets given every 12 hours in patients with moderate to severe cancer pain requiring treatment with opoid analgesics.

Technical Approach: Ambulatory inpatients or outpatients with moderate to severe chronic pain due to disseminated or locally invasive cancer who require narcotic analgesics for pain management will be invited to participate in this trial. After providing informed consent, each patient will be titrated to a stable dose of commercially available immediate-release morphine sulfate (IRMS) oral solution during the 3 to 14 day Lead-In Period. After reaching a stable total daily dose of morphine, each patient will be randomized to one of the following four groups as follows: A. Kapanol capsules - once every 24 hours; B. Kapanol capsules - once every 12 hours; C. MS Contin tablets - once every 12 hours; D. placebo to match active treatments.

Doses of the active treatments will be based on the total daily dose of IRMS after stabilization during the Lead-In Period. IRMS oral tablets will be available as rescue medication during the Treatment Period, as needed.

After seven days (± one day) of treatment, each patient will provide pain assessments in a diary card immediately before the morning dose, every two hours for 12 hours, and at 24 hours after the morning dose.

Progress: Enrollment has just begun. There have been no significant findings.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/009 **Status:** On-going

Title: Fluconazole Versus Amphotericin B as Empiric Therapy in Febrile, Neutropenic Patients. University of Washington

Start Date: 12/06/91 **Est. Completion Date:** Indef.

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

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC

Key Words: neutropenia,fluconazole,amphotericin B

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1836.00	**Periodic Review:** / /

Study Objective: To compare the efficacy of fluconazole versus amphotericin B as empiric antifungal therapy in neutropenic patients with continued fever following initiation of empiric antibacterial therapy and to compare the toxicity profile of fluconazole and amphotericin B in these patients.

Technical Approach: Patients (n=48) with no documented bacterial source of infection who fail to defervesce after 72 hours of antibacterial antibiotic will be randomized into three groups. Group I patients with normal renal function will receive intravenous fluconazole, 800 mg day 1, followed by 400 mg IV daily Group 2 patients with normal renal function will receive oral fluconazole, 800 mg day 1, followed by 400 mg daily and Group 3 patients with normal renal function will receive IV amphotericin B, 0.25 mg/kg Day 1, followed by 0.6 mg/kg/day. Appropriate premedication (e.g., hydrocortisone, meperidine, diphenhydramine, acetaminophen) will be administered as needed. Dosage will be adjusted appropriately (by extent of disease) for renal impairment. Patients who defervesce following initiation of antifungal therapy and in whom no infection is documented will continue therapy until bone marrow recovery occurs. Patients who remain febrile following initiation of antifungal therapy will be monitored closely with repeat cultures, chest radiographs, and other studies as indicated. If no infection is documented, patients will continue receiving antifungal therapy until afebrile and the ANC is above 500/mm^3 for two consecutive days. If a fungal infection is documented. patients receiving an antifungal drug to which the organism is sensitive will continue receiving that drug. If the organism is not sensitive to the study drug assigned to the patient, the study will be terminated and an appropriate antifungal agent begun. In either case, therapy will be continued for a length of time consistent with medically accepted guidelines. Dichotomous variables will be analyzed using either the chi square test or Fisher's exact test. Continuous variables will be analyzed using either ANOVA or T test for comparison. The results from patient randomization will be analyzed to ensure no significant differences in patient populations due to the randomization process alone. Beta errors will also be calculated.

Progress: There has been no significant progress on this project due to slow enrollment.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/001 **Status:** On-going

Title: The Role of Bone Marrow Micrometastases in Breast Cancer. A Two-Year Study funded by the U.S. Army Medical Research and Development Command

Start Date: 10/02/92 **Est. Completion Date:** Dec 94

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

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ George F. Hodeges, MC
LTC Howard Davidson, MC
MAJ Mark E. Robson, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT Katherine H. Moore, MS
MAJ Mark D. Brissette, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Timothy P. Rearden, MC
MAJ Richard C. Tenglin, MC

Key Words: cancer:breast

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

Study Objective: To determine if hormonal or chemotherapy will eradicate bone marrow micrometastases (BMM) in women with breast cancer and to determine if failure to eradicate BMM with system therapy is a prognostic factor for decrease disease-free survival.

Technical Approach: Women who are: (1) between the ages of 18 and 70 years with newly diagnosed or recurrent breast cancer and (2) will be receiving hormonal or chemotherapy will be invited to participate in this study. Bone marrow samples will be aspirated from each posterior iliac crest. The samples will be diluted with phosphate buffered saline (PBS) and layered onto a Ficoll-Hypaque density gradient and centrifuged. The cells at the interface layer will be collected and washed with RPMI-1640 plus fetal calf serum. The cells will then be suspended in PBS and placed, by single drops, onto microscope slides and dried. One slide will be stained with Wright's stain for cytological examination. Ten to twelve slides from each patient will be fixed with 100% ethanol and used for immunofluorescence studies.

The anti-cytokeratin monoclonal antibody AE-1 will be titered against the MCF-7 breast cell line and the optimal concentration used against the bone marrow samples to detect breast cancer cells.

Tumor staging, histology, and hormonal status will be obtained from pathology and surgical reports. Hospital and clinic records will be reviewed to obtain data on the patient's clinical course to include treatment, disease free survival (DFS) and overall survival (OS). The Chi-squared test will be used to evaluate the relationship between the presence of BMM and other known prognostic factors. Standard survival analyses will be used to evaluate the relationship between BMM, DFS and OS.

Progress: Six patients entered. The protocol has been modified to allow women who are going to surgery to have the bone marrow aspirate done while anesthetized for surgery.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/130 **Status:** On-going

Title: Interaction of Breast Cancer and Bone Marrow Cells in Long-Term Culture: Effects on Cell Growth, Growth Factor, and Cytokine Production

Start Date: 07/02/93 **Est. Completion Date:** Mar 97

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

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Richard R. Gomez, MC
LTC Howard Davidson, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Mark D. Brissette, MC
MAJ Patrick L. Gomez, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:breast,cell:bone marrow,cell:growth,cell:cytokine

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

Study Objective: To study the interaction between breast cancer cells and bone marrow cells in a novel long term bone marrow culture system and the effects on cell growth, growth factors and cytokine production.

Technical Approach: This collaborative effort, with the American Lake and Seattle Veterans Administration Hospitals, will study women between the ages of 18 and 78 years with newly diagnosed or recurrent breast cancer. These patients must have sufficient tumor material remaining after all necessary tissue is used for pathologic diagnostic tests to inoculate the Long Term Bone Marrow Culture system and conduct baseline oncogene studies. The overall goal of this project is to establish co-cultures of bone marrow and tumor cells in perfusion bioreactors, examine the cultures for production of tumor and hematopoietic cells, and to characterize the resulting biologic effects of the cellular elements, specifically, compared to bioreactors with only normal bone marrow cells: (1) are there changes in the normal expression of Her-2/neu, p53, and nm23; (2) are there changes in the production of PDGF, bFGF, and IGF; and (3) are there changes in the production of TGF-beta, TNF-alpha, and MIP-1a.

Progress: Awaiting funding before the study begins.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/103 **Status:** On-going

Title: Dolasetron Mesylate Protocol MCPR 0031: A Double Blind, Randomized, Parallel Study of the Antiemetic Effectiveness of IV Dolasetron Mesylate vs IV Zofran in Patients Receiving Cisplatin Chemotherapy

Start Date: 09/04/92 **Est. Completion Date:** Oct 93

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

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: MAJ Kenneth A. Bertram, MC
CPT Curtis S. Hansen, RPH, MSC

Key Words: cisplatin,dolasetron mesylate,zofran,antiemetics

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

Study Objective: To compare the effectiveness of a 2.4 mg/kg single IV dose of dolasetron mesylate to a 32 mg single IV dose of ondansetron for complete prevention of emesis due to >70 mg/m^2 of cisplatin chemotherapy and to compare the effectiveness of a 1.8 mg/kg single IV dose of dolasetron mesylate to a 32 mg single IV dose of ondansetron and to the 2.4 mg/kg single IV dose of dolasetron mesylate for complete prevention of emesis due to >70 mg/m^2 of cisplatin chemotherapy.

Technical Approach: This is a double-blind, randomized, stratified, parallel, multicenter study in which patients with confirmed malignant disease will receive either 1.8 mg/kg or 2.4 mg/kg of dolasetron mesylate or 32 mg of ondansetron. Six hundred patients (20 at MAMC) will be prospectively stratified as to cisplatin dose, i.e., 300 patients receiving 70 to 90 mg/m^2 versus 300 patients receiving >90 mg/m^2. The activity and duration of drug action will be evaluated for 24 hours. If the patient experiences at least three emetic episodes during the 24 hour evaluation period after the start of chemotherapy or request alternative antiemetic therapy, the investigator will initiate escape medication according to institutional practice. Safety, tolerance, and patient satisfaction will also be monitored.

Progress: We are continuing to enroll patients into the study. Data collection continues and analysis will be completed by the sponsor.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/072 **Status:** On-going

Title: Prognostic Significance of Oncogene Amplification and Expression in Human Breast Cancer

Start Date: 06/05/92 **Est. Completion Date:** Jun 93

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

Principal Investigator: MAJ Robert B. Ellis, MC

Associate Investigators:
CPT Robert M. Tuttle, MC
MAJ Richard R. Gomez, MC
CPT Katherine H. Moore, MS

Key Words: cancer,breast,oncogene amplification

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

Study Objective: To clarify the role of oncogenes and their products in the process of malignant transformation as well as determining if an oncogenetic profile of a particular cancer will provide clinically useful prognostic information.

Technical Approach: Although the presence of oncogenes in breast cancer is well documented, the clinical significance of these findings is uncertain. Furthermore, the role of oncogenes in premalignant lesions has not been determined. Many investigators speculate that the presence of certain oncogenes and their products may predict not only clinical course but also the tumor's response to both hormonal and chemotherapeutic intervention. This study will examine the significance of the amplification and expression of the oncogenes Her-2/neu, int-2, nm23, and hst-1 by screening paraffin embedded breast tissues collected over the last ten years at Madigan. Normal breast tissue, benign breast lesions thought to have a high malignant potential, carinoma in situ, and frank breast cancer will be examined. This information will be compared with the patient's medical record in an effort to associate oncogene presence or function with medical outcome. The presence of these oncogenes in the DNA, as well as the expression of the oncogene's mRNA will be determined. Immunohistochemistry will be used to prove for the presence of the specific oncogene proteins. This work will clarify the role of oncogenes in the process of malignant transformation and lead to a better understanding of whether the oncogene profile of a particular breast cancer can provide prognostic information useful in the clinical management of patients with breast cancer.

Progress: The preliminary work of isolating mRNA from paraffin embedded breast tissue to include standardization of procedures is complete. 36 breast cancer samples from males treated in DoD facilities have been collected. We have also acquired and loaded into the database the basic diagnostic and treatment/survival data from the male breast cancer cases seen in DoD facilities.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/070 **Status:** On-going

Title: Comparison of TLC D-99 Doxorubicin Liposome Injection versus Doxorubicin Injection in Metastatic Breast Cancer

Start Date: 06/05/92 **Est. Completion Date:** Aug 95

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

Principal Investigator: MAJ Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
COL Joseph A. Paris, MC
MAJ Paul C. Sowray, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC

Key Words: cancer,breast,TLC D-99 doxorubicin liposome,doxorubicin

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

Study Objective: To compare the cardiac safety of TLC D-99 (liposomal doxorubicin) with free doxorubicin using echocardiography, left ventricular ejection fraction measurements, and endomyocardial biopsies and to compare the efficacy of TLC D-99 with free doxorubicin HCL in the treatment of metastatic breast cancer.

Technical Approach: This will be a multicenter, randomized, parallel, open, comparative study in patients with metastatic breast cancer to compare the safety and efficacy of TLC D-99 and free doxorubicin HCl. Third party blinding will be implemented for evaluation of all radionuclide cardiac angiographies and cardiac biopsies. Growth Colony Stimulating Factor (G-CSF) therapy will be routinely given to both treatment groups in an effort to reduce the myelosuppression associated with doxorubicin administration. Therapy with either treatment will begin at 75 mg/m^2. Dose escalation and reduction steps will be done based on patient tolerance of the drug. Separate randomization series will be used for patients with and without previous exposure to doxorubicin. Cardiac toxicity will be monitored by serial EKG's, echocardiograms, and resting and stress radionuclide cardiac angiography. To document pathologic changes seen with doxorubicin exposure, endomyocardial biopsies will be collected at a cumulative dose of 450 mg/m^2. With any clinical or laboratory evidence of cardiac dysfunction or with progressive disease, treatment will be discontinued and the patient offered an alternate treatment program.

Progress: One patient was enrolled with complete remission to single agent adriamycin. The patient was taken off the agent due to cardiac toxicity judged by endomyocardial biopsy and symptoms.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/121 **Status:** On-going

Title: Clinical Significance of Lymphoid Aggregates in Bone Marrow

Start Date: 05/07/93 **Est. Completion Date:** Oct 93

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

Principal Investigator: CPT James S. D. Hu, MC

Associate Investigators:
MAJ George F. Hodeges, MC
MAJ Luke M. Stapleton, MC
M. D. Brisette

Key Words: bone marrow,lymphoid aggregates

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

Study Objective: To determine the clinical significance of lymphoid aggregates in bone marrow biopsy specimens.

Technical Approach: Approximately 1000 consecutive bone marrow biopsy specimens will be analyzed for the presence of lymphoid aggregates by a hematopathologist who will be blinded to the patient's diagnosis. The lymphoid aggregates will be described by size (in microns), density, morphology, cytology, and distribution. After the clinical diagnosis is matched to the corresponding bone marrow specimen, analysis will be done to determine those features that correlate with a clinically benign or malignant lymphoid aggregate. Logistic regression and tabulation of above variables will be performed.

Progress: Review of 388 consecutive bone marrow biopsy specimens. Lymphoid aggregates were identified in 64. Of these, 20 were characterized by size, morphology, density, pattern of abuttment, and cytology. Analysis of 2 year data with statistical analysis using chi-square revealed significant correlations with density and abuttment.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/031 **Status:** Completed

Title: A Multicenter Clinical Study Using A Technetium-Labelled Monoclonal Antibody for Imaging Patients With Small Cell Lung Cancer

Start Date: 12/04/92 **Est. Completion Date:** Indef.

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

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
COL Stanton R. Brown, MC
LTC John M. Bauman, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
CPT Jennifer L. Cadiz, MC
MAJ Stephen E. Budd, MC
LTC Terry R. Minton, MC

Key Words: cancer:lung,monoclonal antibody

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

Study Objective: To evaluate the normal biodistribution and tumor localization of 99m-TC labelled NR-LU-10 monoclonal antibody prepared with a NeoRX "OncoTrac" kit obtained from a new manufacturer. The results will be compared with historical results from studies with similar kits from a previous manufacturer.

Technical Approach: In-patients with small cell lung cancer will undergo standard staging to determine extent of disease. In addition, they will undergo a single scan using 5.0 - 10.0 mg NR-LU-10 (FAB) labeled with 15 - 30 mCI 99mTc, diluted in 30 mL of normal saline and administered by intravenous injection. Images will be obtained with a gamma camera 14 - 17 hours after injection. The data will be acquired, processed, and stored on a dedicated computer. If the antibody images reveal an abnormality in an otherwise unsuspected area, further diagnostic studies to evaluate this will be performed. Biopsies will be performed when feasible for histologic and immunohistochemical analysis. No therapeutic decisions will be made on the results of the scan.

Progress: Three patients have completed the study. Data forwarded to the sponsor and FDA application is in progress.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/133 **Status:** Terminated

Title: A Multicenter Clinical Study to Compare Imaging of Non-Small Cell Lung Cancer With A Technetium-Labelled Monoclonal Antibody Produced by Two Different Manufacturers

Start Date: 07/02/93 **Est. Completion Date:** Aug 94

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

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC John M. Bauman, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: monoclonal antibody,cancer:non-small cell lung

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review:	/ /

Study Objective: To compare the normal biodistribution and tumor localization of 99m-TC labelled NR-LU-10 Fab monoclonal antibody prepared with a NeoRx "OncoTrac" kit produced by two different manufacturers.

Technical Approach: In-patients with non-small cell lung cancer will undergo standard staging to determine extent of disease. This staging will, at a minimum, consist of a CT scan of the chest, liver, and adrenals. In addition, patients will undergo two scans 3 - 7 days apart using the technetium-labelled monoclonal antibody NR-LU-10. The two scans will be performed with kits from two different manufacturers. Sites of disease as determined by the monoclonal antibody scans will be compared with each other and with those delineated by conventional staging techniques. No therapeutic decisions will be made on the basis of the investigational scan.

Progress: Study closed by sponsor prior to HSC approval.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/105 **Status:** On-going

Title: A Pilot Study of Granulocyte Colony-Stimulating Factor (G-CSF, Filgrastim) in the Empiric Treatment of Febrile Neutropenia Due to Myelosuppressive Chemotherapy

Start Date: 05/07/93 **Est. Completion Date:** May 94

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

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
CPT Steven E. Brilliant, MC
CPT Diana S. Willadsen, MC
CPT Curtis S. Hansen, RPH, MSC

Key Words: neutropenia,GCSF,chemotherapy

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

Study Objective: 1. To determine the median duration of neutropenia after admission for neutropenic fever in patients at Madigan Army Medical Center. 2. To determine whether a policy of delaying G-CSF therapy for 72 hours after admission with neutropenia and fever leads to prohibitively greater morbidity than a strategy of immediate administration of G-CSF.

Technical Approach: Patients with a non-myeloid malignancy who have received myelosuppressive chemotherapy and are admitted to Madigan Army Medical Center with a diagnosis of febrile neutropenia will be entered onto the study at the time of admission. Every attempt will be made to enroll consecutive patients with this diagnosis. Patients who received prophylactic G-CSF during the cycle in which they are admitted will be excluded, as will patients who are neutropenic before they receive chemotherapy. The first 10 patients (group I) will be observed to determine the duration of the nadir (absolute neutrophil count under $1000/mnm^3$) after admission. The second 10 patients (group II) will receive G-CSF at a dose of 300 mcg/day by subcutaneous bolus if they fail to defervesce after 72 hours of broad spectrum empiric antibiotic therapy. Dose escalation will be instituted after 5 days of G-CSF therapy if criteria for discontinuation are not met. The last cohort of 10 patients (group III) will receive G-CSF within 12 hours of admission at the same dose as group II. The dose escalation scheme will be the same as for group II. Differences in mean and median nadir durations between the three groups will be evaluated by use of ANOVA analysis. Outcome of infection and in-hospital mortality will also be evaluated

Progress: Seven patients have been entered to date. Data has not been analyzed due to ongoing accrual.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/082 **Status:** Terminated

Title: A Pilot Study of Carboplatin and Daily Oral Etoposide in the Treatment of Advanced Non-Small Cell Lung Cancer

Start Date: 06/15/90 **Est. Completion Date:** Jun 93

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

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC

Key Words: cancer:lung:non-small cell,carboplatin,etoposide

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$3000.00	Periodic Review:	/ /

Study Objective: To evaluate the effects of carboplatin and oral etoposide in non-small cell lung cancer with respect to response rate, toxicities, and survival.

Technical Approach: Thirty subjects with histologic evidence of non-small cell lung cancer and no prior chemotherapy will be studied. Patients with CNS metastases and simultaneous neoplasms at another site will be excluded. Patients will receive chemotherapy in 28 day cycles. Each cycle will start on day 1. Carboplatin IV will be given on days 1 and 8. The total dose for both days will be determined by the formula 5 x (creatinine clearance [ml/min] + 25). Etoposide will be given 50 mg/m^2 po days 1-14. If cycle 1 nadir AGC is >1000/microL and nadir platelet count is >75,000/microL, the patient will receive etoposide, 50 mg/m^2 po days 1-21 for future cycles. Patients will be evaluated for response after two cycles. Those who have at least a 25% reduction in the product of the bidimensional measurement of the marker lesion will receive two more cycles of therapy and then stop all therapy. Those who do not have a 25% reduction in the cross-dimensional product will stop treatment. Those patients who have non-measurable disease will receive two more cycles if there has been no deterioration in the performance status otherwise, they will also stop therapy. Toxicities will be described as the frequency per patient on study and per cycle of treatment. Response rates will be described using standard criteria. Survival will be measured from study entry. Survival will be displayed graphically and described as duration of survival per quartile of patients.

Progress: No patients were entered in FY 93. Nine subjects have been previously entered. Protocol is terminated because PI has left the Army.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/007 **Status:** Terminated

Title: Treatment of Thrombocytopenia, Hemolytic Anemia, or Neutropenia with Ascorbic Acid

Start Date: 11/17/89 **Est. Completion Date:** Oct 91

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

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: ascorbic acid,thrombocytopenia,hemolytic anemia,neutropenia

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$585.00	**Periodic Review:** / /

Study Objective: To determine if chronic thrombocytopenia, hemolytic anemia, or neutropenia can be improved by ascorbic acid therapy.

Technical Approach: Evaluation will be undertaken of patients who have had a severe cytopenia for at least 30 days and which is expected to continue for a prolonged period. Patients with thrombocytopenia will be evaluated in three categories: thrombocytopenia due to (1) sequestration, (2) production defect, and (3) peripheral destruction. Patients with hemolytic anemia will be evaluated in both immune mediated and non-immune mediated categories. Patients with neutropenia will also be evaluated in immune mediated or nonimmune mediated categories. Fourteen patients per disease category will be studied. Patients will receive ascorbic acid, 2 grams by mouth, daily. Therapy will be continued for as long as effective. It will be discontinued if there is no response after four months of therapy. Serum creatinine and CBCs will be obtained weekly once the clinical condition stabilizes. The clinician will see patients after each blood specimen is obtained to note response and to observe for side effects. Statistical considerations: Each patient will be assessed for the categorical response variable (no response, partial response, or complete response) and the observed event rates will be documented for each disease category with Kruskal-Wallis non-parametric one way analysis of variance to compare rates for different groups. Each patient will be assessed for the continuous response variable of WBC, hemoglobin, platelet count, and absolute lymphocyte count. Observed mean levels for each group will be compared at days 0 and 28 and at time of maximal response by one way analysis of variance. Patients found to be responsive will be evaluated in a non-blinded fashion for crossover to stopping treatment. The crossover treatment will be assessed by the clinical response of each patient. If the study is positive, it will be expanded to include a control group.

Progress: Only one patient has been entered, in FY 91. Protocol is terminated because PI has left the Army.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/021 **Status:** Terminated

Title: A Double Blind, Placebo Controlled, Parallel Group, Multicenter Study of the Use of Weekly Azithromycin as Prophylaxis Against the Development of Mycobacterium avium Complex Disease in HIV Infected...

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

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

Principal Investigator: LTC Ronald H. Cooper, MC

Associate Investigators: None

Key Words: HIV,Mycobacterium avium Complex Disease

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

Study Objective: To evaluate the safety and efficacy of azithromycin administered once a week in the prevention of disseminated mycobacterium avium complex (MAC) in severely immunocompromised HIV infected patients with a CD4 count <100/µl.

Technical Approach: This is a study of the efficacy of azithromycin as prophylaxis against disseminated MAC in HIV infected patients. Patients with confirmed HIV infection and CD4 counts <100/µl will be enrolled. Two blood cultures will confirm MAC bacteremia is not present and stool cultures will be used to document colonization status.

Patients will then be randomized to received either double-blind treatment with azithromycin 1200 mg or matched placebo as a single dose once a week for a minimum of eighteen months or until an end-point is reached (the occurrence of MAC bacteremia or recovery of MAC from normally sterile tissue). Patients who complete eighteen months of therapy will remain in the study until the last patient completes the study (a period expected to be up to 24 months). Patients will be evaluated every 4 weeks. Venous blood will be collected for hematology and biochemistry assessment and blood cultures. Stool cultures will be repeated every 3 months and CD4 counts will be determined every 6 months.

Efficacy will be determined by comparison of the numbers of patients who are removed from each treatment group during the study due to development of MAC bacteremia.

Progress: A decision was made not to procede with the study due to unresolved questions about the placebo arm and the fact that enrollment in this study might preclude patients from other studies that could potentially offer them greater benefit.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/099 **Status:** Completed

Title: Azithromycin in the Treatment of Nongonococcal Urethritis: A Multicenter Double-Blind, Double-Dummy Study Employing Doxycycline as A Comparative Agent

Start Date: 10/04/91 **Est. Completion Date:** Aug 93

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

Principal Investigator: LTC Ronald H. Cooper, MC

Associate Investigators: LTC Rodney A. Michael, MC

Key Words: nongonococcal urethritis,azithromycin,doxycycline

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To compare the efficacy and safety of azithromycin and doxycycline as treatment for nongonococcal urethritis in males.

Technical Approach: This will be a randomized, double-blind, double-dummy, comparative study of azithromycin versus doxycycline. Participants in this study will be patients with acute NGU. All patients must have a Gram-stained urethral smear with five or more PMNL per field (at least three non-adjacent oil immersion fields [X 1000]). All patients will be cultured at baseline. Those with positive cultures for gonorrhea will be discontinued from the study. All others, with or without positive cultures, will be followed. Patients will be randomly assigned in a 2:1 fashion to therapy with a single 1 gm oral dose of azithromycin or oral doxycycline, 100 mg b.i.d. x seven days, respectively, each with placebos for the alternate drug. Evaluations will be performed at baseline and at one and four weeks following completion of treatment. Laboratory safety profiles will also be obtained at these times. The primary measures of treatment efficacy will be the clinical and bacterial outcomes. The distribution of bacterial response will be compared between treatments using the chi-square statistic. If this test leads to a statistically significant result, the percentage of bacterial eradication will be compared using the Fisher Exact test. The percentage of clinical cures will be compared between treatments using the Fisher Exact test.

Progress: Data analysis is currently underway by the sponsor, and it is anticipated that this study will be presented at a future scientific meeting and that a manuscript will be prepared for publication.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/158	**Status:** On-going
Title: Study of Pyelonephritis in Women		
Start Date: 08/06/93	**Est. Completion Date:** Aug 95	
Department: Medicine/Infectious Disease	**Facility:** MAMC	
Principal Investigator: LTC Ronald H. Cooper, MC		
Associate Investigators:	MAJ Joseph T. Morris III, MC	
Key Words: pyelonephritis,women,ofloxacin,trimethoprim-sulfamethoxazole		

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

Study Objective: (1) To investigate the epidemiology of acute pyelonephritis in young women by administering a standardized questionnaire; (2) to investigate the pathogenesis of acute, uncomplicated pyelonephritis in young women by determining secretor status and comparing it to a control population; (3) to evaluate a new therapeutic regimen in the treatment of acute uncomplicated pyelonephritis in young women.

Technical Approach: Fifty female patients between the ages of 18-45 with symptoms of UTI for 7 days or less (flank pain, pyuria, >1000 CFU/ml uropathogen) will be randomized to receive trimethoprim-sulfamethoxazole DS for 14 days or ofloxacin 400 mg QD for 10 days. Follow-up will be on day 3, at termination of treatment, and at 14 and 28 after treatment. At each follow-up visit, the patient will be administered a follow up UTI questionnaire and asked to submit a clean catch urine specimen for analysis and culture.

A subset of 10 secretors and 10 non-secretors will be asked to undergo pelvic examinations at days 14 and 28 after treatment for the purpose of collecting vaginal cells for in vitro studies of cellular receptors. In these same groups, buccal cells will also be collected for the same purpose.

Demographics, treatment effectiveness, and incidence of secretor status will be compared using chi-square. Where required to do small sample size, the Fisher Exact Test will be substituted for the chi-square test.

Progress: The drug has been obtained and enrollment will begin soon.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/057	**Status:** On-going

Title: Swan Ganz Catheteers' Sepsis: Prospective Randomized Study of Replacement of Swan Ganz Catheters

Start Date: 03/05/93	**Est. Completion Date:** Jan 94
Department: Medicine/Internal Medicine	**Facility:** MAMC

Principal Investigator: CPT Kurt W. A. Grathwohl, MC

Associate Investigators:
CPT Bernard J. Roth, MC
CPT James W. Thompson, MC
LTC Anthony S. Sado, MC

Key Words: Swan Ganz catheters:replacement

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

Study Objective: To determine the incidence of infection in Swan Ganz catheter and central venous lines in patients who have lines replaced every three days, every seven days, and for the life of the catheter.

Technical Approach: This study will include all patients greater than eighteen years of age who require swan ganz or central venous catheterization for longer than seventy hours duration and hospitalization in the medical or surgical intensive care unit. This includes triple-lumen, single-lumen and/or pulmonary artery catheters. All sites of access will be included. Pregnant females will be excluded.

Patients will be randomized into one of three groups. Group 1 will have catheter percutaneous sites changed every 3 days to a new site (the current standard of care at MAMC). Group 2 will consist of patients who have the catheter sites changed every 7 days to a new site (The standard of care at some institutions). Group 3 will include patients who have the CVC left in place until it is no longer clinically needed.

Patients will have the CVC/swan ganz placed according to the current protocol for IV insertion. Using sterile technique to include sterile gloves the nursing personnel will change the initial dressings and subsequent dressings every 48 hours. If signs of infection or erythema are apparent the nurse will call the house officer who will evaluate the catheter for removal or necessity of skin culture per the diagnostic criteria. If the catheter is to be removed, the physician will culture the skin and a catheter segment.

The three groups of patients will be compared using the chi-square method. Subgroup analyses may be undertaken to assess different durations of catheter longevity, total parenteral nutrition, and underlying disease. Logistic regression will be used for risk factor infection analysis

Progress: Thirteen patients have been entered.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/035 **Status:** Completed

Title: Deletion From the MAMC Formulary of Nifedipine XL, Patient Effects and Side Effects

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

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

Principal Investigator: MAJ Duane J. Jeffers, MC

Associate Investigators: MAJ David L. Jones, MC
MAJ Francis J. Landry, MC

Key Words: nifedipine XL:pharmacy deletion

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

Study Objective: To access the effect of deleting Nifedipine XL on MAMC patients who were previously treated with that medication and to assess whether the manner in which Nifedipine XL was discontinued significantly affected patient acceptance of this change.

Technical Approach: Pharmacy data for a period of 3 months prior to the deletion of Nifedipine XL from the formulary at MAMC will be collected and from that group a subset will be selected to comprise an anticipated sample size of 200 patients. Numbered questionnaires will be mailed to those patients along with a detachable explanation sheet and a self addressed return envelope. Patients who do not respond to the initial questionnaire will be mailed another copy of that questionnaire and will be called (two attempts) to encourage response. Responses will be tabulated in spread sheet format.

Progress: Data collection and analysis have been completed. Of the agents monitored for two months after intervention the total numbers of prescriptions did not decrease, but total drug costs fell remarkably. Cost savings have been progressive with a 21% overall savings achieved (projected $943,000 per year). Results were presented in abstract form at local and national conferences. A manuscript is in progress.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/062 **Status:** Terminated

Title: Determination of the Sensitivity and Specificity of Light Reflection Rheography for the Diagnosis of Deep Venous Thrombosis in the Lower Extremity

Start Date: 06/16/89 **Est. Completion Date:** Jun 90

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

Principal Investigator: MAJ Duane J. Jeffers, MC

Associate Investigators:
Nancy N. Greenfield, M.S.
SGT Charles Adams
MAJ Dipankar Mukharjee, MC
Michael Bertoglio, B.S.
COL Charles A. Andersen, MC

Key Words: Light reflection rheography,venous thrombosis

Accumulative MEDCASE Cost:	**Est. Accumulative OMA Cost:**	**Periodic Review:**
$6000.00	$760.00	/ /

Study Objective: To measure the sensitivity and specificity of Light Reflection Rheography (LRR) relative to duplex scanning in the diagnosis of deep venous thrombosis (DVT) in the lower extremity.

Technical Approach: Two hundred (200) adult subjects referred for evaluation of suspected lower extremity DVT will be studied. Before entry, standard evaluations will be performed to include history and physical examination. Non-invasive venous evaluation and venography will be excluded. Patients will be tested for DVT using the established method of duplex scanning. Duplex scans will be interpreted and recommendations for patient care will be made based only on established methods. All patients will then be tested for DVT using LRR. Testing and interpretation of LRR will be done independently with the results of the duplex scanning blinded to the interpreter. The sensitivity and specificity of LRR relative to duplex scanning will be calculated.

Progress: Protocol terminated due to malfunction of the LRR device. The manufacturer has gone out of business and replacement parts are no longer available.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/163 **Status:** On-going

Title: Utility of the Physical Examination to Assess Extracellular Volume Status

Start Date: 09/03/93 **Est. Completion Date:** Jul 94

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

Principal Investigator: CPT Mary Jo K. Rohrer, MC

Associate Investigators:
MAJ Francis J. Landry, MC
CPT Paul A. Lester, MC
CPT Jeffrey R. Spina, MC
MAJ Howard M. Cushner, MC
MAJ Agnes K. Ohno, MC
CPT Eric J. Ormseth, MC
Undefined investigator

Key Words: physical examine,volume status

Accumulative		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$285.00	/ /

Study Objective: To determine the sensitivity, specificity, and predictive value of clinical assessment in determination of extracellular volume status.

Technical Approach: A prospective study of 100 medicine ward patients ages 18-80. Patients will have one or more of the following: hyponatremia, elevated BUN of > 20, or elevated serum creatinine (absolute > 1.5). Physical exam will be performed prior to subjective history or chart review and before fluid resuscitation. Chart review will allow ordering of any pertinent test not found. Fluid resuscitation with NS, 2 liters over 24 hours, will be initiation. Post infusion labs will be drawn within 12 hours of infusion. The same investigator will repeat the post-infusion physical exam.

Blinded review of lab data, collected pre- and post-infusion, by two boarded nephrologist will serve as "gold standard" of volume status (volume depleted or not volume depleted). Five of seven predefined criteria must be met to be deemed "volume depleted". Subjects not responding within the 12 hour post volume repletion will be reviewed at 24-72 hours for further correction.

Analysis consists of 2 x 2 contingency tables with independent variable (physical exam criteria) and dependent variable (volume status).

Progress: Four patients have been enrolled in the month since approval. No conclusion can be made at this time.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/066 **Status:** On-going

Title: A Prospective Study of Headache in Pregnancy

Start Date: 05/01/92 **Est. Completion Date:** Indef.

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

Principal Investigator: CPT Renee M. Bernier, MC

Associate Investigators: CPT Linda A. Marden, MC

Key Words: headache,pregnancy

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

Study Objective: To prospectively characterize incidence, type, and outcome of headaches during pregnancy by following women from early first trimester to delivery.

Technical Approach: At the first obstetrics visit, patients (aged 15-45) in the first trimester of pregnancy will fill out a questionnaire regarding previous history of headaches and other related disorders prior to pregnancy. The questionnaire will cover frequency, duration, location, severity, associated symptoms, and type of pain of their headaches and will also cover headache occurrence from time of conception to time of first obstetrics visit. Patients will fill out a short follow-up questionnaire once a month as well as at the six weeks post-delivery appointment. The data will be studied first to determine overall incidence of headache in the study population. Reports of headache will then be analyzed to determine the class of headache and the frequency of each type will be determined. Time of onset will be studied to establish if certain classes of headache are more likely to occur during a particular segment of pregnancy. Subjects with new onset of migraine during pregnancy will be studied separately to determine if this group differs in time of onset and character. Outcome of pregnancy will then be studied in the headache and non-headache groups. These groups will be compared using a chi-square analysis to establish if there is any statistically significant increased morbidity associated with headache. Final outcome will be expressed as either increased morbidity or no increased morbidity associated with headache. Subtypes of headaches will be looked at for evidence of increased risk of morbidity within a specific subtype and new onset migraine will be studied separately for evidence of increased risk.

Progress: Enrollment was completed in Nov. '92. Chart review of delivery records is currently being completed to determine if headache is associated with increased morbidity.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/080 **Status:** On-going

Title: A Randomized Double-Blind, Cross-Over, Placebo-Controlled Clinical Trial of D-alpha-Tocopheryl Acetate (Vitamin E) as Add-On Therapy for Epilepsy in Adults

Start Date: 04/02/93 **Est. Completion Date:** Dec 94

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

Principal Investigator: LTC William L. Clayton III, MC

Associate Investigators:
CPT Curtis S. Hansen, RPH, MSC

Key Words: D-alpha-tocopheryl acetate,vitamin E,epilepsy

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

Study Objective: To prospectively determine the effect of Vitamin E on seizure control in adults with frequent seizures.

Technical Approach: Volunteers of either sex who are over 18 years of age with a seizure disorder requiring treatment with antiepileptic drugs will be included in this study. Patients will be requested to keep a seizure calendar which will be reviewed monthly. After an observation period of 3 months, used to calculate seizure frequency, the pharmacy will issue either Vitamin E or placebo to be taken in addition to standard antiepileptic therapy. After 6 months the pharmacy will cross over the placebo/Vitamin E groups. At the end of 9 months the study will be discontinued. The patients will be informed of the results of the study at its completion. Any patient who benefitted from Vitamin E will have the option of continuing therapy.

Statistical analysis will be by paired T-test for total number of seizures during the treatment period.

Progress: This project is awaiting funding.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/050 **Status:** On-going

Title: Effects of Valproic Acid on Semen Parameters in Male Epileptics

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

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

Principal Investigator: LTC William L. Clayton III, MC

Associate Investigators:
LTC (P) Robert E. Jones, MS
James R. Wright, M.T.
COL Lawrence A. Marden, MC
CPT Katherine H. Moore, MS
Louis A. Matej, B.S.

Key Words: epilepsy,semen parameters,valproic acid

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To prospectively determine the incidence of abnormalities in the semen of epileptic men who are taking valproic acid for seizure prophylaxis and to assess the effects of incubating valproic acid with sperm from nonepileptic donors in vitro.

Technical Approach: Valproic acid, a frequently used antiepileptic, may be linked to a reduction in sperm numbers and sperm function. This possible association is based upon a few case reports and scattered animal studies. In this prospective study, 50 men will be asked to provide two to three ejaculates every three months for one year. These samples will be reviewed for morphology and sperm counts as well as analyzed by computer to assess a variety of motility parameters. Items of particular importance during the computerized evaluation will include morphometric observations as well as movement parameters such as the amplitude of lateral head displacement and swimming velocities. Fixed, stained slides for subjective interpretatin of morphology will also be obtained. In addition, the effects of valproic acid on sperm motility and sperm long chain fatty acid:coenzyme A ligase [AMP] will be measured in vitro. The in vitro studies will be conducted using normal semen samples discarded from the clinical semen analysis lab. Sperm concentrations will be handled using a repeated measures ANOVA to determine statistical significance.

Progress: Only one subject has consented for sperm analysis. He showed a 30 % drop in motility. This suggests that we should continue the study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/094 **Status:** Completed

Title: Effects of Carnitine on Measures of Cognition, Mood, and Sleep in Adolescents with Epilepsy Treated with Valproate

Start Date: 09/04/92 **Est. Completion Date:** Dec 92

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

Principal Investigator: LTC Joseph P. McCarty, MC

Associate Investigators: None

Key Words: epilepsy,carnitine,adolescents

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

Study Objective: To evaluate the effects of L-Carnitine therapy on energy levels and general sense of well-being in adolescent patients who have been previously diagnosed with epilepsy and who are currently receiving valproate as a treatment and to correlate any changes in measures of energy and general well-being with physiologic changes attributable to carnitine.

Technical Approach: Adolescent patients with epilepsy who are currently receiving valproate for control of seizures and who are presently under good control will be eligible for this study. Studies have indicated that one of the metabolic side effects of valproate is lowering of plasma carnitine concentration with a possible negative impact on fatty acid metabolism and resultant decrease in mood and energy levels. Patients will have baseline measures of general sense of well-being and cognition. They will then take carnitine or a placebo for six weeks. At the end of the six week period, data will be collected regarding energy levels and general sense of well-being. The patients will then switch to the opposite experimental treatment for another six week period. At the end of the second six week period the same data will be collected regarding energy level and general sense of well-being. For statistical analysis of psychological measures, changes in mood states and in cognitive scores from period 1 to period 2 in Group A (carnitine) will be compared to Group B (placebo) within each antiepileptic drug condition (valproate monotherapy vs polytherapy). Paired T-tests (parametric) or Wilcoxon Rank Sum tests (non-parametric) will be used for analysis. If changes are seen in the blood chemistry without concomitant changes in behavioral measures, baseline psychological measures will be examined as possible moderating variables.

Progress: This was a cooperative study with Children's Hospital in Seattle. Six patients were enrolled at MAMC with no identifiable effects on mood or cognition noted.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, PULMONARY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/162 **Status:** On-going

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 **Facility:** MAMC

Principal Investigator: CPT Timothy R. Murray, MC

Associate Investigators:
MAJ Rahul N. Dewan, MC
CPT Bernard J. Roth, MC
MAJ 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:** / /

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: Only one patient has been enrolled at this time.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/104 **Status:** On-going

Title: Does Sampling of the Lung With the Guidance of High Resolution CT Scan Improve the Utility of Bronchoalveolar Lavage or Transbronchial Biopsy

Start Date: 05/07/93 **Est. Completion Date:** Jul 94

Department: Medicine/Pulmonary **Facility:** MAMC

Principal Investigator: CPT Joseph S. Pina, MC

Associate Investigators:
CPT Cristopher A. Meyer, MC
CPT Cynthia L. Clagett, MC
MAJ Mary P. Horan, MC
COL James L. Kelley, MS

Key Words: lung,transbronchial biopsy,bronchoalveolar lavage,high resolution CT

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To determine if high resolution CT (HRCT) scanning can be used to improve the yield of bronchoalveolar lavage (BAL) or transbronchial biopsy (TBB) in detecting and diagnosing interstitial lung disease.

Technical Approach: Consecutive patients with suspected interstitial lung disease referred to the pulmonary clinic will be considered for this study. The first twenty-five patients with ground glass opacification on HRCT scanning who pass certain exclusion criteria will be recruited. BAL and TBB will be performed in a segment of lung corresponding to an area of ground glass on HRCT scan and in an uninvolved segment as well. Therefore, "ground glass specimens" will comprise the cohort population and "uninvolved specimens" will act as the control population. Cell counts, cell concentrations and differential counts will be analyzed in each BAL specimen and pathology reviewed in each biopsy specimen. All cell concentrations will be scored to describe the intensity of the alveolitis present. Pathology will be scored based on whether the specimen is diagnostic or not. The cell counts, concentrations and scores from the ground glass BAL specimens will be compared to the uninvolved segment specimens. Pathology will be scored (normal, nondiagnostic, or diagnostic) and compared as well. If the Bal and TBB are nondiagnostic, an open lung biopsy will be recommended to the patient as the standard of care.

Routine chest X-rays, serum studies, skin testing and full pulmonary function testing will be performed on all patients as part of the routine evaluation of interstitial lung disease.

Progress: Ten patients have been evaluated for possible enrollment; however eight patients did not meet all the eligibility requirements. The final two patients who were enrolled have had results which support the contention that alveolitis is not of a higher intensity in abnormal areas of lung seen on high resolution CT scan of the chest than that seen in normal appearing regions. This is not, of course, statistically or clinically significant at this point.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/059 **Status:** On-going

Title: Bleomycin vs. Minocycline in a Randomized Double Blind Prospective Trial of Intrapleural Therapy for Recurrent Malignant Pleural Effusions

Start Date: 05/01/92 **Est. Completion Date:** Sep 94

Department: Medicine/Pulmonary **Facility:** MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators:
CPT John R. Caton, MC
MAJ Stacey B. Young-McCaughan, AN
CPT Lynn M. Keenan, MC
CPT Jennifer L. Cadiz, MC
CPT Curtis S. Hansen, RPH, MSC
LTC William H. Cragun, MC

Key Words: pleural effusions,bleomycin,minocycline,randomized

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

Study Objective: To determine the efficacy of minocycline versus bleomycin for sclerosis of malignant pleural effusions.

Technical Approach: Eighty patients with advanced malignancy and symptomatic pleural effusion recurrent after at least one prior therapeutic thoracentesis will undergo chest x-ray to confirm freely flowing pleural fluid. A data sheet will be kept recording ECOG performance status, chest radiograph results, and demographic information (age, sex, diagnosis, stage of disease, type of chemotherapy received, side effects to the sclerosant including pain, fever, hypotension, allergic reaction, rash, fatigue, anorexia, nausea, vomiting, diarrhea, elevated liver function tests, anemia, neutropenia, and elevated blood urea nitrogen or creatinine). The patient will be randomized to either bleomycin or minocycline. A chest tube will be placed and when it drains less than 100 cc per 24 hour period, the patient will undergo a test dose of the study drug. If the study drug is tolerated, the patients will undergo sclerotherapy with the assigned drug. The chest tube will be clamped for two hours and then placed onto 20 cm suction which will be maintained for at least 24 hours and until pleural drainage is < 150 ml/day. The chest tube will then be removed. Chest radiographs will be obtained at 72 hours to assess for recurrence of the effusion. If the fluid reaccumulates more than 50% of the original volume, the patient will be considered a treatment failure and removed from the study. Liver function tests, blood urea nitrogen, creatinine, and CBC will be obtained at 24 and 48 hours to monitor for side effects. The side effects listed on the data sheet will be monitored during the first 48 hours after sclerosis has been completed. Chest radiographs will be obtained at 7, 14, 30, 60, and 90 days to assess for response. Analysis of variance and regression analysis will be utilized to review the data obtained.

Progress: Three patients have been enrolled this year. WBAMC has agreed to participate in the project to increase accrual.

Detail Summary Sheet

Date: 30 Sep 92 **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 **Facility:** MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators: LTC William H. Cragun, MC

Key Words: pleural effusion,albumin,congestive heart failure

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

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: Six patients have been enrolled at this time. Enrollment is continuing and data analysis will occur after completion of the project.

Detail Summary Sheet

Date: 30 Sep 92 **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 **Facility:** MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators: LTC William H. Cragun, MC
MAJ Bruce S. Grover, MC

Key Words: positive pressure ventilation,air flow obstruction,nasal mask

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$260.00	**Periodic Review:** / /

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-oculogra, 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 nIVPP 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 nCPAPA 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: Two patients have been enrolled but neither has completed the project.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/043 **Status:** On-going

Title: The Effects of Testosterone Replacement in Hypogonadal, Malnourished Patients with Chronic Obstructive Pulmonary Disease (COPD)

Start Date: 03/17/89 **Est. Completion Date:** Oct 89

Department: Medicine/Pulmonary **Facility:** MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators:
MAJ John P. Kushner, MC
COL Stephen R. Plymate, MC
MAJ Bruce S. Grover, MC

Key Words: CPOD,testosterone,hypogonadal,malnourished

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$65.00	Periodic Review: 04/05/91

Study Objective: To determine if testosterone replacement in malnourished, hypogonadal male patients with COPD will result in improved nutritional status, and, if so, does this lead to improved respiratory muscle strength and increased exercise endurance.

Technical Approach: Twenty male patients >40 years will have baseline spirometry, maximum inspiratory and expiratory pressures, maximum voluntary ventilation, 6 minute walking distance, triceps skin fold, midarm muscle circumference, testosterone and lipoprotein profiles, electrolytes, liver function test, ABG, total lymphocyte count, hematocrit, transferrin, albumin, nitrogen balance, creatinine height index, anergy panel, % ideal body weight, and % usual body weight. A clinical assessment (history and physical exam) will be done and a diet history taken. Patients will be allowed to continue usual medications and activities and exercise will be unrestricted. If either total or free testosterone is low, the patient will be admitted to the hospital for five days. A dietary regimen will be initiated with a regular diet, supplemented on Day 3 with Pulmocare, one can three times a day. Calorie counting will be performed to assess nitrogen balance on Days 2 and 5. An interview and patient log will be used to count calories. Patients will be randomized to either testosterone enanthate, 100 mg/ml, or placebo injections. Injections will be given on Day 3 and then once a week for four doses. On Day 5 repeat studies will include: ABG, 24 hr urine urea nitrogen, calorie count, weight, change in weight, and testosterone profile. At the end of weeks 2 and 4 all baseline tests will be repeated except for ABG. This protocol was amended in Sep 89 in order to determine the relationship of testosterone to pulmonary function, as measured by FEV_1, DLCO, and MIP. Initial testosterone (free and total), SHBG, and estradiol will be determined. The investigators will then determine if there is a linear fall in testosterone as FEV_1 falls and if low testosterone is related to weight loss or steroid use. These determinations will then be used to determine entry into the main part of the study.

