# Department of Clinical Investigation

## *Annual Research Progress Report*

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# Madigan Army Medical Center
# Tacoma, Washington

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This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 94. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 94. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during FY 94.

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# ANNUAL PROGRESS REPORT

30 SEPTEMBER 1994

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

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# ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1994

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 94 set records for new protocols submitted and total protocols managed. During this FY DCI processed 180 new protocols and managed 464 total protocols during the year. MAMC investigators continued to attract clinical trials at an increasing rate, augmenting their extramural funding through multiple foundations. MAMC investigators had great success in the competition for Defense Womens' Health Initiative funding, garnering 9 grants totaling over $500,000. MAMC nurses were even more successful, bringing in over $900,000 in DOD nursing research funding. The department continued its strong thrust in molecular biology, training 12 fellows and staff in hands-on techniques and making progress in the areas of characterizing alternate SHBG mRNA transcripts in breast cancer, detection of ANF and NEP mRNA in placentas from pre-eclamptic pregnancy, evaluating bck-2 gene rearrangement in non-Hodgkin's lymphoma and defining cardiac potassium channel gene expression in thyroid dysfunction.

Molecular biology capability was maintained by CPT Wade Aldous who replaced MAJ Robert Stewart, and DCI added LTC Richard Sherman as assistant chief and Director of Surgical Research. The support of BG Leslie Burger, Commander, COL Al Buck, DCCS, COL Thad Krupka, DCA, and COL Charles Mitchell, Director of Medical Education is gratefully acknowledged for their role in the department fulfilling its mission.

# UNIT SUMMARY

## 1. Objective

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

## 2. Technical Approach

| Description | MANPOWER Rank | MOS |
|---|---|---|
| Chief, Clinical Investigation<br>MOORE, Dan C., M.D., COL, MC | 06 | 60P9A |
| C, Clinical Studies Service<br>JONES, Robert E., M.D., COL, MC | 06 | 61C9A |
| C, Surg & Animal Care Svc<br>CALDWELL, Stephen, D.V.M., CPT, VC | 03 | 64A00 |
| C, Microbiology Svc<br>STEWART, Robert S., Ph.D., MAJ, MS (ETS July 94) | 04 | 68A9B |
| C, Bioresearch Svc<br>MARTIN, Keith, Ph.D., CPT, MS | 03 | 68C8Z |
| NCOIC<br>ROBERTS, Teresa, SFC (PCS Apr 94) | E7 | 91T30R |
| NCOIC<br>HERNANDEZ, Carlos, SFC | E7 | 92B |
| Vet Animal Spec<br>FULK, Terry, CPL (PCS Apr 94) | E4 | 91T20 |
| Vet Animal Spec<br>CARREIRO, Frank, SPC (PCS Dec 93) | E4 | 91T20 |
| Lab Tech<br>CARTAGENA, Edward, SPC (ETS May 94) | E4 | 92B |
| Lab Tech<br>WIEGAND, Neil SPC | E4 | 92B |
| Lab Tech<br>POOL, Rosemary PFC | E3 | 92B |

| Description | Rank | MOS |
|---|---|---|
| C, Biochemistry Svc<br>MOORE, Katherine H., Ph.D. | GS13 | 0601 |
| Med Tech<br>MATEJ, Louis A., B.S., M.T. | GS11 | 0644 |
| Med Tech<br>WRIGHT, James R., B.A., M.T. | GS11 | 0644 |
| Med Tech<br>STYNER, M. J., B.S., M.T. | GS11 | 0644 |
| Med Tech<br>THOMSON-ARCHER, Kelly, B.S., M.T. | GS11 | 0644 |
| Statistician Medical<br>PATIENCE, Troy H., B.S. | GS9 | 1530 |
| Edit Asst/Steno<br>WHITTEN, Nancy J., B.A. | GS9 | 1087 |
| Sec/Steno<br>HOUGH, Eugenia R. | GS6 | 0318 |
| Maintenance Worker<br>KAEO, Curtis | WG7 | 4749 |
| Med Tech<br>CRISS-TILLOTSON, Mary "Tilly"* (Dec 92 - Sep 94) | GS9 | 0644 |