Progress: Six patients have been entered. The investigator is concerned that the design of the protocol will cause a negative result. Data are currently being collected to present to an independent reviewer.

Detail Summary Sheet

Date: 30 Sep 92 **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 **Facility:** MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators:
MAJ Miquel J. Rovira, MC
MAJ Frank A. Zimba, MC
MAJ Kevin L. Quinn, MC
MAJ Steven S. Wilson, MC

Key Words: cancer,bronchogenic,MRI

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

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: A total of 24 patients (14 in FY93) have entered the study. Attempts are being made to involve other sites to increase enrollment. No conclusion can be made at this time.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/034 **Status:** Completed

Title: Validation of Infrasonics Adult Star Respiratory Mechanics Package

Start Date: 02/05/93 **Est. Completion Date:** Feb 3

Department: Medicine/Pulmonary **Facility:** MAMC

Principal Investigator: Michael G. Winter, RRT

Associate Investigators: MAJ James D. Pike, MC

Key Words: respiratory mechanics package

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$1930.00	Periodic Review:	/ /

Study Objective: To validate the respiratory mechanics package which includes Negative Inspiratory Force (NIF), Occlusion Pressure (P100/P 0.1), Slow Vital Capacity (SVC).

Technical Approach: Validation of the Infrasonics Adult Star Respiratory Mechanics Package will be accomplished utilizing the Respiratory Pressures Module (RPM) system. The module includes a pressure transducer, waveform analyzer, and apnematic control system. The RPM incorporates a design which allows all tests to be performed using compact valve mechanics. The mechanical respirator will be attached to this valve, the parameter will be tested simultaneously by the ventilator and the RPM system and results printed in hardcopy for interpretation.

The NEV-100 (NPV) will be setup with a rate of 4, Inspiratory Time 1.2 seconds in the control mode. Each measured value for all testing (-10 to -80 cm H_2O) will be printed from internal printer function available on the NEV-100

Five measurements of P 0.1 for each measured value will be done by placing the RPM and Adult Star into modes used to achieve P 0.1 value. Prior to the NEV-100 initiating a negative pressure breath the ENTER button on the Adult Star will be help, preventing inspiration or expiration through the system circuit. All measured values will be printed in hard copy.

Five measurements of NIF for each measured value will be done by placing the Med-Graphics into the Respiratory Muscle Forces screen and Adult Star into NIF measurement screen. Prior to NEV-100 initiating a negative pressure the ENTER button on the Adult Star will be held, preventing inspiration or expiration through system circuit. Values from Manometer will be observed and written down during NEV-100 cycled breath. All measured values from Med-Graphics and Adult Star will be printed in hard copy.

Five measurements on SVC for each measured value will be done by placing the Med-Graphics in Pulmonary Measurements screen and Adult Star into SVC screen. The ENTER button on the Adult Star will be pushed prior to NEV-100 cycling a breath. At a set negative pressure, inspiratory time, and rate, a tidal volume breath will be delivered, measured simultaneously and printed in hard copy from the screen.

A repeated measure analysis will be used to evaluate the difference between results from standard testing device.

Progress: The Infrasonics Adult Star Respiratory Mechanics package is valid and is a clinically acceptable method of obtaining routinely used weaning parameters normally used for the purposes of weaning patients from mechanical ventilation.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/084 **Status:** On-going

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

Start Date: 04/02/93 **Est. Completion Date:** May 95

Department: Medicine/Pulmonary **Facility:** MAMC

Principal Investigator: CPT Lisa L. Zacher, MC

Associate Investigators:
MAJ James D. Pike, MC
CPT Lynn M. Keenan, MC
CPT Cristopher A. Meyer, MC

Key Words: hemoptysis:CT,fiberoptic bronchoscopy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$100.00	**Periodic Review:** / /

Study Objective: To prospectively compare the contributions of high resolution computed tomography technique (HRCT) and fiberoptic bronchoscopy (FOB) in evaluation of patients presenting with hemoptysis.

Technical Approach: Study patients would receive a standardized initial work-up to include history and physical examination, screening labs and a PA and lateral chest X-ray. Demographic data to include age, sex, tobacco history, and frequency and amount of hemoptysis will be noted on the data sheet. Chest X-rays will be designated as normal, abnormal, but non-localizing, or abnormal and localizing. Where there is a discrepancy between the radiologist and the bronchoscopist, the more abnormal interpretation will be utilized.

The radiologist will need to have experience reading HRCT. If such a qualified person cannot be found at other participating institutes, CT scans will be forwarded to MAMC Radiology for interpretation. If more than one radiologist is involved in reading the HRCT examinations, five films will be exchanged to check for interobserver variability. The radiologist will also have access to chest x-rays but be blinded to FOB results and given only the history of hemoptysis. The bronchoscopist ideally will be blinded to CT results but in particular cases where CT scans are available to the bronchoscopist they can be utilized to direct sampling techniques as long as FOB visual findings are properly recorded. If contract CT has already been done and demonstrates source of bleed, additional HRCT views would not be obtained. The order of obtaining HRCT and FOB in all patients need not be uniform. Data will be analyzed looking at clinical characteristics and roentgenographic findings associated with certain diagnosis. HRCT-FOB correlations will focus on the individual and combined efficacy in predicting and/or diagnosing the etiology of hemoptysis.

Statistical significance of observed differences between the two groups (FOB and HRCT) will be by Chi-Square. Multi-variate analysis will be made by the stepwise linear discriminant analysis method to determine risk factors associated with lung cancer.

Progress: This study in on-going with 6 subjects entered in FY93.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE, RHEUMATOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/168 **Status:** On-going

Title: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Oral GR122311X Compared with Ranitidine and GR88502X for the Gastric or Duodenal Ulcers in Patients with Osteoarthritis ... Ulcers

Start Date: 09/03/93 **Est. Completion Date:** Dec 93

Department: Medicine/Rheumatology **Facility:** MAMC

Principal Investigator: MAJ Thomas L. Irvin, MC

Associate Investigators:
MAJ Michael F. Lyons II, MC
CPT Thomas P. Peller, MC
MAJ Amy M. Tsuchida, MC
MAJ Louis J. Dalessandro, MC
MAJ William A. Pearce, MC
MAJ Kathryn K. Riordan, MC

Key Words: gastric ulcers,duodenal ulcres,osteoarthritis,rheumatoid arthritis,ranitidine,GR122311X,GR88502X

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

Study Objective: To compare four treatment groups with respect to cumulative 12-week occurrence rates of NSAID-associated gastric and/or duodenal ulcers ≥ 0.5 cm and for the safety parameters of adverse events and laboratory tests.

Technical Approach: Patients between 18 and 80 years of age with osteo- or rheumatoid arthritis, receiving ASA or one of six specified NSAIDs, not having a documented history of gastric or duodenal ulcer, and an ambulatory outpatient will have a baseline examination and EGD to confirm the absence of ulcers. They will be randomized to receive one of 4 regimens: (1) GR122311X 400 mg B..I.D., (2) GR88502X 240 mg b.i.d., (3) Ranitidine 150 mg b.i.d. or (4) placebo control group. At Week 4, patients will be evaluated and have an EGD. If there is no ulcer occurrence the patient will continue in the study for an additional four weeks of treatment and then return to the clinic for a Week 8 evaluation including EGD. Patients without ulcers after 8 weeks of treatment will continue until Week 12 and a final evaluation with EGD. An additional follow-up exam will be scheduled to determine adverse events only if the study medication was not returned at Week 12.

Progress: We are awaiting receipt of drug for this study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/019 **Status:** Completed

Title: The Efficay and Safety of Misoprostol for the Prevention of NSAID-Induced GI Complications

Start Date: 01/03/92 **Est. Completion Date:**

Department: Medicine/Rheumatology **Facility:** MAMC

Principal Investigator: MAJ Thomas L. Irvin, MC

Associate Investigators: MAJ Kathryn K. Riordan, MC
MAJ Louis J. Dalessandro, MC

Key Words: gastritis,NSAID-induced,misoprostol

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review:	/ /

Study Objective: To determine the efficacy and safety of misoprostol compared to placebo for the prevention of clinically significant and serious nonsteroidal anti-inflammatory drug (NSAID) induced gastrointestinal (GI) events. The events are GI bleeding, ulcer perforation, surgery for ulcer disease, or death due to GU, DU or severe gastrointestinal erosive disease.

Technical Approach: Patients >60 years of age on daily NSAID therapy with rheumatoid arthritis will be enrolled in the study. After baseline demographic and medical information has been recorded, the patients will be randomized to receive either 200 mcg misoprostol or matching placebo four times a day (with meals and a bedtime snack), in addition to the NSAID therapy for six months. Patients may take Amphojel or other nonmagnesium antacids during the study with this usage recorded. Patients will report any GI events to the principal investigator. Patients will be assessed by the principal investigator at three and six months for the occurrence of any of the GI events of interest. Formal statistical testing will be performed on the demographic information (age, gender, vital signs). The primary endpoint is the development of a GI complication during the six months of therapy. A tabular display of the complication development rate across time will be done by institution and then by institutions combined. A survival analysis will be performed to assess the difference in the complication development rate distributions across time. The NSAID-induced GI complication rate will be modeled using logistic regression to assess the significance of risk factors and their impact on treatment outcome. The incidence of adverse events will be tabulated by treatment group, event, and body system. The overall incidence rate will be compared between treatment groups across all patients using the Pearson's chi square test of marginal homogeneity. Vital sign measurement changes from baseline at the end of the study will be analyzed using the *t* test. Between group differences will be assessed using analysis of variance.

Progress: A total of 15 patients were enrolled at MAMC with 11 patients completing the study. There were no significant adverse outcomes experienced.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/083	**Status:** Terminated
Title: Iontophoresis Therapy for Bursitis and Tendinitis		
Start Date: 08/02/91	**Est. Completion Date:**	
Department: Medicine/Rheumatology	**Facility:** MAMC	
Principal Investigator: MAJ Kathryn K. Riordan, MC		
Associate Investigators:	MAJ Thomas L. Irvin, MC	
Key Words: bursitis,tendinitis,iontophoresis		

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

Study Objective: To determine the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of lateral epicondylitis, bicipital tendinitis, subdeltoid burstitis, olecranon burstitis, and achilles tendinitis. The research questions to be answered are: Will iontophoresis be effective in treating bursitis and tendinitis and is iontophoresis more, less, or equally as effective as a local injection of corticosteroid.

Technical Approach: Subjects with acute, subacute, and chronic bicipital tendinitis, lateral epicondylitis, subdeltoid bursitis, olecranon bursitis, and achilles tendinitis will be asked to enter the study. All subjects will receive standard therapeutic exercises, including ice or local heat applications but no ultrasound or "deep heat" therapy. All subjects will receive naproxen 500 mg bid for one month. If not tolerated, the subject will use ibuprofen 800 mg tid. All subjects with lateral epicondylitis will wear an elastic "tennis elbow splint" during the study. The subjects will be randomized as follows: (A) Iontophoresis "treatment" with corticosteroid twice weekly for 3 weeks, and one sham needle "injection" (normal saline) at the third week. (B) One injection of 20 mg of 40 mg/ml triamcinolone acetonide using a 22 gauge needle per standard injection therapy, at the third week following sham iontophoresis, twice weekly for three weeks. (C) Sham iontophoresis without corticosteroid twice weekly for 3 weeks and one sham needle "injection" at the third week. Subjects with achilles tendinitis will be randomized to groups A and C only without a sham injection. The same evaluator will see the patient on each visit and will be blinded as to treatment received. The patient will be unblinded 4 weeks after completion of the treatments. The blinded physician will reexamine the subject after completion of the treatments at 1, 2, 3, 4, 8, and 12 weeks. The following data will be collected on the treated joints: Tenderness and swelling assessment, ROM, subject's evaluation of pain and swelling, subject's evaluation of improvement, and physician's evaluation of improvement. The Phoresor II iontophoretic drug delivery system will be used for all iontophoresis. Dexamethasone sodium phosphate 0. 5 cc will be used in the iontophoresis treatments. Lidocaine hydrochloride 4% will be used in all treatments (including shams).

Progress: Time constraints did not allow for completion of the study.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF NURSING

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/116	**Status:** On-going
Title: Effects of Military Parents' Separation on Children		
Start Date: 06/09/93	**Est. Completion Date:** Oct 93	
Department: Nursing	**Facility:** MAMC	
Principal Investigator: CPT Pamela S. Birgenheier, AN		
Associate Investigators:		
Key Words: parent,child separation,military parents		

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

Study Objective: (1) When separated from a parent for military duty, do school-aged children from military families have more behavior problems than military children not separated from a parent? (2) Do school-aged children separated from their mothers for military duty demonstrate different behaviors than those children separated from their fathers for military duty?

Technical Approach: This is a descriptive study using a questionnaire. A minimum of 360 subjects, children of active duty military, ages 6 - 14 of both sexes will be used. Three main groups will be used consisting of 120 subjects each. These groups will be determined by (1) Father absent, (2) Mother absent, and (3) No Parent absent. Questionnaires will be provided to parents wishing to participate and meeting the entry criteria. They will be instructed to have the child's primary care giver furnish the information required by the questionnaire.

For data analysis the children will be matched as closely as possible across three areas of performance (social, activities, and school) for age, sex and parent rank. An ANOVA will be performed for statistical analysis to compare the children in the three groups in the three different areas of performance.

Progress: Submitted protocol for full funding from the Tri-Service Nursing Research Programs Awards. Funding was approved and will be received 1 October 1993.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/118 **Status:** On-going

Title: Crisis Intervention With Critical Care Families

Start Date: 06/09/93 **Est. Completion Date:** May 94

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Mary Ann Carr, AN

Associate Investigators: None

Key Words: critical care,family intervention

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

Study Objective: To measure the effect of a family crisis intervention program on family need satisfaction, family functioning, and patient stress following acute myocardial infarction (AMI).

Technical Approach: Two groups of 50 patients will be involved in this study. The design is a post-test-only control group design with random assignment of subjects. The experimental group will receive family crisis intervention on a minimum of three occasions during the hospitalization. A family representative will complete the Family Need Satisfaction/Family need Importance and the Family Adjustment of Medical Stressor Questionnaires; patients will complete the Stress of Discharge Assessment Tool (SDAT) within 48 hours of discharge. Multivariate statistics will be done to measure for significant outcomes differences between groups as a result of the independent variable: crisis intervention. Results will also provide military nurses with a theoretical crisis intervention process model to use with all patients and families in similar life-threatening medical and separation crisis.

Progress: Funding will be received on 1 Oct. 93 and study will begin.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/072 **Status:** Completed

Title: Piglet Tracheal Epithelial Injury and Regeneration Following Endotracheal Suctioning

Start Date: 05/18/90 **Est. Completion Date:**

Department: Nursing **Facility:** MAMC

Principal Investigator: Sandra J. Harwood, BSN, RNC

Associate Investigators:
LTC Tom E. Wiswell, MC
MAJ James G. MacMillan, VC
LTC Barbara S. Turner, AN

Key Words: epithelium,regeneration,endotracheal suctioning,Animal Study

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 06/07/92

Study Objective: To determine the difference in: acute cell loss from the tracheal epithelium following six controlled endotracheal suctioning procedures using positive end-expiratory pressure (PEEP) and zero end-expiratory pressure (ZEEP) the process of tracheal epithelial regeneration following PEEP and ZEEP in the length of time for complete tracheal epithelial regeneration between the PEEP and ZEEP groups and the growth of the tracheas of piglets undergoing endotracheal suctioning and those in the sham and control groups.

Technical Approach: Control animals (14) will be sedated and then euthanized (two at a time) acutely on days 3, 7, 10, 14, 17, and 21, and the trachea harvested. Sham piglets (14) will be sedated, intubated, and ventilated for 6 hours, without suctioning taking place. They will be euthanized at time periods as above and the trachea harvested. Group 1 (35) and Group II (35) piglets will be intubated and ventilated. After the piglets have been stabilized on the ventilator each will receive either PEEP (Group 1) or ZEEP (Group II) once every 60 minutes for the six hours of mechanical ventilation. The piglets in Groups 1 and 2 will be euthanized in groups of 5, acutely and at 3, 7, 10, 14 and 21 days post-suctioning and the trachea harvested. At the time of necropsy, the location of the tip of the endotracheal tube will be marked by placing a ligature in the tracheal wall. The heart and lungs will be removed en bloc and grossly examined. The trachea and mainstem bronchi will be dissected free and sectioned into 13 cross sections for examination, including scanning electron microscopy and light microscopy. Descriptive and inferential statistics will be used to determine the total epithelial cell count, goblet cell count, and ciliated cell count from each section. The ratio of ciliated cell to goblet cells will be calculated for all cross sections to determine the tracheal epithelial response to injury. Changes in the cell counts over time will be analyzed. Corrected predicted total epithelial cell counts will be determined, using the control piglets as a standard, correcting for tracheal diameter.

Progress: Subject recruitment, data collection, and individual analysis have been completed. Data were sent to the consultant and to the biostatistician for group analysis. No findings or conclusions are available at this time.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/082 **Status:** Completed

Title: Evaluation of Aftacare Videotaped Programs on Diabetes, Cancer & Heart Disease for Patient Education as an Intervention in Secondary Prevention of Complications Associated with These Chronic Diseases

Start Date: 07/02/92 **Est. Completion Date:** Nov 92

Department: Nursing **Facility:** MAMC

Principal Investigator: MAJ Sandra Hellman, AN

Associate Investigators: MAJ Muriel Metcalf, AN
Ann Lancaster, CHN

Key Words: videotaped education programs,Aftacare,diabetes,cancer,heart disease

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

Study Objective: To evaluate the usefulness of Aftacare videotaped programs on diabetes, cancer, and heart disease for patient education as an intervention in secondary prevention of complications associated with these chronic diseases.

Technical Approach: The community health nurse will collect demographic information and administer a pretest concerning the patients knowledge of his/her medical condition, the patients concerns regarding his/her disease state, resources to help the patient understand how to cope with the condition, and what the patient can do to attain the highest level of health possible. Subjects will then be alternately assigned to a videotape educational program group or to a MAMC standard patient education group. Patients in the videotape group will view the video within two weeks after completion of the pretest. After viewing the video, the participants will be given a post-test, essentially obtaining the same information. Patients assigned to the control group will be given the pretest and be referred to the primary nurse who will be responsible for initiating the medical center's patient education. They will be given the same post-test as the video group two weeks after completing the pretest. The videotape group will have demographic data collected and means determined for age, education, and income. Data on other demographic variables will be categorized by frequency counts. Qualitative data will be obtained from pre/post tests. Common themes will be identified, categorized, and then described for each group. From this, data will be inspected for trends within each group. The demographic variables for each group will be visually compared to determine group equivalence.

Progress: Although patient and family verbal feedback was very positive concerning the Aftacare video tapes, this study did not show an improvement in knowledge or attitudes between the experimental and control groups. This is probably because the tool used to collect the data did not accurately measure a change in knowledge or attitudes, other than the fact that the tapes were not effective. Although not reflected in the data, it is the investigators impression that the tapes did have a significant impact on individuals diagnosed for the first time with heart disease, especially in fear of death or disability.

Detail Summary Sheet

Date: 30 Sep 92	**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: LTC Deborah J. Leander, AN		
Associate Investigators: LTC Barbara S. Turner, AN	MAJ 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:** / /

Study Objective: To examine two types of surfactant (Exosurf & Survanta), 3 methods of adiministration, 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 judgement 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: No patients entered. Funding for this project was received 1 Oct 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/157 **Status:** On-going

Title: Temperature and Capillary Blood Flow Velocity Stability During Nursing Care Procedures in Premature Neonates: A Pilot Study

Start Date: 08/06/93 **Est. Completion Date:** Jun 94

Department: Nursing **Facility:** MAMC

Principal Investigator: Lori A. Loan, AN

Associate Investigators:
Sue Wilson, RN
Sandra J. Harwood, BSN, RNC
Karen A. Thomas, Ph.D.
Roberta Colvin, CCRN
Susan Hicks, CCRN

Key Words: premature neonates,temperature,blood flow velocity

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

Study Objective: This study will explore changes in temperature (axillary, abdominal skin, and foot peripheral skin) and capillary blood flow velocity in the foot of premature neonates associated with nursing care procedures.

Technical Approach: Once the infant has been entered into the study, a skin temperature probe will be placed. A laser doppler flowmeter probe will be placed on the same foot. The abdominal skin temperature probe will already be in place as it is routinely used in NICU. Data for abdominal and foot temperatures and capillary blood flow will be collected at a rate of once per minute beginning 5 minutes before and ending 3 hours after the nursing care procedures. Axillary temperature will be taken at the beginning and end of the nursing care procedures. Heart rate, respiration rate, O_2 saturation, and blood pressure (if available) will be recorded using the Marquette monitoring system. Data will be analyzed descriptively. Temperature and capillary blood flow velocity will be plotted over time.

Progress: The study is being done in conjuction with University of Washington and are awaiting University of Washington Human Use Committee approval before subject recruitment can begin.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/028 **Status:** On-going

Title: The Effect of Two Levels of Hyperoxygenation Given via a Manual Resuscitation Bag and Ventilator During Endotracheal Suctioning of Premature Infants

Start Date: 02/17/89 **Est. Completion Date:**

Department: Nursing **Facility:** MAMC

Principal Investigator: Lori A. Loan, AN

Associate Investigators: LTC Barbara S. Turner, AN

Key Words: endotracheal suctioning,infant,resuscitation bag

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/05/92

Study Objective: To compare two methods of hyperoxygenation delivery [manual resuscitation bag (MRB) and a ventilator] to compare two levels of hyperoxygenation and to examine the interaction effects of the delivery methods and levels of hyperoxygenation during endotracheal suctioning of premature infants.

Technical Approach: Forty premature infants <38 weeks of gestational age and <21 postnatal days, that have been orally intubated and mechanically ventilated for routine treatment will be studied. This will be a within-subject, randomized block design study with repeated measures in which selected physiologic parameters will be monitored during a controlled endotracheal suctioning procedure in a convenience sample of premature infants. The independent variables will be level of hyperoxygenation (FIO_2 increased 10% and 20%) and method of delivery (MRB and ventilator). The dependent variables will to be measured are oxygenation, intracranial pressure, carbon dioxide tension, heart rate, and secretion recovery. Other physiologic variables to be monitored are mean airway pressure, PO_2/FIO_2 ratio, respiratory rate and mean arterial pressure (if there is an indwelling arterial line already in place. Subjects will serve as their own controls during 4 consecutive endotracheal suctioning procedures within a 6-12 hour time period, administered at 1.5 to 3 hour intervals. Each of the following endotracheal suctioning protocols will be implemented in each infant in a random order: 10% increase over baseline FIO_2 by MRB 20% increase over baseline FIO_2 by MRB 10% increase over baseline FIO_2 by ventilator and 20% increase over baseline FIO_2 by MRB.

Progress: Sixteen subjects were entered into the protocol in FY93. Individual data analysis was completed for 45 subjects. No group analysis was done, therefore, no findings or conclusions are available.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/003 **Status:** On-going

Title: A Double Blind, Placebo Controlled Study on the Effect of a Lactobacillus Preparation on the Incidence of Tube-Feeding Related Diarrhea in ICU Patients

Start Date: 10/02/92 **Est. Completion Date:**

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Brenda I. Mygrant, AN

Associate Investigators:
LTC Anthony S. Sado, MC
CPT Robert V. Gibbons, MC
CPT Lynn M. Keenan, MC
CPT Pamela Charney, SP
LTC Debra Savinske, AN
CPT Jeffrey S. Strong, MC

Key Words: diarrhea,lactobacillus,tube feeding,ICU patients

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

Study Objective: To determine if the addition of Lactobacillus species to enteral feedings has an effect on the incidence of tube-feeding related diarrhea in ICU patients receiving antibiotics.

Technical Approach: Patients in either the MICU or SICU, receiving antibiotics and having an order for continuous enteral feeding via nasoenteral feeding tube using MAMC's standard, 1 kcal/cc enteral formula may be entered into the study. They will be given those feedings in a volume to meet the patient's energy and protein intake as estimated by either the Harris-Benedict equation or by use of the metabolic chart. Patients will be randomly assigned to the control group (to receive placebo) or to receive treatment with Lactinex (a mixture of L. acidophilus and L. bulgarticus). Treatment will consist of one packet of lactinex granules mixed with water three times daily for the seven days of the study.

Patients will be monitored daily for one week for the presence of diarrhea. Consistency and volume of stool will be evaluated separately. Stool cultures for C. difficile and ova and parasites will be done on day one and day seven of the study.

Progress: No patients have been enrolled due the difficulty of obtaining informed consent from this group of patients. This study will be modified, with HUC approval, to allow entry into the study with permission of a significant other.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/058 **Status:** Completed

Title: Children's Hospital EMLA Efficacy Research (CHEER) Trial

Start Date: 03/05/93 **Est. Completion Date:** Apr 93

Department: Nursing **Facility:** MAMC

Principal Investigator: CPT Gertrude F. Neill, MC

Associate Investigators:
CPT Robin L. Martin, AN
MAJ Edward J. Walz Jr., MC
CPT Marilie K. Sage, AN
CPT Cynthia A. Bailey, AN
CPT Curtis S. Hansen, RPH, MSC

Key Words: EMLA cream,children

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

Study Objective: To evaluate the efficacy and safety of EMLA Cream in a large general clinical population.

Technical Approach: Two sites, (primary and alternate) where intact skin will be penetrated for an invasive procedure, will be selected. Approximately one half the contents of the EMLA Cream tube (2.5 gms) will be applied to the skin overlying each site. The sites will then be covered with Tegaderm and remain undisturbed for at least 60 minutes. Following the prescribed time of application, the Tegaderm dressing will be removed and the EMLA Cream removed. The site will be disinfected in the normal manner prior to performing the procedure (venipuncture).

As soon as possible following the invasive procedure the patient will be asked to rate perceived pain on a Visual Analog Scale (VAS). The health care professional will also record her/his impression of the patient's pain. If a parent or guardian is present during the procedure, he/she will also be asked to evaluate the pain. From the beginning of the procedure, and for the ensuing 24 hours, the patient will be observed by the hospital staff, parents or guardian for local or systemic reaction to the study medication.

Data evaluation will be performed by the sponsor.

Progress: Twenty patients were included in the study. No adverse effects were noted in any case. Copies of data have been sent to the sponsor for inclusion in a national-wide study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/125 **Status:** On-going

Title: Clinical Information System: Impact on Nursing

Start Date: 08/06/93 **Est. Completion Date:** Sep 94

Department: Nursing **Facility:** MAMC

Principal Investigator: COL Ruth E. R[illegible]N

Associate Investigators:
LTC Pam I. George, AN
MAJ David Williams, AN
Sandra T. Perdue, Ph.D.

Key Words: clinical info system,nursing

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

Study Objective: To examine effects of implementing a clinical information system upon key nursing outputs in an acute surgical nursing unit.

Technical Approach: The planned computerization of a [illegible] ward at MAMC provides a unique opportunity for collecting scientific evidence about the effects of such computerization on specific nursing outcomes. Using a pre- and post-intervention design, work sampling will be utilized to collect information about nursing time utilization by categorizing nursing behaviors into operationally defined categories and mathematically extracting proportions for each category. For both designs, observations will be collected for one work cycle (defined as a 7 day period). To minimize the risk of bias, each one of the seven weekdays (Sunday through Saturday) to be sampled will be randomly selected from within a six week period. There will two randomly selected observation sessions per hour for each of the twenty-four hour collection periods.

Chart audits using a peer review process will be used to quantify the completeness of nursing documentation in the patient's record. A total of 53 charts prior CIS implementation and 53 charts after implementation will be audited by a five member nurse review panel using the JCAHO Profession Nurse Patient Record Review Form.

Appropriate descriptive statistics will be reported for care categories and for documentation completeness for both pre- and post-implementation of the CIS on the acute care unit.

Progress: No patients entered. Funding to be received 1 Oct 93.

Detail Summary Sheet

Date: 30 Sep 92 **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.
MAJ Joanna C. Beachy, MC
Karen A. Thomas, Ph.D.

Key Words: Neonates,modified NICU

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

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 ANOVA-RM 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 ANOVA-RM. Cyclicity of NCASA data will be determined within subject using cosinor analysis.

Progress: This is a continuation grant from FY92. There was no additional modification to the NICU area. Subjects enrolled to date are still inpatients and no data is available.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/102 **Status:** Completed

Title: The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants

Start Date: 09/04/92 **Est. Completion Date:** Aug 93

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Michelle T. Renaud, AN

Associate Investigators:
Susan T. Blackburn, Ph.D.
MAJ Joanna C. Beachy, MC
LTC Barbara S. Turner, AN
Karen Thomas, M.D.

Key Words: high risk infants,NICU environment,physiologic and neurobehavioral effect

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

Study Objective: To evaluate the effects of a modified NICU physical environment on the growth and development of three groups of high risk infants.

Technical Approach: Two groups of preterm infants (<31 weeks and 32 to 37 weeks gestational age) and a group of ill term infants will be evaluated during hospitalization and post discharge; 120 infants will be randomly assigned to an experimental group (n=60 with 20 in each of the groups) or a control group (n=60 with 20 in each of the groups) once they achieve medical stability. The experimental group will be cared for from entry into the study until discharge in a specially designed NICU with a program of care that includes reduction of sound and light levels and day-night cycling of lighting. Controls will receive routine care in the standard NICU environment. All infants will have dependent measures recorded at the same time intervals. Outcome measures include: weight gain, duration of hospitalization, transition to nipple feeding, duration of organized sleep, amount of quiet sleep, diurnal cycling of heart rate, body temperatures, sleep-wake states, neurobehavioral stress cues, neurobehavioral and neurological assessments, and hearing and vision examinations. Analysis will include descriptive statistics, t-tests, analysis of variance procedures (including repeated measures) and cosinor analysis.

Progress: The experimental nursery was set up, equipped and staffed. The NICU was used as the control. Subjects entered received interventions per the protocol. Findings (preliminary) indicate that the infants in the experimental nursery have shorter length of stay, earlier nipple feeding, better neurodevelopmental behaviors, and more sleep.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/034 **Status:** Terminated

Title: Impact of Continuous vs Intermittent Negative Pressure on Tracheal Trauma and Regeneration

Start Date: 03/01/91 **Est. Completion Date:**

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Barbara S. Turner, AN

Associate Investigators: MAJ James G. MacMillan, VC
LTC Tom E. Wiswell, MC

Key Words: tracheal trauma,suctioning,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To examine the trauma and healing of the tracheal epithelium following the two types of negative pressure used during endotracheal suctioning (ETS) by neonatal nurses continuous negative pressure (CNP) and intermittent negative pressure (INP).

Technical Approach: The research questions to be answered are (1) what is the immediate (acute) effect on the tracheal epithelium of ETS using INP versus CNP (2) what is the response of the tracheal epithelium (chronic effect) of ETS using INP versus CNP over the 21 days immediately following ETS and (3) are there differences acutely and chronically in the percentage of tracheal epithelial circumferences that are covered by basal cells, ciliated epithelium and goblet cells based on exposure to suctioning using INP versus CNP. The sample will consist of 98 Chester White swine who will be randomly divided into 4 groups: Control (n=14) sham (n=14) Group I - intermittent negative pressure (n=35) and Group II - continuous negative pressure (n=35). Groups I and II will be intubated, mechanically ventilated, and receive 6 controlled ETS procedures (1 /hour) during 6 hours of ventilation. The swine will either be euthanized immediately after the sixth ETS procedure or recovered and euthanized at 3, 7, 10, 14, and 21 days post ETS. Swine in the control and sham groups will be euthanized at the same time points. All tracheas will be harvested and sectioned into 13 sections beginning at the second tracheal ring and extending to the 9th tracheal ring. Each section will be graded using video image analysis for determination of the percentage of circumference denuded, the numbers of cells, types of cells, and ratio of cell types remaining. Injury scores for each swine in each group at each time period will be determined.

Progress: The grant from NCI was not approved.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/086 **Status:** Completed

Title: Physiologic Responses to Exogenous Surfactant

Start Date: 07/02/92 **Est. Completion Date:** Jul 95

Department: Nursing **Facility:** MAMC

Principal Investigator: Susan B. Webb, AN

Associate Investigators: MAJ Joanna C. Beachy, MC
LTC Barbara S. Turner, AN

Key Words: surfactant

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

Study Objective: To extend prior research on exogenous surfactant administration in premature infants by systematically examining two types of exogenous surfactant, two methods of administration, and the resulting interventions in response to improved pulmonary compliance.

Technical Approach: The sample will consist of 24 intubated and mechanically ventilated premature infants with respiratory distress. The sample will be stratified by two gestational age ranges (<27 wks and 28-30 wks) and then randomized to treatment groups with equal representation in each stratification: Group 1: N=6 for each age range (total 12) Exosurf administered by sideport adpater Group 2: N=3 for each age range (total 6) - Survanta administered by feeding tube through endotracheal tube Group 3: N=3 for each age group (total 6) - Survanta administered through a double lumen endotracheal tube. Data from selected physiologic variables will be recorded continuously and simultaneously for a two hour and 25 minute period, beginning prior to administration of exogenous surfactant through two hours post surfactant administration. Ventilatory interventions will be annotated on the wave forms from the recorder. Data will be analyzed for trends based on type of exogenous surfactant, method of administration, and type of interventions instituted. Results from this pilot study will provide data on infants' response to two types of surfactant and methods of administration, as well as intervention patterns. The data will be used to support a larger multisite study examining physiologic responses following surfactant administration.

Progress: Subject recruitment, data collection and individual analysis have been completed. Results have been sent to a consultant and biostatician for data analysis and preliminary conclusions.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/094	**Status:** Completed

Title: Incidence of Patent Ductus Arteriosus in Premature Infants Receiving Exogenous Surfactant Therapy

Start Date: 04/02/93	**Est. Completion Date:** Aug 93
Department: Nursing	**Facility:** MAMC
Principal Investigator: Susan B. Webb, AN	
Associate Investigators:	LTC Barbara S. Turner, AN
Key Words: patent ductus arteriosus,premature infants,surfactant	

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

Study Objective: To look at the incidence of patent ductus arteriosus (PDA) in the preterm neonate with IRDS, after receiving surfactant replacement therapy. This particular study will investigate the following questions: 1. What is the overall incidence of patent ductus arteriosus in a convenience sample of preterm neonates receiving two types of exogenous surfactant replacement therapy? 2. What is the incidence of PDA in the sample of infants receiving Survanta as compared to the infants receiving Exosurf? 3. What are the demographic and physiologic differences within and between the groups of infants with PDA in preterm neonates between the three different methods of surfactant administration?

Technical Approach: Data collected on MAMC protocol #92/086 will be obtained by chart review. Accompanying medical and nursing progress notes documenting the presence of PDA and electrocardiograms verifying PDA will be reviewed. Data will be analyzed for trends based on type of exogenous surfactant, method of administration and type of intervention instituted. Descriptive statistics will be obtained from the data. Demographic data will be coded and entered into the computer for analysis. Descriptive statistics to include mean, standard deviation, and range as well as nominal data will be generated from the demographic data. Demographic data will include gestational age, age in minutes at the time of the study, birth weight in grams, gender and race. The incidence of PDA between the two exogenous surfactant medications will be analyzed using two different methods. First, a nonparametric inferential statistical test will be used to compare the frequency of the PDA occurrence between the two medication groups. Possibly a Friedman's test will be used to view the difference of the nominal data.

Progress: Data collection was procured by chart review. There was no difference between the two surfactants and the incidence of PDA [Exosurf 54% (n=5/9) and Survanta 50% (n=4/8)]. Using clinical cues of hemodynamically significant PDA as stated in the protocol, nurses documented 89% (n=7/8) of the overall PDAs. The screening tool was 100% accurate and there were no "false positive" PDA documentations.
The findings are currently being used as a foundation for a multi-site nursing research protocol.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/012 **Status:** Completed

Title: Sexual Functioning in Women with Breast Cancer Comparing Women Treated with Systemic Adjuvant Therapy to Women Treated Without Pharmacological Manipulation

Start Date: 10/02/92 **Est. Completion Date:** Aug 93

Department: Nursing **Facility:** MAMC

Principal Investigator: MAJ Stacey B. Young-McCaughan, AN

Associate Investigators: None

Key Words: cancer,breast,sexual functioning

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

Study Objective: To compare sexual functioning in women with breast cancer treated with systemic adjuvant therapy to sexual functioning in women treated without pharmacological manipulation; that is, with surgery and/or radiation therapy alone.

Technical Approach: Subjects with local or regional breast cancer will be identified from the MAMC Tumor Registry. Names will be collected from 1992 going back in time until 300 potentially eligible subjects are identified. Subjects will be sent a cover letter, the questionnaire, and an addressed, stamped return envelope. Return of the questionnaire is deemed sufficient for informed consent. Two weeks after the initial mailing, a follow-up postcard will be mailed to those subjects who have not responded. Four weeks after the initial mailing, a follow-up letter and a second copy of the questionnaire will be sent to those subjects who have still not responded. With two reminder mailings, an estimated 50% return rate is anticipated based on the motivation of women with breast cancer to improve their care and of the military population to return questionnaires. The questionnaire answers of women treated with systemic adjuvant therapy will be compared to answers of women treated without pharmacological manipulation.

Progress: Conclusions evaluating the responses of 59 women who completed the entire questionnaire and who are currently is a sexual relationship are as follows: 1) As expected, the women treated with chemotherapy alone after surgery were the youngest mean group (mean age = 48.0), while the women treated with hormones after surgery were the oldest (mean age = 61.2). There were women in all treatment groups who felt that their treatment for breast cancer brought on their menopause. 2) Women in all treatment groups experienced the menopausal symptoms of weight changes, hot flashes, fatigue, mood swings, and anxiety attacks. However, the women treated with chemotherapy, with and without hormones, experienced these symptoms most frequently. Similarly, women in all treatment groups experienced symptoms interfering with sexual functioning such as vaginal dryness, lack of interest in sex, painful intercourse, and difficulty achieving orgasm. Yet again, the women treated with chemotherapy, with and without hormones, experienced these symptoms most frequently. 3) All of the women scored below the 50th percentile on all of the DSFI scales suggesting that each of these women has experienced insults to her sexual functioning with the diagnosis and treatment of breast cancer. 4) While differences between the treatment groups were expected in libido, satisfaction, and the overall DSFI scores, the scores were not significantly different ($p < .05$). Significant differences were observed

between the groups in psychological symptoms, affects, and body image. The women who received chemotherapy reported significantly more psychological distress ($p = .004$), more negative emotions ($p = .01$), and a more negative body image ($p = .05$). Since only two of the women were currently being treated with chemotherapy, these differences persisted years after treatment.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/106 **Status:** On-going

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 Stacey B. Young-McCaughan, AN

Associate Investigators:
Frances M. Lewis, RN, Ph.D. Sandra L. Underhill, RN, Ph.D.

Key Words: Cancer: breast,home visitation

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

Study Objective: (1) To test the effectiveness of a home intervention program for child-rearing families experiencing non-metas' ic 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: All data are being collected and evaluated by the Univ. of Washington. The study continues to recruit subjects and no reports have been generated thus far.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/010 **Status:** On-going

Title: Predictors of Response to Ovulation Induction with Clomiphene Citrate in the Overweight Patient

Start Date: 12/06/91 **Est. Completion Date:**

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Alicia Y. Armstrong

Associate Investigators: CPT Nathan J. Hoeldtke, MC
CPT Carl A. Gibson, MC

Key Words: ovulation induction,clomiphene citrate,overweight

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$12875.00	**Periodic Review:** / /

Study Objective: To determine if aspects of the patient history and endocrine profile (testosterone, androstenedione, DHEAS insulin, and glucose) are predictive of the response to ovulation induction with clomiphene citrate (CC) in the obese patient.

Technical Approach: Patients (n=50), with ovulatory dysfunction documented by basal body temperatures and history, who are > 30% over ideal body weight and not >100% over ideal body weight will be enrolled at the time of the initial infertility visit. At the initial enrollment, patients will complete a detailed menstrual, pregnancy, and weight history, and waist to hip ratio will be done. Weights will be done at initiation and at the third, sixth, and ninth cycles. At the time of enrollment, the patients will have the following serum studies: DHEAS, estrone, androstenedione, testosterone, SHBG, insulin, and 2 hour glucose tolerance test. These studies (with the exception of the 2 hour GTT) will be repeated at the third, sixth, and ninth cycles. A mid-luteal progesterone will also be drawn at the third, sixth, and ninth cycles. Additional documentation of ovulation will be made with urinary luteinizing hormone levels, using ovulation predictor kits and basal body temperatures. Chi square, Student's t test, and regression analysis will be used where appropriate for data analysis.

Progress: Body mass index (BMI) did not correlate with the measured parameters overall. There was an inverse correlation with BMI and the sum of the insulins. Ovulation and pregnancy did not correlate with BMI. Patients with centripetal obesity had the highest elevations of androgens, the lowest SHBG and the highest glucose and insulin levels. Preliminary data suggests that patients with centripetal obesity are less responsive to ovulation induction.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/093 **Status:** On-going

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

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

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Alicia Y. Armstrong

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

Key Words: spermatozoa,cyropresavation,hyperactivation

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

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: A number of methodologic problems have been identified using specimens submitted for semen analysis rather than cryopreserved specimens. These specimens have been used to identify processing difficulties in order to decrease the cost associated with specimens purchased for the protocol. The pH of the media has been altered as it was found to be too acidic and had a deleterious effect on motility. The centrifugation process has also been altered to produce a specimen with improved motility. Preliminary studies have also helped us to identify the optimum temperature and we have identified alterations in the swim-up technique which allows for a better recovery rate of motile sperm.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/021 **Status:** Completed

Title: Amniotic Fluid Index: A Comparison Between Real Time Ultrasound and Color Flow Doppler Ultrasound in its Determination

Start Date: 01/03/92 **Est. Completion Date:**

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Timothy J. Boley, MC

Associate Investigators:
MAJ Jerome N. Kopelman, MC
MAJ Philip M. Bayliss, MC
COL John A. Read II, MC

Key Words: amniotic fluid index,ultrasound,doppler ultrasound

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

Study Objective: To determine if the use of color flow doppler ultrasound alters the quantitation of the amniotic fluid index (AFI) when compared to the standard technique of real time ultrasound.

Technical Approach: Perinatal morbidity and mortality are significantly increased in the presence of increased or decreased amniotic fluid. Currently, real time ultrasound is used to determine the AFI on pregnant patients. However, in some cases, falsely elevated AFI levels may be obtained because it is not possible to identify a loop of umbilical cord using real time ultrasound and it is counted as part of the amniotic fluid. Color flow doppler capabilities are now available which allow for simple identification of the umbilical cord. This procedure has not been compared to real time ultrasound in the determination of AFI. Patients (n=100) undergoing antepartum testing for indicated obstetrical reasons will have an AFI determination made using real time ultrasound. A second AFI determination will then be performed using color flow doppler. These AFI measurements will be completed by different physicians without knowledge of the other's measurement. Patients found to have oligohydramnios (an AFI value of 5 cm of less) will be managed by current departmental standards. A paired t test will be used to analyze the data.

Progress: Nine patients were enrolled in this study. The study is now complete and the P.I. is preparing a paper for publication.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/071 **Status:** Completed

Title: The Establishment of the Doubly Perfused, Placental Cotyledon Model for the In Vitro Investigation of the Umbilical-Placental Circulation

Start Date: 06/05/92 **Est. Completion Date:** Aug 92

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Timothy J. Boley, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
COL John A. Read II, MC
MAJ Philip M. Bayliss, MC
MAJ Jerome N. Kopelman, MC

Key Words: umbilical circulation,placental circulation

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

Study Objective: To establish an in vitro model using the placental cotyledon perfusion system. This model would simulate as closely as possible the in vivo placenta to study the umbilical-placental circulation.

Technical Approach: A cotyledon chamber will be constructed from Plexiglas. This chamber will consist of a cylinder in which the selected cotyledon will be placed on a supporting mesh screen. The placenta will be examined for tears or gross abnormalities. Suitable chorionic vessels will be identified and followed until they drive down into the placenta. An artery and its adjacent vein will be cannulated with 18 gauge intravenous catheters. Perfusion will be begun into the fetal artery at a rate of 3-8 ml/minutes. Two 21 gauge butterfly needles will be placed into the intervillous space near the site where the chorionic artery and vein enter the cotyledon. Perfusion of the intervillous space will be begun at a rate of 6-10 ml/minute. The perfusate consists of a balanced salt solution to which albumin and heparin have been added. The perfusate will be kept at 38 degrees Celsius and will be bubbled with a gas mixture of 95% oxygen and 5% carbon dioxide throughout the perfusion period. The pH of the solution will be continually monitored and adjusted as needed to keep the pH in the 7.35-7.45 range. Pressure will also be constantly monitored within the system. A second cotyledon will then be cannulated and perfused as above. These two cotyledons will then be separated from the rest of the placenta and placed into a temperature-controlled chamber. Samples will be collected from the system every 30 minutes before and after perfusing the cotyledon. The samples will be assayed for oxygen and glucose consumption, prostacyclin, endothelin, and nitrite levels. Results will be compared between cotyledon pairs and placentas. Total perfusion time is 4-6 hours. Approximately 10 placentas from uncomplicated pregnancies will be perfused to establish baseline levels.

Progress: The study is completed. It was determined that cotelydons from different regions of the same placenta exhibit functional synchronicity when used in a paired perfusion system, thus providing an appropriate control.

Interplacental differences were so great that no basal level of any product measured could be determined with the exception of potassium. This suggests the need for a control cotyledon when performing cotyledon perfusion studies.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/156 **Status:** On-going

Title: The Use of Sertraline in Patients With Chronic Pelvic Pain

Start Date: 08/06/93 **Est. Completion Date:** Sep 94

Department: OB/GYN **Facility:** MAMC

Principal Investigator: CPT William J. Bullis, MC

Associate Investigators: MAJ Alicia Y. Armstrong
C.C. Engel, Jr.

Key Words: pelvic pain,sertraline

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

Study Objective: To determine if patients with chronic pelvic pain will benefit from antidepressant therapy.

Technical Approach: Women between the ages of 18 and 50 with chronic pelvic pain (CPP) will undergo baseline gynecological examination and structured psychiatric interview to determine psychiatric diagnosis as well as mood, anxiety, and sexual abuse status. They will also complete a baseline visual analog pain scale and surveys to assess sociodemographics, dissociation level, level of functioning, medication use, and recent medical and psychiatric service use. Following a 2 week placebo run-in period, patients will then be randomized to receive 6 weeks of therapy with Sertraline or placebo. Following a 2 week wash-out period, patients will be crossed over to the alternate agent for the second 6-week arm of the study. Patients will be reassessed periodically during treatment and with a repeat of the initial evaluation at weeks 6 and 14.

Upon completion of the randomized trial, patients who do not have a response to sertraline will be offered laparoscopy to rule out pelvic pathology if they have not previously undergone surgery. Patients responding to sertraline will have the opportunity to be continued on antidepressant therapy.

Progress: The protocol is pending final approval by HSC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/043 **Status:** On-going

Title: A Crossover Evaluation of Alterations in Glucose Intolerance in Pregnancies Treated With Oral B Mimetic Tocolytic Agents

Start Date: 02/05/93 **Est. Completion Date:** Dec 93

Department: OB/GYN **Facility:** MAMC

Principal Investigator: CPT Colleen C. Foos, MC

Associate Investigators: MAJ Jerome N Kopelman, MC
LTC Arthur S. Maslow, MC

Key Words: glucose intolerance:tocolytic agents

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1125.00	**Periodic Review:** / /

Study Objective: To determine if women with indications of preterm labor demonstrate altered glucose tolerance test results on different oral tocolytic agents.

Technical Approach: Twenty four patient volunteers will be randomized into two groups. Group 1 will receive oral terbutaline 5 mg q4h. On the 5th day of therapy, the patient will be administered a three-hour GTT utilizing a 100 gm glucose dose. After the completion of seven days of terbutaline, the patient will be switched to oral ritodrine 20 mg every 4 hours. On day 5 of ritodrine therapy, another GTT will be performed. After completion of one week of ritodrine therapy, the patient will be returned to the Complicated OB Clinic for routine follow up on oral terbutaline.