* Breast Cancer Program Employee

## Funding FY 94

| | |
|---|---|
| MEDCASE Equipment | $207,142 |
| Capital Equipment | 57,737 |
| Civilian Salaries | 380,955 |
| Military Salaries | 539.869 |
| Consumable Supplies | 146.571 |
| Contractual Services | 3,200 |
| TDY - departmental | 4,619 |
| TDY - presentations | 31.320 |
| | $1,371,413 |

EXTRAMURAL FUNDING:

| | |
|---|---|
| Federal sources: | |
| Tri-service Nursing | $809,794 |
| NIH (thru Duke Univ) | $862,558 |
| USAMRDC | $112,000 |
| Non-federal sources: | |
| FACT | $110,000 |
| PC3 | $18,000 |
| HMJ | $4,500 |
| TOTAL EXTRAMURAL FUNDING: | $1,916,852 |
| **GRAND TOTAL** | **$3,298,295** |

3. Progress

During FY 94, there were 464 active protocols that received administrative and/or technical support during the year. Of these, 303 are presently ongoing; 11 are in a suspended status, 96 were completed; and 54 were terminated. The principal investigator distribution was as follows: 364 staff protocols (includes 165 group oncology protocols); 53 resident protocols, 38 fellow protocols, 2 intern protocols, and 7 other category protocols. There were 180 new protocols and 11 reactivated protocols.

There were 96 publications in nationally recognized journals and 149 presentations at regional or national medical association meetings.

4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 26
81 protocols involving 69 residents
114 protocols involving 27 fellows

5. Other training programs supported by DCI:

US Army Nurse Anesthetists Course: 1 Protocol involving 5 nurses

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) 2/75th Ranger Battalion: 1

6. Other protocols supported:

1 USDA protocol
2 Fort Ord protocols
3 Active duty student protocols
1 Sierra Army Depot 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

# COMMITTEE MEMBERS (CONT'D)

## Human Use Committee

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

Chief or delegated representative of:

Department of Clinical Investigation
Department of Nursing
Department of Radiology
Department of Ministry and Pastoral Care
Pharmacy Service
Social Work Service
Public Affairs Office
Center Judge Advocate
Non-institutional member

# COMMITTEE MEMBERS (CONT'D)

## Animal Use Committee

Chairman
Chief, Clinical Investigation
COL Dan C. Moore, 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 1994:

LTC Cecil A. Dorsett, DC, Resident, Oral and Maxillofacial Surgery for his research protocol: *Influence of the Prophylactic Administration of Intravenous Ondansetron on Post-Operative Nausea and Vomiting and Length of Stay in the Post-Anesthesia Care Unit*

Other nominees were:

*D-Dimer Concentration Before and After A Single Subtherapeutic Dose of Urokinase* by CPT James E.S. Parker, MC, Resident, Dept Radiology

*Hemodilution: Effects of Saline Infusion on Hematologic Parameters in Healthy Euvolemic Subjects* by CPT Kurt Grathwohl, MC, Resident, Internal Medicine

*Changing Physician Prescribing Patterns* by MAJ Eric J. Rube., MC, Resident, Department of Family Practice.

*Comparison of Three Corneal Trephines for Use in Therapeutic Penetrating Keratoplasties for Large Corneal Perforations* by MAJ John D. Ng, MC, Resident, Ophthalmology

*Familial Hemiplegic Migraine: Nystagmus and Cerebellar Atrophy Correlated with Chromosomal Localization* by CPT Michael A. Elliott, MC, Resident, Neurology

## FELLOW'S RESEARCH AWARD

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

Recipient of this award for 1994:

CPT Barrett L. Chapin, MC, Fellow, Endocrinology Fellowship for his research protocol: *Vitamin D Malabsorption and Secondary Hyperparathyroidism Following Biliopancreatic Diversion*

Other nominees were:

*Impact of an Interruption in Family Practice Residency Training on In-training Examination Scores: A Comparison of Two Military Resident Groups* by LTC David D. Ellis, MC Fellow, Faculty Development Fellowship

*The Effect of Atrial Natriuretic Factor on the Ex--Vivo Cotyledon Model* by MAJ Glenn Markenson, MC Fellow, Maternal/Fetal Medicine Fellowship

*Total Lung Capacity Measured by a Medical Diagnostic Imaging Support System* by CPT Lisa Zacher, MC, Fellow, Pulmonary/Critical Care Fellowship

*Clinical Significance of Lymphoid Aggregates in Bone Marrow* by MAJ James S. Hu, MC, Fellow, Hematology/Oncology Fellowship

# PUBLICATIONS

## FISCAL YEAR 94

### ACTIVE DUTY STUDENT

| | |
|---|---|
| Martin D, Day J, Ward G, Carter E, Chesrown S | Effects of Breathing a Normoxic Helium Mixture on Exercise Tolerance of Patients with Cystic Fibrosis. Pediatric Pulmonology 18: 206-210, 1994. |

### FORT ORD, CALIFORNIA

| | |
|---|---|
| Carter PM, Coburn TC, Luszczak M | The Cost Effectiveness of Cervical Cytology During Pregnancy. Journal Amer Board Fam Prac 6(6): 537-45, 1993. |

### FORT WAINRIGHT, ALASKA

| | |
|---|---|
| Levine ME, Milliron AN, Duffy LK | Diurnal and Seasonal Rhythms of Melatonin Cortisol and Testosterone in Interior Alaska. Artic Medical Research 53(53): 25-34, 1994. |

### U.S. ARMY RESERVES

| | |
|---|---|
| Guller G, Reeves RL, Inoue S, Patience TH | Effect of Gallopamil SR on Heart and Circulation in Patients with Essential Hypertension. Herz Kreislauf 26: 132-136, 1994. |

### DEPARTMENT OF CLINICAL INVESTIGATION

| | |
|---|---|
| Moore DC | Body Image and Eating Behavior in Adolescents. J Amer College Nutrition 12(5): 505-510, 1993. |
| Moore KH, Dunbar BS, Bousfield GR, Ward DN | Initial Characterization of Equine Inhibin. Biology of Reproduction 51: 1994. |
| Plymate SR, Swerdloff R | Androgens, Insulin, and Coronary Heart Disease. Annals Internal Medicine, 1994. |
| Powers EM, Hernandez C, Boutros SN, Harper BG | Biocidal Efficacy of a Flocculating Emergency Water Purification Tablet. Applied Environ Microbiol 60(7): 2316-2323, 1994. |

### DEPARTMENT OF DENTISTRY

| | |
|---|---|
| Weber CR, Griffin J | Evaluation of Dexamethasone for Reducing Post-operative Edema and Inflammatory Response After Orthognathic Surgery. J Oral Maxillofacial Surgery 52: 35-39, 1994. |

### DEPARTMENT OF EMERGENCY MEDICINE

| | |
|---|---|
| Burke TF, Rusnak RA, Hurley WT, Champaux A | Refusal to Walk in a 12-Month-Old Child: A Clinical-Pathological Case Conference. Amer J Emergency Medicine 12(4): 472-76, 1994. |
| Casey PD, Youngberg R | Scapholunate Dissociation: A Practical Approach for the Emergency Physician. J Emerg Med 11(6): 701-707, 1993. |
| Herrera J, Gendron BP, Rice MM | Military Emergency Medicine Physician Assistants. Mil Med 159(3): 241-242, 1994. |
| Plotkin FR, Burke TF | Vertex Epidural Hematoma: A Diagnostic Challenge. Annal Emerg Med 24(2): 312-315, 1994. |
| Rice MM | Emergency Department Patients Leaving Against Medical Advice (AMA). Foresight 29: 1-8, 94. |
| Rice MM | Preface by guest editor COL Matthew M. Rice, MC, Dir. Emer Med, Clin North American 11(4): ix, 93. |
| Rice MM | Military Systems IN: Prehospital Systems and Medical Oversight, Second Edition; formerly titled EMS Medical Directors' Handbook; AE Keuhl, Editor, Mosby Lifeline. 1994. |