Group 2 will be treated first with oral ritodrine and then with oral terbutaline. These patients also will have two 3-hour GTT's on the 5th day of therapy on each drug. Due to the short duration of treatment on each drug, the more sensitive and specific 3-hour GTT will be used to diagnose glucose intolerance rather than the routine screening 1-hour GCT.

Each patient will be interviewed weekly at the Complicated OB Clinic regarding compliance with tocolytic therapy, contraction frequency, and side effects. Each patient's heart rate will be monitored for tachycardia as an indicator of compliance with the beta-agonist medications.

Data from the two 3-hour GTT's for each patient will be analyzed by paired T test, or a wilcoxon signed rank test depending upon distribution of the data. Data comparing the terbutaline group to the ritodrine group, may also be analyzed by a chi-square analysis comparing the proportion of abnormal GTTs developed on each drug.

Progress: The principal investigator has been ill, is back at work, and hopes to continue the study. This new protocol has yet to have any patients enrolled.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/041 **Status:** On-going

Title: Correlation of Vaginal Ultrasonographic Findings with Pathology in GYN Surgical Patients

Start Date: 07/02/92 **Est. Completion Date:** Jul 93

Department: OB/GYN **Facility:** MAMC

Principal Investigator: CPT Colleen C. Foos, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
CPT Karen M. Nelson, MC
LTC David J. Magelssen, MC
MAJ Jerome N. Kopelman, MC

Key Words: vaginal ultrasonography,histologic diagnosis,GYN surgery

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

Study Objective: To correlate the preoperative ultrasonographically determined values (ovarian volume endometrial stripe thickness ovarian morphology, outline, internal structure characteristics pulsatility indices of ovarian arteries and color flow doppler characteristics of ovaries and uterus) with operative findings (ovarian volume, uterine volume and weight, endometrial gross appearance, ovarian and uterine morphology) and postoperative histologic diagnosis in women undergoing gynecology surgery.

Technical Approach: Approximately 200 adult patients undergoing gynecological surgical procedures which involve removal or visualization of the ovaries and/or uterus will undergo a vaginal ultrasound examination in addition to the routine preoperative evaluation. Ovarian volumes will be assessed using ovarian dimensions and computing the volume with the formula of an ellipsoid. Doppler flow and color flow doppler will be used respectively to determine ovarian artery pulsatility indices and blood flow characteristics. Maximum endometrial stripe thickness will be measured and ovarian contour, morphology, and echogenicity will be described. At the time of surgery, intraoperative measurements of ovarian dimensions will be measured in vivo. If removed, the uterus will be bivalved to examine the endometrium. For laparoscopic gynecologic surgeries, three ovarian dimensions will be measured on each ovary using a laparoscopic measuring probe. The uterus will be similarly measured. If the uterus is not to be removed, endometrial biopsy will be performed intraoperatively to sample the endometrium. Postoperatively, the surgical specimens will be evaluated in the routine manner. Again ovarian volume will be determined using the above formula. Statistical evaluation correlating preoperative ultrasonography findings with operative and pathologic findings will be performed.

Progress: The principal investigator has been ill, is backt at work, and hopes to continue the study. Seven patients were entered in FY 92, none in FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/002 **Status:** On-going

Title: Changes in Cervical Mucus Following Loop Electrosurgical Excision Procedure (LEEP) for Treatment of Cervical Dysplasia

Start Date: 10/02/92 **Est. Completion Date:**

Department: OB/GYN **Facility:** MAMC

Principal Investigator: CPT David H. Harrison, MC

Associate Investigators: MAJ Alicia Y. Armstrong
Edward Illions, M.D.

Key Words: cervical dysplasia,cerivcal mucus,LEEP

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$3030.00	**Periodic Review:** / /

Study Objective: To determine if the loop electrosurgical excision procedure (LEEP) used in the treatment of cervical dysplasia results in changes in cervical mucus which adversely affects fertility.

Technical Approach: Patients ages 21-35 undergoing evaluation of cervical dysplasia which will be treated by LEEP and who are not currently undergoing hormonal therapy will be asked to participate. Testing, which will involve obtaining a cervical mucus sample at the time of ovulation, will be scheduled based upon ovulation documented by ovulation predictor kits. The mucous will be evaluated by the Penetrak slide test and a cervical mucus score will be assigned. The test will be repeated at 2 and 6 months following the LEEP procedure.

Progress: No patients have been entered. It has been difficult recruiting patients, mostly because of the high percentage of patients on oral contraceptives in our population. An assistant investigator at another institution has likewise discovered the same obstacle. It is planned to pursue other options for enrollment and to continue the study for another year.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/017 **Status:** Completed

Title: Components of Prenatal Care and Low Birthweight

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

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Jerome N Kopelman, MC

Associate Investigators: Shirley A. Beresford, Ph.D.
Susan Brandzel, AN

Key Words: low birthweight,prenatal care

Accu lative		**Est. Accumulative**		**Periodic Review:**
MED E Cost:	$0.00	**OMA Cost:**	$0.00	/ /

Study Objective: To assess acceptability of an exercise program intervention during pregnancy, including barriers to participation; and to obtain consumer input into the planning of an exercise program intervention during pregnancy.

Technical Approach: This study will involve a random sample of two groups of women volunteers recruited by posters in prenatal care waiting rooms at Harborview Hospital and MAMC.

Fifty pregnant women, at any stage in their pregnancies, will be recruited from each site and comprise CPCLP I (the first group) and will complete the questionnaire survey. The receptionist will inform potential participants of the study upon their arrival and, if the patient wishes to participate, will provide the consent form and survey. The receptionist will also indicate that the project coordinator is on site to answer questions. The questions on the survey include information regarding exercise and fitness activities.

Volunteers in their first trimester of pregnancy will be recruited from prenatal care waiting rooms of Harborview and MAMC to attend one of four focus groups and comprise CPCLP II (the second study group). The 90 minute discussion groups will be guided around two questions (1) what kind of exercise program might you attend and (2) what barriers might prevent you from attending. Volunteers, other than active duty military, will be reimbursed $20.00 for their transportation & participation. The discussions will be recorded for purposes of analyses.

Progress: Fifteen women signed up for the class, ultimately only 5 women actually attended the first class. Four of the five who attended the classes found it made them feel healthier and more energetic. One did not feel that is was aerobically challenging. These and the rest of the findings will be used to develop a more helpful program.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/101	**Status:** On-going

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: OB/GYN	**Facility:** MAMC

Principal Investigator: MAJ Jerome N. Kopelman, MC

Associate Investigators: Millie Herd, AN
LTC Glenn C. Tripp, MC

Key Words: herpes simplex virus,pregnancy

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

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: Currently 45 patients are enrolled. Demographics have been compared between those patients enrolled at MAMC and UWMC. The two groups were found to be comparable.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/060 **Status:** Suspended

Title: A Randomized Prospective Evaluation of Bladder Flap Closure at Time of Cesarean Section

Start Date: 05/01/92 **Est. Completion Date:** Apr 93

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Jerome N Kopelman, MC

Associate Investigators: LTC Arthur S. Maslow, MC
COL John A. Read II, MC

Key Words: cesarean section,bladder

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

Study Objective: To determine if the type of closure of the vesicouterine peritoneum affects the postoperative course in low transverse Cesarean section patients.

Technical Approach: Approximately 365 patients having a low transverse Cesarean section will be studied. They will be randomized to either closure or nonclosure of the vesicouterine peritoneal at the time of Cesarean section repair. Patients will be evaluated by ultrasound on day of discharge for fluid collection at the lower uterine segment incision site. Parameters of postoperative morbidity will be compared between the two groups.

Progress: 118 subjectss have been entered. The collection of cases is slower than anticipated and the technical quality of the ultrasounds is poor. The data will be examined at this point to determine if the study is worth pursuing.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/010	**Status:** On-going

Title: Correlation of Single-Void Urinary Protein to Creatinine Ratios vs 24-Hour Urinary Protein Excretion in Pregnant Patients

Start Date: 10/02/92	**Est. Completion Date:** Jun 93
Department: OB/GYN	**Facility:** MAMC

Principal Investigator: CPT Wendy Ma, MC

Associate Investigators:
MAJ Jerome N. Kopelman, MC
CPT Lynda S. Gilliam, MC
MAJ Howard M. Cushner, MC

Key Words: protein excretion,single void vs 24 hour urines

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1424.00	**Periodic Review:** / /

Study Objective: A correlation between single void urinary protein-to-creatinine ratios and 24-hour urinary protein excretion has been shown for nonpregnant populations. This study will investigate the same principal in a unique population subset, pregnant patients.

Technical Approach: The sample population will be selected from MAMC's obstetrical patients who need evaluation for possible preeclampsia, chronic hypertension, or transient hypertension of pregnancy. Twenty-four hour urine collection will be obtained and a spot urine, during that time, will be evaluated for protein, creatinine, and dipstick urinalysis in 100 patients. Blood samples are routinely collected during evaluation and these same serum creatinine results will be used in the study. With the above results, the PI will attempt to plot a correlation between the urine protein/creatinine ratio to the 24-hour total urine protein excretion. She will also investigate the possibility of correlation between the level of protein obtained by dipstick urinalysis and the 24-hour urine protein analysis.

Progress: Data have been collected from 10 patients.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/112 **Status:** On-going

Title: A Randomized, Double-Blind, Placebo-Controlled Study of Parallel Design to Evaluate and Compare the Therapeutic Implant 5-FU-e TI (5003) With and Without Epinephrine to Its Placebo When Administered..

Start Date: 06/09/93 **Est. Completion Date:** Jun 94

Department: OB/GYN **Facility:** MAMC

Principal Investigator: LTC David J. Magelssen, MC

Associate Investigators: CPT Lynda S. Gilliam, MC

Key Words: Condylomata acuminata,5-FU-e TI,epinephrine,collagen

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

Study Objective: 1. To evaluate the safety and efficacy of the therapeutic implant (5-FU-e TI 5003) with and without epinephrine, when administered in 6 weekly injections to male and female patients with external condylomata as compared to placebo gel (collagen). 2. To describe the response rate, the time to recurrence and cumulative recurrence rate of condylomata in patients treated as outlined above. 3. To evaluate the safety and efficacy of treatment in collagen skin test positive patients. 4. To determine fluorouracil levels in plasma after initial injection in patients with a total wart area greater than 100 mm^2 (optional).

Technical Approach: This is a multi-center trial studying 360 male and female patients who have new, recurrent or refractory external condylomata acuminata. MAMC participation will involve 15 patients who may or may not have had previous treatment. Patients will be entered into one of 3 treatment groups and stratified according to total lesion area determined at baseline. Treatment will be with one of the regimens of: (1) 5-FU, Epinephrine, and Collagen; (2) 5-FU, Collagen and Saline; or (3) Collagen and Saline. All treatments will be administered at weekly intervals for 6 doses. Patients will be monitored and target lesions measured during post treatment at week 1, and at months 1, 2, and 3. At the end of three months of follow-up, the randomization will be decoded and patient data will be analyzed to examine response rate and recurrence rate.

Progress: The study is ongoing with 5 subjects entered.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/070 **Status:** Completed

Title: The Effect of Nicotine and Cigarette Smoke Extract on Endothelium-Derived Vasoactive Substances Produced in the Doubly Perfused Placental Cotyledon Model

Start Date: 03/05/93 **Est. Completion Date:** Jun 93

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Glenn R. Markenson, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
COL John A. Read II, MC
MAJ Timothy J. Boley, MC
MAJ Jerome N Kopelman, MC

Key Words: cotyledon:placental,nictotine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$9670.00	**Periodic Review:** / /

Study Objective: Evaluate the effects of nicotine and cigarette smoke extract on the production and release of prostacyclin, thromboxane, nitric oxide and Endothelin 1 by the dually perfused placental cotyledon model.

Technical Approach: Nicotine and cigarette smoke extract will be added to the standard perfusate during a two hour period as described previously (Protocol 92/71). The establishment of the doubly perfused, placental cotyledon model for the in vitro investigation of the umbilical-placental circulation). This solution will then be used to perfuse the cotyledon model to see the effect that these compounds have on the vasoactive substances produced by the model. The viability of the system will be monitored by glucose consumption, potassium levels, and oxygen consumption. Perfusion pressure and pH will also be monitored.

The effluents from the paternal and fetal circulations will be sampled every 15 minutes during the nicotine/cigarette smoke extract infusion. These samples will be analyzed for levels of nicotine, cotinine, nitric oxide, thromboxane (TXB2), 6-keto-PGF1 (stable metabolite of prostacyclin) and Endothelin 1.

Statistical analysis will be performed using the t-test and ANCVA.

Progress: Ten placentas (5 from smokers and 5 from non-smokers) underwent dual perfusion. The addition of nicotine in either situation did not effect perfusion pressure. Assays for vasoactive substances have been performed but the statistical analysis is pending.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/083 **Status:** On-going

Title: A Randomized Trial of Low Dose Aspirin in Pregnancies with Unexplained Elevations of Maternal Serum Alpha-Fetoprotein

Start Date: 04/02/93 **Est. Completion Date:** Jun 94

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Glenn R. Markenson, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
COL John A. Read II, MC
MAJ Timothy J. Boley, MC
MAJ Jerome N. Kopelman, MC

Key Words: alpha-fetoprotein:low dose aspirin

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

Study Objective: 1. To determine if pregnancies with unexplained elevated maternal serum alpha-fetoprotein (MSAFP) would benefit from low dose aspirin therapy. 2. To determine the association between unexplained elevations in MSAFP and antiphospholipid antibodies (APA) and antinuclear antibodies (ANA). 3. To compare placental pathology in those patients with unexplained elevated MSAFP treated with aspirin and with no treatment.

Technical Approach: All patients with unexplained elevated MSAFP, greater than 2.0 multiples of the median, and no history of prior perinatal morbidity or mortality, will be offered entry into the study. All patients will be screened for the presence of autoantibodies, specifically anticardiolipin antibodies, and lupus anticoagulant and antinuclear antibodies. The participants will then be randomized into four groups as follows: Group 1: Unexplained elevated MSAFP with absence of antiphospholipid antibodies, treated with low-dose aspirin. Group 2: Unexplained elevated MSAFP with absence of antiphospholipid antibodies, treated with placebo. Group 3: Unexplained elevated MSAFP with the presence of antiphospholipid antibodies, treated with low-dose aspirin. Group 4D: Unexplained elevated MSAFP with the presence of antiphospholipid antibodies treated with placebo. All patients will be followed in the Complicated Obstetrical Clinic and will receive serial ultrasounds to assess fetal growth. Antepartum fetal testing will consist of biweekly non-stress tests and weekly amniotic fluid indices. Also, uterine artery blood velocity waveform indices will be obtained at initial entry into the study,at 24 - 28 and 32 - 36 weeks gestational age. In addition, all placentas will be sent to pathology for a histologic examination. Students t-test will be used for measured items such as newborn weights, amniotic fluid volume, and Doppler flow systolic/diastolic ratios. Statistical analysis of the grading of chorionic villitis will employ the non-parametric Mann-Whitney U test. Categorical items, such as mode of delivery, preeclampsia, abruptions, presence of autoantibodies, non-reactive non-stress tests, pre-term delivery, and pre-term labor, will be analyzed using the chi-square technique.

Progress: Twenty-three patients have been entered into the study. Only one patient has delivered (uncomplicated but her pregnancy had been complicated by preterm labor). Of those enrolled, 9 of 23 (39%) have at least one antibody (ANA, lupus anticoagulent, anticardiolipin antibody) present. No complications in the undelivered patients have been reported.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/090 **Status:** Completed

Title: The Effects of Estradiol and Progesterone on Vasoactive Substances in the Dually Perfused Cotyledon Model

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

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Glenn R. Markenson, MC

Associate Investigators:
LTC Arthur S. Maslow, MC
COL John A. Read II, MC
MAJ Timothy J. Boley, MC
MAJ Jerome N. Kopelman, MC
MAJ Philip M. Bayliss, MC

Key Words: cotyledon,estradiol,progesterone

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

Study Objective: To document the baseline rate of release/production of estrogens and progesterone in the isolated cotyledon system under varying experimental conditions to delineate the effects of these hormones on the production of eicosanoids and endothelium-derived vasoactive substances and to compare selected other parameters of "viability" of the perfusion system to the steroid production.

Technical Approach: The procedure for initiating, maintaining, and evaluating the integrity/viability of the cotyledon model has been described in the previous protocol "The Establishment of the Doubly Perfused, Placental Cotyledon Model for the In Vitro Investigation of the Umbilical-Placental Circulation." Each substrate listed below will be used in 5 cotyledon perfusions: (1) 17-b-estradiol (E2), 20 ng/ml, and (2) E2, 20 ng/ml plus progesterone (P), 200 ng/ml. Sampling of the fetal and maternal outflow perfusates will be drawn for assays of estradiol, progesterone, and the vasoactive substances TBX2, 6-keto-PGF1, and endothelin 1. Each of these assays will be accomplished with commercially available enzyme immunoassays. Nitric oxide will be measured indirectly from nitrite levels measured in the outflow perfusates. Sampling intervals will be every 15 minutes and the duration of perfusion from the addition of the substrates will be four hours. Each placental cotyledon/lobe will be run as a pair with another cotyledon from the same placenta. This second perfused cotyledon will serve as a control, receiving only the baseline balanced salt solution as a perfusate. Statistical analysis will be performed using the t-test.

Progress: The addition of estrogen and progesterone did not impact on the production of vasoactive substances, O_2 or glucose consumption. We concluded that the addition of estrogen and progesterone is not required in placental perfusion.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/023 **Status:** Terminated

Title: A Comparison of Amniotic Fluid Collected by Amniocentesis versus Amniotic Fluid Collected Via an Intrauterine Pressure Catheter in the Diagnosis of Chorioamnionitis in Laboring Patients at Term

Start Date: 01/03/92 **Est. Completion Date:**

Department: OB/GYN **Facility:** MAMC

Principal Investigator: MAJ Glenn R. Markenson, MC

Associate Investigators:
MAJ Philip M. Bayliss, MC
MAJ Timothy J. Boley, MC
MAJ Jerome N. Kopelman, MC
COL John A. Read II, MC

Key Words:

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

Study Objective: To compare the validity of using amniotic fluid samples collected using an intrauterine pressure catheter versus samples collected by amniocentesis in establishing a diagnosis of chorioamnionitis and to determine the optimum tests to perform on amniotic fluid to establish a diagnosis of chorioamnionitis.

Technical Approach: The study population (n=60) will be divided into Group A, which will consist of term pregnant patients in labor with clinical evidence of chorioamnionitis, and Group B, which will consist of term pregnant patients in labor without evidence of chorioamnionitis. Group A will have a sample collected by amniocentesis and a second sample via an intrauterine pressure catheter. Group A samples will be sent to the lab for gram stain, aerobic and anaerobic cultures, glucose determination, and leukocyte esterase activity. A maternal serum glucose level and CBC will also be done at the time the amniotic fluid sample is drawn. Following delivery, the placenta will be evaluated for evidence of chorioamnionitis. The neonate will be assessed for the presence or absence of neonatal sepsis, and the presence of maternal postpartum endomyometritis will be documented. Group B will have a sample of amniotic fluid collected through an intrauterine pressure catheter which will have the same evaluations as the samples in Group A. A maternal peripheral blood sample will be collected and sent for glucose determination. Results of the data collection for each group will be compared. Differences in results will be evaluated by means of the chi square analysis, paired and unparied t tests, and logistic regression, as needed.

Progress: Two subjects were entered. Subsequently, this study was terminated due to lack of time by the principal investigator.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/022 **Status:** On-going

Title: Continuous Infusion Epidural Analgesia: Its Effects on the Doppler Velocimetry of the Umbilical Arteries of Normotensive and Preeclamptic Patients in Labor

Start Date: 01/03/92 **Est. Completion Date:**

Department: OB/GYN **Facility:** MAMC

Principal Investigator: LTC Arthur S. Maslow, MC

Associate Investigators:
MAJ Jerome N. Kopelman, MC
MAJ Philip M. Bayliss, MC
LTC Joseph J. Mancuso Jr., MC
COL John A. Read II, MC
MAJ Timothy J. Boley, MC

Key Words: umbilical arteries,velocimetry,epidural analgesia

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

Study Objective: To evaluate the effects of continuous infusion epidural analgesia on umbilical artery blood flow in term, laboring pregnancies, including both normotensive and preeclamptic patients.

Technical Approach: Ten normotensive and 10 preeclamptic patients will be studied. The study will involve the measurement of the systolic/diastolic (S/D) ratio of the umbilical arteries in patients electing to have epidural analgesia in labor. All patients will be at term and in the active phase of labor. Continuous infusion epidural technique will be standardized for all patients. The S/D ratio will be determined, using a continuous wave doppler analyzer, in each patient at four intervals: prehydration, posthydraion, at the onset of epidural analgesia, and approximately one hour after the epidural is functional. Pain relief will be documented through skin testing with a needle to record the level of the dermatone achieved and through the patient's own subjective grading, using a standard Glasgow Pain Ruler. Analysis of data will be by paired t test.

Progress: No patients have been enrolled to date, but enrollment is anticipated to begin Jan 94.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/017 **Status:** On-going

Title: Surgical Management of the Bowel and Urinary Tract in Gynecologic Surgery (Swine Model)

Start Date: 01/20/89 **Est. Completion Date:** Indef.

Department: OB/GYN **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators:
COL Richard P. Belts, MC
LTC David J. Magelssen, MC
MAJ John W. Cassels JR, MC

Key Words: gynecologic surgery,training protocol,swine,bowel,urinary tract,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing and stapling techniques and to familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy, and vascular injury repair.

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 training session was held which utilized one pig.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/075	**Status:** Completed
Title: The Management of Minimal Abdominal Trauma in Pregnancy		
Start Date: 04/02/93	**Est. Completion Date:**	
Department: OB/GYN	**Facility:** MAMC	
Principal Investigator: CPT Teresa M. Vanderlinde, MC		
Associate Investigators:	COL John A. Read II, MC	
Key Words: pregnancy,abdominal trauma		

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

Study Objective: To determine the appropriate laboratory analysis and length of monitoring time necessary after mild blunt abdominal trauma in pregnancy by performing a retrospective chart review.

Technical Approach: This retrospective study will consolidate data from all charts of pregnant patients admitted to MAMC for observation after mild, blunt, direct or indirect trauma during the past five years. Charts will be reviewed for independent variables such as description and severity of trauma, vaginal bleeding, uterine tenderness, initial cervical exam, ultrasound evaluation of the placenta and fetus, fetal heart rate, lab data, length of observation and final cervical exam. Review for dependent variables will include pre-term contractions, pre-term labor, need for tocolysis, type of tocolysis, if abruption occurred, and if emergency delivery resulted due to this event.

Statistical regression analysis will be employed to determine the most salient independent variables which can predict any adverse outcomes.

Progress: Insufficient data were available to get conclusive results.

DETAIL SHEETS FOR PROTOCOLS

PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/020	**Status:** Completed
Title: Hepatitis C and Sexual Transmission: A Case-Control Study		
Start Date: 11/06/92	**Est. Completion Date:** May 93	
Department: Preventive Medicine	**Facility:** MAMC	
Principal Investigator: CPT Kent L. Bradley, MC		
Associate Investigators:	MAJ Margot R. Krauss, MC LTC Douglas F. Phillip, MC	
Key Words: hepatitis C,sexual transmission		

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

Study Objective: (1) To better understand the risk factors associated with hepatitis C transmission; (2) To determine the prevalence of risk factors for hepatitis C in relatively asymptomatic patients at a blood donor center.

Technical Approach: Individuals identified by the MAMC blood bank to have been tested Elisa II and Riba positive during March '92 to December '92 and who are currently being followed by the HCV registry in the Department of Preventive Medicine will be mailed a questionnaire to be filled out and returned. Individuals who are notified that they are HCV positive after the study begins will also be given the same questionnaire during their initial counselling session or receive them through the mail. Controls will be selected from blood donor participants who have had negative Elisa II results for antibody to HCV. Three controls will be frequency matched to each case.

The Statistical Analysis System (SAS), Epi-Info crude odds ratios (OR), and standard chi square tests will be used to calculate statistics for the exposure variables. Multivariate analysis will include multiple logistic regression for case or control status based on the variables of interest. Potential confounding will be controlled for by multivariate analysis.

Progress: The results of this study have been prepared for publication and are currently in the review process.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/076 **Status:** Suspended

Title: Early Identification of and Assistance to Pregnant Women Subjected to Domestic Violence

Start Date: 06/05/92 **Est. Completion Date:** Dec 92

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: CPT Heidi A. Fuery, AN

Associate Investigators: MAJ Philip M. Bayliss, MC

Key Words: domestic violence,pregnancy

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

Study Objective: To increase early detection of domestic violence and help direct victims to existing networks by increasing the physician's knowledge of assessing for such signs and symptoms in OB clients. This will be accomplished by teaching the physician the necessary interviewing skills to detect domestic violence and the local resources to assist its victims.

Technical Approach: OB physicians will be assigned to an intervention or a nonintervention group. Each group will be asked to fill out a questionnaire designed to determine their level of assessment in interviewing patients about domestic violence at the start of the study. The nonintervention group will be asked to continue using whatever assessments and interventions they currently use. The intervention group will receive a lecture addressing the signs and symptoms of domestic violence and interviewing techniques. They will be given a list of questions that should be asked of all OB patients and written material to make available to the patients. They will be allowed to intervene with whatever domestic violence interventions are appropriate. They will be asked to document if patients are attending any parenting or other classes. At the end of the study, both groups will be asked to complete a questionnaire to see if they subjectively feel an increase in comfort in asking questions to assess for domestic violence. Charts will be reviewed to ascertain the frequency of documented domestic violence in both populations, physician initiated assessments of the presence of domestic violence, and the use of primary prevention classes by any of the patrons and the FACMT-Spouse report will be used to ascertain if any of the enrolled OB patients were reported as victims of domestic violence. Comparison will be made between the two groups of the number of referrals, the referral rate, the documentation of potential or real domestic violence, interventions used, and physicians comfort level in assessing for and assisting victims of domestic violence during the OB visits. Each question on the pre and post test will be compared for each of the subjects to determine the impact of education and willingness to refer to appropriate interventions.

Progress: No further work was done in FY 93 due to the departure of the P.I. The P.I. is now at Schofield Barracks, where she will submit the protocol. The study has been put in a suspended status until a new investigator can be determined at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/014 **Status:** On-going

Title: Assessment of Risk Factors for HIV Infection Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion - Incident Cases

Start Date: 01/19/90 **Est. Completion Date:** Jun 91

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: MAJ Jeffrey D. Gunzenhauser, MC

Associate Investigators:
COL Kevin M. McNeill, MC
MAJ John G. McNeil, MC
MAJ Margot R. Krauss, MC

Key Words: HIV,risk factors,antibody seroconversion

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/07/92

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 protocol is from WRAIR. The protocol was in the process of being revised during FY93 and no new work was completed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/009 **Status:** On-going

Title: Low-Dose Oral Contraceptives and Cardiovascular Disease

Start Date: 10/02/92 **Est. Completion Date:**

Department: Preventive Medicine **Facility:** MAMC

Principal Investigator: MAJ Margot R. Krauss, MC

Associate Investigators: None

Key Words: from Christina Hrynio,PAD - review to see if need

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

Study Objective: To determine: (1) The relative and attributable risks of acute myocardial infarction among users of all oral contraceptives, and among users of oral contraceptives containing 50 mcg or less of estrogen. (2) The relative and attributable risks of stroke among users of all oral contraceptives, and among users of oral contraceptives containing 50 mcg or less of estrogen. (3) The degree to which age, cigarette smoking, and other risks factors for stroke and acute myocardial infarction modify the relative and attributable risks determined above.

Technical Approach: This is a population-based case-controlled study of the relation between low-estrogen oral contraceptives and cardiovascular diseases (specifically, stroke and acute myocardial infarction) among women 18 - 44 years of age. These cases in King, Pierce, and Snohomish Counties will be identified through a population-based myocardial infarction and stroke ascertainment system through voluntary agreements with institutions in the study area. Information will be obtained from hospital records, paramedic incident reports, autopsy/medical examiner files, and death certificates to document the presence and nature of each myocardial infarction and stroke. After eligibility for the study has been confirmed, each case will be contacted through her physician to obtain permission to approach her and/or a surrogate respondent regarding participation in an in-person interview and blood draw. Subjects and/or surrogates will be interviewed by trained female nurse interviewers.

Progress: Two patients have been identified but not contacted by this date.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PATHOLOGY, BLOOD BANK

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/024 **Status:** Completed

Title: An Anonymous Case-Control Study of Risk Factors for Exposure to the Hepatitis C Virus in Army Blood Donors

Start Date: 12/04/92 **Est. Completion Date:**

Department: Pathology **Facility:** MAMC

Principal Investigator: MAJ Jeffrey A. Schmidt, MC

Associate Investigators: J.V. Writer

Key Words: hepatitis C,blood donors

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To determine the prevalence of selected risk factors for exposure to the hepatitis C virus, e.g., a previous blood transfusion, in a cohort of anti-HCV positive cases and anti-HCV negative controls.

Technical Approach: This study will be done in cooperation with WRAIR. Patients must have had repeatedly reactive (2 of 3 test) anti-HCV enzyme-linked immunosorbant assays (ELISA) and a positive second-generation recombinant immunoblot assay (RIBA) and have completed a Patient Data Form. All serologic tests are performed at the time the subject is enrolled in the HCV Registry; no additional testing will be done. Demographic and risk factor information will be extracted from the Registry files. Controls, volunteer blood donors who are also Army health care beneficiaries, will be asked to volunteer for this study. No serologic evaluations will be carried out in direct support of this research.

All participants will be asked to complete a questionnaire to collect data on HCV antibody positive people for the Registry except that it does not ask for personal identifiers. Consecutive donors will be asked to complete the anonymous questionnaire until 800 usable questionnaires are obtained.

A single data set containing demographic and risk factor variables from the registry cases and blood donor controls will be created. Descriptive statistics will be calculated for each variable for both cases and controls to determine their comparability. Appropriate analysis will be performed on variables to determine the overall relationship between the presence or absence of the virus and various demographic and risk factors. Odds ratios and confidence intervals will be calculated.

Stratified analysis will be conducted to determine the interaction between various characteristics and risk factors. Appropriate multivariate models, such as multiple logistical regression, will be constructed to test the contribution of each variable to the risk of testing positive to anti-HCV.

Progress: Approximately 2000 completed donor questionnaires were collected and forwarded to WRAIR for interpretation. Our participation in the project has been completed.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ 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:** / /

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 on birth weight, length, and head circumference in relation to gestational age have been entered into the computer program database for years '81 to Oct. '93. Preliminary analysis demonstrates that at each gestational age >32-34 weeks, birth weight is greater than in the previously published data. Preliminary analysis of data on twins demonstrates that multiple gestation infants had significantly decreased birth weight at gestational age ≥ 35 weeks. Definitive growth curves will be generated soon.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/095 **Status:** On-going

Title: Effect of Magnesium on Pulmonary Arterial Pressure and Ductal Patency in Newborn Lambs

Start Date: 05/07/93 **Est. Completion Date:** Aug 93

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Joanna C. Beachy, MC

Associate Investigators: MAJ Patrick A. Cambier, MC
MAJ Karl C. Stajduhar, MC

Key Words: magnesium,pulmonary artery pressure,ductal patency,lambs,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$2083.00	**Periodic Review:** 06/07/93

Study Objective: (1) Does an elevated serum magnesium level enhance the normal decrease in pulmonary vascular resistance in the newborn lambs? In other words, in hypermagnesemic newborn lambs, does pulmonary arterial pressure (PAP) decrease more quickly than the normal physiologic decrease or does PAP decrease to a subphysiologic level? (2) Is ductal closure delayed in hypermagnesemic newborn lambs? (3) Is ductal flow altered by increased serum magnesium level in either flow velocity or direction?

Technical Approach: The first part of the experiment will establish the dosing schedule in the newborn lamb that will elevate serum magnesium concentration to 4 - 6 mg/dl. Magnesium 25 mg/kg will be administered by IV injection and the serum level will be measured at 1, 4, and 8 hours after injection. If target magnesium level in not met, the amount of magnesium injected will be increased by 25%. Injections and blood withdrawals will continue until target levels are met or until significant side effects are evident.

In the second part of the experiment, lambs will be randomly placed in 1 of two groups: (1) control lambs and (2) lambs who receive supplemental magnesium by day 3 - 4 of life. Serum magnesium levels will be measured and the dosing schedule adjusted to maintain adequate serum magnesium level. Approximately 3 - 5 days after delivery, lambs will undergo cardiac assessment. Cardiac ECHO will be performed to assess ductal patency and direction and significance of ductal flow. Cardiac angiography will be performed to determine ductal size. Cardiac output will be assessed by thermodilution technique using a Swan Ganz catheter.

Progress: Two lambs were used to establish dosing schedule. The next set of twins were used to verify dosing schedule and adjust ventilation and measure cardiac pressures. The last set of twins were younger on receipt and were given more magnesium sulfate. Complete cardiac data were obtained (pressure & output) in all cases. Magnesium sulfate-treated animals had ductal patency. In the last set of animals, system vascular resistance was similar, but pulmonary vascular resistance was decreased by ~ 8%. Due to problems in establishing adequate dosing schedule 2-3 sets of twins need to be used to complete the study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/058 **Status:** On-going

Title: Neonatal Emergency Procedure Training in the Rabbit Model

Start Date: 04/20/90 **Est. Completion Date:** Indef.

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Joanna C. Beachy, MC

Associate Investigators: LTC Matthew M. Rice, MC

Key Words: training protocol,neonatal,rabbit,neonatal emergency procedure,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$864.00	**Periodic Review:** 06/07/93

Study Objective: To train physicians who have not been previously trained in emergency management of neonates who will be called upon to perform this function in the Neonatal Intensive Care Unit.

Technical Approach: This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands on attempts by the interns and residents. The animal lab will allow the student to observe and practice to proficiency those lifesaving skills necessary in the management and stabilization of the neonatal patient. Telazol, 15 mg/kg, and xylazine, 5 mg/kg IM, will be administered to induce and maintain anesthesia. Additional anesthesia will be administered in increments as needed. The rabbits will be intubated with a 2-3 mm i.d. endotracheal tube and ventilation will be maintained as necessary with 100% oxygen. Tracheal intubation, venous cutdown, needle thoracocentesis, and chest tube insertion will be performed by each intern or resident in attendance.

Progress: This is a training protocol for incoming pediatric interns to learn the correct technique for needling pneumothorax, insertion of chest tubes and clinical signs of pneumothorax. Training is done yearly in the fall. The training session for FY 93 was uneventful and used two rabbits.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/055 **Status:** On-going

Title: Use of the Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Symptom Checklist as an Initial screening Interview for Identification of Obsessive Compulsive Disorder (OCD) and Related .....

Start Date: 04/05/91 **Est. Completion Date:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Robert B. Broadhurst, MC

Associate Investigators: LTC Patrick C. Kelly, MC
Jennifer S. Achilles

Key Words: OCD,screening,Yale Brown Compulsive Scale,symptom checklist,child,n:7 - 18 YO

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

Study Objective: To determine if the short interview is a clinically useful format for identifying Obsessive Compulsive Disorder (OCD) in childhood and to further evaluate the diagnostic screening properties of the CY-BOCS as a semi-structured interview looking for OCD in childhood.

Technical Approach: Approximately 1000 subjects will be selected for interviewing. This will consist of 500 subjects 7 to 12 years old and 500 subjects 13 to 18 years old. Subjects will be randomly selected from appointment rosters. While the parent(s) and child are waiting in the waiting room, they will be asked about participating in this protocol. We will explain that this will involve a 10 minute interview of parent(s) and child in a private exam room. Using the chi-square test, comparisons will be made between the positive and negative short interview groups, between the positive and negative CY-BOCS interview groups, between the positive and negative physical exam finding groups, between the positive trichotillomania/eating behavior and negative groups. Concordance of all positive groups will be assessed. Demographic data in positive and negative groups will be compared. From analysis of the above groups, information on the selectivity of the short interview versus the CY-BOCS for OCD diagnosis at followup will be formulated. Minimal prevalence rates of OCD will be assessed for this clinic sample. All positive interview groups and physical exam findings will be compared with diagnoses and medical problems at followup evaluation. All diagnoses and medical problems will be determined at followup interview, as the gold standard for establishing any diagnosis or medical problem in this study. Data in all the negative groups will be assessed for frequency of "1" level symptoms, trichotillomania symptoms, and eating disorder symptoms on the CY-BOCS according to age, sex and sponsor rank. This will also be correlated with any later DSM diagnoses, which may come about on followup clinical interviews.

Progress: No subjects were enrolled into this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/040 **Status:** On-going

Title: The Short-Term Use of Helium-Oxygen Mixture in Children Hospitalized With Acute, Severe Asthma

Start Date: 12/04/92 **Est. Completion Date:** Apr 93

Department: Pediatrics **Facility:** MAMC

Principal Investigator: LTC Edward R. Carter, MC

Associate Investigators: COL Donald R. Moffitt, MC
CPT Jennifer L. Leathe, MC

Key Words: asthma:heliox

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$802.00	**Periodic Review:** / /

Study Objective: To determine whether the inhalation of helium-oxygen mixture (heliox) will improve pulmonary function and respiratory clinical status in children hospitalized with severe asthma.

Technical Approach: Patients admitted to the hospital for treatment of asthma will be stabilized, and baseline pulmonary function tests, clinical score, heart rate, and transcutaneous carbon dioxide will be recorded. They will 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 10 minutes, pulmonary function testing, assessment of clinical score, and the other measurements will be repeated again. Patients will then be changed to the second gas mixture, and after 10 minutes all the measurements will be repeated. The patients, their parents 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. Difference in continuous variables (i.e. FEV_1 and heart rate) will be analyzed with the two sample Studen's t test, and difference in clinical score (median) will be assessed with the Wilcoxon rank sum test.

Progress: Patient enrollment will begin in Oct 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/041 **Status:** On-going

Title: The Short-Term Use of a Helium-Oxygen Mixture in Indfants Hoszpitalized With Bronchiolitis

Start Date: 12/04/92 **Est. Completion Date:** May 93

Department: Pediatrics **Facility:** MAMC

Principal Investigator: LTC Edward R. Carter, MC

Associate Investigators: COL Donald R. Moffitt, MC
CPT Anthony R. Neri, MC

Key Words: bronchiolitis: helium-oxygen,infants

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1258.72	**Periodic Review:** / /

Study Objective: To determine if the inhalation of a 30% oxygen - 70% helium mixture (heliox) will improve the ventilation and clinical status of infants hospitalized with bronchiolitis.

Technical Approach: Patients will be stabilized and placed in a special plastic box which is placed over the head and chest into which oxygen enriched air can be placed. Baseline measurements will be recorded with the patient breathing 30% oxygen. The patient will then be randomized to receive first either heliox or enriched air with a fractional inspired oxygen concentration (FIO_2) of 30%. Measurements will be taken at baseline and then 10 minutes after breathing the first gas mixture. The subject will then receive the second gas mixture and measurements recorded again in 10 minutes. The primary measurements will be respiratory rate, a clinical score adapted from an established clinical scoring system for bronchiolitis, heart rate, oxygen saturation, and transcutaneous partial pressure of carbon dioxide ($TcPCO_2$). If an arterial line has been placed for clinical reasons we will also measure the partial pressure of carbon dioxide in arterial blood ($PaCO_2$).

Primary end points are changes in PCO_2 (transcutaneous and possibly arterial), clinical score, respiratory rate and heart rate. Differences between continuous variables will be analyzed with the two tailed Student's t test, and differences in clinical score (median) will be assessed with the Wilcoxon rank sum test.

Progress: Patient enrollment will begin in Oct 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/129 **Status:** On-going

Title: Placebo Controlled Trial of Cromolyn Sodium (Intal) in the Prevention of Airway Inflammation in Ventilated Premature Neoantes

Start Date: 07/02/93 **Est. Completion Date:** May 94

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Thomas D. Carver, MC

Associate Investigators:
MAJ Margaret G. Richardson, MS
LTC Deborah J. Leander, AN
CPT Katherine M. Hermann, MC
LTC Robington J. O. Woods, MC

Key Words: Neonates: airway disease,cromolyn sodium,Intal

Accumulative		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$4379.00	/ /

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: No patients have been enrolled. This protocol was approved on 1 Sept with anticipation of enrolling 1-3 patients per month.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/044 **Status:** Completed

Title: Lead Levels and Their Relationship to Attention Deficit Hyperactivity Disorder and Developmental Delay

Start Date: 06/05/92 **Est. Completion Date:** Mar 93

Department: Pediatrics **Facility:** MAMC

Principal Investigator: CPT Cynthia A. Kahn, MC

Associate Investigators: COL Stephen Stephenson, MC
LTC Patrick C. Kelly, MC

Key Words: lead,ADHD

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

Study Objective: To determine if children with attention deficit hyperactivity disorder (ADHD) or developmental delay have elevated lead levels at the time of diagnosis as compared to age matched controls.

Technical Approach: Two hundred controls, 50 children with ADHD, and 50 children with developmental delay will be entered. Controls will be selected at random in the Pediatric Clinic. All newly diagnosed children with ADHD or developmental delay will be asked to participate. Parents will complete a questionnaire after informed consent has been obtained and a blood sample will be obtained from the child for a lead level. The questionnaire will elicit information about the child's attention span, previous testing for lead levels, any diagnosis of anemia, family members or playmates who have had a high lead level, and demographic data to include age, sex, socioeconomic status, length of time in Washington state, other areas lived, and time of year. The following information will be examined: demographic data presence or absence of developmental delay presence or absence of attention problems and lead levels. Using standard statistical tests (chi-square, t-test), comparisons will be made between the control and sample groups based on lead levels. Demographic data will be analyzed with an ANOVA table to insure that these variables are not a cause for difference between groups.

Progress: It has been recommended that children diagnosed with ADHD or developmental delay be evaluated for lead poisoning as a potential etiology for their problem. We have not found this recommendation to be beneficial in the population studied. Therefore, we recommend that there is no need to check blood lead levels routinely at the time of diagnosis in a low risk population. Further investigation of this issue in a high-risk area is warrented to better define the relationship between ADHD, developmental delay, and blood lead levels.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/004 **Status:** Terminated

Title: Incidence of Group A Beta Hemolytic Streptococcus Colonization and Infection in Association with Varicella

Start Date: 11/01/91 **Est. Completion Date:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: LT Kenneth L. Brooks, MC

Key Words: varicella,streptococcus,colonization,infection

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$748.00	**Periodic Review:** / /

Study Objective: To determine the frequency at which Group A beta hemolytic streptococcus (GABHS), in association with varicella, will colonize the pharynx, the rectum, and the varicella lesion and to determine the attack rate of GABHS in patients with, or without, positive cultures of GABHS.

Technical Approach: This will be a multicenter study with a total of 520 patients entered. Patients who have been diagnosed with Varicella will have a culture taken from an intact Varicella lesion and from the pharynx and the rectum. Patients will be recultured between days 5 and 7 of the rash with at least 48 hours between cultures. Data to be collected will include: age, sex, day of rash at presentation, treatment before and after enrollment, month of year, first and second culture results from each site, estimate of the number of Varicella lesions, presence or absence of Varicella mucosal lesions, and infectious complications during the Varicella illness, which may include any of the following: local cellulitis, bacteremia/sepsis, osteomyelitis, streptococcal toxic shock-like syndrome, arthritis, pneumonia, gangrenosa, abscess, erysipelas, endocarditis, and acute glomerulonephritis. The end points that will be evaluated include: the culture results in the pharynx and rectum being positive or negative for GABHS, the culture results in the Varicella lesions being positive or negative for Streptococcus and/or Staphylococcus, and the presence or absence of infection with GABHS. Confounders may include: the patient's age, sex, day of presentation, number of lesions, presence or absence of Varicella mucosal lesions, and month of year. Chi square analysis will be used to evaluate the results.

Progress: The project was terminated due to lack of adequate access to the desired patient population.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/071 **Status:** Terminated

Title: Pyridoxine as Specific Therapy and Prophylaxis in the Treatment of Theophylline-Induced Seizures in Mouse and Rabbit Models

Start Date: 05/18/90 **Est. Completion Date:** May 91

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators:
COL Michael R. Weir, MC
LTC Patrick C. Kelly, MC
CPT Gregory M. Glenn, MC
LTC Joseph P. McCarty, MC

Key Words: seizures,prophylaxis,pyridoxine,mouse,rabbit,Animal Study

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$420.00	Periodic Review: 06/07/93

Study Objective: To investigate the therapeutic efficacy of pyridoxine in seizures secondary to theophylline overdose in rodent models.

Technical Approach: Part I: Inbred male mice will be divided into a control group of 10 mice (250 mg/kg aminophylline, 75% expected to seize) and a pretreatment group. The pretreatment group will be subdivided into four groups of 10 mice and given 25, 50, 100, and 250 mg/kg of IP pyridoxine, respectively. A third group will be given 250 mg/kg of IP aminophylline and then pyridoxine at the onset of seizure, and subdivided into four groups of 10 mice, given 25, 50 100, and 250 mg/kg, respectively. Time to seizure and mortality rate will be observed. In this fashion, it is anticipated that a dose-response range can be established based on human models. Part II: After a successful dose-response range has been established in Part I, initial EEG trials with external electrodes will be attempted on conscious untreated rabbits. If reliable EEG results can not be obtained in this manner, then the rabbits will be anesthetized and stainless steel screw electrodes will be placed overlying the dura in both centroparietal areas with a reference electrode placed in the frontal sinus. Bipolar recording of EEG activity will be recorded on a Grass recorder and EKG and respirations will also be monitored using the Grass recorder. Six New Zealand white rabbits will be anesthetized and given 115 mg/kg of IV aminophylline over 50 minutes with an expected seizure rate of 80% with a mean time to seizure of 108 minutes. The first group of 3 animals will be pretreated with the same mg/kg dose of pyridoxine as found to be effective in Part I. The second group of 3 animals will be given a mg/kg dose of pyridoxine as found to be effective in Part I at the onset of seizures. If apnea occurs, assisted ventilation will be given for a maximum of 10 minutes to minimize the mortality secondary to apnea alone. Time to seizure, duration of seizure and mortality rates will be noted. Pre and post aminophylline PLP levels will be determined as well as PLP, theophylline, and standard chemistries at the onset of seizure. Once seizures are controlled with the pyridoxine, PLP and theophylline levels will again be determined. These findings will be correlated with EEG findings. Revision I (20 Jul 90): Initial findings (using mice) indicated that pyridoxine may have an effect in preventing theophylline seizures. The investigators then did a pilot study in an attempt to maximize the therapeutic effect by providing 500 mg/kg pyridoxine, after 250 mg/kg theophylline and noted a significant delay in time to seizure. The protocol was revised to allow the investigators to serially inject 250 mg/kg of pyridoxine at 5, 15, and 50 minutes after the theophylline dose in order to provide pyridoxine levels over the time frame of seizures in the control group and to achieve an experimental number, balanced

by sex. In previous experimental groups, female mice appeared to predominate in the seizure group. Therefore, 20 additional control females will be studied in order to alleviate any effect due to sex. If results are promising, the investigator will then commence with Part II of the protocol, using larger animals. Revision II (17 Aug 90): A revision was approved to add a study of the use of propranolol in place of pyridoxine in the acute model with the 30 mice given theophylline as before. Instead of a large single dose of pyridoxine, a large single dose of propranolol will be given. Several doses will be given in order to find a dose-range. Also a chronic model using 30 mice will be studied. Animals will be given half the acute dose of theophylline daily for five days. Half of the animals will be given the mg equivalent dose of pyridoxine while the remainder will be given isovolemic saline. Revision III (21 Sep 90): The studies showed that EEG changes caused by aminophylline could be reversed with acute pyridoxine, followed by a 230 mg/kg/50 min pyridoxine infusion. The animals developed theophylline levels of 192 mg/ml immediately and fell to 99 mg/ml at 3-4 hours and were asymptomatic when returned to their cages. Six of 6 animals died shortly thereafter, raising the question of whether prolonged infusion of pyridoxine until blood levels fell to therapeutic ranges in 3 half-lifes would result in saving the subject. Therefore, the protocol was amended to study 6 rabbits with prolonged pyridoxine infusion (approximately 12 hours).

Progress: No work has been done on this protocol since November 1990 therefore the protocol was terminated.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/022 **Status:** On-going

Title: A Randomized Controlled Trial of Penicillin to Evaluate the Clinical Response in Group C Streptococcal Pharyngitis

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

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: CPT James P. Guevara, MC
LTC Christopher B. White, MC

Key Words: pharyngitis,streptococcus,penicillin

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

Study Objective: To determine the effect of penicillin therapy on the clinical course of group C streptococcal pharyngitis in children. To determine the efficacy of penicillin in eradicating group C streptococci from the pharynx of children.

Technical Approach: Patients eligible for enrollment will be those ranging in age from 3 to 19 who have acute group C streptococcal pharyngitis diagnosed by rapid strep test and/or throat culture. To obtain an alpha error of 0.05, a beta error of 0.20, a clinical difference of 3 on the mean symptom scores between the control and treatment groups, with a standard deviation of 1/6 and 3.4 respectively for the two groups, an enrollment of 32 patients (16 in each arm) will be needed. Patients will be stratified into two groups by virtue of whether they were enrolled on the basis of a rapid strep or throat culture and then randomized using a table of random numbers to receive either penicillin V 250 mg or a placebo (formulated to have a similar appearance and taste) three times a day for 10 days. Patients will be asked to withhold antipyretic medications for the first 72 hours and to have temperatures measured every 8 hours. However, if patients develop a fever greater than 103 degrees fahrenheit, Tylenol may be given in an age appropriate dose and doses recorded. Patients will receive follow-up in clinic at 48 hours to obtain repeat throat culture and urine specimens to detect the presence of penicillin and again at 14 days to obtain repeat throat cultures of antibiotics or placebo. A clinical scoring system will be used to quantitate symptoms and signs at the time of enrollment and at the 48 hour follow-up.

Differences in mean symptom scores and mean temperatures over time between treatment and control groups will be analyzed by ANOVA with repeated measures. Any statistically significant differences will have further follow-up by a Newman-Keul's test to detect which differences are statistically significant. Differences in throat culture positivity will be assessed by Fisher's Exact Test.

Progress: No patients have been entered into this study because of the difficulties in obtaining the necessary placebo medication.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/053 **Status:** Terminated

Title: Role of Glutamine and 4-aminobutyraldehyde in Pyridoxine-Treated Theophylline Toxicity

Start Date: 04/05/91 **Est. Completion Date:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators:
COL Michael R. Weir, MC
CPT Katherine H. Moore, MS
LTC Patrick C. Kelly, MC
John Enriquez
MAJ John W. McBurney, MC

Key Words: seizures,glutamine,4-aminobutyraldehyde,theophylline toxicity,Animal Study

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 06/07/93

Study Objective: To test whether seizure activity can be altered with glutamine or 4-aminobutyraldehyde in theophylline toxicity that has been altered with pyridoxine.

Technical Approach: Female mice will be given aminophylline for toxicity, followed by equivalent doses of pyridoxine. They will then be given varying doses of glutamine and 4-minobutyraldehyde in order to determine the maximal effective doses. For the next phase, the study animals will receive theophylline and pyridoxine and the dose chosen above of either glutamine (6 animals) of 4-aminobutyraldehyde (6 animals). Groups of six will also receive half and twice the chosen amount of theophylline and pyridoxine. Control groups will consist of three animals and will use test drugs in: each drug alone (mid range dose) with pyridoxine and with theophylline theophylline alone, and with pyridoxine and pyridoxine alone. The animals will be observed for time to seizure and time to death. Eighteen rabbits will have baseline EEG recordings done and then will be returned to the cage and observed to explore the limits of EEG changes and variation in rabbits. Six animals will receive 115 mg/kg aminophylline followed by pyridoxine 115 mg/kg plus glutamine as derived from the mouse studies. The most effective mouse dose will be reduced by a fraction that corresponds to the reduction in aminophylline dose, i.e., 115/250. With that as a base dose, double and half doses will again be used. Six animals will be similarly treated with 4-aminobutyraldehyde. Two animals will receive theophylline only, two theophylline and pyridoxine, and two will receive the best dose of both study medications with theophylline and pyridoxine in two. EEG recordings will be obtained at 15 minute intervals. Baseline blood samples will be drawn for pyridoxal-5'-phosphate and again after aminophylline, pyridoxine, and glutamin/aminobutyrate. Spinal taps will be attempted on some animals for determinations of GABA and glutamine. The animals will be observed for a period of three hours with EEG monitoring, followed by three days in cages. Consistent presence or absence of effect on the EEG is expected. Analysis of blood levels of PLP and CSF levels of GABA and glutamine will be by repeated measures ANOVA with post-hoc testing by paired t-tests. The resulting paper will be descriptive.

Progress: Work has never been initiated on this protocol.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/076 **Status:** Terminated

Title: Protective Role of Pyridoxine in Gentamicin Nephrotoxicity

Start Date: 09/15/89 **Est. Completion Date:** Sep 90

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: LTC Jose D. Masi, MC
COL Michael R. Weir, MC

Key Words: nephrotoxicity,gentamicin,pyridoxine,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$3135.00	**Periodic Review:** 06/07/93

Study Objective: To test whether pyridoxine has a protective effect on gentamicin nephrotoxicity.

Technical Approach: Following a period of quarantine and observation, rabbits will be premedicated with xylazine and ketamine and then taken to the operating suite in groups of seven. One animal will receive 100 mg of pyridoxine as a control. The remaining animals will receive either 20 mg/kg or 60 mg/kg of gentamicin intramuscularly. One animal at each gentamicin dose will then receive either saline or 10 mg pyridoxine or 100 mg pyridoxine. These medications will be repeated daily for five days. Blood will be drawn for pyridoxal 5'-phosphate (PLP), gentamicin, and creatinine on days 1 (before injection), 3, and 5. Following the last injection in the morning, the animals will be sacrificed in the late morning or early afternoon using pentobarbital or suitable substitute, and one kidney from each animal will be recovered for fixation for blinded and pathologic interpretation. In each of two subsequent weeks, seven more animals per week will be studied similarly. This is a descriptive study in which the investigators hope to show that there is a general relationship between renal pathology and the average fall in PLP or, potentially, a relationship between pathology and gentamicin blood levels. BMDP and SPSS will be used to analyze data. If there are striking differences between the renal pathology of the various animals, the pathology will be scored for rank testing versus PLP, creatinine, gentamicin levels, and B6 dose.

Progress: No work has been done on this study since Mar 91. Delays have ensued because the dose of gentamicin did not produce significant renal pathology and new arrangements were needed for blood PLP assays.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/007 **Status:** Completed

Title: A Comparative Study of the Safety and Efficacy of Clarithromycin and Eryped (Erythromycin Ethylsuccinate) Suspensions in the Treatment of Children with Community-Acquired Pneumonia

Start Date: 12/06/91 **Est. Completion Date:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators:
MAJ Arlene E. Roots, AN
COL Donald R. Moffitt, MC
LT Kenneth L. Brooks, MC

Key Words: pneumonia,Clarithromycin,Aaugmentin,children

Accumulative		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$150.00	03/05/93

Study Objective: To compare the efficacy and safety of clarithromycin and erythromycin ethylsuccinate suspensions in the treatment of children with community-acquired pneumonia who are suitable candidates for oral macrolide therapy.

Technical Approach: Children from 3 to 12 years of age with community-acquired pneumonia will be treated with either clarithromycin 7.5 mg/kg/dose b.i.d., or 20.0 mg/kg/dose b.i.d, or 13.3 mg/kg three times a day. About 300 patients will be enrolled nation-wide, with approximately 10 patients enrolled at Madigan. Patients must have x-ray confirmation of the diagnosis of pneumonia. They must not have underlying chronic disease, renal disease, or hepatic disease. At the initial visit, the children will have CBC, CRP, blood chemistries, blood culture, sputum culture, and serology and culture for chlamydia and mycoplasma. The children will return in 5-7 days for repeat clinical evaluation. Urine will be obtained to check for compliance. The child will receive antibiotics for 10 days and return to the clinic within 48 hours of stopping treatment. A repeat chest x-ray will be done and sputum will be cultured, if possible. CBC and chemistries will be retested. The patient will be evaluated for culture, x-ray, and clinical response to treatment. Laboratory and clinical side-effects of treatment will be noted. A final visit will be at 4-6 weeks. Convalescent serum will be obtained at that time. Results will be used to compare the safety and efficacy of clarithromycin and erythromycin.

Progress: Two patients were entered into this study at MAMC. The data were sent to the sponsor for analysis.

Detail Summary Sheet

Date: 30 Sep 92 **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: COL Marvin S. Krober, MC

Associate Investigators:
MAJ Thomas A. Perkins, MC
COL James S. Rawlings, MC
MAJ Joanna C. Beachy, MC

Key Words: HIV,diagnostic assays,children

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

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: Data have been forwarded to a central file at WRAIR which has been used to provide useful information on age-related CD_4 lymphocyte parameters.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/093 **Status:** Terminated

Title: Epidemiology of HIV in Pediatric and Perinatal Patients: A Natural History Study

Start Date: 07/20/90 **Est. Completion Date:** Jul 93

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators:
COL James S. Rawlings, MC
MAJ Thomas A. Perkins, MC
MAJ Joanna C. Beachy, MC

Key Words: HIV,epidemiology,pediatric

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 12/04/92

Study Objective: To establish a Pediatric AIDS Center (PAC) to identify at-risk dependents of HIV positive individuals, compile a high-risk HIV pediatric registry, collect basic epidemiological data, and conduct longitudinal follow-up studies to assess the transmission and progression of HIV infection following heterosexual and/or perinatal exposure.

Technical Approach: This is a multicenter study, which originated at Walter Reed Army Medical Center and is being funded by an NIH grant. The Armed Forces are required, by Department of Defense directive, to screen all active duty personnel for antibody to HIV. Army personnel who are positive for HIV antibody are reported to the US Army HIV Data System (USAHDS). The PAC will identify and follow all eligible pediatric beneficiaries of HIV positive soldiers by comparing USAHDS reports with computer linked family records in the Defense Enrollment Eligibility Reporting System data files. Dependents who are identified from matching records will be entered into an HIV high-risk patient registry. To validate the matching process and to facilitate evaluation of high-risk families, a physician network with coordinators at each Army regional medical center will be established. The regional coordinators will work with the PAC to provide an accurate clinical evaluation, obtain appropriate laboratory studies, and organize regular followup for high-risk patients. Each patient will be evaluated for HIV infection with antibody screening, HIV culture, and antigen assay. Infection will be staged according to current Center for Disease Control (CDC) recommendations. Clinical information from the initial evaluation and subsequent follow-up visits will be entered into computer-managed patient files at the PAC. CDC classifications will be updated with results from the most current evaluation. Once the PAC has been established, the investigators anticipate that the HIV registry and PAC could be expanded to follow patients from all three branches of the Department of Defense.

Progress: Data were forwarded to a central file at WRAMC. The project was terminated because of loss of NIH funding.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/107 **Status:** Terminated

Title: Perinatal HIV Infection: Epidemiology and Natural History

Start Date: 09/21/90 **Est. Completion Date:** Apr 95

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators:
MAJ Thomas A. Perkins, MC
MAJ W. Kim Brady, MC
COL James S. Rawlings, MC
MAJ Joanna C. Beachy, MC

Key Words: HIV,epidemiology,natural history

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To develop a clinical perinatal center for the diagnosis and management of pregnant women with human immunodeficiency virus (HIV) infection and their newborn infants and to systematically collect clinical, laboratory, and epidemiologic data describing the course and natural history of perinatal HIV infection.

Technical Approach: Preliminary screening will be performed with the ELISA test and positives will be confirmed by Western blot assay, and the women will be staged according to the Walter Reed Staging System. The initial evaluation will include a physical examination, assessment of fetal growth and well being, HIV culture, quantitative T-cell subset analysis, CBC, serology for CMV, toxoplasmosis and herpesvirus, and blood samples for p24 antigen assay, in situ hybridization, and polymerase chain reaction (PCR). Reassessment will be done during each trimester of pregnancy and at the time of birth using the same test measures as in the initial evaluation. At the time of birth, the placenta and a segment of the umbilical cord will be sent for electron-microscopic, histochemical, and immunofluorescent analysis. Postpartum cervical cultures will be obtained for CMV and Herpes virus cultures. A sample of breast milk will be obtained for HIV culture in women who forego suppression of lactation. Infants will be evaluated at birth and then every three months for two years. Laboratory tests will be the same as for the mother with the addition of urine, rectal, and nasopharyngeal cultures for CMV. Physical exam in infants will also include assessment for fetal embryopathy. Subjects will be divided into two subsets: (1) HIV+ mother and HIV+ infant and (2) HIV+ mother and HIV- infant. Descriptive statistics will be used to describe the entire sample and prevalence comparisons will be made for the two major subsets. Analytic methods may involve both univariate and multivariate techniques.

Progress: Data were forwarded to a central file. Project was terminated due to loss of NIH funding.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/018 **Status:** Terminated

Title: Role of Pyridoxine in Gentamicin-Lasix Nephrotoxicity in Rabbits

Start Date: 12/07/90 **Est. Completion Date:**

Department: Pediatrics **Facility:** MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: COL Michael R. Weir, MC

Key Words: nephrotoxicity,gentamicin-Lasix,pyridoxine,rabbit,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To test whether or not the nephrotoxicity and altered blood-brain barrier associated with a gentamicin-lasix combination can be altered by pyridoxine.

Technical Approach: Twenty-two New Zealand white rabbits will be divided into the following groups: gentamicin + lasix + saline (7 rabbits) gentamicin + lasix + pyridoxine (7 rabbits) pyridoxine only (2 rabbits) gentamicin only (2 rabbits) lasix only (2 rabbits) saline only (2 rabbits). On day one of the study, baseline blood samples will be obtained for measurement of creatinine, gentamicin, and PLP (the active form of pyridoxine) levels. The animals will receive IM injections by group for five days. On days 5, 8, and 12 blood samples will again be obtained to measure creatinine, gentamicin, and PLP levels. The IM injections will be repeated on days 8 - 12. The animals will be sacrificed on day 12 and the kidneys and the brains will be sent to the pathologist who will grade the pathology on the following 5 point scale: (1) no significant pathology (2) focal ATN involving <10% of the tubules (3) mild ATN involving 10-25% of the tubules (4) moderate ATN involving 26-50% of the tubules, widespread ballooning necrosis of tubular epithelium, definite nuclear degeneration (at least focally) proteinaceous material in tubules ± interstitial inflammation and tubular regenerative changes and (5) severe changes involving over 50% of the tubules with changes as in #4 but more wide spread. Changes in blood levels of creatinine, gentamicin, and PLP will be compared between the two study groups by ANOVA.

Progress: Work was never initiated on this protocol.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/071 **Status:** Terminated

Title: Comparison of Effectiveness of Lidocaine HCL vs Hyaluronidase in the Early Treatment of Soft Tissue Extravasation Injuries in Swine

Start Date: 07/28/89 **Est. Completion Date:** Oct 89

Department: Pediatrics **Facility:** MAMC

Principal Investigator: CPT John S. Scott, MC

Associate Investigators: COL Michael R. Weir, MC

Key Words: extravasation injuries,lidocaine HCL,hyaluronidase,swine,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$614.00	**Periodic Review:** 06/07/93

Study Objective: To determine if Lidocaine HCl is a superior therapeutic agent in the treatment of soft tissue extravasation when compared to more traditional therapy.

Technical Approach: The agents which produce cell death by direct cellular toxicity when extravasated include such drugs as Adriamycin, methotrexate, and Renografin. This study will focus on the efficacy of lidocaine HCl versus hyaluronidase as a primary therapeutic agent in the treatment of soft tissue extravasation injury produced by the subcutaneous infusion of Renografin. One pig will be used to attempt to create an extravasation injury. If this attempt is successful, then an extravasation injury will be created in three additional pigs. Each animal will have its flank closely shaven. Renografin will be injected subcutaenously into two areas of the flank in order to created the extravasation injury. X-rays will be used to determine the distribution of the Renografin. After the injury has been created, one injection site on each pig will be infused with normal saline and the other site injected with either hyaluronidase alone, lidocaine HCl alone, or a combination of lidocaine HCl and hyaluronidase. In this manner each pig will serve as its own control. Lesions will be monitored daily for the presence or absence of blister formation and these results photographed and recorded. Measurements will include necrosis and induration. The data will be analyzed by comparing the daily induration and blister or ulcer size to healing or to scar.

Progress: The P.I. requested termination of this study. This study was never implemented at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/067 **Status:** Completed

Title: Cervical Human Papillomavirus Infection Prevalence in Female ROTC College Cadets

Start Date: 06/05/92 **Est. Completion Date:** Aug 92

Department: Pediatrics **Facility:** MAMC

Principal Investigator: MAJ Elisabeth M. Stafford, MC

Associate Investigators:
MAJ Gilbert R. Teague, MC
MAJ Barbara A. Crothers, MC
COL Terrel J. Michel, MC
MAJ Robert S. Stewart, MS
COL Dan C. Moore, MC

Key Words: papillomavirus,college cadets

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To determine the prevalence of cervical HPV (Human Papillomavirus) infection in ROTC college students from a geographically diverse sample.

Technical Approach: Five hundred young adult women reporting for inprocessing ROTC physicals will be asked to participate in this cervical Human papillomavirus infection screening study. Participation will include completion of a questionnaire and processing of an endocervical sample for HPV obtained from the routine PAP smear sampling. PAP smears revealing squamous or glandular cell abnormalities will require cervical colposcopy as standard of care. Cadets with negative PAP smears and positive HPV DNA screen will not undergo colposcopy, but will be informed of the positive result with the recommendation that they make this information available to their private physician. After determining the prevalence of HPV cervical infection, data will be further analysed using chi-square analysis and stepwise logistic regression to determine significant variable associations with HPV status.

Progress: 332 women representing 42 states, mean age of 21.9 years, were studied. Racial composition included 70% Caucasian, 16% Black, 4% Hispanic, 4% Asian, and 6% others. Eight-six percent had a history of heterosexual activity, mean age at onset of 17.7 years. One in eight had a past sexually transmitted disease.

Pap smears yielded 7.8% abnormal results. Colposcopic biopsy results were available for 24 of 26 abnormal Paps. There was 84% agreement between positive Paps and colposcopic biopsy results. HPV screening resulted in 9.1% positives. Of the abnormal Paps verified by colposcopy, 62% were HPV positive. Of the negative Pap smears, 5.6% were HPV positive. In conclusion, DNA amplification technique did enhance overall HPV detection rate. Its role as an indicator for colposcopic evaluation, however, is still unclear and should be addressed in a future study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/046 **Status:** On-going

Title: Single Dose Cefixime Therapy for the Treatment of Uncomplicated Urinary Tract Infections in Female Children and Adolescents

Start Date: 02/05/93 **Est. Completion Date:** Jul 94

Department: Pediatrics **Facility:** MAMC

Principal Investigator: LTC Christopher B. White, MC

Associate Investigators:
LTC Janet L. Rowe, MC
COL Marvin S. Krober, MC
MAJ Elisabeth M. Stafford, MC

Key Words: urinary tract infections:female children,cefixime

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

Study Objective: Using a medically-approved oral cephalosporin (cefixime) with a broad antimicrobial spectrum and a long half-life, we will attempt to show that a single oral dose of cefixime can be used successfully to treat uncomplicated lower urinary tract infections in females between the ages of 3 - 21 years of age. Additionally, the impact (if any) of giving extra oral fluids in the first three days of therapy on the successful treatment of lower urinary tract infections in the same patient population will be studied.

Technical Approach: Children and adolescents presenting to the pediatric clinic with signs and symptoms of lower urinary tract infection, who are toilet-trained (avoiding the need for catheterized urine sample) and without fever will be candidates for the study. If urinalysis reveals evidence of infection, they will be given an opportunity to participate in the study. Confirmation of urinary tract infection will be by urine culture. Patients will be randomized to one of three treatment regimens: (1) oral cefixime, 8 mg/kg/day as one dose x 7 days; (2) Oral cefixime, 8 mg/kg as a single dose; (3) Oral cefixime, 8 mg/kg with extra fluid supplementation (approximately 90 - 100% daily maintenance fluid requirement) given for the first three days of treatment. Maximum dosage for cefixime will be 400 mg/day. Four follow-up visits will be done: (1) 2 - 3 days after initiation of therapy, (2) 10 - 14 days after initiation of therapy, (3) approximately 30 days after initiation of therapy, and (4) approximately 60 days after initiation of therapy at which times urine cultures will be obtained. Patients with positive cultures at 2 days will be considered failures and have therapy modified as appropriate based on the sensitivities of the organism(s) on initial culture. Patients with positive culture at later follow-up visits will be considered relapses or recurrences, depending on the organism and/or the antibiotic sensitivity pattern of the organism. Outcomes for each treatment arm will be analyzed by the chi-square test to compare frequency distribution between groups. Differences with a probability of less than 0.05 will be considered significant.

Progress: Progress on the study was interrupted due to an unexpected deployment to Somalia. Slow enrollment has been a problem and is being addressed.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF RADIOLOGY

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/028	**Status:** On-going
Title: Quantitative Pulmonary Perfusion		
Start Date: 12/04/92	**Est. Completion Date:** Jan 93	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: LTC John M. Bauman, MC		
Associate Investigators:	MAJ Stephen E. Budd, MC	
Key Words: pulmonary perfusion		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1490.00	**Periodic Review:** / /

Study Objective: To determine the normal split lung function and reproducibility of quantitative lung perfusion with technetium macro aggregated albumin (99mTc-MAA).

Technical Approach: All volunteers will receive pulmonary spirometry and a chest x-ray to determine normalcy of volunteers. All female volunteers and in child bearing age will have a negative serum beta-HcG documented. While in the supine position an IV injection of approximately 1.5 millicuries 99mTc-MAA (less than half the usual dose given at MAMC for diagnostic pulmonary studies) will be administered. Both anterior and posterior images of 800,000 counts will be computer acquired and a geometric mean will be calculated and reported. A second study utilizing the same dose will be done within 2 weeks of the initial study, but will not require repeat spirometry or chest x-ray.

Progress: Work on this project has been delayed by the illness of the PI.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/098 **Status:** On-going

Title: Establishing Normal Gastric Emptying Times for MAMC

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

Department: Radiology **Facility:** MAMC

Principal Investigator: LTC John M. Bauman, MC

Associate Investigators: MAJ Stephen E. Budd, MC

Key Words: gastic emptying:normal time

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$30.00	**Periodic Review:** / /

Study Objective: To determine the normal range for gastric emptying times using the new MAMC Nuclear Medicine SOP.

Technical Approach: Ten volunteers will be studied twice. The volunteers will be NPO after midnight and on the morning of the study will be fed a meal per the new MAMC protocol for gastric emptying, but the meal will include only 50% of the 500 microcuries of 99mTc sulphur colloid stated in the new MAMC protocol. The protocol consists of 2 medium raw eggs which are injected with approximately 500 microcuries of 99mTc sulfur colloid, incubated 5 minutes, then scrambled, and eaten by the patient between 2 slices of bread/toast as an egg sandwich. Approximately 100 cc of juice are included with the meal. The volunteer has 5 minutes to ingest the meal. The volunteer will be placed in a sitting position, and a 45 degree left anterior oblique acquisition will be obtained. Serial one minute images will be computer acquired for a total of 60 minutes. This will be repeated within 2 weeks with another 250 microcuries of 99mTc sulfur colloid. The data will be processed by the technologist using the proprietary gastric emptying software provided by MEDASYS, which generates a half emptying time for statistical evaluation.

Mean, range, and standard deviation for each set of data will be calculated. A repeated measures ANOVA will be calculated.

Progress: Work on this project has been delayed by illness of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 92	**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	J. Billingsley LTC Clifford L. Simmang, MC	
Key Words: gallbladder,ejection fractions		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $6166.00	**Periodic Review:** / /

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/kilogram 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: This study has been delayed due to the illness of the PI.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/124 **Status:** On-going

Title: Measurement Accuracy of Reformatted MR Images in Cardiac Imaging Using 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

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

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: The MRI data on the cadaveric pig hearts (n=4) has already been obtained. The data has yet to be processed and analyzed.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/053	**Status:** Completed
Title: Juvenile Huntington Disease: CT and MR Features		
Start Date: 03/05/93	**Est. Completior Date:** Feb 94	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	Sylvester H. Chuang, M.D.	
Key Words: Huntington disease:CT and MR features		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To retrospectively (1) review CT and MR studies of the brain performed on children with juvenile Huntington disease, (2) determine if radiologic criteria established for adult Huntington disease are valid for juvenile Huntington disease and (3) determine imaging criteria for the radiologic diagnosis of juvenile Huntington disease based on comparison with the CT scans performed on normal children.

Technical Approach: This is a retrospective review of 5 patients with the clinical diagnosis of juvenile Huntington disease. The radiologic diagnosis of Huntington disease is primarily of caudate atrophy which is measured using internal linear measurement ratios (e.g. bicaudate ratio = ratio of the intercaudate distance to that of the calvarial width at the same level) as measured on axial CT or MRI. The norms for these ratios exist only on adult patients. We will determine the norms for children and compare them to those obtained in juvenile Huntington patients with known caudate atrophy. Because the ventricles are smaller in children, the intercaudate distance "should" be less than that of adults. The resultant normal pediatric values for the bicaudate ratio are expected to be lower than that of the adult; and the normal pediatric frontal horn width/intercaudate distance ratio higher than that of the adults.

Progress: The FH/CC and CC/IT ratios of juvenile patients with Huntington disease were noted to be statistically different from that of normal (n=24) children. These ratios in association with abnormal signal intensity on T2 weighted MRI of the brain were found to be good diagnostic tools in these patients.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/122 **Status:** On-going

Title: A Modern Approach to Congenital Metabolic and Neurodegenerative Diseases of Childhood

Start Date: 08/06/93 **Est. Completion Date:** Jul 94

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: Sylvester H. Chuang, M.D.

Key Words: neurodegenerative disease,metabolic disease,children

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

Study Objective: To retrospectively review CT, MR, MR Spectroscopy (MRS) and positron emission tomography (PET) studies of the brain performed on children with congenital metabolic and neurodegenerative illnesses.

Technical Approach: This retrospective review of 80 to 100 patients, seen at MAMC and the Hospital for Sick Children (Toronto), with known congenital metabolic and neurodegenerative diseases will focus on the clinical-radiographic presentation and progression of these disorders. Studies, including the MRS and PET when available, will be evaluated for disease distribution and progression when more than one study is available. Based on the review, it is intended to formulate a systematic approach to these diseases with the inclusion of MRS and PET.

Progress: The radiologic findings of 80-100 patients with known congenital metabolic and neurodegenerative diseases of childhood are being retrospectively reviewed. We intend to develop an approach to these disorders using currently available technology. The review is on-going and not yet completed.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/007	**Status:** Completed
Title: Scintographic Artifacts: A Systematic Approach		
Start Date: 10/02/92	**Est. Completion Date:** Nov 92	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:		
Key Words: scintigraphic artifacts		

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

Study Objective: The objectives of this protocol are (1) to retrospectively review artifacts produced on routine radionuclide imaging, (2) to det e variety of artifacts created, and (3) to delineate an organized approach t ecognition of artifacts in nuclear medicine -- to insure accurate interpretation of scans.

Technical Approach: This is a retrospective review of approximately 27,000 nuclear medicine studies (e.g. Tc-MDP bone scan, Thallium cardiac scan, Gallium scan, Indium-WBC scan, Tc/I Thyroid scan...) for images plagued by artifacts (overall less than 1 percent). In this study, we plan to determine the variety of artifacts which were produced and formulate an organized approach to these entities which will aid in the prospective recognition of artifacts.

This study is one of description and illustration. The recognition of artifact from true abnormality is crucial for the accurate interpretation of any nuclear medicine study.

Progress: A simplified approach to artifacts encountered on nuclear medicine was formulated. Three different patterns (diffuse, multifocal and localized) were found. Once recognized, each pattern's artifact etiology could be isolated to faulty instrumentation, radiopharmaceutical problems, tracer administration or imaging technique.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/008 **Status:** Completed

Title: Bone Scintigraphy in Sports Medicine

Start Date: 10/02/92 **Est. Completion Date:** Nov 92

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators:

Key Words: bone scintigraphy,sports medicine

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

Study Objective: (1) To retrospectively review bone scans (tc-MDP) performed for the evaluation of sport-related injury; (2) to determine the variety of injuries which were detected; and (3) to delineate an organized approach to these injuries in hopes of improving the diagnostic value of bone scanning.

Technical Approach: This is a retrospective review of approximately 20,000 bone scans to locate and review those performed to evaluate sports injury (15-20%). The spectrum of injuries which may be encountered in sports medicine will be determined and an organized approach will be formulated for the recognition of these entities on bone scan.

Progress: A review of over 400 T_cMDP scans performed to evaluate sports-related injuries was undertaken. Two broad categories (acute/isolated and chronic/repetitive) were observed. Acute injuries occurred following isolated excessive trauma to a normal body part. Repetitive or sequential performance of unaccustomed activity resulted in chronic damage and overuse syndromes.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/146	**Status:** Completed
Title: Abnormal Soft Tissue Tc-MDP Uptake: Incidence and Clinical Significance		
Start Date: 09/03/93	**Est. Completion Date:** Nov 93	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:		
Key Words: soft tissue,Tc-MDP uptake,scintigraphy		

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

Study Objective: (1) To determine the incidence of abnormal soft tissue Tc-MDP uptake on routine bone scintigraphy and (2) to evaluate the frequency at which these findings alter patient management.

Technical Approach: This study is a retrospective review of approximately 8,500 Tc-MDP scans performed over the 3 year period of 1989-92. The scans will be reviewed for the presence of abnormal soft tissue activity (muscular, hepatic, pulmonary, renal...). By reviewing the clinical records of patients with demonstrated abnormal soft tissue activity on Tc-MDP, the clinical significance of each incidence of abnormal Tc-MDP activity can be assessed. Descriptive statistical analysis will be utilized for this project.

Progress: A retrospective review of 8472 Tc-MDP scans revealed abnormal soft tissue uptake in 584 (6.9%) cases. In 314 of these cases (314/516, 55%) the abnormal uptake was unexpected; and in 170 cases (170/566, 30%) the abnormal studies altered patient diagnosis, evaluation, or therapy. Soft tissue activity on Tc-MDP scans, if identified, often has significant clinical importance.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/016 **Status:** On-going

Title: CT and MR Imaging of Radiculopathy

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

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: MAJ Miquel J. Rovira, MC

Key Words: radiculopathy,lateral recess,pathology

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

Study Objective: This is a retrospective study to review CT and MR studies of the spine in patients presenting with radiculopathy in order (1) to determine if a threshold of neural foraminal or "lateral recess" (the transitional region between which the nerve roots exit the spinal cord and enter the neural foramina) size exists for the symptomatology and (2) to determine the range of pathologic conditions (e.g. osteophyte, facet arthropathy, ligamentum flavum hypertrophy, tumor, idiopathic which resulted in the radiculopathy.

Technical Approach: The total of approximately 2,700 CT and MR scans performed at MAMC over the past year will be reviewed for those performed in patients with radicular symptoms. The diagnoses of pathologic entities will be based on the interpretation of the CT and/or MR study.

The dimensions (liner measurements and area) of the neural foramina and "lateral recess" in symptomatic individuals will be compared to that of normal individuals (to be determined by another protocol). The degree of statistical significance of disparities in the study group from those of the control group will be performed using the Student's t-test analysis.

Progress: An ongoing review of abnormal scans in patients with radiculopathy is being undertaken. The direction of this project is in part dependent upon the findings of protocol 93/014 (Normal CT and MR Anatomy of the Lateral Recess). A spectrum of pathologies have been found.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/037	**Status:** On-going
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:	MAJ Miquel J. Rovira, MC	
Key Words: arachnoid granulations:MRI		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

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: The review of MR venograms performed at our institution is near completion. We are awaiting pathologic data in a parallel study being performed at the Uniformed Services University of the Health Sciences.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/145 **Status:** Completed

Title: High Dose Gadoteridol MR in the Detection of Neuropathology

Start Date: 09/03/93 **Est. Completion Date:** Jul 93

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: MAJ Miquel J. Rovira, MC

Key Words: MRI,neuropathology,gadoteridol

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

Study Objective: (1) To determine the efficacy of high dose godateridol-enhanced MR in the detection of neuropathology, and (2) expand the adverse event profile for high dose godateridol usage.

Technical Approach: This is a multi-center, limited prospective study of the efficacy of godateridol to detect neuropathology. Following the acquisition of traditional post-contrast MR images (following 0.1 mmol/kg dose), an additional 0.2 mmol/kg dose (cumulative 0.3 mmol/kg) will be administered and additional post-contrast images will be performed.

Data will be compiled with that of the other participating centers to be published in a major radiologic journal.

Progress: The data on the 10 patients entered in this protocol have been forwarded to Commonwealth Clinical Research Services, an independent research organization, for compilation with data from 49 other institutions as part of a multicenter project.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/014	**Status:** On-going
Title: Normal CT and MR Anatomy of the "Lateral Recess"		
Start Date: 11/06/92	**Est. Completion Date:**	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators: CPT Theodore A. Dorsay, MC	MAJ Miquel J. Rovira, MC	
Key Words: spine,lateral recess		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To retrospectively review CT and MR studies of the spine interpreted as "normal" to determine the variations in the normal appearance (size, length, changes related to age...) and of the "lateral recess" (the transitional region between which the nerve roots exit the spinal cord and enter the neural foramina) in the cervical, thoracic and lumbar regions.

Technical Approach: The "lateral recess" is a frequent site for pathologic conditions. Approximately 2,700 CT and MR scans performed at MAMC over the past year will be reviewed for those interpreted as "normal" and which were not associated with focal or specific neurologic symptomatology. The "lateral recess" as imaged by CT and MR will then be measured for linear dimensions (width, height, length...) and area.

Progress: A search of "normal" spinal MRIs was undertaken and formulation of a good mode of measurement for the nerve root canal was investigated. The determination of a sound geometric and reproducible means of nerve root canal measurement is ongoing. All techniques thus far are flawed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/078 **Status:** Completed

Title: Gadolinium Enhanced Computed Tomography (CT) in a Pig Model

Start Date: 04/01/93 **Est. Completion Date:** Jun 93

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: MAJ Miquel J. Rovira, MC
MAJ James H. Timmons, MC

Key Words: Computed tomography:gadolinium enhanced,animal model,Animal Study

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$625.00	Periodic Review: 06/07/93

Study Objective: To determine the effectiveness of intravenous Gadolinium-diethylenetriamine-pentacetic acid (Gd-DTPA) as an alternative CT contrast agent.

Technical Approach: CT scanning with iodinated contract agents (Iopromide) is the gold standard for most chest, abdominal and brain processes. However, certain individuals who (1) have allergies to iodinated contrast agents or (2) have renal failure are not able to undergo CT with iodinated contrast. Gd-DTPA is a radiologic non-iodinated contrast agent currently being used for MRI with characteristics similar to that of iodinated contrast agents; however, it can be used in patients with allergies to iodinated contrast agents and in patients with renal failure. Gd-DTPA, however, has never been specifically utilized for CT scanning. In this limited pilot study, we intend to explore the possibility of Gd-DTPA as an alternative CT contrast agent utilizing five pigs. The protocol is without morbidity or mortality and the pigs, once utilized may be issued to another protocol.

Progress: Gadolinium was found to be less effective than iodine for CT's of the abdomen. An abstract has been submitted for the 94 Radiology Society of North America meeting..

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/071	**Status:** Completed
Title: Pineal Region Masses: A Simplified Approach to Differential Diagnosis		
Start Date: 03/05/93	**Est. Completion Date:** Feb 94	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Vincent B. Ho, MC		
Associate Investigators:	James G. Smirniotopoulos, M.D.	
Key Words: pineal tumors		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: (1) To review pineal region tumors found in the collective radiologic experiences of Madigan Army Medical Center and the Armed Forces Institute of Pathology and (2) to formulate a simplified differential approach to pineal region masses.

Technical Approach: The pineal region is bounded by the cisterns of the quadrigeminal plate and velum interpositum, the posterior third ventricle, the brain stem, the thalami and the splenium of the corpus callosum. A variety of lesions may occur in this location and include germinoma, teratoma, choriocarcinoma, pineoblastoma, astrocytoma, cyst, lipoma and vascular malformation. This study reviews these entities diagnosed at Madigan Army Medical Center and the Armed Forces Institute of Pathology. The review will attempt to identify distinguishing radiologic and/or clinical features of each entity.

Progress: A simplified approach to the pineal region based on lesion epicenter and patient age can limit the list of differential considerations.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/015 **Status:** Completed

Title: Von Hippel-Lindau Disease: Radiologic-Pathologic Correlation

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

Department: Radiology **Facility:** MAMC

Principal Investigator: MAJ Vincent B. Ho, MC

Associate Investigators: James G. Smirniotopoulos, M.D.
MAJ Frank H. Yackovich, MC

Key Words: Von Hippel-Lindau Disease:radiologic pathology

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

Study Objective: To review the spectrum of radiologic pathology (CNS hemangioblastoma, renal cell carcinoma, pheochromocytoma, paraganglioma, visceral cysts, pancreatic tumors...) in von Hippel-Landau disease found in the collective radiologic experiences of MAMC and the Armed Forces Institute of Pathology.

Technical Approach: The radiographic archives of the Armed Forces Institute of Pathology and MAMC will be reviewed for patients with von Hippel-Lindau disease (roughly 75 - 100 patients). The radiographic (CT, MR angiography, plain film) will then be reviewed for features of von Hippel-Lindau disease with correlation to pathology.

Progress: One hundred patients with Von Hippel-Lindau disease were reviewed. We were able to illustrate the spectrum of radiologic features of this disorder.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/054	**Status:** On-going
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:** / /

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: Stones of chemical content are currently being saved for the project. When approximately 2 dozen samples have been acquired they will be analyzed. We are also awaiting the building of a holder for the technical aspect of the study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/113 **Status:** On-going

Title: A Clinical Comparison of Nodule Detection Utilizing A Modified ROC Study: Conventional vs. Digital vs. Digital-AMBER Chest Radiography

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

Department: Radiology **Facility:** MAMC

Principal Investigator: CPT Cristopher A. Meyer, MC

Associate Investigators:
CPT Robert Leckie, MC
Jon R. Carter, M.S.
CPT Kyle L. Colvin, MC
MAJ Donald V. Smith, MC
LTC William H. Cragun, MC

Key Words: radiography:AMBER,digital,conventional

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$224.00	Periodic Review:	/ /

Study Objective: To evaluate the efficiency of combined AMBER-Storage Phosphor Digital Radiography (AMBER-SPDR) in the detection of pulmonary nodules versus conventional radiography alone and storage phosphor digital radiography (SPDR) alone, using a modified receiver operating characteristic study.

Technical Approach: Patients with one or multiple pulmonary nodules, the largest measuring less than 2 cm, will be identified for inclusion by previously obtained CT. Patients will receive in addition to conventional radiography, SPDR and AMBER-SPDR chest studies. These films will be randomized and numbered. Four board certified chest radiologists and two senior residents in radiology will review the films in sets of 25/session with 75 minutes to finish each session. Each set of films will be restricted to a single modality (i.e. conventional, digital, AMBER-digital) to permit familiarity with modality and prevent inadvertent inclusion of patient images in more than one modality at the same session. All images will be viewed one at a time on standard illuminator under low ambient light conditions. A true positive is recorded if the location is within 1 cm of the center of the actual nodule.

Modified receiver operating characteristic as described by Bunch (Bunch PL, et al: A Free Response Approach to the Measurement and Characterization of Radiographic Observers Performance. J Appl Photogr Eng 1978:4,166-171.) will used to interpret the data. In this method the ordinate is the joint probability for detection and location and the abscissa is the mean number of false positive responses per image.

Progress: At present, 63 patients have been enrolled in the protocol. Thirty of the image sets have been processed for viewing. The "keys" are being prepared prior to the radiologist interpretation of the data sets.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/038 **Status:** Completed

Title: Nipple to Lesion Distance Discrepancy on Mammographic Craniocaudal and Mediolateral Oblique Views

Start Date: 02/05/93 **Est. Completion Date:** Mar 93

Department: Radiology **Facility:** MAMC

Principal Investigator: CPT James E. S. Parker, MC

Associate Investigators:
CPT Cristopher A. Meyer, MC
CPT John C. Pestaner, MC
COL Sankaran S. Babu, MC

Key Words: mammograms:nipple to lesion distance

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

Study Objective: To determine if significant discrepancy exists between nipple to lesion distance (NLD) on standard mammographic craniocaudal (CC) and mediolateral oblique (MLO) views based on zonal anatomy, increasing distance from the nipple, or benign appearing calcification versus malignant mass.

Technical Approach: Measurement of the NLD in the CC and MLO projections will be performed in a retrospective review of approximately 100 mammograms including 90 which demonstrate characteristic benign calcifications and 10 which demonstrate characteristic malignant masses. Measurements will be made from the base of the nipple to the center of the calcification or mass. The position of each lesion will be categorized into one of nine zones: retroareolar, direct superior, direct inferior, direct lateral, direct medial, superolateral, superomedial, inferolateral, or inferomedial.

Statistical analysis will consist of: (1) regression analysis of the relationship between discrepancy (the absolute value of the difference between CC NLD and MLD NLD) and average NLD, and (2) the unpaired t-test to see if significant differences in discrepancy exist for malignant masses vs benign calcifications or lesions in different zones of the breast.

Progress: Of the 89 lesions studied, 85 (95.5%) had a discrepancy of less than or equal to 10 mm. The mean discrepancy for all lesions was 7.9 mm with a standard deviation (SD) of 7.3 mm. The unpaired t-test showed no significant difference in discrepancy for lesions in different zones of the breast ($p > 0.05$). Regression analysis show no correlation between NLD and discrepancy ($r^2 = 0.007$). The mean discrepancy for malignant masses was 5.5 mm with a SD of 4.4 mm which was not significantly different from benign appearing calcifications ($p > 0.05$)

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/050 **Status:** Terminated

Title: Kinetics of D-Dimer Concentration After A Single Subtherapeutic Dose of Urokinase in Patients with Pulmonary Embolism or Deep Venous Thrombosis

Start Date: 02/05/93 **Est. Completion Date:** Mar 93

Department: Radiology **Facility:** MAMC

Principal Investigator: CPT James E. S. Parker, MC

Associate Investigators: MAJ Peter P. Taillac, MC
MAJ James H. Timmons, MC

Key Words:

Accumulative		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$3408.00	/ /

Study Objective: To determine the time to peak concentration of D-dimer following an intravenous bolus of urokinase in patients with known deep venous thrombosis (DVT) or pulmonary embolism (PE).

Technical Approach: Within twelve hours of the diagnosis of deep venous thrombosis (DVT) or pulmonary embolism (PE) in an adult, and after Informed Consent is obtained, patients not in the ICU will be moved to the Emergency Medicine Department where proper monitoring and nursing support are available. Vital signs will be taken and recorded and if no intravenous access exists, an intravenous catheter will be placed with simultaneous removal of 3cc of blood for baseline determination of D-dimer level. If an existing line exists, the baseline D-dimer level is to be drawn via peripheral venipuncture at a site remote from the existing I.V. line to avoid dilution of the blood. Urokinase, 250,000 units IV over 10 minutes, will be administered and vital signs will again be checked and recorded. A second and third D-dimer level will be drawn 15 and 30 minutes after the urokinase infusion. A fourth, fifth, and sixth D-dimer sample will be obtained at one, two, and three hours, from the time of completion of the urokinase infusion.

D-dimer ELISA quantification and latex agglutination will be performed on the collected specimens.

Data will be displayed utilizing a simple cartesian plot of time vs. D-dimer concentration with calculation of mean and standard deviation of time to peak concentration.

Progress: This study was terminated after the d-dimer levels from the first six patients were analyzed. No significant rise in serum D-dimer concentration occurred after the single dose of 250,000 units of urokinase I.V. was given in these patients with documented deep venous thrombosis.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/039	**Status:** On-going
Title: Normal MR Angiography of the Cerebral Venous System		
Start Date: 02/05/93	**Est. Completion Date:** Feb 94	
Department: Radiology	**Facility:** MAMC	
Principal Investigator: MAJ Miquel J. Rovira, MC		
Associate Investigators:	MAJ Vincent B. Ho, MC	
Key Words: cerebral venous system:MR angiography		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To retrospectively review normal MR angiograms of the cerebral venous system to determine the patterns of venous drainage and caliber of normal venous structures.

Technical Approach: Approximately 50 MR angiograms of the cerebral venous system have been performed at MAMC. These studies will be reviewed for those interpreted as "normal". A diagnosis of "normal" will be based on the MR study as interpreted by two staff radiologists in addition to additional radiologic studies (e.g. cerebral venogram). The major cerebral venous structures will then be measured for linear dimensions.

The average "normal" measurements for the cerebral venous structures will be evaluated for standard deviation. Degree of error analysis will also be performed.

Progress: Sixty-eight MR venograms have been performed on 56 different patients. Data on anatomical variants correspond to previously reported angio data. Data to this point suggest that 2D phase contrast is sufficient to assess patency while 3D techniques are valuable for luminal detail.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/079 **Status:** Terminated

Title: Use of Metoclopramide With Chloral Hydrate for Sedation

Start Date: 06/15/90 **Est. Completion Date:** Jan 91

Department: Radiology **Facility:** MAMC

Principal Investigator: Alfred N. Stanford, M.D.

Associate Investigators:
CPT George D. Patrin, MC
LTC Joseph P. McCarty, MC
CPT Vincent A. Dubravec, MC

Key Words: sedation,metoclopramide,chloral hydrate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$42.06	**Periodic Review:** 05/03/91

Study Objective: To demonstrate a more complete and reliable sedative effect with chloral hydrate, utilizing less drug, by adding metoclopramide to the preprocedure regimen.

Technical Approach: Approximately 100 children, age range 6 months to 12 years, requiring sedation for CT, MRI, or EEG, will be studied. One hour prior to the exam time, the subjects will be given 50 mg/kg of chloral hydrate PO along with either 0.4 mg/kg (maximum 5 mg) Reglan or placebo, in a randomized fashion. If not asleep within 45 minutes, they will get an additional 25 mg/kg of chloral hydrate. Questionnaires will be completed immediately after the procedure by the parent and by the technician detailing the time of onset of sedation, its completeness, and any failed events or untoward effects. Placebo will be compared to Reglan regarding dose of chloral hydrate needed, effect on onset of action, duration, and completeness in terms of allowing the test procedure to be done.

Progress: Data on the first 20 patients were lost in the move to the new MAMC. A new investigator (Dr. Stanford) was named in June upon the departure of Dr. Dubravec. No patients were entered by the new PI, who has decided to terminate the protocol because of other previous commitments.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, ANESTHESIA SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/030 **Status:** Completed

Title: An In Vitro and In Vivo Assessment of Elevated Magnesium Levels on the Visco-elastic Measurement of Whole Blood Clot Formation

Start Date: 12/04/92 **Est. Completion Date:** Jun 93

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ Frederick W. Burgess, MC

Associate Investigators: None

Key Words: blood clot formation:magnesium levels

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$1695.00	Periodic Review: / /

Study Objective: 1. To demonstrate the concentration-dependent inhibitory effects of magnesium sulphate on blood coagulation, as measured by thromboelastography. 2. To illustrate the failure of conventional in vitro coagulation testing to detect the anticoagulant effects of magnesium.

Technical Approach: Healthy male volunteers will have an 16 or 18 gauge intravenous cannula inserted into a peripheral vein for the purpose of drawing sequential blood samples. Baseline specimens will be obtained and submitted for serum magnesium and calcium measurements, platelet count, PT, and PTT. A bleeding time will be performed by the investigator using the commercial Simplate technique. Serial blood specimens (2 ml) will be withdrawn into syringes containing sufficient magnesium sulfate to provide 2, 4, and 6 mEq/L of magnesium over the normal serum magnesium concentration. These specimens will be assayed on the thromboelastograph. The remainder of the magnesium spiked sample will be stored in heparinized tubes. The plasma will be separated, and assayed for final magnesium concentration by the investigator. A duplicate set of samples will be conducted on anticoagulated blood (citrate). These samples will be recalcified and assayed on the thromboelastograph. Upon completion of these serial in vitro measurements, each volunteer will receive a loading dose of 4 gm of magnesium sulfate in 250 ml of 5 % dextrose and water, over a 20 minute period. Ten minutes following the completion of the magnesium infusion, 12 ml of blood will be obtained for the purpose of repeating the baseline studies. Electrocardiographic and blood pressure monitoring will be instituted prior to and for 1 hour following the administration of the magnesium sulfate infusion.