## DEPARTMENT OF FAMILY PRACTICE

| | |
|---|---|
| Ellis DD | Association of an Interruption in Family Practice Residency Training with Change in In-Training Examination Scores: A Comparison of Two Military Resident Groups, 1994. |
| Kugler JP | A symptom-oriented approach IN Handbook of Sports Medicine. Handbook of Sports Medicine: 222-230, 1993. |
| O'Connor FG, Marlowe SM | Low Back Pain in Military Basic Trainees, A Pilot Study. Spine 18(10): 1351-1354, 1993. |
| Runkle GP | The Vasectomy Reversal Experience: A qualitative investigation using life histories, 1994. |
| Runkle GP, Zaloznik AJ | Malignant Melanoma. American Family Physician 49(1): 91-98, 1994. |

## DEPARTMENT OF MEDICINE, ALLERGY/IMMUNIZATION SERVICE

| | |
|---|---|
| Douglas DM, Andrade WP, Brown JS | Biphasic Systemic Anaphylaxis: An Inpatient Study and Outpatient Study. J Allergy Clin Immunology 93(6): 977-985, 1994. |
| Douglas DM, Ward L, Brown JS | Nonsteroidal Antiinflammatory Drug Desensitization Using Flurbiprofen (Ansaid). Annals of Allergy 71(5): 459-460, 1993. |

## DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

| | |
|---|---|
| Nottestad SY, Mascette AM | Nitroglycerin-Induced Heparin Resistance: Absence of Interaction at Clinically Relevant Doses. Military Medicine 159(8): 569-571, 1994. |

## DEPARTMENT OF MEDICINE, DERMATOLOGY SERVICE

| | |
|---|---|
| Vanderhooft SL, Stephan MJ, Sybert GP | Severe Skin Erosions and Scalp Infections in AEC Syndrome. Pediatric Dermatology 10(4): 334-340, 93. |

## DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

| | |
|---|---|
| Chapin BL, Jones RE | Infertility IN Endocrinology Secrets: 249-253, 1994. |
| Gibson CA, Jones RE | Endocrine Abnormalities in Human Immunodeficiency Virus Infection. Jour US Army Med Dept, Fall, 1994. |
| Jones RE | Adrenal Insufficiency IN Endocrinology Secrets: 156-160, 1994. |
| Jones RE, Plymate SR | Synthesis of Docosahexaenoyl Coenzyme A in Human Spermatozoa. Journal of Andrology 14(6): 428-432, 1993. |
| Reed HL, Quesada M, Hesslink RL, D'Alesandro MM, Christopherson RJ, Turner BV, Young BA | Changes in Serum Triiodothyronine (T3) Kinetics and Hepatic Type I 5'-Deiodinase Activity of Cold Exposed Swine. Journal of Endocrinology, 1994. |
| Reed HL, Quesada M, Hesslink RL, D'Alesandro MM, Hays MT, Christopherson RJ, Turner BV, Young BA | Changes in Serum Triiodothyronine Kinetics and Hepatic Type I 5' -deiodinase Activity of Cold-exposed Swine. Am J Physiol 266(5): E786-795, 1994. |
| Tuttle RM, Loop S, Jones RE, Meikle AW, Ostenson RC, Plymate SR | Effect of 5-a-Reductase Inhibition and Dexamethasone Administratin on the Growth Characteristics and Intratumor Androgen Levels of the Human Prostate Cancer Cell Line PC-3. The Prostate 24: 229-236, 1994. |

## DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE

| | |
|---|---|
| Morris JT, Konkol KA, Longfield RN | Chemical Meningitis Following Epidural Methylprednisolone Injection. Infections in Medicine 11(6): 439-40, 1994. |

| | |
|---|---|
| Morris JT, Longfield RN | Sarcoidosis and ELISA for Borrelia burgdorferi. Southern Medical Journal 87(6): 590-91, 1994. |

**DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE**

| | |
|---|---|
| Landry FJ, Pangaro L, Kroenke K, Lucey C, Herbers J | A Controlled Trial of a Seminar to Improve Medical Student Attitudes, Knowledge, and Use of the Medical Literature. Journal of Gen Internal Med 9: 436-439, 1994. |
| Salerno SM, Zugibe FT | Calcium Channel Antagonists: What do the Second-Generation Agents have to Offer?. Postgrad Med 95(5): 51, 1994. |

**DEPARTMENT OF MEDICINE, INTENSIVE CARE UNIT**

| | |
|---|---|
| Low LL | Non-Operative Management of Gastric performation Secondary to Cardiopulmonary Resuscitation. Intensive Care Medicine, 1994. |

**DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE**

| | |
|---|---|
| McBurney JW, Teiken PJ, Moon MR | Propofol for Treating Status Epilepticus. Journla of Epilepsy 7(1): 21-22, 1994. |

**DEPARTMENT OF MEDICINE, PULMONARY SERVICE**

| | |
|---|---|
| Roth BJ, Cragen WH | Serum-Effusion Albumin Gradient in Separation of Transudative and Exudative Pleural Effusions. Chest 3(105): 974-75, 1994. |
| Thompson JW, Irvine TW, Grathwohl KW, Roth BJ | Misuse of Metered-Dose Inhalers in Hospitalized Patients. Chest 105: 715-717, 1994. |

**DEPARTMENT OF NURSING**

| | |
|---|---|
| Mygrant BI, Renaud MT | Infant Botulism. Heart Lung 23(2): 164-168, 1994. |

**DEPARTMENT OF OBSTETRICS/GYNECOLOGY**

| | |
|---|---|
| Adams MM, Harlass FE, Sarno AP, Read JA, Rawlings JS | Antenatal Hospitalization Among Enlisted Servicewomen, 1987-1990. Obstetrics and Gynecology 84(1): 35-39, 1994. |
| Kopelman JN, Maslow AS | Fetal Testing. Infert Reprod Med Clinics NA, 1994. |

**DEPARTMENT OF PEDIATRICS**

| | |
|---|---|
| Carter ER | Albuterol Administered by Metered-Dose Inhaler and Spacer to Young Children with Wheezing. Arch Pediatr Adolesc Med 148: 1352-1353, 1994. |
| Carter ER, Stecenko AA, Pollock BH, Jaeger MJ | Evaluation of the Interrupter Technique for the Use of Assessing Airway Obstruction in Children. Pediataric Pulmonology 17: 211-17, 1994. |
| Fisher RG, Kelly P, Krober MS, Weir MR, Jones R | Necrotic Arachnidism. Western Journal of Medicine 160(6): 570-572, 1994. |
| Kinney JB, Schofield TD, Kawabori I, Budd SE, Bauman JM | Quantitative Perfusion Imaging Assessing Acquired Discrete Peripheral Pulmonary Artery Stenosis. Journal of Nuclear Medicine 34(11): 1995-1997, 1993. |
| Stephan MJ, Brooks KL, Moore DC, Coll EJ, Goho K | Hypothalamic Hamartoma in Oral-Facial-Digital Syndrome Type VI (Varadi Syndrome). Amer Journal Medical Genetics 51: 131-136, 1994. |