Progress: The study is completed. Magnesium sulphate appears to act as an anticoagulant. This effect is not appreciated with routine coagulation studies, possibly because citrate may chelate the magnesium. Subsequent recalcification appears to partly reverse the anticoagulant effect of magnesium.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/090 **Status:** Terminated

Title: Selective Blockade of the Vagus Nerve to Relieve Referred Shoulder Pain Associated with Pulmonary Surgery in Human Subjects

Start Date: 09/06/91 **Est. Completion Date:** Dec 92

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ Frederick W. Burgess, MC

Associate Investigators:
LTC Richard M. Dearman, MC
MAJ James D. Helman, MC
COL Daniel G. Cavanaugh, MC
LTC Douglas M. Anderson, MC

Key Words: shoulder pain,pulmonary surgery,vagus nerve

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$50.45	**Periodic Review:** / /

Study Objective: To determine if the referred shoulder pain associated with thoracotomy for lobectomy and pneumonectomy can be blocked by the infiltration of local anesthetic around afferent vagal fibers of the involved lung.

Technical Approach: This study is designed as a double blind, random assignment clinical trial with a control and treatment group. The target sample size is 8-10 subjects per group. Subjects will be assigned in a random fashion to receive either 0.9% NaCl or 0.5% bupivacaine for infiltration into the pulmonary ligament prior to closure of the thoracic cavity. Postoperative pain management will be provided with a thoracic epidural infusion of narcotic/local anesthetic. Each subject will be evaluated at 1 and 24 hours postoperatively for the presence of referred shoulder pain. Demographic data on each patient to include height, weight, age, sex and surgical procedure will be collected and analyzed where appropriate by Chi-square analysis or an unpaired t-test. Pain scores at 1 and 24 hours will be analyzed by the Mann-Whitney rank sum test. The presence or absence of referred pain will be analyzed by Chi-square analysis.

Progress: Results were not promising so the PI terminated the protocol when he was reassigned.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/061 **Status:** Completed

Title: A Double Blind, Placebo-Controlled Comparison Between 0.125%, 0.25%, and 0.5% Ropivacaine, When Used for Post-operative Infiltration in Herniorraphies: A Dose Resposne Study

Start Date: 05/01/92 **Est. Completion Date:** May 93

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ Frederick W. Burgess, MC

Associate Investigators: MAJ Christopher R. Kaufmann, MC

Key Words: herniorraphies,ropivacaine

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To establish the dose-response analgesic effect of ropivacaine, given postoperatively by local wound infiltration, using three different concentrations of ropivacaine in equal volumes and saline.

Technical Approach: Male outpatients scheduled for elective inquinal herniorraphy will be randomized to receive local infiltration during wound closure with one of three concentrations of ropivacaine (0.125%, 0.25%, or 0.5%) or saline, using equal volumes. Surgery will be performed under a short acting regional block and pre-anesthetic medication will be standardized according to usual practice at Madigan. Infiltration of the surgical wound during closure will be done using 30 ml of the study drug (15 ml in the deep layer and 15 ml in the superficial layer). In the first 32 patients, the plasma concentration of ropivacaine will be followed during the first 2 hours after end of infiltration. Assessments of perceived pain will be assessed by the patient using a visual analogue scale (VAS) at premedication, and at 60, 120, 180, 240, and 300 minutes and at 8 and 24 hours after the end of drug infiltration and again on the first postoperative visit (6-14 days postoperatively). Tolerance to pressure-induced pain will be at the same time periods as the VAS while in the hospital. Postoperative analgesic therapy will be standardized in regard to drug, dose, and minimum interval between doses. The time to first request for analgesics and the amount of analgesics required during the first 6 days postoperatively will be recorded. A follow up VAS and pressure-induced pain test will be done at the first postoperative visit. Adverse events will be recorded intraoperatively, in the post-anesthesia recovery room, at the first postoperative visit, and at a telephone follow-up 2-3 weeks after surgery. The presence of a dose-response relationship (increasing effect with increasing dose) will be the primary analysis and will be done using a regression analysis.

Progress: Patient entry is complete at MAMC. The study was done in conjunction with Virginia Mason Med Center in Seattle. Data have been sent to Virginia Mason where data analysis will be done.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/046 **Status:** On-going

Title: Can the Combination of Intramuscular Ketorolac and Continuous Epidural Bupivacaine Eliminate the Need for Narcotic Analgesia Post-Thoracotomy

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

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: CPT Gary D. Gridley, MC

Associate Investigators:
CPT Ronald L. Hurst, MC
MAJ Frederick W. Burgess, MC
COL Daniel G. Cavanaugh, MC

Key Words: thoracotomy,ketorolac,bupivacaine

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

Study Objective: To demonstrate a substantial reduction or complete elimination of the need for narcotic analgesics following thoracic surgery, with the analgesic combination of intramuscular ketorolac and a continuous epidural bupivacaine infusion.

Technical Approach: Patients presenting for open thoracotomy who have chosen epidural anesthesia for postoperative pain control will be randomized to one of four groups: (1) fentanyl plus 0.625% bupivacaine plus an IM placebo (saline) every six hours (2) fentanyl plus 0.125% bupivacaine plus an IM placebo (saline) every six hours (3) fentanyl plus 0.625% bupivaciane plus 30 mg ketorolac IM every six hours (4) fentanyl plus 0.125% bupivacine plus 30 mg ketorolac IM every six hours Groups 1 and 2 will receive a 60 mg injection of placebo prior to awakening from the surgical procedure and Groups 3 and 4 will receive a 60 mg injection of ketorolac before awakening. Patients will control their pain using a Patient Controlled Analgesia Device to administer fentanyl (10 mcg of fentanyl with an initial 10 minutes lock out period). Patients will quantify their pain once every four hours using a visual analog scale (scale of 1-10). For pain more severe than 5 on the scale, a supplemental epidural injection of 50 mcg of fentanyl will be provided. Total fentanyl requirements will be analyzed between groups. VAS pain scores will be quantitated at 4 hours intervals to ascertain that comparable levels of analgesia were provided.

Progress: Patients eligible for this project are being recruited into another study. The competing study should be completed in the next couple of months and entry into this project will begin in the spring.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/087 **Status:** On-going

Title: Patient-Controlled Analgesia and the Risk of Postoperative Myocardial Ischemia

Start Date: 07/02/92 **Est. Completion Date:** Indef.

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ James D. Helman, MC

Associate Investigators:
LTC Michael J. Sborov, MC
D. Mangano Ph.D, M.D.
MAJ Frederick W. Burgess, MC
CPT Ronald L. Hurst, MC

Key Words: analgesia,myocardial ischemia

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

Study Objective: To identify the most efficacious post-operative pain modality which will reduce the incidence and or severity of postoperative myocardial ischemia in high-risk patients undergoing noncardiac surgery.

Technical Approach: This study will evaluate the relative effectiveness of IV patient-controlled analgesia (PAC) morphine sulfate and epidural PCA fentanyl alone or combined with dilute local anesthetic for continuous epidural analgesia in patients with coronary artery disease undergoing upper abdominal surgery. Patients will be randomized in a blinded fashion to receive either IV PCA with morphine sulfate or PCA epidural fentanyl and a separate epidural infusion of saline or to PCA epidural fentanyl and a separate epidural infusion of 0.0625% bupivacaine. The effectiveness will be determined by observing the incidence and severity of myocardial ischemia measured electrocardiographically and the incidence of adverse cardiac outcomes: cardiac-related death, myocardial infarction, and ventricular failure.

Progress: Holter monitors were received but were dysfunctional. We are now awaiting replacements.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/082	**Status:** On-going

Title: Allo-priming of Mivacurium Neuromuscular Blockade With Steroidal Nondepolarizers

Start Date: 04/02/93	**Est. Completion Date:** Jun 93
Department: Surgery/Anesthesia	**Facility:** MAMC

Principal Investigator: MAJ William A. Hughes, MC

Associate Investigators:
CPT R. Michael Tuttle, MC
LTC Anthony S. Sado, MC
CPT Ronald J. Place, MC
CPT Ronald L. Hurst, MC

Key Words: mivacurium neuromuscular blockade,steroidal nondepolarizers

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$15.35	**Periodic Review:** / /

Study Objective: This study will evaluate the effect of a priming dose of steroidal neuromuscular blockade (NMB) on the onset and duration of mivacurium.

Technical Approach: Thirty patients, ASA class I or II, receiving general anesthesia for operative procedures (pilot study) will be administered an anesthetic technique limited to thiopental + narcotic induction and nitrous-narcotic maintenance. This technique is known as a "nitrous-narcotic", a common anesthetic technique. The study population will be randomly assigned to three groups of ten each: Group I (Control) will receive a priming dose of mivacurium; Group II will receive a priming dose of vecuronium; Group III will receive a priming dose of pancuronium. Each patient will be fitted with a neuromuscular blockade monitor capable of recording twitch height and time. The anesthetist will be blinded to the group assigned. A priming dose of the unknown NMB agent will be administered prior to induction. Five minutes after priming dose and induction of anesthesia, an intubating dose of mivacurium will be administered. If the duration of the procedure will not allow for spontaneous NMB recovery, then NMB will be reversed in the usual fashion (i.e., administration of neostigmine and glycopyrrolate).

Data will be analyzed for statistically significant differences in time to onset and duration of action for NMB and subsequent power analysis will determine the number of subjects needed to achieve statistical significance.

Progress: This project cannot procede until funding is received for a neuroblockade monitor.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/028 **Status:** On-going

Title: The Influence of Prophylactic Administration of Intravenous Crystalloid and Colloid Solutions on the Incidence of Hypotension Following Subarachnoid Anesthesia

Start Date: 02/01/91 **Est. Completion Date:**

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: CPT Michael L. Plyman, MC

Associate Investigators:
MAJ David M. Colonna, MC
MAJ Frederick W. Burgess, MC
LTC Douglas M. Anderson, MC
LTC Michael J. Sborov, MC

Key Words: anesthesia,hypotension,prophylactic agents

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

Study Objective: To determine if the routine administration of an intravenous (IV) crystalloid solution prior to the administration of a subarachnoid anesthetic decreases the incidence of hypotension in euvolemic patients undergoing extremity surgery and to show that avoidance of an IV fluid preload prior to spinal anesthesia will diminish the incidence of postoperative urinary retention.

Technical Approach: Patients presenting for lower extremity or lower abdominal procedures to be performed under spinal anesthesia and associated with minimal blood loss will be divided into three groups of 120 subjects per group. Group I will receive no additional prophylactic fluids beyond maintenance requirements Group II will receive 12 ml/kg of lactated Ringer's solution and Group III will receive 4 ml/kg of Hespan immediately prior to injection of the subarachnoid anesthetic. Surgery and anesthetic care will be conducted by standard operative and anesthesia protocol. Data collection will involve documentation of the total amount of ephedrine administered. Evaluations during surgery will include blood pressure determinations at 3 minute intervals throughout the surgery and at one minutes intervals for at least 10 minutes immediately following the block peak level of sensory anesthesia as determined by pinprick and continuous monitoring of heart rate and oxygen saturation. Patients will be evaluated within 18-24 hours postoperatively for evidence of urinary retention. The need for bladder catheterization will be documented and the amount of residual urine obtained will be recorded. Residual urine volumes of <5 ml/kg will not be considered as representative of urinary retention. The results to be analyzed include the proportion of patients in each group requiring ephedrine for a fall in blood pressure of >20%, the peak sensory level of anesthesia and the proportion of patients in each group with urinary retention. Differences between groups will be analyzed for statistical significance via chi square analysis.

Progress: Fifty-three patients have been entered into this study. At this point, no significant differences are apparent between the control and study group. At completion of enrollment, statistical analysis will begin.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/073 **Status:** On-going

Title: The Efficacy of Epinephrine as an Epidural Test Dose for Predicting Intravascular Injection During Halothane Anesthesia in Infants and Children

Start Date: 03/05/93 **Est. Completion Date:** May 93

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: David M. Polaner, M.D.

Associate Investigators: None

Key Words:

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$300.00	**Periodic Review:** / /

Study Objective: This study will determine whether the intravenous injection of small doses of epinephrine will result in a predictable increase in heart rate during halothane anesthesia, thereby allowing "test doses" of epinephrine-containing local anesthetics to serve as an accurate and reliable marker for inadvertent intravascular injection.

Technical Approach: Each child will be randomized to receive either 0.75 ug/kg or 1.0 ug/kg of intravenous epinephrine after the induction of anesthesia and the establishment of a steady state of anesthesia with 1.5 MAC of halothane (adjusted for age) delivered in a 60% nitrous oxide / 40% oxygen mixture. The induction technique will be left to the discretion of the anesthesiologist as will premedication, except that patients will not receive atropine. Ventilation will be regulated to achieve an end tidal CO^2 concentration between 28 and 43 mm/Hg. Vital signs will be recorded continuously for three minutes using standard non-invasive techniques. Data will be analyzed using a two tailed t-test with the groups and ANOVA for repeated measures for analysis of data between the groups.

Progress: Due to constraints imposed by limited non-clinical time, the protocol was not implemented this year.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/008 **Status:** On-going

Title: Influence of Phrenic Nerve Blockade on the Incidence of Referred Shoulder Pain in Patients Undergoing Thoracic Surgery for Pneumonectomy

Start Date: 12/06/91 **Est. Completion Date:**

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ Edward J. Walz Jr., MC

Associate Investigators:
LTC Douglas M. Anderson, MC
COL Daniel G. Cavanaugh, MC
CPT Michael J. Decker, MC
COL Michael J. Barry, MC
MAJ Frederick W. Burgess, MC

Key Words: referred shoulder pain,phrenic nerve

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

Study Objective: To evaluate the contribution of the phrenic nerve to the referred shoulder pain associated with thoracic surgery for pneumonectomy.

Technical Approach: Pneumonectomy operations may be associated with referred pain symptoms conducted by the phrenic nerve. Blockade of the phrenic nerve may inhibit these pain symptoms. This will be a double-blind randomized trial using patients greater than 18 years of age who are presenting for thoracotomy. Individuals will be assigned in a random fashion to receive either 0.9% NaCl or 0.5% bupivacaine for infiltration around the phrenic nerve above the hilum prior to closure of the thoracic cavity. There will be 8-10 patients in each group. Postoperative pain management will be provided according to standard MAMC practice with a thoracic epidural infusion of narcotic/local anesthetic. Each patient will be evaluated at 1 and 24 hours postoperatively for the presence of referred shoulder pain. Severity of pain will be assessed by the patient using a visual analog scale. Demographic data on each patient, including height, weight, age, sex, and surgical procedure will be collected and analyzed where appropriate by chi-square analysis or an unparied t-test. Pain scores at 1 and 24 hours will be analyzed by the Mann-Whitney rank sum test. The presence or absence of referred pain will be analyzed by chi-square analysis.

Progress: Accrual into this study is slow due to the low number of pneumonectomies performed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/047 **Status:** On-going

Title: Identification of the Optimal Bupivacaine Concentration for Epidural Analgesia in Combination with Patient Controlled Epidural Fentanyl Analgesia

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

Department: Surgery/Anesthesia **Facility:** MAMC

Principal Investigator: MAJ Edward J. Walz Jr., MC

Associate Investigators:
CPT David J. Bower, MC
CPT Michael J. Decker, MC
MAJ Frederick W. Burgess, MC

Key Words: epidural analgesia,bupivacaine,fentanyl

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

Study Objective: To identify the optimal concentration of dilute local anesthetic for continuous epidural analgesia that will produce the greatest reduction in the total amount of narcotic required for postoperative analgesia following major thoracic and upper abdominal surgery.

Technical Approach: At Madigan, virtually all patients undergoing major abdominal or thoracic surgery receive epidural anesthesia for postoperative pain relief. In this study, patients greater than 18 years of age who have been scheduled by the anesthesiologist to receive patient-controlled epidural analgesia for postoperative pain relief will be randomized to four groups: (1) fentanyl plus a placebo, (2) fentanyl plus 0.03% bupivacaine (3) fentanyl plus 0.0625 % bupivacaine or (4) fentanyl plus 0.125% bupivacine. Patients will rate postoperative pain using a visual analog scale every four hours for 24 hours and arterial blood gases will be obtained at one hour postoperatively and at 24 hours after the start of the epidural infusion. The total amount of fentanyl and the amount of additional fentanyl provided in the form of a bolus will be recorded and totaled for the 24 hour period. Arterial blood gas data and total fentanyl requirements will be analyzed between groups for statistical significance, using analysis of variance and the Student-Newman-Keuls test.

Progress: Preliminary data suggest that epidural bupivacaine infusions, in concentrations as low as 0.03%, substantially reduce the need for patient controlled delivery of epidural fentanyl analgesia following thoracotomy and abdominal aortic surgery. The findings are highly significant, not only in showing up to 60% reduction in narcotic usage, but also may indicate that bupivacaine concentrations greater than 0.063% offer little analgesic advantage and may even increase the risk of complications secondary to local anesthesia.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, ENT SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/026 **Status:** On-going

Title: Atrial Natriuretic Factor as a Mediator of Airway Obstruction Induced Enuresis

Start Date: 12/04/92 **Est. Completion Date:** Jun 93

Department: Surgery/ENT **Facility:** MAMC

Principal Investigator: CPT Philemon L. Anderson, MC

Associate Investigators: CPT Karen L. Della-Giustina, MC
MAJ John W. McBurney, MC

Key Words: enuresis,airway obstruction,atrial natriuretic factor

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$2794.00	**Periodic Review:** / /

Study Objective: 1. To demonstrate a correlation between the presence of tonsillar hypertrophy in children who exhibit significant airway obstructive symptoms and overnight urine volumes and natriuresis. 2. To demonstrate a correlation with relief of enuresis following tonsillectomy, with or without adenoidectomy, and change in overnight urine volume. 3. To demonstrate that enuresis occurring in a child with obstructive airway symptoms can be shown to correlate with the function of atrial natriuretic factor and the renin/angiotensin system.

Technical Approach: Thirty male patients between the ages of 5 - 12 who have an indication for tonsillectomy and who also have obstructive airway symptoms and/or enuresis will undergo an overnight in-hospital sleep study both before and after their scheduled surgical procedure. Females will be excluded because anatomic considerations make performance of the testing procedures technically difficult, leading to unreliable data collection. The sleep study is to consist of a standard polysomnogram along with urinary collection for determination of aldosterone, antidiuretic hormone and cyclic-GMP, which serves as a marker for plasma atrial natriuretic factor. Cortisol will also be measured to provide an indicator of ACTH, which can be used to infer the effect of ACTH on aldosterone production. The collections will be designed to measure the total urinary production of these substances during early, mid and late periods of the night. Also measured will be the urine volume and the urine electrolytes as these are expected to be affected by one or more of the above hormones. A blood sample will be obtained as a reference point for the urine electrolyte values. The polysomnogram will be used to document the presence or absence of obstructive sleep apnea syndrome. It will further document changes in this condition as a result of surgery. Data will be compiled to allow correlation of urinary c-GMP levels with urine volume and sodium excretion as well as correlation by the measured apneic and hypoapneic events. Similar correlations between these parameters will be performed for urinary aldosterone and urinary antidiuretic hormone. Each of these correlations will be performed for the three periods of the night. The postoperative study is expected to show reduced overnight production of the atrial natriuretic factor as measured by it's marker, c-GMP, as a result of the relief of airway obstruction by the surgical procedure. Similar alteration in urinary ADH is not predicted. Improvement in the enuresis symptoms is expected to correlate with the reduction in c-GMP postoperatively.

Progress: We have been unable to begin the study because the protocol is dependent on services to be provided by an EEG technician from the Neurology Svc. The Neurology Svc has lost a techician and has been unable to hire another due to budget constraints.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/026 **Status:** Terminated

Title: Shoulder Morbidity in Head and Neck Surgery

Start Date: 01/01/01 **Est. Completion Date:** Apr 92

Department: Surgery/ENT **Facility:** MAMC

Principal Investigator: CPT Domenic M. Canonico, MC

Associate Investigators:
MAJ Michael R. Morris, MC
1LT David Paulson, MS
CPT Jonathan A. Perkins, MC

Key Words: surgery,head & neck,morbidity

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$200.00	Periodic Review:	/ /

Study Objective: To compare postoperative shoulder morbidity with regard to strength, work function, and range of motion in patients subjected to radical neck dissection and/or regional musculocutaneous flap reconstruction during course of treatment for a head and neck malignancy.

Technical Approach: Patients will be examined and the trapezius muscle function and bulk will be noted and each subject will complete a questionnaire as a measure of the patient's perception of the functional results of surgery. Patients will then be identified by groups. Group 1 will include those with post radical neck dissection alone Group 2 will include those with a pectoralis myocutaneous flap only, and group 3 will have had both a radical neck dissection and a pectoralis myocutaneous flap. The three groups will then be evaluated by history, physical exam, and physical therapy protocol. The physical therapist will test for available passive range of motion and active range of motion for shoulder flexion, extension, abduction, and internal and external rotation, as well as scapular mobility. Shoulder/shoulder girdle strength will be tested by a licensed physical therapist and gross strength will be tested using the LIDO isokinetic machine. Each subject will act as his/her own control. The uninvolved side will be compared to the involved side and statistically analysed.

Progress: This protocol was not started because the PI did not have time to revise the study and then conduct it because of out-of-hospital rotation.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/160 **Status:** On-going

Title: Analyzing the Dynamic Behavior of the Eustachian Tube Through A Sonometric Monitor

Start Date: 08/06/93 **Est. Completion Date:**

Department: Surgery/ENT **Facility:** MAMC

Principal Investigator: MAJ Charles V. Edmond Jr, MC

Associate Investigators: None

Key Words:

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

Study Objective: To develop and investigate an ambulatory monitoring eustachian tube (ET) system that will record ET events in a dynamic fashion, utilizing the technique of sonometry.

Technical Approach: This is a team approach whereby an instrument capable of dynamic testing of ET function is developed and clinically used to define the signature of selected otologic disorders and normal function. This four phase approach will utilize the capabilities of private industry and the MAMC Otolaryngology Service. Phase I will consist of fabricating and testing an improved bench top system, modeled after the Pittsburgh-Carnegie-Mellon system and will provide the formulation for the dynamic measurements. Phase II will entail development of a portable data acquisition unit which will allow the patient to wear a self contained measurement system. Upgrades will continue on the bench top system. Phase III will begin the clinical trials to investigate the dynamic nature of the ET and the characteristics of opening and closing patterns as they relate to normals and specific otologic disorders. Phase IV will emphasize the transfer of technology to a medical instrument vendor of a portable ambulatory ET monitor, that is diagnostic, user friendly, and cost efficient.

Progress: Funding was declined by DOD/VA. The protocol will be resubmitted.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/068 **Status:** On-going

Title: The Effect of Radial vs Circumferential Myringotomy on Ventilatory Tube Retention

Start Date: 03/05/93 **Est. Completion Date:** Dec 93

Department: Surgery/ENT **Facility:** MAMC

Principal Investigator: CPT Jeffrey L. Silveira, MC

Associate Investigators: CPT Philemon L. Anderson, MC
MAJ Charles R. Souliere, MC

Key Words: myringotom:tube retention

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

Study Objective: To determine if a statistical difference in ventilatory tube retention of greater than or equal to 3 months duration exists between radial vs. circumferential myringotomy.

Technical Approach: Approximately 100 children will be entered in this study. Each child will have a radial myringotomy in one ear and a circumferential myringotomy in the other ear; thus serving as his/her own control. Children will be randomly assigned between a right or left radial myringotomy and a left or right circumferential myringotomy by date of surgery and the surgeon performing the procedure. All children will be otherwise healthy and undergoing only first sets of ventilatory tubes with no additional procedures. The children will be followed every 2 months until such time that both tubes have been extruded or 18 months has elapsed since surgery. Patients will be placed in one of four groups at the close of the study: 1) tubes in place bilaterally at close of study, 2) simultaneous extrusion, 3) earlier radial extrusion, or 4) earlier circumferential extrusion. The date that the tube is first noticed to be extruded will be used as the extrusion date and duration will be calculated from this date to the time of the original surgery. Data will be analyzed by using the student t-test.

Progress: Followup has been completed on 50 participants. No conclusions have been drawn.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE

Detail Summary Sheet

ıte: 30 Sep 92 **Protocol No.:** 93/161 **Status:** On-going

tle: Multicenter, Single-Blind Clinical Trial To Determine the Efficacy of Dermagraft, A Living Dermal Replacement, in the Treatment of Full-Thickness Chronic Venous Insufficiency Ulcers

art Date: 08/06/93 **Est. Completion Date:** Aug 94

epartment: Surgery/General Surgery **Facility:** MAMC

rincipal Investigator: COL Charles A. Andersen, MC

ısociate Investigators: LTC David F. J. Tollefson, MC

ey Words:

ccumulative EDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** / /

udy Objective: To establish the safety and efficacy of Dermagraft in the promotion of aling chronic venous insufficiency ulcers.

chnical Approach: This multicenter study will be stratified by medical center and by cer size. Two ulcer size strata are defined: ulcers ≤ 50 cm^2 and ulcers >50 cm^2. The rpose of this stratification is to ensure approximately equal allocation of patients tween treatments within each stratum. Dermagraft will be applied to the wound bed ıder a paste boot and elastic bandage. Control treatment wounds will receive a nventional paste boot and elastic bandage only. All patients will be followed at weekly tervals for 12 weeks or until one week after the wound achieves complete closure. ıereafter, all patients will be seen at 16, 20, and 24 weeks. Patients will also complete a ort series of health status questionnaires that will assess overall health, quality of life, tivity level, pain and discomfort, and labor force participation.

ogress: Enrollment in the trial has now been closed. We are currently following 4 tients on a weekly basis to determine a rate of healing of the venous ulcers. It is too rly to draw any conclusions.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 85/021	**Status:** On-going
Title: Advanced Trauma Life Support Course		
Start Date: 01/18/85	**Est. Completion Date:** Indef.	
Departmen . Surgery/General Surgery	**Facility:** MAMC	
Principal Investigator: MAJ Christopher R. Kaufmann, MC		
Associate Investigators: COL Stanley C. Harris, MC	MAJ Leslie W. Yarbrough, VC LTC William E. Eggebroten, MC	
Key Words: training protocol,ATLS,Animal Study		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1600.00	**Periodic Review:** 06/07/93

Study Objective: To provide training to general surgery, emergency medicine, and family practice residents and, specifically, to teach proper management of the initial one hour following major trauma.

Technical Approach: During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

Progress: Three sessions involving three animals each were conducted this fiscal year.

Detail Summary Sheet

te: 30 Sep 92 **Protocol No.: 93/079** **Status:** Suspended

le: Serum Levels of Tumor Necrosis Factor in Postoperative Patients

rt Date: 04/02/93 **Est. Completion Date:** Jun 93

partment: Surgery/General Surgery **Facility:** MAMC

incipal Investigator: CPT Ronald J. Place, MC

sociate Investigators:
CPT Robert M. Tuttle, MC
LTC Anthony S. Sado, MC
CPT Robert A. Avery, MC
CPT Ronald L. Hurst, MC

y Words: Tumor necrosis factor:serum levles,postop patients

cumulative		Est. Accumulative		Periodic Review:
EDCASE Cost:	$0.00	OMA Cost:	$2865.00	/ /

udy Objective: 1. To determine whether tumor necrosis factor (cachectin) can be tected in the serum of postoperative patients. 2. To determine whether post-op Tumor crosis Factor (TNF) levels differ according to the operation performed. 3. To determine TNF can be used to predict post-op course.

chnical Approach: Patients admitted to the vascular surgery service who are greater an 18 years of age, undergoing either abdominal aortic aneurysm or carotid darterectomy will be invited to participate. Pregnant females and patients with idence of sepsis, malignancy, shock or hemodynamic instability prior to the study will excluded.

A standard history and physical along with standard preoperative laboratories ll be done. A baseline serum TNF will be drawn on the day of admission and serve as e control TNF measurement. Intraoperatively, a serum TNF level will be drawn at duction of anesthesia at 30, 60 and 120 minutes after incision. In addition, a serum NF level will be drawn at cross clamp placement and 30 minutes after the cross clamp released from the aorta or the carotid artery. In the event of a hypotensive episode, fined as a systolic BP less than 90 lasting greater than one minute, a serum TNF level ll be drawn. Daily laboratories to include a serum TNF will be drawn for the first 72 urs after surgery.

Other data to be evaluated include fluid status monitored by input and output, ily weights, and IV fluid intake including the amount of crystalloid, albumin, other lloids, and packed red blood cells. Serial blood pressure following admission to ICU ll be reviewed for any episode of hypotension. Daily Apache scores will be obtained for e day of surgery and for the first 72 hours postoperatively. Patients will also be onitored for temperatures of greater than 101.6°F, evidence of positive blood cultures, fection, myocardial event, congestive heart failure, and fluid overload.

Repeated measurements of TNF will be analyzed by ANOVA analysis.

ogress: CPT Avery, who has been reassigned, was the original PI. A new P.I. (Dr. ace) was named in July 93. A decision is being made whether to continue the protocol.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/007 **Status:** On-going

Title: General Surgery Stapling Familiarization Lab (Swine Model)

Start Date: 10/17/86 **Est. Completion Date:** Oct 87

Department: Surgery/General Surgery **Facility:** MAMC

Principal Investigator: LTC Clifford L. Simmang, MC

Associate Investigators:

COL Stanley C. Harris, MC
MAJ Stephen B. Smith, MC
COL Michael J. Barry, MC
LTC James A. Knight, MC
COL Charles A. Andersen, MC
COL Preston L. Carter, MC
LTC Richard A. Hall, MC
MAJ Michael J. O'Reilly, MC
COL Daniel G. Cavanaugh, MC
LTC Richard M. Dearman, MC
LTC William E. Eggebroten, MC

Key Words: training protocol,stapling,swine,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$500.00	**Periodic Review:** 06/07/93

Study Objective: To familiarize residents in General Surgery with the proper use of surgical stapling devices.

Technical Approach: For each laboratory session, two animals will be anesthetized (ketamine HCl 20 mg/kg body weight and atropine 0.088 mg/kg body weight, IM) as a pre-anesthetic. The animals will then be intubated endotracheally and surgical anesthesia will be induced and maintained using a mixture of Halothane and nitrous oxide. Once a surgical level of anesthesia has been achieved, the abdominal cavity will be entered via a midline incision. A demonstration of stapling techniques (under the direct supervision of staff surgeons and representatives from the staple manufacturer) will be performed on the animal by the surgical residents. After the demonstration, all animals will be euthanized without being allowed to recover from anesthesia.

Progress: There was no activity on this ongoing teaching protocol during FY93.

Detail Summary Sheet

: 30 Sep 92	**Protocol No.:** 93/029	**Status:** On-going
: Laparoscopic Assisted Colon and Rectal Operations		
t Date: 12/04/92	**Est. Completion Date:** May 93	
artment: Surgery/General Surgery	**Facility:** MAMC	
cipal Investigator: LTC Clifford L. Simmang, MC		
ciate Investigators:	MAJ William C. Williard, III, MC	
MAJ Timothy F. Deaconson, MC	MAJ Daniel Jorgenson, MC	
Words: laparoscopy:colon,rectal		

umulative		**Est. Accumulative**		**Periodic Review:**
OCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

y Objective: The determine the feasibility of performing laproscopic-assisted colon rectal surgical procedures at MAMC.

nical Approach: Laparoscopic-assisted colon and rectal surgery have been ormed in both medical centers and com..unity hospitals throughout the country. se procedures have been demonstrated to often reduce postoperative pain, ileus, and ital stay, and to have an earlier return to regular activities. Our procedure will not r from those previously done.

Laproscopic-assisted colon and rectal resection differs from standard open edures in that the dissection and mobilization is performed with laparoscopic niques using endoscissors and endocautery. Vascular structures are divided veen endoclips instead of clamps and ligatures. A small (average 7 cm) incision is e to deliver the specimen. Standard open techniques through the small incision are l to complete the bowel resection and anastomosis. The patients will be followed in hospital with usual postoperative until normal bowel function has returned and the ent can tolerate self care. A review of the procedure, complications, hospital course, patient's level and rate of return to normal activity will be assessed. Because these niques will be new to MAMC, it is felt that review of the initial procedures should be itored to determine the impact on our facility.

ress: One more patients is needed to complete this project. Advanced laproscopic ery appears to be feasible. Cost comparisons have yet to be done.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/069	**Status:** On-going

Title: Hemodynamic Consequences of Pneumoperitoneum in Patients with Cardiopulmonary Disease

Start Date: 03/05/93	**Est. Completion Date:** Jan 93
Department: Surgery/General Surgery	**Facility:** MAMC

Principal Investigator: CPT Steven E. Weber, MC

Associate Investigators:	CPT Michael J. Decker, MC
MAJ Daniel Jorgenson, MC	LTC Joseph A. Scaniffe, MC

Key Words: cardiopulmonary disease,pneumoperitoneum

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

Study Objective: To determine if significant hemodynamic compromise occurs during laparoscopic procedures in patients with cardiopulmonary disease.

Technical Approach: Patients scheduled to undergo laparoscopic cholecystectomy on the general surgery service will be stratified according to the degree of cardiopulmonary disease as defined by the New York Heart Classification, Goldman's criteria, ASA Classification and Pulmonary Function Tests. These patients will undergo cholecystectomy using the standard laparoscopic technique presently being performed. The general anesthetic technique will be standardized. As part of the anesthetic protocol, minute ventilation will be maintained at a level to obtain a $PaCO_2$ equal to baseline (+/- 5 mm HG), thus eliminating an elevated $PaCO_2$ as a variable. In addition to having the standard hemodynamic parameters monitored intraoperatively, the patients will have an arterial line placed for frequent arterial blood gas analysis and continuous monitoring of cardiac wall movement and ejection fraction by means of transesophageal echocardiography. The data will then be compared between the groups and analyzed using repeated measures ANOVA and logistic regression for statistical significance.

Progress: The study has been on hold because the transesophageal echo obtained for this study was returned to the manufacturer. The supplier has not been cooperative in returning the equipment.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, OPHTHAMOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/111	**Status:** On-going
Title: Refractive Changes at Altitude Following Radial Keratotomy Surgery		
Start Date: 06/09/93	**Est. Completion Date:** Jul 93	
Department: Surgery/Ophthamology	**Facility:** MAMC	
Principal Investigator: COL Thomas H. Mader, MC		
Associate Investigators: MAJ John D. Ng, MC CPT Carl A. Gibson, MC Walter Hubickey, M.D.	MAJ Lawrence J. White, MC Jon R. Carter, M.S. MAJ Vernon C. Parmley, MC Michael Caputo	
Key Words: keratotomy:altitude,refractive changes		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

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 are exposed to simulated high altitude.

Technical Approach: Two groups will be selected for the study. The first group will consist of 10 volunteers who have had radial keratotomies within the last two years. Several ocular parameters will be examined and recorded at sea level and at a simulated altitude of 14,000 feet, including cycloplegic refraction, intraocular pressure, corneal keratometry, corneal computer topographic analysis and central corneal thickness. Barometric pressure will be monitored and recorded. Oxygen saturation will also be monitored and recorded using a pulse oximeter. The altitude chamber at Ft. Rucker will be used to achieve a simulated altitude of 14,000 feet. This altitude was chosen because military aircraft crew members may fly to this altitude without supplemental oxygen.

The second study will consist of 10 normals. The above parameters will also be measured in these subjects at sea level and at a simulated altitude of 14,000 feet. The data will be compared using Analysis of Variance to see if a significant difference exists between the two groups.

Progress: Altitude chamber data is to be collected during Oct 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/128 **Status:** Completed

Title: The Effect of Weightlifting on Intraocular Pressure

Start Date: 05/07/93 **Est. Completion Date:** Apr 93

Department: Surgery/Ophthamology **Facility:** MAMC

Principal Investigator: CPT Mark A. Nekola, MC

Associate Investigators: MAJ John D. Ng, MC

Key Words: intraocular pressure,weightlifting

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

Study Objective: To document the change in intraocular pressure that occurs with weight-lifting.

Technical Approach: Ten volunteers will be selected from clinic staff. Level of baseline exercise, height/weight, age, sex and blood pressure will be documented. Each volunteer will undergo a full ophthalmic exam. Each subject will perform five standard exercises on Nautilus machines. Each exercise will be performed according to manufacturers instructions. Resistance weight used is the maximum a subject could perform for five repetitions (determined prior to study). Subjects will be encouraged to perform a valsalva maneuver breath during muscle contraction. In addition, intraocular pressure (IOP) will be measured during valsalva alone. Prior to exercise, baseline intraocular pressure will be measured in the standard manner with the pneumatonometer. The subject will then be asked to perform the given exercise with the pneumatonometer remaining in place. The intraocular pressure tracing will then be examined for the magnitude of IOP during exercise. This will be done for each of the five exercises and the valsalva maneuver. Mean IOP change and standard deviation will be calculated for each exercise to characterize the change. Statistical significance will be determined by comparing baseline IOP mean for each exercise with mean IOP during that particular exercise employing a paired t-test.

Progress: A paper is being prepared describing the outcome of this study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/155 **Status:** Completed

Title: Comparison of Three Corneal Trephines for Penetrating Keratoplasties to Treat Large Central Corneal Perforations

Start Date: 08/06/93 **Est. Completion Date:** Aug 93

Department: Surgery/Ophthamology **Facility:** MAMC

Principal Investigator: MAJ John D. Ng, MC

Associate Investigators:
COL Thomas H. Mader, MC
MAJ Margaret G. Richardson, MS
CPT Mark A. Nekola, MC
MAJ Vernon C. Parmley, MC

Key Words: trephines,corneal perforations,keratoplasty

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

Study Objective: To determine which of three different corneal trephines provides the sharpest and cleanest corneal cut in eyes with large corneal perforations.

Technical Approach: Fifteen human donor eyes (not fit for human transplantation use) will be obtained and inspected to ensure there were no pre-existing perforations or surgical procedures performed. Balanced Salt Solution will be injected into the vitreous cavity to maintain intraocular pressures at 10 to 18 mm Hg. A 4 mm diameter punch will be used to create a full thickness opening in each eye to simulate a large corneal perforation. Six eyes will be used for each trephine type (Hanna, Hessburg-Barron and Free blade). Each will be used according to manufacturers guidelines to create a corneal trephine opening. Technical difficulties inherent for each type of trephine will be recorded. The globes will be fixed in formalin and sent for plastic embedding, sectioning, and staining. The corneas and anterior segment structures will be microscopically examined for quality of trephination by a surgeon blinded to the type of surgery. The data will be used to determine whether the Hanna Trephine has any advantage over the other two corneal trephines.

Progress: All work has been completed. The rough draft of the results is being completed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/114 **Status:** On-going

Title: Clinical and Microbiological Study Comparing Ciprofloxacin Opthalmic Solution to TOBREX Ophthalmic Solution for Treating Bacterial Conjunctivitis in Children

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

Department: Surgery/Ophthamology **Facility:** MAMC

Principal Investigator: MAJ Vernon C. Parmley, MC

Associate Investigators:
CPT Benjamin N. Gilbert, MC
MAJ William R. Raymond IV, MC
CPT Lilia A. Fannin, MC
MAJ Benny T. Gee, MC
COL Thomas H. Mader, MC

Key Words: conjunctivitis,ciprofloxacin,TOBREX,children:1-12 YO

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

Study Objective: The objectives of this study are to compare clinical and bacterial efficacy and incidence of adverse reactions for topical Ciprofloxacin ophthalmic solution against Tobrex in children (ages 1 - 12), with acute bacterial conjunctivitis.

Technical Approach: One hundred thirty evaluative patients diagnosed with acute bacterial conjunctivitis, of any race and either sex, and between 1 and 12 years of age, will be randomized to either a Ciprofloxacin or TOBREX study group. Prior to enrollment, the patients will undergo bacteriologic culture from the lower conjunctiva. At each follow-up visit, the investigator will evaluate the patient's progress objectively and by bacteriologic culture.

Primary statistical analyses will be based on physician impression of cure, and microbiological comparison on the Day 0 and Day 7 (± 2 days) conjunctival cultures. Ocular symptoms and signs will also be analyzed.

Progress: Recruitment for this project is ongoing. There are no data available at this time.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/092 **Status:** Completed

Title: Gram Negative Endotoxin Monoclonal Antibody as an Adjunct to Treating Gram Negative Endophthalmitis in the Rabbit

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

Department: Surgery/Ophthamology **Facility:** MAMC

Principal Investigator: MAJ Vernon C. Parmley, MC

Associate Investigators:
COL Thomas H. Mader, MC
LCDR John H. Varga, MC
CPT Lilia A. Fannin, MC
CPT (P) Kent Karren, MC
CPT Curtis S. Hansen, RPH, MSC
MAJ Anthony R. Truxal, MC
MAJ Benny T. Gee, MC

Key Words: monoclonal antibody,endophthalmitis,animal model,animal study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 06/07/93

Study Objective: To determine the tolerance of rabbit retina and corneal endothelium to intraocularly administered gram negative endotoxin monoclonal antibody (GNEMA) and to determine if GNEMA, in combination with intraocularly injected antibiotic, is more effective than intraocularly injected antibiotics alone in decreasing the amount of retinal necrosis associated with gram negative endophthalmitis.

Technical Approach: The study will be conducted in two parts. Part one will determine if GNEMA is safe when administered intraocularly. One rabbit will be injected only with a balance salt solution and serve as a control. The other rabbits will receive a specified amount of GNEMA in both eyes, starting at one fourth the required effective systemic dose needed for treating gram negative sepsis and increasing to four times the required systemic dose. The rabbits will be euthanized and their eyes examined histopathologically for evidence of toxicity.
The second part of the study will determine efficacy. Gram negative bacterial endophthalmitis will be reproduced in the rabbits with two species of bacteria. In 16 rabbits, one eye will serve as a control and be treated according to accepted standard of care with vitrectomy and intraocular antibiotics. The other eye will be treated the same except it will also receive the maximum safe amount of GNEMA that can be injected intraocularly. One rabbit will be a non-infected control. After time intervals of one day and one week, the rabbits will be euthanized and their eyes examined for retinal and corneal viability. The study will be blinded to the pathologist performing the determination of viability. A viability score will be determined based on the normal or abnormal appearance of the retina and cornea. The viability score of each group will be compared with the Fisher exact test or Student's t test to determine statistical significance between the two groups.

Progress: Daily eye evaluation showed no evidence of E5 toxicity in the control or E5 injected eyes, even with the highest concentration of E5 used. Histopathologic assessment of the retina and cornea demonstrated no abnormalities in the control of E5 injected eyes.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, ORTHOPEDIC SURGERY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 86/016 **Status:** On-going

Title: Teaching Program for Practical Microsurgery

Start Date: 11/15/85 **Est. Completion Date:** Indef.

Department: Surgery/Orthopedic Surgery **Facility:** MAMC

Principal Investigator: MAJ Michael Q. Cosio, MC

Associate Investigators:
COL Jackie L. Finney, MC
LTC Donald B. Blakeslee, MC
MAJ Stephen D. Clift, MC
LTC Bruce R. Wheeler, MC
COL Richard A. Camp, MC
COL Thomas G. Griffith, MC
LTC Robert J. Kenevan, MC
MAJ Viswanatham Piratla, MC
MAJ Michael R. Morris, MC

Key Words: training protocol,microsurgery,Animal Study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$690.00	**Periodic Review:** 06/07/93

Study Objective: To perfect the techniques needed to perform clinical microsurgery and to establish formal training programs in clinical microsurgery at MAMC for use of those surgeons desiring to develop this expertise.

Technical Approach: A schedule of one or two afternoons per week will be set aside for teaching sessions. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques. Staff and residents from the Orthopedic, Plastic Surgery, and Thoracic Surgery Services will train in the following procedures: (1) reimplantation of extremities, (2) re-anastomosis of peripheral vessels and nerves, (3) repair of avulsion wounds, (4) graft transplants, (5) free cutaneous, myocutaneous and composite tissue transfer for traumatic lesions and reconstructive procedures, (6) re-anastomosis of facial nerve lesions. The training will begin with small vessels and nerves in cadaver specimens of small laboratory animals. When the anatomy of the area is learned as well as the use of the microsurgical instruments and the operating microscope, then microsurgical procedures in living rats, guinea pigs, and rabbits can be learned.

Progress: Four sessions were held with one animal used at each session.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/081 **Status:** On-going

Title: Postarthroscopy Analgesia Following Intra-articular Morphine and Bupivicaine

Start Date: 04/02/93 **Est. Completion Date:** Mar 94

Department: Surgery/Orthopedic Surgery **Facility:** MAMC

Principal Investigator: CPT Steven M. Crenshaw, MC

Associate Investigators:
CPT Patrick J. Fernicola, MC
CPT Gary D. Gridley, MC
MAJ John D. Pitcher Jr., MC

Key Words: Postarthroscopy Analgesia:morphine and bupivicaine

Accum	**tive**	**Est. Accumulative**		**Periodic Review:**
MEDC	**Cost:** $0.00	**OMA Cost:**	$21.00	/ /

Study Objective: To determine the effectiveness of intra-articular morphine when combined with bupivicaine compared to bupivicaine alone for post arthroscopy analgesia.

Technical Approach: Over 100 patients undergoing knee arthroscopy will receive an injection of a 30 ml solution into the knee, consisting of either 100 mg of bupivicaine with mg of morphine or 100 mg of bupivicaine alone. Post operative assessment will begin in the post-anesthesia care unit and continue on the ward. These assessments will include a graded pain scale to be filled out at set intervals by the patient or health care provider. The contents of the injection will remain unknown until the study is completed. Supplemental analgesics required for pain will be recorded.

The pain scores and supplemental medications will then be analyzed to determine statistical correlation to the injection given by the ANOVA test.

Progress: Eleven patients have been entered. This study is designed for inpatients. Most arthroscopy patients are presently going home immediately following surgery. We will continue the present study as designed but will most likely need to modify the protocol to include outpatients.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/096 **Status:** On-going

Title: Thumb Flexor Retinaculum and Tendon Sheath Pulley Study

Start Date: 05/07/93 **Est. Completion Date:** Jun 93

Department: Surgery/Orthopedic Surgery **Facility:** MAMC

Principal Investigator: CPT Vermon S. Esplin, MC

Associate Investigators: MAJ Michael Q. Cosio, MC

Key Words: thumb:carpal flexor retinaculum,metacarpophalangeal joint,interphalangeal joint

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$2208.00	**Periodic Review:** / /

Study Objective: To analyze the impact of cutting the carpal flexor retinaculum and the three flexor pulleys on the motion of the metacarpophalangeal (MP) and interphalangeal (IP) joints of the thumb.

Technical Approach: Twenty five specimens amputated at the mid forearm, will be obtained from the University of Washington Anatomy Department. These specimens will each have x-ray evaluation to determine presence or absence of arthritis. Those who have significant arthritic changes will be excluded from the study. These specimens will be carefully dissected at MAMC morgue to expose the flexor pollices longus tendon (FPL), the carpal flexor retinaculum, and the three flexor tendon sheath pulleys. They will then be transported to the Harborview Medical Center Lab for testing. The forearm and the finger metacarpals will be stabilized with modified "C" clamps mounted on a board. Each of the 15 groups of hands will then undergo the tests, first in a neutral position, and then in 45 degrees of wrist dorsiflexion. A fixed tendon excursion will then be performed recording joint motion and required force. A standard force will then be applied, recording tendon excursion and joint motion.

Range of motion will be compared using a repeated measure ANOVA analysis. Differences that are found will be isolated using paired t-tests and/or post-hoc ANOVA testing.

Progress: Testing of specimens is currently being done at Harborview. It was necessary to construct a special clinic and monitors to accomplish our goal. It is anticipated that testing will be finalized by 1 Jan 94

Detail Summary Sheet

ate: 30 Sep 92 **Protocol No.:** 90/015 **Status:** Terminated

tle: Investigation of Cryotreatment on the Epiphysis of Growing Rabbit Bone

art Date: 01/19/90 **Est. Completion Date:** Jan 91

epartment: Surgery/Orthopedic Surgery **Facility:** MAMC

rincipal Investigator: CPT James S. StLouis, MC

ssociate Investigators:
COL D. Scott Smith, MC
MAJ Michael Tidwell, MC
CPT Harvey Montigo, MC
COL Roberto Barja, MC

ey Words: bone,epiphysis,cryotreat,rabbit,Animal Study

ccumulative		**Est. Accumulative**		**Periodic Review:**
EDCASE Cost:	$0.00	**OMA Cost:**	$150.00	06/07/93

tudy Objective: To determine if cryotreatment to the epiphysis of 6 week old rabbits will :unt growth, slow growth, or cause deformity.

echnical Approach: Number or rabbits studied: 15. The lateral aspect of the distal :mur of the right leg will be exposed and the CT-73 cryosurgical system will be applied ith a microprobe to freeze the area. The left rear leg will be operated in the same anner, except the cryoprobe will not be applied. After a six week period for bone rowth, the animals will be euthanized. A pathologist will then determine the gross ffect on growth plates and any deformities present on the right versus the left femur. licroscopic specimens of the cryotreated epiphyses will be examined to evaluate emaining potential growth of microvascular structures and uniformity of cryological ffects. Data will be evaluated using a paired t test between right and left sides to ompare the legs at an alpha level of 0.05.

rogress: This study has not been implemented because the P.I. has been assigned to hildren's Hospital in Seattle, WA for most of his residency. The P.I. requested ermination.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, PLASTIC SURGERY SERVICE

Detail Summary Sheet

e: 30 Sep 92 | **Protocol No.:** 92/099 | **Status:** On-going

.e: The Implantation of Bone Morphogenic Protein Using Vascularized Omentum in a Predetermined Size and Shape in Swine

rt Date: 09/04/92 | **Est. Completion Date:** Dec 92

›artment: Surgery/Plastic Surgery | **Facility:** MAMC

ncipal Investigator: MAJ Stephen M. Davis, MC

ociate Investigators: MAJ Cecil R. Dorsett, DC
MAJ Robert J. Wygonski, DC | MAJ Richard R. Gomez, MC

r Words: bone protein,omentum,animal study,Animal Study

:umulative DCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$600.00	**Periodic Review:** 06/07/93

dy Objective: To determine if a vascularized graft utilizing omentum with bone phogenetic protein can induce bone formation in a three dimensional shape; and to ermine bone produced in this manner can survive transplantation to a different ıtion.

hnical Approach: Bone grafting is a commonly performed procedure. The best bone ft is a vascular autogenous graft (one obtained from the patient complete with its own od supply). However, this is not always possible and does have certain risks, even en properly performed. Bone morphogenetic protein (BMP) is a substance which uces new bone to form in intra- or extra-skeletal sites and has recently been cloned by ombinant DNA techniques. Six pigs will be used for this study. Each pig will undergo ıparotomy with the placement of six tubular molds around individual omental licles. Two molds will contain only omentum, two will contain omentum and ogenous bone, and two will contain omentum and bone morphogenetic protein. Forty days after being implanted, each mold will be opened and visually examined. The molds containing bone morphogenetic protein will have their vascular supply tched by microsurgical techniques. After an additional 45 days, all molds will be vested and examined to determine if bone has been produced in a three dimensional ıpe with its own blood supply. If present, an attempt will be made to determine if it is tical, cancellous, or corticocancellous bone.

gress: Due to the significant cost of obtaining bone morphogenic protein and the iculty of obtaining the substance we have submitted a modification to utilize cell ture autologous pig bone marrow.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY, UROLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/098 **Status:** On-going

Title: Randomized Prospective Study Comparing Intermittent Pneumatic Compression of the Calf to Intermittent Sequential Pneumatic Compression of the Whole Leg

Start Date: 10/04/91 **Est. Completion Date:** Nov 93

Department: Surgery/Urology **Facility:** MAMC

Principal Investigator: MAJ Kurt L. Hansberry, MC

Associate Investigators:
COL Charles A. Andersen, MC
MAJ Ian M. Thompson, MC
MAJ James H. Timmons, MC

Key Words: pneumatic compression,intermittent,sequential,calf,leg

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$3055.00	**Periodic Review:** / /

Study Objective: To determine the best mechanical device used to prevent deep venous thrombosis (DVT) and subsequent pulmonary embolism, taking into consideration patient comfort and cost effectiveness.

Technical Approach: Patients undergoing open urologic procedures that wish to participate in the study will sign the consent form and will be categorized by specific organ system. Then using a random numbers table, subjects will be randomized to one of two prophylactic groups within that category. One of these modalities is normally used in these procedures. One day prior to the surgery, a duplex venous scan will be performed on both lower extremities. At the time of surgery, the compression devices will be placed on the subjects and be worn for at least 72 hours post operatively and longer if the patient is not fully ambulatory. Duplex scans will be done on each patient on post operative day 3 or 4 and 7. Appropriate therapy will be instituted (anticoagulants) once a diagnosis is made. Once the patient is discharged from the hospital, surveillance for DVT will cease and that patient's involvement in the protocol will end. Incidence of DVT will be compared using chi-square analysis.

Progress: Patients have undergone pre and post operative duplex venous ultrasound and randomization to one of two groups of pneumatic compression stockings (PCS). One pulmonary embolus was diagnosed in the thigh high PCS group without evidence of precedent deep venous thrombosis (DVT). In addition one DVT was discovered by duplex ultrasound in the thigh high PCS group. Patient accrual is ongoing but at a slower rate than originally projected. Preliminary data suggest no difference in the rate of formation of DVTs with either form of compression but statistical significance may not have been reached because of the small population studied this far.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/091	**Status:** Completed
Title: Transurethral Prostatectomy and Associated Erectile Dysfunction		
Start Date: 09/06/91	**Est. Completion Date:**	
Department: Surgery/Urology	**Facility:** MAMC	
Principal Investigator: CPT Richard W. Knight, MC		
Associate Investigators: COL John N. Wettlaufer, MC	MAJ Kurt L. Hansberry, MC	
Key Words: sexual function,prostatectomy		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To use objective data to measure erectile function after transurethral prostatectomy.

Technical Approach: All patients who have medical indications for transurethral resection of the prostate (TURP) will be asked to participate in this study, with the expectation of from 100-200 consenting subjects. Prior to undergoing the surgery the subjects would be asked to answer a questionnaire concerning sexual function/dysfunction. They would then undergo three nights of NPT (nocturnal penile tumescence) measurements at home with a computerized device called the Rigiscan. This device measures the "hardness" (rigidity) of the erect penis and the size (width) of the erect penis and records duration and number of events (erections) each night. The subject would then undergo the TURP. Approximately three to six months after the surgery the subjects will again undergo NPT for three nights, just like the before surgery procedure. Pre-op and post-op NPT measurements will be compared to determine any objective change in erectile function. The questionnaire will also be used to determine any subjective change in function.

Progress: No statistical difference was found between preoperative and postoperative erections; however, 28% of men entered in the study noted a decrease in their overall quality of erection on the written questionnaire. In depth detailed interviews discovered patients equated retrograde ejaculation with decreased potency.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/132 **Status:** On-going

Title: Fluoroquinolones As Prophylaxis in Penile Prosthesis Surgery

Start Date: 07/02/93 **Est. Completion Date:** Jun 96

Department: **Facility:** MAMC

Principal Investigator: CPT Bradley F. Schwartz, MC

Associate Investigators: J.B. Thrasher
MAJ Kurt L. Hansberry, MC

Key Words: penile prosthesis,fluoroguinolones,prophylaxis

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

Study Objective: To deteermine if oral Fluoroquinolones afford efficacious alternatives to the current regimens in penile prosthetic surgery prophylaxis.

Technical Approcach: All patients undergoing elective penile prosthesis surgery at Madigan Army Medical Center will be given one of the following preoperative antibiotic prophylaxis regimens: Fluoroquinolone two hours prior to surgery, the evening of surgery and for seven days following surgery; or a combination of gentamycin 75 mg and Cefazoline 1 gm two hours preoperatively and cephradine 250 mg qid for seven days postoperatively. Intraoperatively, a 1 cm^3 sample of the corpus cavernosum will be taken and sent to the University of Washington Department of Pathology for quantitative tissue determinations of the antibiotic using a bioassay. At the same time, a determination of serum concentration of the drug will be made.

Progress: Initiation of this project is delayed pending exploration of possible sources of funding.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/045	**Status:** On-going
Title: The Normal Flora of the Human Epididymis		
Start Date: 02/05/93	**Est. Completion Date:** Jul 96	
Department: Surgery/Urology	**Facility:** MAMC	
Principal Investigator: CPT Bradley F. Schwartz, MC		
Associate Investigators: COL John N. Wettlaufer, MC	J.B. Thrasher	
Key Words: epididymis:normal flora		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To provide quantitative and qualitative identification of normal flora of the human epididymis.

Technical Approach: Males undergoing orchiectomy for other than non-infectious causes will be evaluated preoperatively in the usual fashion and, in addition, a urinalysis, urine culture and a blood culture will be performed (a positive urinalysis or blood culture will exclude the subject). Upon orchiectomy the specimen will be properly labeled and sent to the microbiology lab for quantitative and qualitative tissue cultures to include routine bacteria, chlamydia, mycoplasma and mycobacteria. Any colonies of growth will be considered significant. A numerical statistical analysis will be performed to determine occurrence of organisms in the normal human epididymis

Progress: There have been no complications or adverse events in the 30 patients enrolled. There have been three positive aerobic cultures felt to be contaminants. All other cultures have revealed no growth. Initial conclusion is that there is no normal bacterial flora of the human epididymis.

DETAIL SHEETS FOR PROTOCOLS

FORT ORD MEDDAC

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/055 **Status:** On-Going

Title: Infant Feeding Practices in the Military Community: The Incidence and Duration of Breast Feeding in the Military Community and the Factors Affecting This Decision

Start Date: 03/05/93 **Est. Completion Date:** Nov 93

Department: Fort Ord MEDDAC **Facility:** MAMC

Principal Investigator: Cindy B. Lee, MD

Associate Investigators:
Dana Andersen, M.D.
Kathy Holder, M.D.
B. Wayne Blancke, M.D., MPH
LTC John P. Kugler, MC
LCDR Euelya L. Lewis
B.W. Blount

Key Words: breast feeding:military

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

Study Objective: (A) To determine the incidence and duration of infant feeding methods of women in the military community. (B) To determine the incidence and duration of breast feeding in active duty women as a subset of employed mothers. (C) To identify the factors affecting womens' infant feeding decisions, specifically those affecting active duty women.

Technical Approach: All women delivering at five U.S. military medical treatment facilities who agree to participate will be asked to complete a survey form resulting in a total of 400-500 postpartum patients over four to six months at each site. From this number a total of 400 active duty patient surveys should be obtained. The forms will be collected at discharge and forwarded to the study site coordinator. Subjects will be contacted by telephone for follow-up surveys information at six months. This data will be compiled at each site and sent to the study primary investigator for analysis.

The primary independent variables will be categorical, interval, and ordinal. The dependent variables will be ordinal and categorical. Categorical independent and dependent variables will be compared by chi-square and relative risk values, with corresponding 95% confidence intervals. Ordinal and categorical data will be compared by the Mann-Whitney U as well as other non-parametric methods. Ordinal and ordinal data comparisons will be analyzed by Somer's D Logistic Regression analysis will be used to assess statistical significance with multiple variables.

Progress: Enrollment is completed with approximately 600 participants. The data will be analyzed in the next few weeks. Dr. Lee has resigned from the Army and Dr. Andersen will direct the remainder of the project from MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/036 **Status:** Completed

Title: Seroprevalence of Human Babesia Infections in High Risk Individuals in Northern California: A Pilot Study

Start Date: 11/06/92 **Est. Completion Date:** Sep 93

Department: Fort Ord MEDDAC **Facility:** MAMC

Principal Investigator: LTC Douglas F. Phillip, MC

Associate Investigators:
Glaser C
Krause P
Kohl S
Conrad P

Key Words: babesiosis

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

Study Objective: To determine if (a) there is a significant prevalence of human babesial infections in Northern California and (b) to characterize the babesial parasites infecting humans in Northern California.

Technical Approach: Patients for this study will be selected by convenience sampling using serum obtained for other purposes. Serum will be collected which was saved from individuals with a positive Lyme titer (defined as >1 optical density by Elisa) at various locations in Northern California. Serum collected from individuals at Fort Ord who are enrolled in an independent Shigella vaccine trial will also be tested.

Individuals identified will be contacted by mail, informed about the study, and asked permission to run the stored serum for Babesia antibody. A stamped self-addressed postcard which can be returned by those individuals who do not wish to participate will be included. Additional medical history(e.g. history of tick bite, episodes of febrile illness) will be obtained by a telephone interview. In the initial phase of the study 100-200 individuals will be tested for babesial antibodies. Inclusion criteria for the second phase of the study will be based on results of antibody titers to various Babesia species (titer >1:80).

In the second phase of the study serum samples will be requested for a follow-up titer. A separate consent form will be used for this phase of the study. The blood sample will be collected at the same laboratory as the original blood sample.

Progress: Eight patients were entered from Ft Ord. The project has been completed and a paper is being written for publication. A new human pathogen was discovered through the DNA testing.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/170	**Status:** Suspended
Title: A Prospective Study of the Treatment of Functional Ovarian Cyst		
Start Date: 05/07/93	**Est. Completion Date:**	
Department: Fort Ord MEDDAC	**Facility:** MAMC	
Principal Investigator: CPT Kenneth K. Vu, MC		
Associate Investigators: None		
Key Words: cyst:ovarian,oral contraceptives		

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

Study Objective: To determine if estrogen/progestin therapy in the form of oral contraceptive pills is effective in the treatment of functional ovarian cyst.

Technical Approach: Female patients ranging in age from 18 through 35 with ovarian cysts diagnosed by pelvic exam will be invited to join this study. Subject will be randomized into an oral contraceptive group versus placebo group. Prior to the initiation of medication, an endovaginal ultrasound will be performed but will not affect the treatment. The patient will be followed for 8 weeks or two cycles with an examination both by bimanual examination and endovaginal ultrasound at the end of 5 and 8 weeks of treatment or placebo.

A second arm to the study will derive information which will indicate how effective the physician's bimanual examination is as compared to the endovaginal ultrasound in the identification and follow-up of these functional ovarian cysts.

Progress: No status report is available. The P.I. is now a fellow at Johns Hopkins University and is out of town for several weeks. A review for continuation of the study will be conducted as soon as he returns.

DETAIL SHEETS FOR PROTOCOLS

FORT WAINWRIGHT, AK

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/054	**Status:** Completed
Title: Melatonin and Cortisol Secretion in the Arctic, Effects of Photoperiod on Circadian Rhythms and Mood		
Start Date: 05/03/91	**Est. Completion Date:**	
Department: Fort Wainwright, AK	**Facility:** MAMC	
Principal Investigator: COL Matthew E Levine, MC		
Associate Investigators:	LT Lawrence K. Duffy, USNR	
Key Words: melatonin,arctic,photoperiod,circadian rhythm		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To establish basic knowledge and understanding of the effects of extreme latitude on the circadian secretory patterns of the primary hormones of the pineal and adrenal glands, and to determine possible effects on mood and behavior.

Technical Approach: Melatonin and serum cortisol levels will be determined on approximately 100 individuals on a quarterly basis, as close to the solstices and equinoxes as practical, at 0200, 0800, 1030, and 1700 hours on those days. Sufficient blood will be obtained for additional endocrine studies, such as reproductive hormones, and possibly thyroid hormones. Subjects will be screened verbally for recent acute stress or geographic changes, and, if either is present, the blood draw will be delayed by one week to allow for diminution of physiologic stress response or readjustment to arctic photoperiod. On the day of the first sampling, a Seasonal Pattern Assessment Questionnaire will be administered. The Beck Depression Inventory will be administered to each subject at each sampling period. Data will be compared with that from other studies at similar and different latitudes. Seasonal variations in hormone levels and mood rating scores will be compared in individual subjects, as well as in the study group. Relationships between mood behavior, endocrine physiology, and season will be subjected to statistical analysis using a repeated measures multi-variate analysis with season and sex as factors, and age as a co-variant. Aposteriori multiple contrasts will be made with Bonferroni tests.

Progress: Prominent finds included unusually high levels of cortisol at 0200 and 0800 in the fall and elevated daytime levels (1030) of melatonin in the winter. These results indicate a delayed phase secretory pattern when compared to the normal pattern at lower latitudes. These findings imply possible underlying physiological causes for the high incidence of behavior disorders such as depression and alcoholism in Alaska and circumpolar environments in general.

DETAIL SHEETS FOR PROTOCOLS

LETTERMAN MEDDAC

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/065	**Status:** Completed
Title: Racial Differences in Responses to the Rorschach Inkblot Test in a Psychiatric Population		
Start Date: 05/01/92	**Est. Completion Date:**	
Department: Letterman MEDDAC	**Facility:** MAMC	
Principal Investigator: Lisa M. Tobin, M.A.		
Associate Investigators:	CPT James J. Picano, MS	
Key Words: Rorschach Inkblot Test,racial differences		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To examine racial differences in responses to the Rorschach Inkblot Test in a clinical population and to determine if such response differences exist, and whether or not they are a function of clinical diagnosis.

Technical Approach: While inquiry has been made into biases inherent in other areas of psychodiagnostic testing, little has been done to examine racial differences in responses to projective measures, such as the Rorschach. The population will be male and female persons evaluated and diagnosed in a military psychiatric inpatient setting. In this study, approximately 40 records of African- American subjects will be matched for diagnosis, age, education SES, and rank to records of Euro-American subjects. All subjects will have a valid Rorchach protocol in the record. Valid Rorchach protocols will be those that contain 14 or more responses and reflect standardized administration procedures. The following psychiatric variables will be obtained: admission, testing and discharge dates, prior hospitalizations, number of days hospitalized medication used as well as presence/absence of medication at the time of testing an estimate of intellectual abilities, and discharge diagnosis. Descriptive statistics such as frequency distributions on a variety of Rorschach variables will be generated and displayed in table form. In addition, descriptive statistics for demographic and psychiatric variables will be generated, both for the total sample and for black and white subject groups separately.

Progress: This study was completed according to schedule and a dissertation was presented. There were few racial differences in the responses to the measure. One exception was that black subjects with a lamba within normal limnits had fewer responses to the measure than white counterparts. This may be attributable to different approaches by examiners during free association verses inquiry.

DETAIL SHEETS FOR PROTOCOLS

U.S. DEPARTMENT OF AGRICULTURE

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 92/001	**Status:** Suspended
Title: Methods for Assessing Vitamin A Status in Healthy Adults		
Start Date: 10/04/91	**Est. Completion Date:** Jul 92	
Department: U.S. Dept. of Agriculture	**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:** / /

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 retinyl 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 (preingestion, 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: This project was temporarily suspended during 1992 so that a metabolic research unit could be organized. The estimated date of resumption is Oct. 94.

DETAIL SHEETS FOR PROTOCOLS

WALTER REED ARMY MEDICAL CENTER

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/046	**Status:** Completed
Title: Pregnancy Attitudes, Ambivalence, and Symptom Distress		
Start Date: 02/01/91	**Est. Completion Date:**	
Department: WRAMC/Nursing	**Facility:** MAMC	
Principal Investigator: LTC Irene M. Rich, AN		
Associate Investigators:	LTC Susan L. Burroughs, AN	
Key Words: pregnancy:attitudes,ambivalence,symptom distress		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To determine the changes that occur in the measures of general pregnancy attitudes, ambivalence, and psychological symptom distress during the three trimesters of pregnancy and to determine the relationships (correlational and predictive) among measures of general pregnancy attitudes, ambivalence, psychological symptom distress, and selected demographic variables during the three trimesters of pregnancy.

Technical Approach: A total of 420 research subjects from three military treatment facilities will be entered in the study. The proposed research employs a combination of quantitative and qualitative research methodologies. The Pregnancy Questionnaire is an investigator-developed, 86 item, modified visual analogue tool which contains two scales. The first scale, the Rich Pregnancy Attitude scale, is used to assess general pregnancy attitudes quantitatively. The second scale, the Rich Ambivalence Scale, is used to assess ambivalence in pregnant women quantitatively. The Pregnancy Questionnaire: Focused Interview Guide will be used to conduct interviews for the qualitative portion of the research. The Rich Visual Analogue (RVA) is an investigator-developed tool designed to quantify levels of ambivalence and general pregnancy attitudes. A panel of experts will score the RVA on review of transcripts from focused interviews. Psychological symptom distress will be measured using scores obtained on Derogatis (1977) Symptom Checklist -90-Revised (SCL-90-R). The women will be systematically assigned to one of three study groups. Group I will provide the quantitative data by completing the demographic data form, the RPA/RA Scales, and the SCL-90-R. Women in Group 2 (a subsample of 45 women - 15 per pregnancy trimester) will provide both quantitative and qualitative data. These women will complete the demographic data form, the RPA/RA scales, and the SCL-90-R and will be interviewed using the Focused Interview Guide. Women in Group 3, a subsample of 120 women (40 per pregnancy trimester) will provide information on the test-retest reliability of the RPA/RA scales by completing the same questionnaires as in Group 1, and then repeating the procedure one week later.

Progress: Relationships between general pregnancy attitudes, ambivalences, and psychological symptom distress were explored using correlation matrixes and a series of multiple regression analyses and analyses or variance. Findings supported three hypothesized relationships between the key variables. There was a direct relationship between PSD and ambivalence, an inverse relationship between PSD and pregnancy attitudes, and an inverse relationship between pregnancy attitudes and ambivalence. Suprisingly, hypothesized differences based on pregnancy trimester were not found. Preliminary content analysis was performed on the qualitative data.

DETAIL SHEETS FOR PROTOCOLS

GYNECOLOGY ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:** 02/05/93

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 were entered in this group of protocols in FY 93. GOG 26 NN was closed Jun 93 due to sufficient patient accrual and GOG 26EE was terminated.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:pelvic,cisplatinum

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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 were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/067 **Status:** On-going

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:** Indef.

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:** 02/05/93

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 have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/082 **Status:** Terminated

Title: GOG 0026EE: A Phase II Trial of Didemnin B (NSC #325319) in Patients with Advanced Pelvic Malignancies

Start Date: 09/16/88 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:pelvic,didemnin B

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

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: Patient must demonstrate a normal prothrombin time to be eligible for this protocol. Didemnin B will be administered at a dosage of 4.2 mg/m^2 every four weeks. The dosage will be calculated using the GOG standard monogram. Prophylaxis against nausea and vomiting using metoclopramide, diphenhydramine, and dexamethasone will be required. Dose modifications will be permitted. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of Didemnin B and demonstrating progression more than or equal to four weeks from study entry will be considered for response and progression. Toxicity, however, may be assessed as soon as drug is given. Each patient should remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/023 **Status:** On-going

Title: GOG 0026GG: A Phase II Trial of Fazarabine (ARA-AC,1-BETA-D-Arabinofuranosyl-5-Azacytosine, NSC 281272, IND 29722) in Patients with Advanced/Recurrent Cervical Cancer

Start Date: 01/19/90 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix,fazarabine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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: 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, and SGOT <5 IU. Fazarabine will be administered at a dose of 40 mg/m^2/day for five days. Cycles of therapy will be repeated every 28 days. Patients with a response or stable disease will continue therapy until progression of disease is documented or adverse effects prohibit further therapy. Patients with progressive disease will have Fazarabine discontinued. Patients will be monitored for adverse effects and dose levels modified as necessary.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Ind x

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: 02/05/93

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 were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 91/085	**Status:** On-going

Title: GOG 0026KK: A Phase II Trial of Merbarone (NSC336628) in Patients with Advanced and Recurrent Epithelial Ovarian Carcinoma

Start Date: 08/02/91	**Est. Completion Date:**
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian:epithelial,merbarone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. In this protocol, the agent will be merbarone, a thiobarbituric derivative. The intent of the protocol is to determine the efficacy of this agent in patients whose advanced malignancy has been resistant to high priority methods of treatment.

Technical Approach: Only patients with ovary epithelial, cervical, or endometrial cancer will be eligible. Because of severe phlebitis induced by peripheral infusion, each patient must have a central line prior to administration of merbarone. Patients must have adequate hepatic function as demonstrated by bilirubin and SGOT less than 2 x normal and creatinine must be < 1.5 mg, with a creatinine clearance of 60 ml/min. Merbarone will be administered as a continuous IV infusion via central line at a starting dose of 1000 mg/m^2/day for five days and repeated every three weeks depending upon adverse effects. Maximum dose per day will be 2 grams. Courses will be given once every three weeks providing there is adequate bone marrow, renal function, and hepatic function. An adequate trial is defined as receiving one course of drugs and living at least 4 weeks for additional tumor assessment. Severe irreversible adverse effects and/or progression of disease will require being removed from the study.

Progress: No patients were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Dec 93

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:** / /

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: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 83/024 **Status:** On-going

Title: GOG 0026N: A Phase II Trial of Diahydroxyanthracenedione (DHAD) (NSC #30179) (CL232315) in Patients with Advanced Pelvic Malignancies

Start Date: 11/19/82 **Est. Completion Date:** Indef.

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:pelvic,DHAD,diahydroxyanthracenedione

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To determine the efficacy of DHAD 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 prior therapies will be offered DHAD as a Phase II drug to determine its efficacy. The drug will be given as 12 mg/m^2 I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy. This protocol was closed to uterus/MMT patient entry in Aug. 87.

Progress: No patients were entered in this study during FY 93. In previous years, 3 patients were entered and all died of the disease.

Detail Summary Sheet

ate: 30 Sep 92 **Protocol No.:** 93/072 **Status:** Completed

itle: GOG 0026NN: A Phase II Trial of Piroxantrone in Patients With Advanced and Recurrent Ovarian Epithelial Carcinoma

tart Date: 03/05/93 **Est. Completion Date:** Feb 94

epartment: GOG **Facility:** MAMC

rincipal Investigator: LTC Mark E. Potter, MC

ssociate Investigators: None

ey Words: cancer:ovarian epithelial carcinoma, piroxantrone

ccumulative		**Est. Accumulative**		**Periodic Review:**
EDCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

Study Objective: 1. To evaluate the activity of Piroxantrone, an anthrocycline derivative, n advanced ovarian carcinoma. 2. To evaluate the toxicity profile in these patients.

Technical Approach: Patients with advanced and recurrent ovarian carcinoma, who have failed standard chemotherapy are eligible for participation in this protocol. Patients must have a tumor present which is measurable either on physical examination or by radiologic tests. Pyroxantrone will be administered at a starting dose of 160 mg/m^2 infused over one-hour every three weeks. If toxicity is not noted with treatment, the dose will be escalated to the next highest level to a maximum dose of 190 mg/m^2. Each patient should remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: This study was closed to patient entry on 7 June 93. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 83/026 **Status:** On-going

Title: GOG 0026Q: A Phase II Trial of Aminothiadiazole in Patients with Advanced Pelvic Malignancies

Start Date: 11/19/82 **Est. Completion Date:** Indef.

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:pelvic,aminothiadiazole

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To determine the efficacy of aminothiadiazole in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer who have failed higher prior therapies will be offered aminothiadiazole as a Phase II drug to determine its efficacy. The drug will be given as 125 mg/m^2 I.V. once a week. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patients were entered in FY 93. One patient was entered in FY 85 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 85/087 **Status:** On-going

Title: GOG 0026U: A Phase II Trail of Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #25232) in Patients with Advanced Pelvic Malignancies

Start Date: 09/20/85 **Est. Completion Date:** Indef.

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:pelvic,ifosfamide,uroprotector mesna

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/03/95

Study Objective: To determine the efficacy of ifosfamide plus mesna in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All eligible patients who have failed higher priority therapies will be offered ifosfamide plus mesna as a Phase II drug regimen to determine its efficacy. Ifosfamide will be given at a dosage of 1.8 g/m^2 daily for five days and mesna will be given 400 mg/m^2 t.i.d. every four weeks. Patients will be followed for toxicities to the drug and the drug dosage will be modified according to the severity of the toxicities. Response to the drug will be followed; progression of disease and/or excessive toxicities will terminate the study for the patient.

Progress: No patients were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 86/075 **Status:** Terminated

Title: GOG 0026W: A Phase II Trial of Echinomycin in Patients with Advanced Pelvic Malignancies

Start Date: 06/20/86 **Est. Completion Date:** Indef.

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:pelvic,echinomycin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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: Echinomycin will be administered at a dosage of 1500 mcg/m every 4 weeks. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of drug and demonstrating progression < 4 weeks from study entry will be considered eligible for response and toxicity. Each patient will remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients were entered at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/058 **Status:** Completed

Title: GOG 0026X: A Phase II Trial of Gallium Nitrate (NSC #15200) in Patients with Advanced Pelvic Malignancies

Start Date: 05/20/88 **Est. Completion Date:** Indef.

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:pelvic,gallium nitrate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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: Gallium nitrate will be given as a slow intravenous infusion over 30-60 minutes at a dose of 750 mg/m^2. The dose will be repeated once every three weeks. Patients will be hydrated with at least three liters of fluid the day prior to treatment. An additional 500 cc normal saline will be infused in the two hours prior to administration of gallium nitrate. Hydration of three liters of fluid orally or intravenously will be continued during the first 24 hours after therapy. Patients receiving concurrent radiotherapy are ineligible for this study. An adequate trial will be defined as receiving one course of therapy and living three weeks. Each patient will continue receiving gallium nitrate until disease progression or death or until adverse effects prohibit further therapy.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 81/079 **Status:** On-going

Title: GOG 0040: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas

Start Date: 05/15/81 **Est. Completion Date:** Indef.

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: sarcoma:uterine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To determine the incidence of pelvic and aortic lymph node metastases associated with Stages I and II uterine sarcomas, the relationship of these node metastases to other important prognostic factors such as mitotic index of the tumor, and the complication rate of the procedures. These findings will then be used as a guide for treatment protocols.

Technical Approach: Patients with histologically proven uterine sarcoma clinical Stages I or II who undergo total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, peritoneal cytology sampling and omentectomy (optional) as described in the protocol are eligible. Patients who have had prior preoperative adjuvant pelvic radiation or chemotherapy will be ineligible. The following pathologic evaluation will be done: a. Peritoneal cytology will be evaluated for malignant cells. b. The uterus will be evaluated at least in regard to: (1) location of tumor; (2) depth of myometrial invasion; (3) differentiation of tumor; (4) size of uterus; (5) number of mitoses per 10 HPF; (6) histologic type of tumor. c. The adnexa will be evaluated for presence of metastasis. d. The lymph nodes will be evaluated as to metastasis and location and number of involved lymph nodes. After surgical staging, patients may be transferred to an appropriate treatment protocol if all criteria are met. If no protocol is available, further treatment will be at the discretion of the physician.

Progress: No patients were entered in this study during FY 93. One patient continues to be followed

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 81/035 **Status:** On-going

Title: GOG 0041: Surgical Staging of Ovarian Carcinoma

Start Date: 01/16/81 **Est. Completion Date:**

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,surgical staging

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

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: No patients were enrolled during FY 93. In previous years, 13 patients were enrolled and 2 have been lost follow up, 2 have died and 9 are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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: 08/21/82 **Est. Completion Date:** Feb 94

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:** 02/05/93

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: Six patients were entered in this study. Five have died of the disease and one was apparently lost to follow-up. Therefore, the study was closed at MAMC in FY 91. However, this patient was relocated and is now being followed at MAMC. Therefore, the study was reactivated in December 1992. No patients were enrolled in this protocol at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 82/036 **Status:** Completed

Title: GOG 0063: A Clinical Pathologic Study of Stages IIB, III, and IVA Carcinoma of the Cervix

Start Date: 03/19/82 **Est. Completion Date:**

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:cervix,pathologic study

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To evaluate the sensitivity and specificity of non-invasive procedures such as sonography, computerized transaxial tomography and lymphangiography in detection of metastases; to better understand the significance of various surgical and pathologic factors involved in staging and therapy for advanced cervical cancer. The accumulated clinical/surgical/pathological data may then play a role in modification or design of future protocols; to determine by observations of five-year survival and disease-free interval, the validity of current FIGO staging in comparison to histopathologic prognostic factors such as size of lesion, location of lesion, histology, grade, pelvic lymph node metastases, and aortic lymph node metastases, in patients with Stages IIb, III, and IVa carcinoma of the cervix.

Technical Approach: All eligible patients with invasive carcinoma of the cervix, Stages IIb through IVa, will undergo preoperative clinical staging, including traditional staging as permitted by FIGO rules. Extended clinical staging utilizing sonography, lymphangiography, and computerized transaxial tomography are mandatory. When these tests reveal an aortic nodal metastasis, the patient will have a fine needle biopsy; however, if the tests are negative, the patient will have an aortic lymphadenectomy. Patients who have a positive fine needle biopsy or positive aortic lymphadenectomy will undergo scalene node biopsy before consideration for a GOG treatment protocol. It is anticipated that all patients will be considered for entry into a GOG protocol for which they are suitable when such protocols are available.

Progress: No patients were enrolled in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 84/033 **Status:** On-going

Title: GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phse II Trial of Melphalan an[illegible] Secondary Treatment with Cisplatin in Patients with Progressive Disease

Start Date: 02/17/84 **Est. Completion Date:** Dec 88

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:ovarian,melphalan,cisplatin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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: No patients were enrolled at MAMC during FY 93. In previous years, 10 patients were enrolled, 1 has died and 9 are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jul 89

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: 02/05/93

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: One patient was enrolled in FY 92 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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: 08/15/96 **Est. Completion Date:** Feb 94

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, Radiothearpy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

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. After further review it was discovered that this was a mistake. Therefore, the protocol was reopened in Feb 93 in order to follow these two patients.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/044 **Status:** Completed

Title: GOG 0086O: A Phase II Trial of Taxol (NSC #125973) and G-CSF in Patients With Advanced or Recurrent Endometrial Carcinoma

Start Date: 02/05/93 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:endometrial

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

Study Objective: To evaluate the activity of Taxol in chemotherapy naive patients with advanced or recurrent endometrial carcinoma.

Technical Approach: Patients will be those who present with advanced, measurable adenocarcinoma of the endometrium documented histologically prior to entry in the protocol. They must not have a recent history of angina or congestive heart failure nor have active arrhythmias. Enrolled patients will be given Taxol as a 24-hour continuous infusion at an initial dose of 250 mg/m^2/24 hour every 3 weeks following premedication with Benedryl, Decadron, and Cimetadine. This infusion will be repeated every 3 weeks (no treatment course is to begin until all toxicity from the previous course has resolved). Additionally, daily subcutaneous injections of G-CSF will be given beginning 24 hours after the completion of chemotherapy for 14 days or until the white blood cell count is > 10,000. During the course of therapy, weekly CBCs and platelet counts will be obtained to follow for bone marrow toxicity. Physical examinations will be performed at the time of every treatment. Radiologic imaging will be repeated every other cycle.

The principal parameters employed to evaluate the efficacy of each agent are: 1) The frequency and duration of objective response. 2) The frequency and severity of observed adverse effects. 3) Survival time for all patients. 4) Duration of progression-free interval for all patients.

Progress: One patient was enrolled and later died of the disease.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:** 02/05/93

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 were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/104 **Status:** On-going

Title: GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervis After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

Start Date: 08/21/87 **Est. Completion Date:** Indef.

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: 02/05/93

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: One patient was enrolled in FY 88 and is still in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:** 02/05/93

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 were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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: 02/05/93

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: One patient was entered in FY 93 and is in follow-up. Five patients were entered in previous years and 1 remains in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:**	**Periodic Review:** 02/05/93

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: No patients were enrolled at MAMC during FY 93. The two patients enrolled in previous years are both in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/105 **Status:** Completed

Title: GOG 0100: Monoclonal Antibody Against Free Beta HCG to Predict Development of Persistent Gestational Trophoblastic Disease (PGTD) in Patients with Hydatidiform Mole

Start Date: 08/21/87 **Est. Completion Date:** Indef.

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: hydatidiform moles,monoclonal antibody,free beta HCG,PGTD

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

Study Objective: To measure the serum concentration of free beta HCG and total beta HCG in patients with molar pregnancies in order to determine whether the ratio of free beta HCG to total beta HCG may be of value in predicting which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent gestational trophoblastic disease.

Technical Approach: Patients with gross and microscopically verified diagnosis of hydatidiform mole, either classic (true) or partial (incomplete), obtained by evacuation of the uterus with uterine conservation will be eligible. Patients will have a pelvic ultrasound within two weeks of evacuation and the first serum will be drawn within 48 hours (prior to if at all possible) of evacuation for beta HCG and free beta HCG determinations. Following histologic confirmation of the hydatidiform mole (within one week of evacuation) the patient will be placed on study. Serum samples will be obtained weekly until a negative assay is attained or until a plateau or rise in titer is observed. All patients will remain on study for a minimum of twelve weeks after primary evacuation of the molar pregnancy. After spontaneous remission, patients will have beta HCG titers monthly for six months (free beta HCG assay is not necessary). After persistent disease, the patient will remain on study until remission. The principle parameters employed to investigate the prediction of which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent trophoblastic disease are free beta HCG, total HCG concentration, ratio of free beta HCG to total HCG, and remission of disease as determined by weekly titers.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/106 **Status:** On-going

Title: GOG 0101: A Phase II Evaluation of Preoperative Chemoradiation for Advanced Vulvar Cancer

Start Date: 08/21/87 **Est. Completion Date:** Indef.

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:vulva,chemoradiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To determine: the feasibility of using preoperative chemoradiotherapy to obviate the need for pelvic exoneration for patients with advanced vulvar cancer involving the proximal urethra, bladder, anal canal, or rectum; the feasibility of allowing a less extensive vulvar and vaginal resection in patients with a T3 primary tumor by using preoperative chemoradiotherapy; the survival rate for patients with Stage III or IV-A disease associated with this technique of therapy; the morbidity of a combined chemoradiosurgical approach to advanced vulvar cancer and to attempt to improve survival in patients with N3 groin nodes.

Technical Approach: Patients with primary, previously untreated, histologically confirmed invasive squamous or adenocarcinoma of the vulva clinically determined to be Stage III or IV will be treated with chemoradiation therapy according to the sub-stage. Regimen I: Patients with T4 or unresectable T3 primary tumor and NO or N1 groin nodes will receive a split course of radiation therapy to the vulva by AP-PA fields. Twice daily fractions of 150 cGY will be given on days 1-4 and 1'-4'; once daily fractions of 180 cGY will be given on days 5, 8-12 and 5', 8'-12'. A 1 1/2 to 2 1/2 week split will be allowed between the two courses. Total midplane dose will be 4560 cGY. During the twice daily radiation (days 1-4 and 1'-4'), patients will receive concurrent chemotherapy of 5-FU, 1000 mg/m^2 over 24 hours, allopurinol, 300 mg p.o., and cisplatin, 50 mg/m^2 IV, (days 1 and 1' only). Four to eight weeks following completion of chemoradiotherapy, patients considered to have resectable disease without the need for an exenterative procedure will undergo excision of the area previously replaced by primary tumor. An inguinal/femoral lymphadenectomy will also be performed. Regimen II: The same as Regimen I with the addition of radiation to the inguinal/femoral and low pelvic lymph

Progress: No patients were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/065 **Status:** On-going

Title: GOG 0102N: Intraperitoneal Administration of Recombinant Alpha-2 Interferon Alternating with Cisplatin in Patients with Residual Ovarian Carcinoma

Start Date: 03/05/93 **Est. Completion Date:** Nov 94

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian carcinoma, interferon, cisplatin

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

Study Objective: 1) To further evaluate the role of intraperitoneal chemotherapy in patients with recurrent refractory ovarian carcinoma. 2) To assess the hypothesis that alternating Cisplatin with Alpha-2 Interferon on two of the three off weeks results in improved response rates and less toxicity over concomitant administration of Cisplatin and Alpha-2 Interferon.

Technical Approach: Patients with persistent or recurrent ovarian carcinoma with less than or equal to 1 cm residual tumor and a previous documented response to Cisplatin chemotherapy will be treated with intraperitoneal Cisplatin 90 mg/m^2 on weeks 1, 5, 9 and 13 and intraperitoneal Alpha-2 Interferon 50 million units on weeks 2, 3, 6, 7, 10, 11, 14, and 15. Patients will be treated as an inpatient during each administration of chemotherapy. This will require a one day hospitalization for each weekly treatment. After the completion of the four treatment cycles a reassessment operation will be performed to evaluate response to therapy. This reassessment operation is strongly encouraged for all patients who have no evidence of disease at the completion of therapy. Patients participating in this study will have a intraperitoneal access port placed prior to the initiation of therapy. With any clinical evidence of progressive disease treatment will be discontinued and an alternative treatment plan will be determined by the patient and the GYN Oncology service.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 88/081	**Status:** Completed
Title: GOG 0106: Evaluation of the Serum Marker, CA-125, in the Management of Carcinoma of the Endometrium		
Start Date: 09/16/88	**Est. Completion Date:** Indef.	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: cancer:endometrial,CA-125,serum marker		

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To evaluate the sensitivity of CA-125 for endometrial carcinoma; to correlate CA-125 levels with surgical pathologic criteria (stage, grade, sites); to evaluate the efficacy of CA-125 in monitoring response to therapy (surgery, radiation, chemo, hormonal) in endometrial carcinoma; and to evaluate the efficacy of CA-125 in predicting survival and/or recurrence in endometrial cancer.

Technical Approach: Patients with endometrial carcinoma who are eligible for designated concurrently active GOG treatment protocols for endometrial cancer will be eligible. Specific protocols are selected to obtain a population of patients with tumor burdens and risks for recurrence appropriate to accomplish the study objectives. Serum for CA-125 will be collected according to a schema individually developed for each treatment protocol to be consistent with the regimen and anticipated findings. The collection schedules developed will follow the general schema that follows, modified as appropriate: 1. prior to surgery, if surgery is needed; 2. prior to initiation of therapy; 3. prior to each chemotherapy treatment; 4. monthly during hormonal therapy; 5. prior to initiation of postoperative radiation and at two week intervals during therapy; 6. at the completion of therapy; 7. at regular follow-up intervals, approximately every three months for the first year, every four months the second year, and every six months thereafter, on patients who are free of disease; 8. in patients who progress, follow-up blood samples will not be required after progression is well documented and sera at those time points has been obtained. The duration of this study will be determined by the designated concurrently active GOG treatment protocols with five years of follow-up thereafter.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/037 **Status:** Completed

Title: GOG 0107: A Randomized Study of Doxorubicin (NSC #123127) versus Doxorubicin Plus Cisplatin (NSC #119875) in Patients with Primary Stage III and IV Recurrent Endometrial Adenocarcinoma

Start Date: 03/17/89 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:endometrial,doxorubicin,cisplatin

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

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 were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Indef.

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:** 02/05/93

Study Objective: To confirm reported high response rates of advanced or recurrent mixed mesodermal tumors of the uterus to Ifosfamide/ Mesna; to determine the toxicity and whether the addition of Cisplatin to Ifosfamide/Mesna improves response rates or survival in patients with these tumors.

Technical Approach: Patients will be randomized to either Regimen I or to Regimen II. Regimen I: Ifosfamide 1.5 g/m^2/d IV for 5 days plus Mesna 120 mg/^{2} IV bolus 15 minutes prior to Ifosfamide, first day only; then 1.5 g/m^2/d infusion over 5 days; repeated every 21 days. Regimen II: cisplatin 20 mg/m^2/d IV for five days before administration of Ifosfamide as given in Regimen I; repeated every 21 days. The Ifosfamide starting dose will be 1.2 g/m^2 if the patient has had prior radiotherapy. One course of chemotherapy and living three weeks for repeat lesion measurement will be the minimal trial to evaluate response. One course (or part of one course) of therapy and receiving any follow-up information for observation of toxicity will be the minimal trial to evaluate toxicity.

Progress: No patients were entered in this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix,5-Flourouracil,cisplatin,radiotherapy

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

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: No patients were enrolled at MAMC during FY 93. The one patient enrolled in previous years is still in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/009 **Status:** On-going

Title: GOG 0110: A Randomized Study of Cisplatin versus Cisplatin Plus Dibromodulcitol (NSC #104800) versus Cisplatin Plus Ifosfamide and Mesna in Advanced Stage III or IV), Recurrent or Persistent ....

Start Date: 10/19/90 **Est. Completion Date:**

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix,squamous cell,chemotherapy,cisplatin,dibromodulcitol

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$1440.00	**Periodic Review:** 02/05/93

Study Objective: To determine if mitolactol plus cisplatin or ifosfamide plus cisplatin improves response rate, response duration, progression-free interval and/or survival in advanced squamous cervical cancer compared to cisplatin alone; and to compare the toxicity of these three regimens in advanced cervical cancer.

Technical Approach: Patients, with a Karnofsky performance scale of 50-100, who have histologically confirmed advanced, recurrent, or persistent squamous cell carcinoma of the cervix which is not suitable for curative treatment with surgery and/or radiotherapy will be eligible. Lesions must be measurable by physical examination or chest x-ray. Patients will be randomized to one of the following regimens: Regimen I: cisplatin 50 mg/m^2 every three weeks; Regimen II: cisplatin 50 mg/m^2 plus dibromodulcitol, 180 mg/m^2 daily x 5, every three weeks; Regimen III: cisplatin 50 mg/m^2 plus ifosfamide 5 gm/m^2 infused over 24 hours plus Mesna 6 gm/m^2 during and for 12 hours following ifosfamide, every three weeks. Therapy will continue for 6 courses or until cumulative adverse effects dictate cessation of therapy.

Progress: No patients were entered in this study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/010 **Status:** On-going

Title: GOG 0111: A Phase III Randomized Study of Cyclophosphamide (NSC #26271) and Cisplatin (NSC #119875) versus Taxol (NSC #125973) and Cisplatin (NSC #119875) in Patients with Suboptimal Stage III and ...

Start Date: 10/19/90 **Est. Completion Date:**

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian,chemotherapy,cyclophosphamide,cisplatin,taxol

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

Study Objective: To determine response rate, response duration, and survival in suboptimal Stage III and Stage IV ovarian cancer treated with different platinum-based combination chemotherapy regimens; to evaluate the relative activity of a new combination (cisplatin/taxol) as compared to the standard regimen (cisplatin/cyclophosphamide; to further evaluate the toxicities of the new combination of cisplatin/taxol in this larger patient population; and to compare the relative toxicities and therapeutic indices of the two regimens.

Technical Approach: Patients with established ovarian epithelial cancer, suboptimal (>1 cm in diameter) Stages III and IV who have had optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue submitted for histologic examination, will be eligible. Following optimal initial surgery, patients will be randomized to either cisplatin plus cyclophosphamide or to cisplatin plus taxol given every 21 days for six courses. Patients with partial response, stable disease, or increasing disease will then go off study to be treated on other appropriate GOG protocols. Patients who are clinically free of disease at the completion of therapy will undergo a reassessment laparotomy to determine disease status unless CA-125 is >100. A 21 item patient self-report questionnaire and a five item nurse neurological assessment will be completed prior to the first course of therapy and at 4-6 weeks after the last course of therapy, regardless of the total number of courses. An adequate trial for response is defined as receiving one course of therapy and living three weeks for repeat measurement to be performed. An adequate trial for toxicity is defined as receiving one course of therapy and receiving any follow-up information for observation of toxicity.

Progress: No patients were enrolled at MAMC during FY 93. Two patients were enrolled in previous years and 1 is still in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/011 **Status:** On-going

Title: GOG 0112: A Randomized Comparison of Chemoprophylaxis Using Methotrexate versus Routine Surveillance in the Management of the High Risk Molar Pregnancy

Start Date: 10/19/90 **Est. Completion Date:**

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: molar pregnancy,methotrexate,routine surveillance

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$18.00	Periodic Review: 02/05/93

Study Objective: To determine the incidence of post-molar trophoblastic disease after evacuation of the high risk molar pregnancy in those patients receiving chemoprophylaxis versus those randomized to usual post-evacuation surveillance; to evaluate the toxicity associated with chemoprophylaxis; and to develop a clinical pathologic scoring system for risk of post-molar trophoblastic disease which highly correlates with the serum free beta HCG assay.