**PHYSICAL MEDICINE AND REHABILITATION SERVICE, PHYSICAL THERAPY**

| | |
|---|---|
| Dettori JR, Pearson BD, Basmania CJ, Lednar WM | Early Ankle Mobilization, Part 1: The Immediate Effect on Acute, Lateral Ankle Sprains (A Randomized Clinical Trial). Military Medicine 159(1): 15, 1994. |

| | |
|---|---|
| Dettori JR, Basmania CJ | Early Ankle Mobilization, Part 2: A One Year Follow-up of Acute, Lateral Ankle Sprains (A Randomized Clinical Trial). Military Medicine 159(1): 20, 1994. |

**PREVENTIVE MEDICINE SERVICE**

| | |
|---|---|
| Kirchner DB, Gaydos JC, Battigelli MC | Combustion Products of Propellants and Ammunition. IN Textbook of Military Medicine. R. Zajtchuk, DP Jenkins, Bellamy FR (eds), Office of The Surgeon General, Dept Army, Falls Church, VA, 1993. |

**DEPARTMENT OF RADIOLOGY**

| | |
|---|---|
| Barohn RJ, Bazan C, Timmons JH, Tegeler C | Bilateral Diabetic Thigh Muscle Infarction. J Neuroimaging 4: 43-44, 1994. |
| Bauman JM | Scintigraphic Diagnosis of Inflammatory Processes IN Fundamentals of Diagnostic Radiology: 1220-1233, 1994. |
| Bender GN, Lane JD, Tsuchida AM, Clark JA | Small Bowel Biopsy Through an Enteroclysis Catheter to Augment Findings at Enteroclysis and Hypotonic Duodenography. Radiology 191(2): 573-575, 1994. |
| Bender GN, Myers MA, Reichle JL, Tsuchida AM, Peller T, Jackson F, Malcolm B | Nonendoscopic Gastric Mucosal Biopsy to Augment Double-Contrast Upper Gastrointestinal Barium Examination. Radiology 191(1): 285-87, 1994. |
| Burke TF, Guertler AT, Timmons J | A Comparison of Sinus X-Rays with Computed Tomography in Acute Sinusitis. Academic Emergency Medicine 1: 235-239, 1994. |
| Casey PD, Youngberg R | Scapholunate Dissociation: A Practical Approach for the Emergency Physician. J Emerg Med 11: 701-707, 1993. |
| Cook JF, Hansen M, Francoise JJ, Leckie RG, Smith DV | Digital Imaging Access Library. SPIE Proceedings 2165: 709-713, 1994. |
| Do-Dai DD, Bender GN | Decompression of Colonic Pseudo-Obstruction With A Tri-Component Coaxial System (TAS) Under Fluoroscopy. Radiology, 1994. |
| Do-Dai DD, Stracener JC, Youngberg RA | Oblique Sagittal MRI of Anterior Cruciate Ligament. J Comp Assisted Tomography 18(1): 160-62, 1994. |
| Myers MA, Youngberg RA, Bauman JM | Congenital Absence of the Major Salivary Glands and Impaired Lacrimal Secretion in a Child: Case Report and Review of Literature. J Am Dental Assoc 125: 210-212, 1994. |
| Romlein JR, Weiser JC, Willis CE, Smith S, Buinther R, Quillin E | Transitioning Process of a Film-based Radiology Department to Direct Digital Imaging. SPIE Proceedings 2165: 850-857, 1994. |
| Smith DV, Smith S, Bender GN, Carter JR | PACS: Design and Evaluation. SPIE Proceedings 2165: 538-555, 1994. |
| Timmons JH | Central Nervous System Scintigraphy IN Fundamentals of Diagnostic Radiology: 1234-1242, 1994. |
| Wilson DL, Smith DV | Distribution of Workload Over the Working Day in a PACS SPIE Proceedings: PACS: Design and evaluation. SPIE Proceedings 2165: 2165-2183, 1994. |
| Yackovich FH, Bender GN, Tsuchida AM | Peri- and Episiotomy Scar Endometrioma Imaged by CT and Sector Endoluminal Ultrasound. Clinical Radiology, 1994. |