Technical Approach: Patients who are categorized as at high risk for molar pregnancy and who have a gross and microscopically verified diagnosis of classic (true) hydatidiform mole, obtained by evacuation of the uterus with uterine conservation, will be eligible. Patients will be randomized to either a methotrexate prophylactic regimen or surveillance. Patients will have a pelvic ultrasound performed in the two week period prior to evacuation or in the two week period immediately following evacuation. The first HCG serum determination will be performed in the 48 hour period immediately prior to or after evacuation. HCG serum determinations will be repeated weekly. The methotrexate prophylactic regimen (40 mg/m^2 IM weekly x 3 courses) will be initiated within 14 days after evacuation and prior to obtaining the day 15 post-evacuation titer. If remission occurs, patients will have monthly beta HCG titers for 12 months, then every three months for one additional year. The principal parameters employed to examine the relative therapeutic value of chemoprophylaxis are the frequency of post molar trophoblastic disease after evacuation and the frequency and degree of toxicity associated with chemoprophylaxis.

Progress: No patients were entered in this study aty MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

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: 02/05/93

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: No patients were enrolled at MAMC during FY 93. Two patients were enrolled in FY 92 and are in follow-up.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/059 **Status:** On-going

Title: GOG 0114: A Phase III Randomized Study of Intravenous Cisplatin and Cyclophosphamide vs Intravenous Cisplatin and Taxol vs High Dose Intravenous Carboplatin Followed by Intravenous Taxol and ....

Start Date: 03/05/93 **Est. Completion Date:** Oct 96

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian carcinoma, cisplatin, cyclophosphamide, Taxol, carboplatin

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

Study Objective: 1) To compare the efficacy of the combination of Cisplatin & Taxol to the standard therapy of Cyclophosphamide and Cisplatin in patients with optimally debulked Stage III Ovarian Carcinoma. 2) To investigate the theory that intravenous high dose therapy will render patients more sensitive to intraperitoneal therapy with Cisplatin and intravenous Taxol. The rate of fall of serum CA-125 will be correlated with response to chemotherapy.

Technical Approach: Patients who have had appropriate surgery for ovarian carcinoma with a histologic diagnosis of epithelial ovarian carcinoma, Stage III optimal, and who are not more than six weeks post-operative will be considered for this study. Upon entry, patients will be stratified according to whether or not gross residual disease is present (gross disease being any visible unresected tumor remaining after surgery). They will then be randomized to 1 of 3 regimens. Regimen I: - Cisplatin 75 mg/m^2 IV & Cyclophosphamide 750 mg/m^2 IV every 21 days X 6 courses. Regimen II: Taxol 135 mg/m^2 24 hour continuous infusion, Day 1, Q 21 days followed by Cisplatin 75 mg/m^2, Day 2 Q 21 days X 6 courses. Regimen III: Carboplatin (dose mg = target AUC X (GFR + 25) Q 4 weeks X 2 administered intraperitoneally through an implantable peritoneal dialysis catheter followed by Cisplatin 100 mg/m^2 intraperitoneally Q 21 days X 6 and Taxol 135 mg/m^2 IV X 6. While being treated, patients will have blood samples performed on a weekly basis to assess the serum CA-125 levels which will be correlated in response to chemotherapy. Response evaluations will be based on second-look surgical reassessment.

There will be two interim analyses conducted when approximately 188 patients and 375 patients are evaluable for second-look response. The critical values of the chi-square test statistic are 5.41, 5.41, and 3.283 at final analysis. These critical values correspond to the following probabilities (one-sided favoring the experimental therapy): 0.010, 0.010, and 0.035. The over-all error (rejecting either hypothesis) is 0.0754.

Progress: No patients were enrolled at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

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: 02/05/93

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: The one patient enrolled at MAMC (FY 84) is still being followed.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/060	**Status:** Completed

Title: GOG 0117: Adjuvant Ifosfamide and Mesna with Cisplatin in Patients with Completely Resected Stage I and II Mixed Mesodermal Tumors of the Uterus

Start Date: 03/05/93	**Est. Completion Date:** Nov 94
Department: GOG	**Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:uterine, mesodermal tumor, ifosfamide cisplatin

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

Study Objective: To determine whether cisplatin and Ifosfamide/Mesna can reduce the recurrence rates in patients with completely resected Stage I or II mixed mesodermal tumors of the uterus.

Technical Approach: Following complete resection of Stage I and II mixed mesodermal tumors of the uterus the patients will receive Ifosfamide 1.5 mg/m^2 IV for four days. The Mesna dose 120 mg/m^2 IV bolus on day 1 THEN 1.5 gm/m^2/day continuous IV infusion X 4 days plus Cisplatin 20 mg/m^2/d. This therapeutic regime will be repeated every three weeks from day one for 3 cycles. After the completion of the chemotherapy, patients will be followed every three months for two years, then every six months for an additional three years.

The primary statistical parameters to be collected, analyzed and reported are: 1) Proportion of patients progression-free after 12 months of follow up. 2) Proportion of patients alive after 12 months of follow up.

Progress: No patients participated in this protocol at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Oct 97

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: / /

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. The critical values of the chi-square test statistics are 11.1, 10.8, 10.6, 10.6, and 3.81. The last critical value is for the final analysis which will be a one-sided pair-wise test. These critical values correspond to the following tail probabilities from the two degrees of freedom chi-square distribution: 00.0039, 0.0045, 0.0050 and 0.0050. This early stopping rule will increase the type I error from 0.025 to 0.0386 for each test. The over-all type I error will be 0.0757.

Progress: No patients were enrolled at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/062	**Status:** Completed
Title: GOG 0121: A Phase Two Trial of High Dose Megestrol Acetate (Megace) in Advanced or Recurrent Endometrial Carcinoma		
Start Date: 03/05/93	**Est. Completion Date:** Nov 93	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: cancer:endometrial, megestrol acetate, Megace		

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

Study Objective: 1) To evaluate the response rate and progression free interval in patients receiving high dose megestrol acetate (Megace) for advanced and recurrent endometrial carcinoma. 2) To determine toxicity of high dose megestrol acetate in such patients. 3) To determine if estrogen/progesterone receptor status is predictive of response.

Technical Approach: Patients with histologically confirmed advanced, persistent or recurrent endometrial carcinoma who have failed local therapeutic measures or are considered incurable with local therapy and have measurable disease consisting of abdominal, pelvic or other masses (which can be defined in at least two dimensions by palpation, x-ray, scans, or ultrasound) may be invited to participate.

Patients who agree to participate will be treated with Megace 800 mg/day PO in divided doses unless toxicity or disease progression requires discontinuing the medication. Patients will be evaluated by physical examination or x-ray studies every month for three visits and then every three months. If CT scans or ultrasounds are necessary for evaluation they will be performed every three months.

Data analyses to evaluate the effectiveness of therapy are: a) the frequency of complete (CR) and partial (PR) response; b) the duration of response; c) the frequency of observed adverse effects. A response (CR+PR) rate of 30% or more would be clinically significant and would indicate that further investigation of this therapy is appropriate. A response rate of 15% would indicate that the therapy has insufficient activity to warrant further investigation. A decision will be made after twenty evaluable patients are entered whether to continue accrual based on the number of responders observed and the observance of no atypical severe toxicity. The study will continue if there are 3 or more responses out of 20 evaluable patients.

Progress: There were no participants in the study from MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Oct 97

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: / /

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: No patients were enrolled at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/064 **Status:** On-going

Title: GOG 0125: Extended Field Radiation Therapy with Concomitant 5-FU Infusion and Cisplatin Chemotherapy in Patients with Cervical Carcinoma Metastatic to Para-aortic Lymph Nodes

Start Date: 03/05/93 **Est. Completion Date:** Apr 95

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervical, radiation therapy, 5-FU, cisplatin, para-aortic lymph nodes

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: To evaluate the safety and efficacy of combined extended field radiation with cisplatin and 5-FU given as a radiation sensitizer.

Technical Approach: All patients who consent to participate in this study will be treated with both external radiation therapy and a local application of radiation therapy (brachy therapy). This technique is standard treatment in the management of cervical carcinoma. The treatment fields will be extended to include the para-aortic lymph nodes. Intravenous cisplatin and 5-FU will be administered during radiation. Cisplatin 50 mg/m^2 IV will be given on the first day of the first week and again four weeks subsequently in an intravenous bolus infusion. The 5-FU 1000 mg/m^2 will be given by a continuous infusion over four consecutive days (Days 2, 3, 4, 5, and 30, 31, 32, 33) starting on the second day of radiation therapy through the fifth and repeated four weeks later. Intracavitary radiation will be delivered by cesium utilizing standard or commonly used applicators providing that acceptable radiation dose symmetry can be determined. Following the completion of therapy, patients will be seen every three months for two years and every six months for an additional three years after which time they will be seen at yearly intervals.

The variables to be collected, analyzed and reported to evaluate the effectiveness of extended field radiation and cisplatin/5-FU are divided into the outcome variables and covariates. The Outcome Variables are: 1) Recurrence-free survival 2) Survival time 3) Morbidity of extended field radiation therapy and cisplatin/5-FU 4) and Degree of adherence to the protocol treatment.

Progress: No patients were enrolled at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/152 **Status:** On-going

Title: GOG 0126B: Evaluation of Cisplatin (NSC #119875) and Cyclosporin in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer

Start Date: 08/06/93 **Est. Completion Date:** Aug 94

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian, cisplatin, cyclosporin

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

Study Objective: 1. To determine if the addition of cyclosporin to cisplatin therapy reduces drug resistance and thereby increases chemo-sensitivity of platinum refractory ovarian cancer to cisplatin. 2. To determine if the addition of cyclosporin to cisplatin is tolerated without significant toxicity.

Technical Approach: Patients with platinum refractory epithelial ovarian carcinoma who progress while on treatment or recur within six months of the most recent treatment with platinum containing compounds are eligible for this study. Patients will be treated as inpatients. Cyclosporin 4 mg/kg over two hours followed six hours later by cisplatin 75 mg/m^2 given at 1 mg/min followed the next day by cyclosporin 4 mg/kg (again over two hours). This cycle will be repeated every 21 days until disease progression or significant toxicity precludes further treatment.

Progress: There have been no participants in the study during FY 93.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/085	**Status:** Completed
Title: GOG 0127B: Evaluation of Isotretinoin and Alpha Interferon in Advanced or Recurrent Squamous Cell Carcinoma of the Cervix		
Start Date: 04/02/93	**Est. Completion Date:** Mar 94	
Department: GOG	**Facility:** MAMC	
Principal Investigator: LTC Mark E. Potter, MC		
Associate Investigators: None		
Key Words: Cancer:cervix, isotretinoin, alpha interferon		
Accumulative MEDCASE Cost: $0.00	**Est. Accumulative OMA Cost:** $0.00	**Periodic Review:** / /

Study Objective: To determine the activity of the combination of oral isotretioin and interferon in the treatment of advanced or recurrent squamous cell carcinoma of the cervix.

Technical Approach: This study will assess the efficacy of daily oral isotretinoin at 1 mg/kg in combination with alpha interferon 6 million units per day subcutaneously in the treatment of recurrent curative therapeutic modalities. Patients eligible are patients who have been previously treated for advanced and recurrent Squamous Cell Carcinoma of the cervix including up to one previous chemotherapeutic regimen. Daily administration of these agents will be undertaken for a minimum of four weeks. If progression of disease or toxicity is significant, therapy will be discontinued. As long as a tumor response is noted therapy will continue at those doses. Once stabilization of the disease has been achieved or after a minimum of three months of treatment, a maintenance dose of isotretinoin at 0.5 mg/kg per day orally will be initiated and the alpha interferon will be reduced to 3 million units, three times a week subcutaneously. This maintenance therapy will continue until disease progression or irreversible side effects preclude further therapy. Tumor measurements by physical examination and, if necessary, radiological evaluation will be obtained during the course of treatment. After treatment is discontinued alternative treatment plans will be discussed with the patient.

Progress: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/150 **Status:** On-going

Title: GOG 0127C: Evaluation of Cisplatin and Pentoxifylline in Advanced or Recurrent Squamous Cell Carcinoma of the Cervix

Start Date: 08/06/93 **Est. Completion Date:** Aug 94

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:cervix, cisplatin, pentoxifylline

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: 1. To determine if the addition of methylxanthine pentoxifylline enhances the cytotoxicity of cisplatin in patients with recurrent or advanced squamous cell carcinoma of the cervix. 2. To determine if the side effects when combining pentoxifylline with cisplatin are acceptable.

Technical Approach: Patients with measurable, recurrent or advanced squamous cell carcinoma of the cervix consenting to participate will be entered into a treatment regimen consisting of cisplatin 75 mg/m^2 given every three weeks. Pentoxifylline will be given at 1600 mg orally every eight hours for nine doses (3 days). Treatment will continue for six cycles or until progression or toxicity precludes further therapy.

Progress: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/023 **Status:** On-going

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:** Oct 95

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:** / /

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: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/006 **Status:** On-going

Title: GOG 0134: A Phase III Trial of Taxol at Three Dose Levels and G-CSF at Two Dose Levels in Platinum-Resistant Ovarian Carcinoma

Start Date: 10/02/92 **Est. Completion Date:** Oct 95

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: cancer:ovarian, Taxol

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: / /

Study Objective: 1. To determine if the dose of taxol affects response rate, progression free interval or survival in patients with platinum-resistant ovarian cancer. 2. To compare the toxicities of the three regimens. 3. To compare the efficacy and toxicity of two dose levels of G-CSF (5 ug/kg/day versus 10 ug/kg/day) in patients who receive the highest taxol dose (250 mg/m^2). 4. To determine the relationship between peak taxol plasma concentration and toxicity/response.

Technical Approach: Patients with platinum-resistant ovarian carcinoma will be stratified according to the presence of measurable disease. They will then be randomized to Regimen I, II, IIIa, or IIIb. Regimen I: Taxol 135 mg/m^2 by 24 continuous infusion, Day 1, every 21 days x 6 doses. Regimen II: Taxol 175 mg/m^2 by 24 hr continuous infusion, Day 1, every 21 days x 6 doses. Regimen IIIa: Taxol 240 mg/m^2 by 24-hour continuous infusion Day 1 and G-CSF 5 ug/kg/day day 3 through the nadir until ANC is greater than or equals 10,000/ul, every 21 days. Regimen IIIb: Taxol 250 mg/m^2 by 24-hour continuous infusion Day 1 and G-CSF 10 ug/kg/day Day 3 through the nadir until ANC is greater or equals 10,000/ul, every 21 days. At the completion of six courses of therapy surgical reassessment, if done, should be performed in those patients with clinically complete responses within eight weeks following the last cycle of chemotherapy. Minimum length of trial to evaluate response is defined as receiving one course of therapy and surviving three weeks for repeat measurement to be performed.

Progress: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/139 **Status:** On-going

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:** Nov 20

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:** / /

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: No patients have been enrolled in the study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/086 **Status:** On-going

Title: GOG 0138: A Phase II Trial of Cisplatin and Cyclophosphamide in the Treatment of Extraovarian Peritoneal Serous Papillary Carcinoma

Start Date: 04/02/93 **Est. Completion Date:** Dec 93

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: Cancer:papillary, cisplatin, cyclophosphamide

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

Study Objective: To systematically evaluate through a large group cooperative study the clinical behavior of Extraovarian Peritoneal Serous Papillary Carcinoma to similarly staged ovarian carcinoma with a similar residual disease.

Technical Approach: Patients with advanced Extraovarian Peritoneal Serous Papillary Carcinoma with greater than 1 cm residual tumor at the completion of initial debulking surgery will be eligible for this protocol. This is largely a registry protocol, dictating the mode of standard treatment. This standard treatment utilizes Cyclophosphamide 750 mg IV per meter squared and Cisplatin 75 mg per meter squared administered at three week intervals for a total of six cycles. Subsequent to completion of chemotherapy, a second look procedure will be performed to ascertain disease status in those patients who have either demonstrated a complete response as noted on physical examination, radiologic studies or patients who never demonstrated measurable disease. A clinical-pathological correlation will be made with the disease progression as well as a comparison made to previous GOG protocols with similarly staged and graded ovarian tumors of serous origin. Patients will be followed in a standard fashion at three month intervals for at least two years and at potentially decreased intervals there after.

Progress: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Mar 96

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:** / /

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 entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/140 **Status:** On-going

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:** May 94

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:** / /

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: No patients entered this study at MAMC during FY 93.

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/149	**Status:** On-going
Title: GOG 0143: Familial and Reproductive Factors in Ovarian Cancer		
Start Date: 08/06/93	**Est. Completion Date:** Aug 95	
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:** / /

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 during FY 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/039 **Status:** Completed

Title: GOG 8809: Flow Cytometrically Determined Tumor DNA Content in Ovarian Tumors of Low Malignant Potential

Start Date: 03/17/89 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Pot MC

Associate Investigators: None

Key Words: tumor:ovarian,low malignant potential,DNA,flow cytometry

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 02/05/93

Study Objective: To determine if the DNA content of borderline ovarian tumors (carcinoma of low malignant potential) can be correlated with extent/stage of tumor, potential for recurrence, and patient survival.

Technical Approach: This study proposed to determine the [illegible] ontent in paraffin-embedded tumor specimens in patients with any stage of disease entered on GOG Protocol #72. These data will be correlated with stage of disease at entry, as well as recurrence/ progression of disease. Specimens of recurrent tumor will also be analyzed to determine the effect of treatment on DNA content. At least one representative paraffin-embedded ovarian tumor specimen from the pretreatment laparotomy must be available as well as follow-up information including second look laparotomy findings (if done) or time to progression and follow-up after negative second look laparotomy and survival. When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:32733, 1985).

Progress: There was no activity at MAMC during FY 93 on this study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/026 **Status:** On-going

Title: GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia

Start Date: 01/19/90 **Est. Completion Date:** Indef.

Department: GOG **Facility:** MAMC

Principal Investigator: LTC Mark E. Potter, MC

Associate Investigators: None

Key Words: trophoblastic neoplasia,DNA,hydatidiform moles

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 02/05/93

Study Objective: To determine: if aneuploidy identifies a subset of high-risk hydatidiform moles; if ploidy status has sufficient predictive value to justify prophylactic chemotherapy of certain molar pregnancies; if proliferative activity, as estimated from cell cycle distribution, has any prognostic value; the number of paraffin blocks that constitutes an appropriate sampling of a molar pregnancy in order to establish presence of aneuploid cell lines; and if ploidy or proliferative index, as measured on either the mole or subsequent biopsy material, can predict the pattern of post-molar gestational trophoblastic neoplasia to be either metastatic or nonmetastatic and the response to various treatment regimens; and to assess persistence of ploidy status by comparing ploidy of molar tissue with ploidy status of subsequent tissue samples obtained after development of post-molar gestational trophoblastic disease.

Technical Approach: Flow cytometry will be used to measure ploidy and proliferative rate on archival tissues on patients identified as having complete hydatidiform mole pregnancies. These patients have previously been identified by entry on GOG Protocol #55. Results of lab measurements on tissue will be compared to clinical characteristics of post molar course, treatment received, if any, and response to such treatment. The incidence of aneuploidy in tissue samples from staging work-up in those patients who have developed persistent gestational trophoblastic neoplasia will be assessed. Information regarding cell cycle kinetics and growth fraction will be used to correlate tumor responses to treatment regimens in consideration of cell cycle phase specificity for various agents.

Progress: No patients entered this study at MAMC during FY 93.

DETAIL SHEETS FOR PROTOCOLS

NATIONAL CANCER INSTITUTE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 81/033 **Status:** Completed

Title: NCI 7602: All Stage IC and II 9A,B,C) and Selected Stage IAii and IBii Ovarian Cancer

Start Date: 01/16/81 **Est. Completion Date:** Jun 85

Department: NCI **Facility:** MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: cancer:ovarian,surgery,melphalan,radiotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/89

Study Objective: To define the natural history of patients treated with surgery plus either chemotherapy or radioisotope; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to determine the patterns of relapse for each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

Technical Approach: All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 2A, 2B, 2C, 1Aii, 1Bii, or 1Ai or 1Bi with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If IIB, IIC, residual disease is found, will be randomized to pelvic radiotherapy plus melphalan alone. If after 18 months of therapy, the patient remains free of disease, chemotherapy will be discontinued. Second look will be done if the patient is free of disease after 18 months of chemotherapy.

Progress: This study was closed to patient entry in September 1986. All subjects at MAMC are now deceased and the study has been closed.

DETAIL SHEETS FOR PROTOCOLS

NATIONAL SURGICAL ADJUVANT BREAST & BOWEL PROJECT

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/171 **Status:** On-going

Title: NSABP B-21: A Clinical Trial to Determine the Worth of Tamoxifen in the Management of Patients with Node-Negative, Occult, Invasive Breast Cancer Treated by Lumpectomy

Start Date: 09/03/93 **Est. Completion Date:** Sep 98

Department: NSABP **Facility:** MAMC

Principal Investigator: MAJ Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT James S. D. Hu, MC
LTC Robert D. Vallion, MC
CPT John R. Caton, MC

Key Words: cancer:breast, tamoxifen, lumpectomy

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

Study Objective: This study's primary aim is to test the hypothesis that long-term treatment with tamoxifen (with and without breast radiation) is effective in prolonging disease free survival in patients with occult, invasive cancer.

Technical Approach: Patients who have had a lumpectomy with tumor free margins and negative axillary nodes will be randomly assigned to one of three groups: lumpectomy and breast irradiation plus placebo; lumpectomy and breast irradiation plus tamoxifen; or lumpectomy and tamoxifen with irradiation. Tamoxifen (10 mg BID) or placebo will be started within 35 days of surgery. Breast radiation will begin as soon as wound healing permits but within 56 days of lumpectomy. Patients will be followed, at least annually, thereafter. The primary endpoints to be used for statistical analysis will be ipsilateral breast tumor reoccurrence and disease free survival.

Progress: No patients have yet been enrolled.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jul 98

Department: NSABP **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
CPT 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:** / /

Study Objective: 1). To determine whether the administration of chemotherapy (5-FU-LV with radiotherapy preoperatively is more effective than the administration of the chemotherapy and radiotherapy 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 chemotherapy and radiotherapy preoperatively results in improvement local recurrence rates when compared with the regimen administered postoperatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative chemotherapy and radiotherapy and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative chemotherapy and radiotherapy on the tumor size and the pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdominoperineal resection. Furthermore, to estimate the proportion of patients who can be converted from sphincter-saving surgical procedures to local excision alone.

Technical Approach: This trial in patients with operable adenocarcinoma of the rectum compares the worth of 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. Radiotherapy 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 radiotherapy (cycles 2 and 3). Surgery will be performed after completion of the 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. Chemotherapy 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. Radiotherapy will begin after completion of cycle 1. Cycle 4 should begin after

completion of radiotherapy 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.

The primary endpoints are diseases free survival and survival.

Progress: No patients have yet been enrolled.

DETAIL SHEETS FOR PROTOCOLS

PEDIATRIC ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92	**Protocol No.:** 93/141	**Status:** On-going
Title: POG 8650: Intergroup National Wilms' Tumor Study - 4		
Start Date: 06/09/93	**Est. Completion Date:** Oct 97	
Department: POG	**Facility:** MAMC	
Principal Investigator: LTC Bruce A. Cook, MC		
Associate Investigators: None		
Key Words: cancer:pediatric, Wilms'		

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

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: There has been one patient enrolled at MAMC in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/164 **Status:** On-going

Title: POG 9047: Neuroblastoma Biology Protocol

Start Date: 09/03/93 **Est. Completion Date:** Feb 96

Department: POG **Facility:** MAMC

Principal Investigator: LTC Bruce A. Cook, MC

Associate Investigators: COL Stephen R. Stephenson, MC

Key Words: cancer:neuroblastoma, biology

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

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 entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/135 **Status:** On-going

Title: POG 9226: Treatment of Stages I, IIA, and IIIA Hodgkin's Disease With ABVE and Low Dose Irradiation

Start Date: 07/02/93 **Est. Completion Date:** Jun 95

Department: POG **Facility:** MAMC

Principal Investigator: LTC Bruce A. Cook, MC

Associate Investigators: COL Stephen R. Stephenson, MC

Key Words: pediatric cancer: Hodgkin's disease

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

Study Objective: 1) 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 or IIIa Hodgkin's Disease; 2) establish the response (CR and PR) rate following four cycles of ABVE; 3) determine the incidence of major therapy related immediate and late effects of the above regimen; 4) reduce the morbidity associated with therapy without decreasing the efficacy of treatment in Early Stage Hodgkin's Disease; 5) correlate the results of clinical, imaging, and laboratory staging with surgical/pathological staging where performed.

Technical Approach: All patients meeting the enrollment criteria will receive 2 of the 4 courses of Adriamycin, Bleomycin, Vincristine on days 1 and 15, and Etoposide on days 1 through 5 (ABVE). Patients will be evaluated after the 2nd course and if a response is seen, then 2 more courses will be given. If no response is seen the treatment will be changed.

Patients will again be evaluated after the 4th cycle and irradiation (2550 cGy) given >28 but <40 days after ABVE. If 4 cycles ABVE + low-dose RT is determined to be worthy of further study as described above, current plans are to compare it to ABVE + MOPP + low dose RT in a randomized trial.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jun 95

Department: POG **Facility:** MAMC

Principal Investigator: LTC Bruce A. Cook, MC

Associate Investigators: COL Stephen R. Stephenson, MC

Key Words: cancer:CNS, pediatric, chemotherapy, radiotherapy

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

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: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/134 **Status:** On-going

Title: POG 9340/41/42: Treatment of Patients Greater than or = 365 Days 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:** Aug 95

Department: POG **Facility:** MAMC

Principal Investigator: LTC Bruce A. Cook, MC

Associate Investigators: COL Stephen R. Stephenson, MC

Key Words:

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

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: No patients have entered this study at MAMC.

DETAIL SHEETS FOR PROTOCOLS

PUGET SOUND ONCOLOGY CONSORTIUM

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/079 **Status:** Completed

Title: PSOC 615: Intraperitoneal Consolidation Therapy Following Second-Look Operation in Ovarian Cancer

Start Date: 05/15/87 **Est. Completion Date:** Indef.

Department: PSOC **Facility:** MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: COL Roger B. Lee, MC
COL William L. Benson, MC

Key Words: cancer:ovarian,P32,cisplatin,5-Flourouracil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 11/17/89

Study Objective: To examine the effect of intraperitoneal therapy on disease free survival in patients with no disease or minimal residual disease following second-look surgery and to document the complication rate associated with the use of intraperitoneal chromic phosphate or chemotherapy in patients previously treated with systemic chemotherapy.

Technical Approach: Following standard induction chemotherapy, patients with Stage IIb, IIc, or III epithelial carcinoma of the ovary will have second-look laparotomy in the standard fashion. The second look procedure will include resection of any remaining female genital organs. If the patient has no evidence of gross persistent disease greater than 1.0 cm at the time of second look, a Tenckhoff catheter will be inserted. If the pathologic findings from the second look procedure show no evidence of persistent tumor, the patient will receive 15 millicuries of intraperitoneal P-32 in 1000-1500 ml of normal saline, with appropriate rotation of position to assure proper distribution of the P-32. If the patient has positive disease within the peritoneal cavity, she will receive chemotherapy with cisplatin (100 mg/m^2) and 5-FU (1000 mg/m^2) through the Tenckhoff catheter every three weeks for a maximum of four doses unless there are unacceptable side effects.

Progress: This study is closed to patient entry. One patient was entered in FY 87 and is now deceased.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/066 **Status:** On-going

Title: PSOC 1007: Adriamycin and Cefoperazone for Treatment of Carcinoma and Sarcoma Refractory to Adriamycin

Start Date: 06/14/91 **Est. Completion Date:**

Department: PSOC **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC

Key Words: adriamycin,cefoperazone

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

Study Objective: To determine the complete and partial response rates to a combination of adriamycin and cefoperazone in patients who have had progression of non-Hodgkin's lymphoma, small cell lung carcinoma, sarcoma, breast or ovarian carcinoma while on an adriamycin-containing chemotherapeutic regimen or have progressed within six months of receiving such a regimen and to determine the toxicities of the addition of high dose cefoperazone to adriamycin in the treatment of refractory malignant disease.

Technical Approach: Adriamycin has been used extensively in the therapy of a number of malignancies. In many instances, the malignant cells become resistant and adriamycin becomes ineffective and is one of the agents implicated in multiple drug resistance (MDR). Because of its clinical value, the mode of action of adriamycin and the possible mechanisms of drug resistance have been the subject of extensive research. Cefoperazone has been purported to act as a modulator of MDR. It is hoped that high-dose cefoperazone will block the MDR capability of the cancer cells which will allow the adriamycin to remain within the cancer cells for a longer period of time, thereby allowing patients to go back into remission. All patients will receive intravenous cefoperazone weekly at a dose of 5 grams in 30 minutes, followed by a continuous IV infusion for three hours at 4 grams per hour. After the 30 minutes loading dose, patients will be given a bolus of adriamycin. Patients will be reevaluated after eight weeks. Patients will continue on treatment until there is evidence of disease progression; there is a decrease in ejection fraction by MUGA scan to <40% or a fall of 20 percentage points; or the patient develops symptoms of congestive heart failure.

Progress: One patient entered in FY 91 is still being followed.

DETAIL SHEETS FOR PROTOCOLS

SOUTHWEST ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92	**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:** Jan 88	
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:** 12/04/92

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. Seven patients were enrolled in previous years and 5 are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Sep 81

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:** 12/04/92

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 l yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for l 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: Thirty-five patients were enrolled prior to closure of patient enrollment 15 Aug 90. Twenty-four patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Sep 85

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:** 12/04/92

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.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Feb 85

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: 12/04/92

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. Eleven patients were enrolled in previous years and 10 continue to be followed. One patients has expired.

Detail Summary Sheet

Date: 30 Sep 92 **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:** May 86

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:** 12/04/92

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 92 **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:** Sep 87

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:** 12/04/92

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 Jan 93. No patients were enrolled at MAMC in FY93 but 5 patients had been enrolled previously. All patients enrolled at MAMC have died but 1 patient has transferred in and is being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Dec 89

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:** 12/04/92

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 92 **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:** Aug 90

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:** 12/04/92

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 92 **Protocol No.:** 88/003 **Status:** On-going

Title: SWOG 8520: Cis-Diamminedichloroplatinum (II), Methotrexate and Bleomycin in the Treatment of Advanced Epidermoid Carcinoma of the Penis, Phase II

Start Date: 10/16/87 **Est. Completion Date:** Sep 90

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ David M. Dunning, MC
CPT Denis Bouvier, MC
MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC
MAJ Ruben D. Sierra, MC
COL William D. Belville, MC

Key Words: cancer:penis,cis-diamminedichloroplatinum,methotrexate,bleomycin

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To determine the response rate in patients with advanced epidermoid carcinoma of the penis treated with cisplatinum, methotrexate, and bleomycin and to evaluate the toxicity of this three-drug combination in this patient population.

Technical Approach: Cis-platinum, 75 mg/m^2, will be administered by IV infusion at 1 mg/min in normal saline (1 mg/cc) on day 1. Prior to, during, and after treatment with cis-platinum, the patient will be vigorously hydrated, intravenously and orally. Lasix, 40 mg IV bolus, will be given prior to cis-platinum. Patients will also receive methotrexate, 25 mg/m^2, IV bolus on days 1 and 8 and bleomycin, 10 units/m^2, IV bolus on days 1 and 8. Courses will be repeated every 21 days provided absolute granulocyte count is >1500/ ml and platelet count is >100,000/ ml. Dosage modifications will be made for all three drugs following the initial and all subsequent cycles of chemotherapy, using standard Southwest Oncology Group chemotherapy toxicity criteria for any of the following toxicities: hematopoietic, renal, pulmonary, and neurotoxicity. Chemotherapy with bleomycin will be discontinued when a total cumulative dose of 200 units/m^2 has been reached. Two cycles of chemotherapy will constitute an adequate trial. Patients with stable or responding disease will continue on treatment beyond two cycles until evidence of disease progression or unacceptable toxicity. Patients who have achieved a complete remission will discontinue all chemotherapy after six cycles. Patients who achieve a complete response will receive 6 courses of treatment.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** May 87

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:** 12/04/92

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.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Apr 87

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:** 12/04/92

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 92 **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:** Feb 90

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:** 12/04/92

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 92	**Protocol No.:** 89/045	**Status:** On-going

Title: SWOG 8621: Chemohormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III

Start Date: 03/17/89	**Est. Completion Date:** Mar 92
Department: SWOG	**Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	COL Irwin B. Dabe, MC
MAJ Mark H. Kozakowski, MC	MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC	MAJ Kenneth A. Bertram, MC

Key Words: cancer:breast,postmenopausal,chemohormonal therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$2316.00	**Periodic Review:** 12/04/92

Study Objective: To compare initial combined chemo-hormonal therapy with initial hormonal therapy with respect to survival; to compare chemo-hormonal therapy using tamoxifen with that using DES with respect to survival; and to compare combined chemohormonal therapy with initial hormonal therapy with respect to response in patients with measurable disease.

Technical Approach: Postmenopausal females with recurrent or disseminated breast cancer, tumor positive for estrogen receptor or progesterone receptor, and adequate bone marrow and hepatic function will be eligible. Patients who have received prior hormonal therapy or chemotherapy will not be eligible. Prior adjuvant chemotherapy will be allowed if disseminated disease developed more than six months after completing adjuvant therapy, except for tamoxifen and DES. Patients with a history of deep vein thrombosis, cerebral embolus, stroke, congestive heart failure, or ischemic heart disease will not be eligible. No concurrent malignancy is allowed except for cured non-melanoma skin cancer, in situ cervical cancer, or other cancer from which the patient has been disease-free for five years. Patients will be stratified by dominant disease (osseous vs soft tissue vs visceral) and disease status. Descriptive factors will be prior adjuvant therapy; presence or absence of ascites or pleural effusions; performance status; disease free interval; number of metastatic sites, and receptor status. Patients will be randomized to: Arm I (DES); Arm II (Tamoxifen); Arm III (DES + 5-FU + cyclophosphamide + methotrexate); or Arm IV (Tamoxifen + 5-FU + cyclophosphamide + methotrexate). Patients who respond (or have prolonged disease stabilization at six months and then relapse) to tamoxifen or DES will be treated with sequential secondary and tertiary hormonal therapy if they continue to have endocrinereceptor tumors. Patients with progressive disease or short term stable disease will go off study.

Progress: One patients was enrolled in this study prior to closure to patient entry 1 Aug 91. This patient continues to be followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/058 **Status:** On-going

Title: SWOG 8692 (INT 0075): Therapy in Premenopausal Women with Advanced, ER Positive or PgR Positive Breast Cancer: Surgical Oophorectomy vs the LH-RH Analog, Zoladex: Phase III, Intergroup

Start Date: 05/19/89 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
COL Irwin B. Dabe, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC

Key Words: cancer:breast,surgical oophorectomy,Zoladex,ER,PgR positive

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 12/04/92

Study Objective: To compare the response rate, the time to treatment failure, and survival of medical castration using Zoladex to surgical castration in premenopausal women with advanced, ER+ or PgR+ breast cancer; to assess the response rate to surgical castration in patients failing to respond to or relapsing on Zoladex and the response rate to Zoladex in patients failing to respond to or relapsing on surgical castration; to compare toxicities of medical castration and surgical castration; to assess the value of post-treatment hormone levels in predicting response to medical castration; and to asses the effect of long term Zoladex treatment on hormone levels in responding patients.

Technical Approach: Patients must have a performance status of 02. Patients with extensive liver metastases, lymphangitic lung metastases, or prior hormone therapy or chemotherapy for advanced disease will be ineligible. Prior adjuvant chemotherapy is allowed; adjuvant tamoxifen is allowed provided relapse occurred > 6 months after completion of therapy. Patients will be stratified by disease status, dominant site of disease, performance status, and prior adjuvant tamoxifen (yes or no). Patients will be randomized to receive either surgical oophorectomy or Zoladex, 3.6 mg subcutaneously every four weeks. Surgical castration patients clearly progressing after six weeks will be crossed over to Zoladex. Patients then developing progressive disease will be taken off study. Zoladex patients with clearly progressive disease after six weeks will cross over to surgical oophorectomy. Upon development of progressive disease, patients will be removed from the study.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Mar 92

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
MAJ Robert L. Sheffler, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ 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:** 12/04/92

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 92 **Protocol No.:** 90/084 **Status:** Completed

Title: SWOG 8719: Evaluations of Didemnin B or Ifosfamide/Mesna in Endocrine Resistant Prostate Cancer and of Ifosfamide/Mesna in Patients Without Prior Endocrine Manipulation, Phase II

Start Date: 06/15/90 **Est. Completion Date:** May 92

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Mark H. Kozakowski, MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: cancer:prostate,Didemnin B,Ifosfamide,Mesna,endocrine resistance

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate the likelihood of response for each regimen in order to assess whether either treatment should be advanced to further studies; to evaluate the qualitative and quantitative toxicities of the regimens; and to explore the response rate, toxicity, and time to progression of patients with no prior or concomitant endocrine treatment who are treated with Ifosfamide/ Mesna for measurable Stage D2 prostatic cancer.

Technical Approach: Patients must have a histologically confirmed diagnosis of adenocarcinoma of the prostate and advanced (Stage D2) disease with objective evidence of progression following prior endocrine treatment. Newly diagnosed Stage D2 patients without prior endocrine manipulation will be placed directly on Arm II. Patients will be randomized to either Arm I (Didemnin B, IV, once every 28 days) or to Arm II (Ifosfamide and Mesna, IV, days 1-5, every 21 days). After two courses of treatment, patients will be evaluated, and will continue on the same arm until progression of disease.

Progress: This study was closed to patient entry 15 Mar 93. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jun 91

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
MAJ 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: 12/04/92

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: Eight patients have been enrolled at MAMC (2 in FY93) and all continue to be followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Sep 91

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ 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: 12/04/92

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. Five patients were enrolled at MAMC in previous years and 2 continue to be followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Apr 93

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ 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:** 12/04/92

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 92 **Protocol No.:** 90/040 **Status:** Terminated

Title: SWOG 8793 (EST-3883): Randomized Phase III Evaluation of Hormonal Theray versus Observation in Patients with Stage D1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prost

Start Date: 02/16/90 **Est. Completion Date:**

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
MAJ Robert L. Sheffler, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC

Key Words: cancer:prostate,hormonal therapy,lymphadenectomy

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 12/04/92

Study Objective: To determine the time to progression and survival in patients with histologically confirmed Stage D1 adenocarcinoma of the prostate, following radical prostatectomy and pelvic lymphadenectomy, treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy; to determine the effect of early hormone therapy on local control of D1 prostate cancer; to determine whether the effects of hormonal manipulation on progression or patterns of failure are modified by tumor grade, prior TUR, number and grade of involved nodes; to determine if an initially elevated acid phosphatase level predicts a poor response to therapy; to determine whether pretreatment hypogonadism is predictive of a poor response to hormonal therapy; and to evaluate the role of the prostate specific antigen in assessing response, progression, and survival.

Technical Approach: Patients must have undergone a radical prostatectomy within 12 weeks prior to randomization and must have no evidence of disease. Patients with a history of previous hormonal, radiation, systemic or intravesical chemotherapy, a history of other neoplasms in the past 5 years, and those previously treated for prostate cancer (except for prostatectomy and/or pelvic lymph node dissection) are ineligible. Patients will be randomized to hormonal therapy (Zoladex or orchiectomy) or to observation. The treating physician, after consultation with the patient, will determine if the patient receives Zoladex or orchiectomy therapy. Patients randomized to observation, who subsequently progress systemically, will have hormonal management instituted within 6 weeks of systemic progression. Patients randomized to hormonal therapy or who are later put on hormonal therapy will be taken off study if disease progression occurs.

Progress: This study was terminated Mar 93 due to poor patient accrual. No patients were enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jun 91

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: COL Irwin B. Dabe, MC
CPT Denis Bouvier, MC

Key Words: Hodgkin's Disease,chemotherapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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. On patient was enrolled at MAMC (FY88)

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/165 **Status:** On-going

Title: SWOG 8807: An Investigation of the Relationship Between an Integrated, System Education Approach and Breast Self Exam (BSE) Compliance, Phase III

Start Date: 09/03/93 **Est. Completion Date:** Sep 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
CPT John R. Caton, MC

Key Words: cancer:breast, self exam

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

Study Objective: This is a short-term randomized Phase III cancer control study to compare three educational approaches for teaching breast self exam (BSE) to healthy women who do not have learning disabilities.

Technical Approach: Healthy women, 20-65 years, with no history of breast cancer and consenting to participate will be administered the Intake Compliance Measurement Evaluation, scheduled for a six month follow-up visit, and told they will receive a phone contact at six and 12 months. They will then be randomized to one of three arms. ARM I participants will receive BSE instruction by physician only; ARM II will receive physician instruction + BSE class by a registered nurse; ARM III will receive physician instruction + BSE class + reinforcements in the form of calendar sticker, phone calls and monthly follow-up reminders. All BSE participants will receive a packet of educational material and be able to demonstrate a knowledge of the steps/methods for effective BSE.

Accuracy and frequency of BSE will be evaluated at six months. The Compliance Measurement Evaluation will again be administered and the participant will be asked to demonstrate BSE on the breast plate model. Twelve month follow up will be conducted by phone to determine accuracy and frequency (utilizing the Compliance Measurement form). All data will be submitted to the SWOG statistical center.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Apr 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: l[illegible]oma,alpha-interferon,ProMACE-Mopp,chemo

Accumulativ		**Est. Accumulative**		**Periodic Review:**
MEDCASE Cost:	$0.00	**OMA Cost:**	$0.00	12/04/92

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: Three patients have been entered at MAMC (1 in FY93). All patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/054 **Status:** Completed

Title: SWOG 8810: Six Courses of 5-Fluorouracil & Cisplatinum with Correlation of Clinical & Cellular DNA Parameters in Patients with Advanced, Untreated, & Unresectable Squamous Cell Carcinoma of the.....

Start Date: 03/16/90 **Est. Completion Date:** Mar 93

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC
MAJ Michael R. Morris, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: cancer:head & neck,DNA,5-Fluorouracil,cisplatinum

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$8200.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate, following three and six courses of treatment, the likelihood of increased numbers of patients achieving complete response rates when given three additional courses of the same regimen; to evaluate the qualitative and quantitative toxicities of 5-fluorouracil and cisplatinum following three and six courses of treatment; and to evaluate by serial biopsy and flow cytometry the correlation of the cellular DNA parameters of degree of aneuploidy (DNA index) and proliferative activity (SPF) with the patients clinical characteristics, tumor morphology, cytotoxic response, disease free interval, and survival.

Technical Approach: Patients must have a histologically confirmed diagnosis of advanced unresectable squamous cell carcinoma of the head and neck, Stage IV, and not be eligible for SWOG protocol of higher priority. Nasopharyngeal primary tumor will be excluded. Biopsy specimens for flow cytometry will be taken before treatment. Patients will be treated with three courses of 5-FU and cisplatinum combination chemotherapy. Patients achieving a partial response or complete response will continue for an additional three courses of therapy. Patients who have no response after three courses will be taken off study and a biopsy will be taken for flow cytometry. Patients will have a triple endoscopy and re-biopsy of the primary site and lymph nodes for flow cytometry analysis within four weeks of completion of treatment following the full six courses of therapy or at any time that disease recurs. All patients will be followed until death.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/065 **Status:** On-going

Title: SWOG 8812: Treatment of Limited Small Cell Lung Cancer With Concurrent Chemotherapy, Radiotherapy, With or Without GM-CSF and Subsequent Randomization To Maintenance Interferon or No Maintenance

Start Date: 06/16/89 **Est. Completion Date:** Jun 92

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark H. Kozakowski, MC
COL Irwin B. Dabe, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC

Key Words: cancer:lung:small cell,chemo,radiotherapy,GM-CSF,interferon

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To compare the days of neutropenia, the days of leukopenia, the incidence and severity of infections, the incidence and duration of fever, the days on antibiotics, and the days of hospitalization between patients receiving GM-CSF and those not receiving it; to evaluate the toxicities of GM-CSF; to evaluate the ability of rHuIFN a2 a to prolong remission duration and survival; and to evaluate the toxicities of rHuIFN a2 a.

Technical Approach: Patients must have histologically proven small cell carcinoma of the lung. Prior to treatment patients will be staged as to the extent of disease. Only patients with limited disease are eligible for this study. Patients must have evaluable or measurable disease, a pretreatment WBC >4,000 ml, absolute granulocyte count >1500 ml, platelet count >100,000/ ml, serum creatinine of <2.0 mg%, creatinine clearance of >50 ml/min, and performance state of 0-2 by SWOG criteria. Pregnant patients or those with prior radiation therapy, chemotherapy, colony stimulating factors, or interferon are not eligible. Patients with malignant pericardial or pleural effusions, a past medical history of congestive heart failure, extensive pulmonary disease, poor pulmonary reserve, or a history of seizures are ineligible. Patients will be stratified at initial registration by institution and at second registration according to performance status (0-1 vs 2); sex; response; and induction arm. Patients will be randomized to receive induction chemotherapy (cis-platinum + VP-16) and concurrent chest radiotherapy with or without GM-CSF. Consolidation chemotherapy will be as in induction but with no radiotherapy. Those patients achieving a complete remission will be randomized to receive or not receive maintenance therapy with recombinant alpha interferon. All patients who have achieved a complete response by week 33 will receive prophylactic cranial irradiation to the brain. Patients with stable disease, progression, or relapse at any point will be taken off study.

Progress: This study closed to patient enrollment 1 Jan 92. Three patients were enrolled at MAMC, 2 have died and 1 is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Sep 99

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ 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:** 12/04/92

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: Six patients have been entered in this study at MAMC (1 in FY93). All six of the patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC
MAJ 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:** 12/04/92

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 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC

Key Words: lymphoma:tissue procurement

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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 fom other SWOG protocols. Thus far 2 samples have been collected (none in FY93).

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/041 **Status:** Completed

Title: SWOG 8828: A Phase II Trial of Carboplatin (CBDCA) in Relapsed or Refractory Acute Myeloid Leukemia

Start Date: 02/16/90 **Est. Completion Date:** Feb 92

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: leukemia:myeloid,carboplatin,CBDCA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate the complete remission rate of carboplatin (CBDCA) in patients with relapsed or refractory acute myeloid leukemia (AML); to assess the qualitative and quantitative toxicities of these patients; and to identify the pattern of treatment failure by the criteria of Preisler.

Technical Approach: Patients must have a bone marrow aspiration and biopsy demonstrating AML with FAB subtype M1-M7. Patients must be in relapse or must have had a treatment failure of Preisler type 1 or 2 on the most recent induction attempt. Patients must have received only one prior remission induction regimen for AML. Patients with prior CML or myelodysplastic syndrome or those who have received prior radiotherapy or chemotherapy for non-AML conditions are ineligible. Induction: Carboplatin, 300 mg/m^2/day continuous intravenous infusion daily for 5 days. Second induction course: If the bone marrow on Day 21 shows >10% blasts and cellularity >30%, patients will be treated with carboplatin 300 mg/m^2/day continuous intravenous infusion daily for 5 days beginning Day 22. Patients who do not achieve a remission after two induction courses will be removed from protocol treatment. Consolidation: If A-1 marrow is achieved: carboplatin 210 mg/m^2/ day continuous intravenous infusion daily for 5 days. Patients will receive only one consolidation course. There will be no maintenance treatment. Patients will be removed from the protocol at any time unacceptable toxicity occurs.

Progress: No patients were enrolled at MAMC

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/055 **Status:** Completed

Title: SWOG 8842: Dihydroxyazacytidine in Malignant Mesothelioma, Phase II Study

Start Date: 04/03/92 **Est. Completion Date:** Dec 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, mesothelioma

Accumulative MEDCASE Cost:	$0.00	Est. Accumulative OMA Cost:	$0.00	Periodic Review: 12/04/92

Study Objective: To assess the response rate and survival of patients with unresectable malignant mesothelioma treated with Dihydroxyazacytidine (DHAC, NSC-264880); to further evaluate the toxicity of DHAC given by continuous infusion; and to prospectively evaluate the use of CA-125 as a tumor marker in mesothelioma.

Technical Approach: Mesothelioma is an uncommon tumor and, if not localized, is not amenable to therapy with either surgery or radiation therapy. Chemotherapy has shown moderately good response rates. Whether there has been any benefit in survival is unclear. Therefore, use of a new agent which may have activity against mesothelioma will be undertaken. DHAC causes an inflammatory response in the pleura and it is felt that in the presence of a malignancy of the pleura, this anti-trial continuity response may be tumoricidal. Therefore, all patients on the study will receive two cycles of DHAC by continuous infusion over five days. Cycles will be repeated every four weeks. Patients will continue to receive treatment if they have a partial response or stable disease; otherwise they will be taken off the medication.

Progress: This study was closed to patient entry on 15 Nov 92. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Dec 99

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ 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:** 12/04/92

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: Six patients have been enrolled at MAMC (3 in FY93). These patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Mar 98

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:** 12/04/92

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 is a companion study using tissue from SWOG 8814. Three samples were used in FY93. A total of 7 samples have been studied.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert B. Ellis, MC

Key Words: cancer:head & neck,cytometry,DNA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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: 03/19/90 **Est. Completion Date:** Mar 93

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC
MAJ Michael R. Morris, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
CPT Denis Bouvier, MC
MAJ 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:** 12/04/92

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: One patient was enrolled in FY91 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/086 **Status:** On-going

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:** Apr 93

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: cancer:prostate,orchiectomy,flutamide

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: Three patients have been entered in this protocol (1 in FY93). Two patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jan 93

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ Robert L. Sheffler, MC

Key Words: cancer:breast,chemotherapy,endocrine therapy

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$5000.00	**Periodic Review:** 12/04/92

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.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Feb 92

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ 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: 12/04/92

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: Seventeen patients were enrolled at MAMC prior to closure to patient entry on 30 Jul 92. Three patients have died from their disease and 14 continue to be followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/030 **Status:** On-going

Title: SWOG 8905: Phase II/III Study of Fluorouracil and Its Modulation in Advanced Colorectal Cancer

Start Date: 01/19/90 **Est. Completion Date:** Jun 92

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Mark H. Kozakowski, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC

Key Words: cancer:colorectal,5-Fluorouracil,leucovorin,PALA

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$20780.00	**Periodic Review:** 12/04/92

Study Objective: To determine and compare response rates and toxicities of 5-fluorouracil given by different schedules and/or with biochemical modulators to patients with advanced colorectal cancer and to compare patient survival on the different 5-FU regimens.

Technical Approach: All patients must have disseminated or recurrent colorectal cancer. Patients will be randomized to one of seven regimens: Arm I: 5-FU, IV push x 5 days every 5 weeks; Arm II: Low dose Leucovorin, IV push x 5 days followed by 5-FU IV push x 5 days every 4 weeks x 2, then every 5 weeks; Arm III: High dose Leucovorin IV, Days 1, 8, 15, 22, 29, 36 followed by 5-FU (same days) every 8 weeks; Arm IV: 5-FU continuous infusion, days 1-28, every 5 weeks; Arm V: 5-FU continuous infusion, days 1-18 preceded by Leucovorin IV push, days 1, 8, 15, 22 every 5 weeks; Arm VI: 5-FU alone, 24 hour infusion, days 1, 8, 15, 22, every 4 weeks; Arm VII: PALA IV, days 1, 8, 15, 22 followed by 5-FU, 24 hour infusion, days 2, 9, 16, 23, every 4 weeks. Patients will be continued on study until progression of disease or unacceptable toxicity. Patients will be followed to death.

Progress: Two patients have been enrolled prior to FY93. One patient has died and the other is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/079 **Status:** On-going

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:** Jul 97

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ Paul C. Sowray, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** 12/04/92

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 92 **Protocol No.:** 90/112 **Status:** Completed

Title: SWOG 8931 (EST-3189): Phase III Comparison of Cyclophosphamide, Doxorubicin, and 5-Fluorouracil (CAF) and 1 16-Week Multi-drug Regimen as Adjuvant Therapy for Patients with Hormone Receptor Negative..

Start Date: 09/21/90 **Est. Completion Date:** Sep 93

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert B. Ellis, MC

Key Words: cancer:breast,cyclophosphamide,doxorubicin,5-Fluorouracil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To compare disease-free and overall survival and toxicities in node positive receptor-negative breast cancer patients receiving adjuvant CAF or a 16-week multidrug chemotherapy regimen.

Technical Approach: Patients must be female and must 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. Prior malignancies are limited to a curatively treated basal or squamous cell carcinoma of the skin, carcinoma in situ of the cervix, or other cancer if the patient has been disease-free > five years. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be stratified by the number of positive axillary nodes, menopausal status, and pathologic size of the primary tumor at the largest dimension. Patients will be randomized to CAF (cyclophosphamide, doxorubicin, and 5-FU), given every 28 days for six cycles or a 16-week multidrug regimen: cyclophosphamide, doxorubicin, vincristine, methotrexate, 5-FU (600 mg/m$^{2)}$, and leucovorin, given weeks 1, 3, 5, 7, 9, 11, 13, and 15, with 5-FU, 300 mg/m^2, given on alternate weeks.

Progress: The study was closed to patient entry in April 93. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Luke M. Stapleton, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
MAJ Kenneth A. Bertram, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC

Key Words: lymphoma:serum repository

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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 (none in FY93).

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/006 **Status:** On-going

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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ William A. Phillips

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Everardo E. Cobos Jr., MC
MAJ 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:** 12/04/92

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: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/032 **Status:** Completed

Title: SWOG 8956: A Phase II Study of Cisplatin and 5-Fluorouracil Infusion for Treatment of Advanced and/or Recurrent Metastatic Carcinoma of the Urinary Bladder

Start Date: 02/01/91 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC

Key Words: cancer:bladder,cisplatin,5-Fluorouracil

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To assess efficacy and feasibility of utilizing cisplatin (CDDP) and 5-fluorouracil infusion (5-FU-I) in patients with advanced and/or recurrent carcinoma of the urinary bladder and to evaluate the toxicity of cisplatin and 5-FU in this group of patients.

Technical Approach: Bladder cancer is the sixth most common cancer in the United States, accounting for 10,000 deaths per year. Treatments have been developed which provide 15% long term disease-free survival equated with cure. However, the toxicities have been profound, including treatment related mortalities. As a consequence, this potential less toxic regimen has been devised for evaluation in metastatic bladder cancer. In this study, all patients will receive the same treatment which includes cisplatin on the first day of treatment and continuous infusion of 5-FU on each of the first five days of treatment. These treatments will be repeated every 21 days. Patients response to treatment will be assess every other course (every six weeks). The patients will continue on therapy until they have progression of disease.

Progress: This study was closed to patient entry on 15 June 93. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ 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: 12/04/92

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: One patient was enrolled in FY92 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ William A. Phillips

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ 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:** 12/04/92

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 92 **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:** Mar 93

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
LTC John A. Vaccaro, MC
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC
MAJ 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: 12/04/92

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 92 **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:** Mar 98

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** / /

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 this fiscal year.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/094 **Status:** On-going

Title: SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary

Start Date: 09/06/91 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC

Key Words: cancer:leukemia,cytogenetic studies

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: The complex nature and diversity of numerical and structural chromosomal changes in hematologic malignancies have been increasingly recognized in the last 15 years as cytogenetic techniques have improved and the knowledge base expanded. It has been shown that the majority of malignancies have non-random chromosomal anomalies such that specific cytogenetic aberrations are generally associated with particular leukemia subtypes. Previous studies have shown the remarkable consistency of the recurring chromosome abnormalities in the leukemias and their current and potential usefulness as diagnostic and prognostic indicators. Strong correlations with certain clinical immunological and morphologic features have been shown and in certain cases a molecular mechanism has been discovered. Large prospective studies which include responsiveness to the various treatments have not been done and for most leukemias the molecular mechanisms and correlations remain to be elucidated. 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 (4 in FY93) have been entered in this study at MAMC and are being followed.

Detail Summary Sheet

Date: 30 Sep 92	**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:** Mar 95
Department: SWOG	**Facility:** MAMC

Principal Investigator: MAJ Luke M. Stapleton, MC

Associate Investigators:

MAJ Rahul N. Dewan, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, gastric, adenocarcinoma, chemoradiation

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0	**Periodic Review:** 12/04/92

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: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
COL Joseph F. Homann, MC
MAJ Everardo E. Cobos Jr., MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ 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:** 12/04/92

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: Two patients have entered this study (1 in FY93) and both are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/142 **Status:** On-going

Title: SWOG 9015: A Randomized Trial of Pre- and Post-Operative Chemotherapy Compared to Surgery Alone for Patients With Operable Non-Small Cell Carcinoma of the Lung, Phase III

Start Date: 06/09/93 **Est. Completion Date:** Jun 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** / /

Study Objective: To: 1) compare the survival experience of patients with clinical stages T2N1, T1N1, T2N0 T3N0, and T33N1 NSCLS (mediastinoscopy negative) (Clinical stages 1b, 11, 111a) treated with either surgical resection alone (control) or a regimen of pre- and post-operative chemotherapy (experimental arm); 2) estimate the response rate to pre-operative chemotherapy; 3) test the association between response to pre-operative chemotherapy and survival of those patients who receive chemotherapy; 4) establish the toxicity, including operative complications, of combined pre- and post-operative chemotherapy.

Technical Approach: Young adult patients with non-small cell carcinoma of the lung who are mediastinoscopy negative will be randomized to ARM I pre-operative chemotherapy and then surgical resection followed by post-operative chemotherapy or ARM II surgical resection alone. Chemotherapy will be with VP-16 IV days 1-3 and carboplatin IV on day 1 for each of 2 cycles. Cycles will be 21 days duration. Patients whose tumors do not progress will have the tumor surgically resected, followed by an additional 3 courses of the same chemotherapy.

Progress: No patients have been enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** May 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Timothy P. Rearden, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** / /

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: One patient entered this study in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/045 **Status:** Completed

Title: SWOG 9028: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD to VAD/Verapamil/Quinine for Induction; (2) Alpha-2b Interferon or Alpha-2b Interferon Plus ..

Start Date: 03/01/91 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Luke M. Stapleton, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ William A. Phillips
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC

Key Words: myeloma,alpha 2b interferon, VAD, VMCP

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To determine if multidrug resistance can be prevented during remission induction by adding chemosensitizers (verapamil or quinine) to the VAD (vincristine, adriamycin, and dexamethasone); to determine if Interferon alone or plus VMCP (vincristine, melphalan, cytoxan, and prednisone) represents better maintenance therapy for myeloma; to examine the prognostic significance of pretreatment LDH level, Ki-67 level, and presence of P-glycoprotein; and to evaluate the relationship between the magnitude of cytoreduction and survival.

Technical Approach: Previously untreated patients with all stages of multiple myeloma are eligible. Protein criteria must be present but patients with IgM myeloma are not eligible. Patients must not have symptoms of congestive heart failure and may not be on digitalis preparations, beta blockers, or calmodulin inhibitors. Cardiac ejection fraction must be at least 50%, the EKG must be free of serious cardiac arrhythmias, and systolic blood pressure must be >90 mm/Hg. Patients who have had a prior malignancy within the last five years except for basal or squamous cell carcinoma or in situ cervical cancer are not eligible. Patients will be randomized to VAD every 21 days or to VAD plus verapamil and quinine every 21 days. Patients with >75% disease regression and at least 6 months of treatment and those with at least 50% regression after 9 months of treatment will be randomized to maintenance therapy. Maintenance therapy will consist of either alpha-2B interferon 3 times weekly or to alpha-2B interferon plus CVMCP 3 times weekly every 3 months until relapse.

Progress: No patients entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/040 **Status:** On-going

Title: SWOG 9030: Phase II Study of High Dose Ara-C/Mitoxantrone for the Treatment of Relapsed/Refractory Acute Lymphocytic Leukemia

Start Date: 02/07/92 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT James S. D. Hu, MC

Key Words: cancer, leukemia, lymphocytic, ara-C, mitoxantrone

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To assess the complete response rate achieved in adult patients with relapsed or refractory ALL using the combination of high-dose Ara-C with mitoxantrone and to evaluate the toxicities associated with this induction regimen.

Technical Approach: Patients who have relapsing or refractory acute lymphocytic leukemia (ALL) have only one chance of being cured, and that is by a bone marrow transplant, which is available only to about one in four patients. For those patients without the possibility of bone marrow transplant, more effective chemotherapy regimens need to be developed. Preliminary studies suggest the effectiveness of high-dose Ara-C and mitoxantrone, in combination. On this study, patients would receive Ara-C once daily for five days and mitoxantrone will be given as a 30 min infusion beginning 12-20 hours after the first dose of Ara-C (one dose only). Both drugs will be given at very high doses. This will be a one time only regimen that will not be repeated.

Progress: No patients have been enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jun 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, leukemia, myeloid

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: Two patients have been enrolled in this study in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, myelogenous, leukemia

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/067 **Status:** On-going

Title: SWOG 9034 (EST 3489, CALGB 9120): Phase III Study of Three Intensive Postremission Therapies in Adult Acute Nonlymphocytic Leukemia: Comparison of Autologous Bone Marrow Transplantation, Intensive....

Start Date: 03/05/93 **Est. Completion Date:** Apr 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:leukemia, autologous bone marrow, allogenic bone marrow, idarubicin, Ara-C, busulfan, cyclophosphamide

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

Study Objective: 1. To compare complete remission (CR) duration and survival in de novo acute myelogenous leukemia resulting from post-remission therapy with 4-HC treated marrow versus conventional chemotherapy versus one course of high-dose cytarabine. 2. To examine differences in outcome for allogeneic bone marrow transplantation versus consolidation therapy or autologous transplant. 3. To examine the results of differing post-remission therapies in patient subsets defined by age, cell surface markers, and karyotype abnormalities.

Technical Approach: Patients having morphologic proof of non-lymphocytic leukemia, who have not been previously treated with radiation therapy or cytologic chemotherapy, are eligible for this study. Following registration, induction with Idarubicin 12 mg/m^2/day on days 1, 2, & 3 and Cytabine 25 mg/m^2 IV push, then 100 mg/m^2 by continuous infusion on days 1, 2, 3, 4, 5, 6, & 7. Patients will receive a second course of the induction medication (Ida/Ara-C) if a remission is not achieved from the first. Patients failing to receive a complete remission (CR) after the 2nd induction Ida/Ara-C course are off study. Patients achieving CR who have a histocompatible sibling will receive an Allogeneic Bone Marrow Transplantation (using Busulfan-Cyclophosphamide as the preparative regimen. Patients not qualified for allogeneic transplant will then be randomized to either an Autologous Bone Marrow Transplantation or Consolidation Chemotherapy with Cytarabine 3 gm/m^2 IV over 1 hour every 12 hours X 12 doses (6 days). The preparative therapy for the autologous transplant is Busulfan 1 mg/kg q6 hr X 16 (4 days) followed by Cyclophosphamide 50 mg/kg IV q.d. X 4.

Progress: One patient entered in this study in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/068 **Status:** Completed

Title: SWOG 9037: Prediction of Recurrence and Survival in Node-Negative Breast Cancer Patients Using a Panel of Prognostic Factors: A Companion Protocol to SWOG 8897 (EST-2188, CALGB-8897, INT-0012)

Start Date: 06/14/91 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC

Key Words: cancer:breast,prognostic factors,recurrence,survival

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To measure histologic and nuclear grade, estrogen and progesterone receptors, HER-2 oncogene, cathepsin D, EGF receptor, PS2, and hsp 27, 70, and 90 in paraffin-embedded histopathological specimens; and to correlate the above factors with biological and clinical features including recurrence and survival in patients entered on SWOG 8897.

Technical Approach: There is now evidence in prospective randomized clinical trials that adjuvant endocrine therapy and adjuvant chemotherapy can be of benefit in axillary node-negative (ANN) breast cancer patients. This study will be done in concert with a current prospective trial (SWOG 8897) of ANN good risk patients assigned to observation or chemo plus or minus endocrine therapy based upon low and high proliferative rate and in tumors too small for estrogen receptor measurement. In the paraffin-embedded histopathological specimens submitted to the laboratory for DNA flow cytometry, extra 5 microgram sections will be cut for measurement of histological and nuclear grade, estrogen and progesterone receptors; HER-2 oncogene; cathespin D; EGF receptor; PS2; and hsp 27, 70, and 90. This represents the most popular proposed prognostic factors for predicting recurrence and survival in ANN patients. A critical aspect of this study will be the multivariate analysis (Cox model) which will indicate the relative importance of these factors as well as tumor size and DNA flow cytometry in predicting recurrence and survival in good risk ANN patients. This study should help decide if prognostic factors can and should be used in treatment decisions in ANN patients.

Progress: This is a tissue study involving patients that are registered on other protocols. One patient was enrolled prior to study closure to patient entry, 15 May 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/077 **Status:** On-going

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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ William A. Phillips
MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC

Key Words: cancer:prostate,quality of life

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: One patient was enrolled in this protocol in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Rahul N. Dewan, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC
MAJ Steven S. Wilson, MC
MAJ 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: 12/04/92

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 92	**Protocol No.:** 92/002	**Status:** On-going

Title: SWOG 9045: Evaluation of Quality of Life in Patients with Advanced Colorectal Cancer Enrolled on SWOG 8905

Start Date: 10/04/91	**Est. Completion Date:** Jun 92
Department: SWOG	**Facility:** MAMC
Principal Investigator: MAJ Timothy P. Rearden, MC	
Associate Investigators:	MAJ Paul C. Sowray, MC
Key Words: cancer:colorectal,quality of life	

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: (1) To compare the following primary aspects of quality of life according to treatment assignment: treatment specific symptoms, physical functioning, and emotional functioning; and (2) to compare four secondary quality of life variables according to treatment assignment: general symptoms, role functioning, social functioning, and global perception of quality of life.

Technical Approach: This cancer control intervention study measures quality of life in patients with advanced colorectal cancer; specifically, patients registered on SWOG 8905: Phase II/III Study of 5-FU and Its Modulation in Advanced Colorectal Cancer. SWOG 8905 compares survival, response rates, and toxicities of 5-FU given by different schedules and/or with biochemical modulators (seven arms). 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 8905 and become a critical consideration if no difference is demonstrated in survival between the treatment arms. A Quality of Life questionnaire will be administered prior to treatment, and at 6, 11, and 21 weeks after randomization on SWOG 8905.

Progress: This study was closed to patient entry 15 Jan 93. Two patients were enrolled in previous years and are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Nov 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** / /

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: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/144 **Status:** On-going

Title: SWOG 9107: A Phase II Pilot Study of High-Dose 24-Hour Continuous Infusion 5-FU and Leucovorin and Low-Dose PALA for Patients With Colorectal Cancer

Start Date: 06/09/93 **Est. Completion Date:** Jun 96

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:colorectal, 5-FU, Leucovorin, PALA

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

Study Objective: To evaluate response rates and toxicities of 5-FU 2600 mg/m^2 as a 24 hour continuous intravenous infusion given once a week, in combination with Leucovorin 500 mg/m^2 as a 24 hour continuous infusion and PALA 250 mg/m^2 intravenously.

Technical Approach: Patients with histologically proven diagnosis of colorectal cancer with distant metastasis who have received no more than one adjuvant chemotherapy will receive PALA IV on day 1 and Leucovorin and 5-FU 24 hours later. This regimen will be repeated on 7 day cycles and will continue until disease progression.

Progress: One patient entered this study at MAMC in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/096 **Status:** On-going

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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT 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:** 12/04/92

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 to avoid treatment imbalance within institutions.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/104 **Status:** On-going

Title: SWOG 9110: A Phase II Evaluation of Diademnin B in Central Nervous System Tumors

Start Date: 09/04/92 **Est. Completion Date:** Sep 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:nervous system

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate the likelihood of response in order to assess whether didemnin B should be advanced to further studies and to evaluate the qualitative and quantitative toxicities of didemnin B.

Technical Approach: Didemnin B will be administered IV over 30 mins once every 28 days. Patients will be evaluated for response at least every two courses of treatment. Those achieving complete response, partial response or stable disease will continue on study. Liver function tests and measurable and evaluable disease will be assessed at least every other course of therapy (every eight weeks). Didemnin B therapy and parameters will continue at these intervals until progression of disease occurs.

Progress: Two patients were entered into this study in FY 93. One patient continues to be followed (1 patient expired.) The study was closed to patient entry 15 Nov. 93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/078 **Status:** On-going

Title: SWOG 9111: Post-Operative Adjuvant Interferon Alpha 2 in Resected High-Risk Primary and Regionally Metastatic Melanoma, Intergroup

Start Date: 07/12/91 **Est. Completion Date:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
MAJ Everardo E. Cobos Jr., MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
MAJ Paul C. Sowray, MC

Key Words: melanoma,interferon alpha 2

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To establish the efficacy of one year at maximally tolerable dosages (IV and SC) interferon alpha-2 as an adjuvant to increase the disease free interval and overall survival in patients at high risk for recurrence after definitive surgery for deep primary lesions or after regional lymph node recurrence; and to evaluate the efficacy and tolerance of long-term alpha-2 at 3 MU/d (Sc TIW) as an adjuvant in similar patients in comparison to 1 year of treatment of maximally tolerable dosages.

Technical Approach: Patients must fulfill one of the following criteria: TA NO MO - Deep primary melanoma (>4.0 mm Breslow depth) with or without lymph node involvement; T1-4 N1 MO - Primary melanoma with regional lymph node metastases found at lymphadenectomy, but clinically undetectable (occult); T1-4 N1-2 MO - primary melanoma with clinically apparent (overt) regional lymph node metastases confirmed by lymphadenectomy; or T1-4 N1-2 MO - recurrence of melanoma at the proximal regional lymph node(s) resection. Patients must have an ECOG performance status of 0-1. This is a three arm Phase III study. Patients will be randomized to treatment groups and staged according to the criteria above plus the number of nodes positive at lymphadenectomy. Arm A will be alpha-2 interferon at high dose for one year. Arm B will be alpha-2 interferon at low dose for two years or more. Arm C will consist of observation alone. This study is designed to utilize group sequential analysis procedures to allow multiple comparisons throughout the trial without inflating the Type I error rate. At each planned analysis, two treatment comparisons, one year vs observation and two year vs observation, will be performed using a logrank test stratified by stage of disease. If either one of these primary comparisons crosses the group sequential boundary, then the observation arm may be dropped.

Progress: No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT 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: 12/04/92

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 92 **Protocol No.:** 93/088 **Status:** On-going

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:** Aug 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ 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:** / /

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: One patient was enrolled at MAMC in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/138 **Status:** On-going

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:** Aug 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Robert B. Ellis, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ 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:** / /

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: There are no participants in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Oct 92

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
CPT 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:** 12/04/92

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 92 **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:** Sep 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Timothy P. Rearden, MC
CPT James S. D. Hu, MC
LTC Robert D. Vallion, MC
CPT 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:** / /

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.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/048 **Status:** On-going

Title: SWOG 9129: Phase III Randomized Study of All-Trans Retinoic Acid Versus Cytosine Arabinoside and Daunorubicin as Induction Therapy for Patients with Previously Untreated Acute Promyelocytic Leukemia

Start Date: 02/05/93 **Est. Completion Date:** Jan 96

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:leukemia, promyelocytic

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

Study Objective: The objectives of this study are: (1) to compare the complete remission rate and disease-free survival of all-trans retinoic acid (TRA) to that achieved with conventional remission induction therapy, including cytosine arabinoside (Ara-C) plus daunorubicin (DNR) in patients with previously untreated acute promyelocytic leukemia (APL); (2) to compare the toxicities of TRA to those of Ara-C plus DNR as induction therapy in APL; (3) to determine the value of maintenance therapy with TRA.

Technical Approach: Patients with morphologically proven acute promyelocytic leukemia, untreated with radiation therapy or cytotoxic chemotherapy, will be considered for inclusion into this study. This study is designed as a Phase III prospective trial which involves two randomizations. Patients will be initially randomized to either TRA or Daunorubicin plus Cytosine Arabinoside as induction therapy. Consistent with other SWOG studies, one or two cycles of Daunorubicin plus Cytosine Arabinoside will be permitted to achieve complete remission (CR) since approximately 20% of patients not achieving CR with one cycle do so with a second cycle. Following two cycles of consolidation chemotherapy for patients achieving CR, patients will be randomized (second randomization) to either maintenance TRA or observation until relapse. Ancillary laboratory studies will explore biological correlations of TRA responsiveness and the pathophysiology of the coagulopathy.

Progress: One patient was enrolled in this study at MAMC in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
MAJ George F. Hodeges, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT 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: 12/04/92

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 92 **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:**

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, osteogenic sarcoma

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

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: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/049 **Status:** On-going

Title: SWOG 9147: Evaluation of Tamoxifen in Desmoid Tumors, Phase II

Start Date: 02/05/93 **Est. Completion Date:** Jan 95

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
CPT James S. D. Hu, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
MAJ 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:** / /

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: There have been no patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/089 **Status:** On-going

Title: SWOG 9148: A Phase II Study of Cisplatin Preceded by a 12-Hour Continuous Infusion of Concurrent Hydroxyurea and Cytosine Arabinoside ... Extensive Stage Small Cell and Non-small Cell Lung Carcinoma

Start Date: 04/02/93 **Est. Completion Date:** Apr 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:small cell, cancer:Non-small cell, cisplatin, hydorxyurea, Ara-C, G-CSF

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

Study Objective: 1. To evaluate the response rate of this 3-drug program in patients with extensive non-small cell lung cancer. 2. To evaluate the response rate of this program in patients with extensive-stage small cell lung cancer. 3. To assess the qualitative and quantitative toxicities of this regimen in each patient population.

Technical Approach: Patients with histologically or cytologically proven disease who have not received prior chemotherapy for lung carcinoma and entering this study will have received blood work and/or other body fluid analyses, x-ray, scans or physical examination used for tumor measurement within the 14 days prior to registration.

Patients will receive allopurinol, 600 mg po, at least 12 hours before start of therapy, and then 300 mg po q.d. continuously until off study. Patients will be hydrated with normal saline, 150 ml/hr or higher rate to maintain urine output ≥ 100 cc/hr with intake and output measurements every 4 hours. The hydration must begin at least 8 hours prior to the start of chemotherapy and continue for at least 12 - 24 hours after completion of cisplatin (or until adequate oral intake, whichever is longer). Patients will received Hydroxyurea 1260 mg/m^2 in 150 ml 0.9 NS or D5 0.9 NS IVPB over 1 hour via an infusion pump followed immediately by Ara-C 100 mg/m^2 plus hydroxyurea 5040 mg/m^2 mixed in the same bag of 1 liter of NS or D5NS and given IVPB over exactly 12 hours using an infusion pump. At the start of the last hour of Ara-C plus hydroxyurea, piggyback Mannitol, 25 gms in 100 ml D5W will be infused into the chemotherapy line over 1 hour. Cisplatin 100 mg/m^2 in 250 ml NS or D5NS IVPB via an infusion pump will be administered immediately upon completion of the Ara-C, hydroxyurea, and Mannitol. This regimen will be completed every 28 days if absolute granulocytes are > 1500, platelets are > 100,000, and measured creatinine clearance > 50. The treatment should be delayed one week, then a second and third week until these criteria are met. If the parameters are not up to these levels after three 1-week delays the patient will be removed from the study.

Progress: There have been no patients enrolled in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/080 **Status:** Completed

Title: SWOG 9151: Evaluation of Topotecan in Hepatoma, Phase II

Start Date: 06/05/92 **Est. Completion Date:** Jun 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard C. Tenglin, MC
LTC Howard Davidson, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC

Key Words: cancer, hepatoma, topotecan

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	**Periodic Review:** 12/04/92

Study Objective: To evaluate the response rate of hepatomas treated with topotecan and to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study.

Technical Approach: Hepatoma is an uncommon malignancy which is usually far advanced by the time diagnosis is made. The median survival after diagnosis is six months. There is no effective chemotherapeutic regimen for this disease. Topotecan is a new chemotherapeutic agent which has been shown to have activity in early cancer trials. An attempt will therefore be made to see whether or not topotecan will be effective against hepatomas. Patients will receive topotecan through an IV for five consecutive days. This treatment will be repeated every three weeks. Patients will continue on this schedule as long as they show either complete response, partial response, or stable disease. If the disease progresses, the patient will be taken off study.

Progress: This study was closed to patient entry, 15 Jun 93. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Jan 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT 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:** / /

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: Two patients were enrolled in FY93. One patients is still be followed and the other died of the disease.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/167 **Status:** On-going

Title: SWOG 9157: Trial of All Trans-Retinoic Acid in Hepatoma, Phase II

Start Date: 09/03/93 **Est. Completion Date:** Sep 98

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT 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
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
MAJ Robert B. Ellis, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

Key Words: cancer:hepatoma, all trans-retinoic acid

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

Study Objective: (1) To evaluate the response rates in patients with hepatomas treated with all trans-retinoic acid; (2) To evaluate the qualitative and quantitative toxicities of all trans-retinoic acid administered in a Phase II study; (3) To describe the number of responses for (a) high versus medium versus low alphafetoprotein and (b) for patients positive and negative for hepatitis B.

Technical Approach: Patients must have a histologically proven, unresectable, bidemensionally measurable hepatoma. They will be described according to: (1) Alpha-fetoprotein level, (2) Hepatitis-B antigen, (3) SWOG performance status, (4) Prior RT or surgery for hepatoma. This is a primary treatment and includes no plans for any concurrent treatment of the primary tumor. Patients will receive All-trans retinoic acid 50 mg/m^2 t.i.d. x 21 days followed by 7 days of rest. Therapy will be open-ended for responding or stable disease patients who are not experiencing serious toxicities. Disease assessment will be done at least every 8 weeks. Statistical evaluation will be based on time to treatment failure/time to death.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/097 **Status:** On-going

Title: SWOG 9205: Central Prostate Cancer Serum Repository Protocol

Start Date: 05/07/93 **Est. Completion Date:** Mar 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ 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:** / /

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: One patient was entered in this study in FY93.

Detail Summary Sheet

e: 30 Sep 92 **Protocol No.: 93/107** **Status:** On-going

e: 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 ....

rt Date: 05/07/93 **Est. Completion Date:** May 98

)artment: SWOG **Facility:** MAMC

ncipal Investigator: CPT James S. D. Hu, MC

ociate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
MAJ Robert B. Ellis, MC
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MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC
CPT Jennifer L. Cadiz, MC
LTC Robert D. Vallion, MC

y Words: Cancer:myeloma, VAD-P, VAD-P,Quinine

cumulative		**Est. Accumulative**		**Periodic Review:**
:DCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

dy Objective: (1) To compare the effectiveness of the VAD-P chemotherapy regimen en administered alone or in combination with the chemosensitizer quinine intended block the emergence of multidrug resistance during remission induction in viously untreated patients with multiple myeloma; (2) To evaluate the emosensitizing potential of quinine to reverse drug resistance in myeloma patients ndomized to VAD-P induction who fail to achieve at least 25% regression with emotherapy alone. 3. To compare the value of alternate day prednisone 10 mg versus mg for remission maintenance for patients proven to achieve at least 25% regression.

chnical Approach: Patients with proven multiple myeloma (all stages) who have not eived prior chemotherapy are eligible for participation in this trial. A dynamic ocation scheme will be used to randomize patients to one of the two induction atment arms.

INDUCTION: ARM I patients will receive Vincristine 0.4 mg IV q.d. on days 1-4, xorubicin 9 mg/m^2 q.d. IV on days 1-4, Dexamethasone 40 mg q.d. PO on days 1-4, and ednisone 50 mg Q.O.D. on days 9, 11, 13, 15, 17, and 19. This cycle will be repeated Q 21 ys for a minimum of 6 to 8 cycles (6 months) or a maximum of 17 cycles (12 months). tients who fail to achieve ≥ 25% tumor regression after 12 months of treatment on m I (VAD-P) or relapse or progress on Arm I, will be eligible for crossover to VAD-Q.

ARM II and Crossover schedule patients will receive VAD-P as outlined above on ys 2-5 and will also receive Quinine 400 mg t.i.d. on days 1-6 (VAD-P/Q).

Patients with ≥ 25% tumor regression after 9 to 12 months of induction therapy or tients who achieve ≥ 50% tumor regression after 6 months of induction therapy will be ndomized to either of two maintenance regimens. If, in the judgement of the ysician the patient will continue to benefit from induction therapy, they may continue to 12 months.

MAINTENANCE: ARM III patients will receive Prednisone, 10 mg Q.O.D., until apse and ARM IV patients will receive Prednisone 50 mg Q.O.D. until relapse.

ogress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/066 **Status:** Completed

Title: SWOG 9215: Quality of Life on Breast Cancer Adjuvant Trial (SWOG 8931)

Start Date: 03/05/93 **Est. Completion Date:** Mar 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
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Key Words: cancer:breast

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

Study Objective: To determine if adjuvant chemotherapy given to breast cancer patients for SWOG 8931 has an adverse effect on performance status and lifestyle.

Technical Approach: This companion protocol will assess the quality of life for breast cancer patients undergoing adjuvant chemotherapy on SWOG 8931. This protocol requires that the patient complete a quality of life questionnaire at set time intervals.

Comparison will be made of biodemographic characteristics of patients on the quality of life study with patients on the parent trial to determine the extent to which the quality of life samples are representative of the samples in the parent trial.

Progress: No patients were entered at MAMC prior to closure to patient entry, 29 Apr 93.

Detail Summary Sheet

e: 30 Sep 92 **Protocol No.: 93/090** **Status:** On-going

le: SWOG 9216: A Randomized Phase III Study of CODE Plus Thoracic Irradiation Versus Alternating CAV and EP for Extensive Stage Small Cell Lung Cancer

rt Date: 04/02/93 **Est. Completion Date:** Mar 98

)artment: SWOG **Facility:** MAMC

ncipal Investigator: MAJ Timothy P. Rearden, MC

)ociate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
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CPT Diana S. Willadsen, MC

y Words: Cancer:lung, cisplatin, adriamycin, vincristine, etoposide, lophosphamide, irradiation

cumulative		**Est. Accumulative**		**Periodic Review:**
:DCASE Cost:	$0.00	**OMA Cost:**	$0.00	/ /

dy Objective: To determine if chemotherapy dose intensification and thoracic adiation will improve the response rate and overall survival rate in patients with ensive small cell lung cancer.

:hnical Approach: Patients with extensive, measurable or evaluable disease will be domized to 1 of 2 arms. Those randomized to Arm 1 will receive CODE (cisplatin, cristin, doxorubicin, and etoposide) administered as follows: Cisplatin 25 mg/m^2 IV r 15 minutes weekly; Vincristine 1 mg/m^2 IV over 15 minutes weeks 1, 2, 6, 8; xorubicin 40 mg/m^2 IV over at least 10 minutes weeks 1, 3, 5, 7, 9; Etoposide 80 mg/m^2 over 20 - 30 minutes day 1 of weeks 1, 3, 5, 7, 9 and Etoposide 80 mg/m^2 PO days 2 & 3 of eks 1, 3, 5, 7, 9. Those randomized to Arm 2 will receive alternating CAV/EP eduled as follows: Cyclophosphamide 100 mg/m^2 IV 100 mg every 1 - 2 minutes of eks 1, 7, 13; Doxorubicin 50 mg/m^2 IV over at least 10 minutes on day 1 of weeks 1, 7, and Vincristine 1.2 mg/m^2 IV over 2 - 3 minutes day 1 of weeks 1, 7, 13 and Etoposide) mg/m^2 IV over 20 - 30 minutes days 1, 2 & 3 of weeks 4, 10, 16; Cisplatin 25 mg/m^2 VI r 15 minutes days 1, 2, & 3 of weeks 4, 10, 16. Supportive drugs (corticosteroid, troprotective agent, antifungal agent, prophylactic antibiotic Colony-stimulating tor, will be given according to set criteria.

After complete protocol cytotoxic chemotherapy, all patients will be re-staged, with eat of any investigation that was abnormal prior to entry. If a patients should refuse staging, but appears on the available evidence to be in complete response, prophylactic nial irradiation may be offered at the discretion of the investigator.

Patients on ARM 1 who achieve a complete response or partial response at the mary site with a complete response at all known metastatic sites will receive both racic irradiation to the mediastinum and site of the primary and prophylactic nial irradiation beginning 3 to 4 weeks after completion of systemic therapy. These y be given concurrently and are obligatory.

Patients on Arm II who achieve a complete response will receive at least phylactic cranial irradiation and this is obligatory. Other radiation therapy for ients in this arm is non-obligatory but may be given at the discretion of the estigator 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: No patients have entered the study at MAMC.

Detail Summary Sheet

: 30 Sep 92	**Protocol No.:** 93/136	**Status:** On-going

: 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

: Date: 07/02/93	**Est. Completion Date:** Jul 98
artment: SWOG	**Facility:** MAMC

cipal Investigator: MAJ Timothy P. Rearden, MC

ciate Investigators:	MAJ Luke M. Stapleton, MC
LTC Howard Davidson, MC	MAJ Kenneth A. Bertram, MC
MAJ Patrick L. Gomez, MC	MAJ Mark E. Robson, MC
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Words: cancer:non-small cell lung, 13-cis retinoic acid

umulative		**Est. Accumulative**		**Periodic Review:**
DCASE Cost:	$0.00	**OMA C st:**	$0.00	/ /

dy Objective: To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing incidence of SPTs in patients who have been treated for Stage I non-small cell lung cer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13- in a daily administration schedule; and (3) compare the overall survival of patients ted with 13-cRA vs. patients treated with placebo.

hnical Approach: Patients enrolling into this study will be stratified according to ology, T stage and smoking status then registered into a Single-Blind, 8 week run-in iod to test compliance. All patients will receive placebo during this period. After n-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg /d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up iod.

The final analysis will be undertaken shortly after seven years. The primary othesis for the study is whether 13-cRA lowered the rate of second primary tumors T). All patients randomized will be grouped according to the assigned treatment. ients who are either purely lost to follow up or died without a SPT occurring will be uded in the actuarial analysis with a censored status on the last day of contact. The nary hypothesis of treatment benefit will be tested using the proportional hazards lel.

gress: No patients have entered the study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** May 98

Department: SWOG **Facility:** MAMC

Principal Investigator: CPT James S. D. Hu, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
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Key Words: Cancer: myeloma; topotecan

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

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: One patient was entered in this study in FY93.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/109 **Status:** On-going

Title: SWOG 9240: A Phase II Trial of CVAD for Treatment of Non-Hodgkin's Lymphoma

Start Date: 05/07/93 **Est. Completion Date:** May 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC

Key Words: Cancer:non-Hodgkin's lymphoma, cyclophosphamide, vincristine, doxorubicin, dexamethasone

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

Study Objective: 1) To evaluate the effectiveness, toxicities, and side effects of the CVAD chemotherapy regimen in previously untreated patients with intermediate and high-grade non-Hodgkin's lymphomas. 2) 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 markers of outcome. These objectives will be addressed in a companion study to this protocol (SWOG 8819). 3) A further secondary objective will be to further utilize the central serum repository enabling clinicopathologic correlations with the results of studies on the material collected (see SWOG 8947).

Technical Approach: Treatment with CVAD chemotherapy will be administered every 21 days for 8 courses in the following doses: Cyclophosphamide 750 mg/m^2 IV on day 1, Vincristine 0.5 mg/day IV on day 1-4, Doxorubicin 12.5 mg/m^2/day on day 1-4, and Dexamethasone 40 mg/day PO on day 1-4. Retreatment interval is 21 days for 8 courses. Patients who develop objective evidence of disease progression during treatment, patients who relapse following a complete remission, and patients who fail to achieve a complete remission after completing the specified protocol treatment may be treated according to the physician preference. Performance status will be graded according to the current Southwest Oncology Group grading scale.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 93/091 **Status:** Terminated

Title: SWOG 9244 (MSKCC-92-106, NCI-T92-0130): A Randomized Study of Cisplatin (CDDP) & Etoposide versus Carboplatin (CBDCA) + Etoposide in the Treatment of Good Risk Patients With Advanced Germ Cell Tumors

Start Date: 04/02/93 **Est. Completion Date:** Apr 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
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CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: Cancer:germ cell, etoposide carboplatin

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

Study Objective: 1. To determine, in a randomized trial, the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens used in the treatment of good risk patients with disseminated germ cell tumors. 2. To validate prospectively the prognostic value of serum tumor marker decline in good risk patients treated with chemotherapy.

Technical Approach: Patients agreeing to participate in this study will be randomized to receive Cisplatin (CDDP) (20 mg/m^2/day X 5 days) and etoposide (100 mg/m^2/day X 5 days q 21 days X 4 cycles or Carboplatin (CBDCA) to be dosed for AUC (area under the curve) of 5.0 mg/ml-min (minimum dose of 400 mg/m^2 on Day 1 and Etoposide 100 mg/m^2 IV on Day 1-5. The treatment course is recycled at 21 days to a total of 4 cycles. Responding patients will be treated for all 4 cycles after which a complete assessment of all sites of disease should be performed. Following completion of four cycles of chemotherapy and radiographic and marker assessment, surgical resection of all residual masses should be considered. Retroperitoneal lymph node dissection, mediastinal node dissection, excision of pulmonary metastases, and/or resection of supraclavicular disease may need to be performed when residual disease is present. If residual malignant tumor is found but is completely excised, then two cycles of chemotherapy using Vinblastine .11 mg/kg/(day 1 and 2), Ifosfamide 1.2 gm/m^2 (days 1 - 5) and Cisplatin 20 mg/m^2(days 1 - 5) should be administered. O'Brien/Fleming stopping rules are being used for the calculation of the overall sample size. As the data accumulate, five analyses will be undertaken after successive groups of 32 patients per arm. Each time the data are analyzed, two one-sided confidence intervals will be calculated. If the lower confidence limit (with one-sided error of 0.1) excludes a treatment difference of 10% then the trial will be stopped and the treatments will be declared equivalent. If the upper confidence limit (with one sided error of 0.2) excludes zero then the trial will be stopped and the carboplatin arm will be declared inferior. To make sure that one of these conditions occurs a sample size of 320 will be needed.

Progress: This study was closed to patient entry 15 May 93 due to poor patient accrual. No patients were enrolled at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** May 95

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
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MAJ Patrick L. Gomez, MC
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MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
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CPT 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:** / /

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 92 **Protocol No.:** 93/110 **Status:** On-going

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:** Jun 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Mark E. Robson, MC

Associate Investigators:
LTC Howard Davidson, MC
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CPT James S. D. Hu, MC
LTC Robert D. Vallion, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Timothy P. Rearden, MC
MAJ Robert B. Ellis, MC
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:** / /

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 92 **Protocol No.:** 93/137 **Status:** On-going

Title: SWOG 9248: A Phase II Trial of Paclitaxel (Taxol) in Patients With Metastatic Refractory Carcinoma of the Breast

Start Date: 07/02/93 **Est. Completion Date:** Aug 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Robert B. Ellis, MC

Associate Investigators:
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 Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC
CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

Key Words: cancer:breast, taxol

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

Study Objective: To evaluate: 1) the subjective improvement in patients with symptomatic refractory carcinoma of the female breast treated with paclitaxel; 2) the clinical response rate of paclitaxel in patients with refractory carcinoma of the female breast; and 3) the qualitative and quantitative toxicities of paclitaxel in a Phase II study.

Technical Approach: Women with breast cancer who have failed one chemotherapy program for metastatic disease will receive Paclitaxel 210 mg/m^2/21 days IV over 3 hrs. Because of the high frequency of hypersensitivity reactions noted in previous clinical trials, patients will be premedicated with decadron, benedryl and tagamet. Objective responses will be assessed by standard criteria. Subjective response will be measured by use of a Patient Symptom Monitoring Questionnaire which will be completed by the patient and scored by the study coordinator.

Patients will be treated for a minimum of two cycles or until objective progression or unacceptable toxicity is noted. The primary endpoints are symptom response and objective tumor response.

Progress: No patients have entered this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **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:** Oct 98

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Mark E. Robson, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
CPT 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:** / /

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: No patients have entered this protocol at MAMC.

DETAIL SHEETS FOR PROTOCOLS

UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/073 **Status:** Completed

Title: UWNG 86-01: Phase II Study of External Brain Irradiation and Hydroxyurea Followed by Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Primary Malignant Brain Tumors

Start Date: 08/19/88 **Est. Completion Date:** Jul 91

Department: UWNG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
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Key Words: tumor:brain,irradiation,PCV,procarbazine,CCNU,vincristine

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$0.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate radiation therapy plus hydroxyurea and PCV in terms of the following parameters: time to progression from start of therapy, response rates and stabilization rate, survival time from start of therapy, and quality of life and activity level (Karnofsky).

Technical Approach: Patients must have a primary intracranial malignant glioma. Most patients will have had some form of surgery. Treatment will begin within four weeks of the operation at which the current diagnosis was made or within four weeks of clinical diagnosis. No prior cytotoxic, chemotherapy, or radiation therapy will be permitted. Local field radiotherapy will be employed. Only one course of radiotherapy will be given. The total dose to the tumor will be 5940 cGy delivered in a period of 6-7 weeks. The tumor volume will include at least the enhanced portion of tumor based on CT scan and a 2-3 cm margin of normal tissue in all directions. Every other day during radiotherapy, beginning day 1, patients will receive hydroxyurea, 300 mg/m^2 every six hours. PCV treatment will begin within two weeks after radiotherapy. CCNU, 110 mg/m^2 po, will be given on day one of each course. Procarbazine, 60 mg/m^2 po will be given days 8-14. Vincristine, 1.4 mg/m^2, will be given IV push on days 8 and 29. Patients will be evaluated and courses given at six to eight week intervals in the absence of irreversible toxicity. Patients will remain on protocol until the completion of two full courses of PCV. If tumor progression is documented after the second course, the patient will be taken off protocol. If tumor progression is not demonstrated, PCV will be given for one year or a minimum of 6 courses (not to exceed 8 courses) and then stopped. All patients will be followed for survival. Patients who expire from tumor progression early in the course of therapy will be evaluable for analysis if one full course of PCV was administered.

Progress: No patients participated in this study at MAMC.

Detail Summary Sheet

ate: 30 Sep 92 **Protocol No.:** 88/017 **Status:** On-going

itle: UWNG 87-01: Phase II Study of TPDCFH for Recurrent Malignant Brain Tumor

tart Date: 12/11/87 **Est. Completion Date:** Sep 90

epartment: UWNG **Facility:** MAMC

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ey Words: tumor:brain,chemotherapy,TPDCFH

ccumulative		**Est. Accumulative**		**Periodic Review:**
IEDCASE Cost:	$0.00	**OMA Cost:**	$100.00	12/04/92

tudy Objective: To determine whether TPDCFH chemotherapy for recurrent malignant lioma will increase time to progression and survival rate and to document the toxicity ttendant on combined treatment.

echnical Approach: Patients will be eligible for this study if: they have received primary urgical treatment, radiotherapy, or adjuvant chemotherapy but no radiotherapy or hemotherapy for 8 weeks prior to entry; the tumor is a histopathologically confirmed ecurrence of a malignant supratentorial glioma; liver and renal function are not eriously impaired (liver enzymes and serum creatinine within 1.5 x normal for aboratory; Karnofsky performance status is >60%. Recurrence will be signaled by orsening neurologic symptoms and signs measured by a neurologic examination. Enlargement of tumor volume as measured in contrast and noncontrast CT scans will erve as an additional criterion of recurrence. All patients will receive the following chedule: 0-66 hr: 6-thioguanine, 30 mg/m^2, q. 6 hr p.o. x 12 doses; 60-78 hrs: rocarbazine, 50 mg/sq.m., q. 6 hr p.o. x 4 doses; 60 hrs: dibromodulcitol, 400 mg/sq.m., .o.; 72 hrs: CCNU, 100 mg/sq.m., p.o.; Days 14 & 15: 5-FU, 1 g/sq.m. continuous infusion ver 48 hrs; Day 15: hydroxyurea, 1 g/sq.m. p.o., 4 hours before the 5-FU infusion ends nd at 4 hr intervals for a total of 3 doses. The cycle will be restarted on day 37-48, epending on toxicity level. In general WBC and platelets should increase to WBC >4000/cu mm and platelets >125,000/cu mm. Exceptions may be made to restart when WBC >3600/cu mm for patients with chronically depressed bone marrow.

Progress: No patients participated in this study at MAMC

Detail Summary Sheet

Date: 30 Sep 92 **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

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Key Words: lymphoma:central nervous system,chemoradiotherapy,methotrexate

Accumulative MEDCASE Cost:	$0.00	**Est. Accumulative OMA Cost:**	$328.00	**Periodic Review:** 12/04/92

Study Objective: To evaluate this regimen; the endpoints 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 functions 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 can be treated with other therapy as indicated. Patients will be followed until death.

Progress: This study is ongoing. One patient participated without any unusual adverse events.

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