## DEPARTMENT OF SURGERY, ANESTHESIA SERVICE

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| Burgess FW, Anderson DM, Colonna D, Cavanaugh DG | Thoracic Epidural Analgesia With Bupivacaine and Fentanyl for Postoperative Thoracotomy Pain. Jour Cardio Vasc Anesthesia 8(4): 420-424, 1994. |

## DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SURGERY SERVICE

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| Chismire KJ, Witkop G | The Association of the Blepharophimosis Syndrome With Optic Nerve Hypoplasia, Angle Dysgenesis and Glaucoma. AJO, 1994. |
| Chismire KJ, Witkop GS | Optic Nerve Hypoplasia and Angle Dysgenesis in a Patient With Bleparophimosis Syndrome. American J Ophthalmology 117(5): 676-77, 1994. |
| Morris MR, Morris WJ | Esthesioneuroblastoma: An Unusual Presentation Complicating the Surgical Approach. Am J Otolaryngol 15(3): 231-236, 1994. |
| Perkins JA, Moore KH, Canonico DM, Morris MR | Neuropeptide Levels in the Nasal Secretion and Nasal Mucosa of Patients with Chronic Sinusitis and Nasal Polyposis. American J Rhinology 8(3): 117-21, 1994. |
| Souliere CR, Quigley SM, Langman AW | Cochlear Implants in Children. Otolaryngol Clin North Am 27(3): 533-56, 1994. |

## DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE

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|---|---|
| Allshouse MA, Holland RM, Lilly JR | The Toupet Fundoplication for Gastroesophageal Reflux in Infants and Children. Pediatric Surg Residents Conf 14(5): 37, 1993. |
| Healy JT | Effect of Peritoneal and Gastric Irrigation with Ozone Saline on Arterial Blood Gases and Venous Blood Gases. Life Sciences 53: 1867-1872, 1993. |
| Holland RM, Lilly JR | Treatment of Choledochal Cyst in Kuala Lumpur. Pediatr Surg Int 9(1): 156, 1994. |
| Holland RM, Stewart BA, Karrer FM, Lilly JR | Endorectal Pullthrough Operation for Massive Rectal Trauma in Children. J Pediatr Surg 27(4): 570, 1993. |
| Tran LP, Velanovich V, Kaufmann CR | Familial Multiple Glomus Tumors: Report of a Pedigree and Literature Review. Ann Plast Surg 32(1): 89-91, 1994. |
| Velanovich V | Preoperative Laboratory Screening based on Age, Gender, and Concomitant Medical Diseases. Surgery 115(1): 56-61, 1994. |
| Williard WC, Brennan MF | Primary Retroperitonial Masses IN Surgical Decision Making, 1993. |

## DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

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|---|---|
| Bigham WJ, Mazzoli RA, Flanagan JC | Lid Management and Avoidance of Complications of Lid Reconstruction After Tumor Excision. Man Avoid Comp Eyelid Surgery, 1994. |
| Fannin LA, Thrasher JB, Mader TH | Valsalva Retinopathy Associated With Transectal Prostate Biopsy. British Journal Urology, 1994. |
| Flanagan JC, Mazzoli RA, Bigham WJ | Reconstruction of the Lower Lid. Surg Eyelid Orbit Lacrimal Sys, 1993. |
| Hansen EA, Stein EA, Mader TH, Mazzoli RA | Spitting Cobra Ophthalmia in United Nations Forces in Somalia. American J Ophthalmology 117(5): 671, 1994. |
| Karren KA, Mader TH | Wound Adhesives for Eyelid Retraction. Amer Journal of Ophthalmology 117(1): 109, 1994. |

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| Mader TH, Aragones, Chandler, Hazlehurst, Heier, Kingham, Stein | Ocular and Ocular Adnexal Injuries Treated by US Military Ophthalmologists During Operations Desert Shield and Desert Storm. Ophthalmology, 1993. |
| Mader TH, Aragones JV, Chandler AC, Hazelhurst JA, Heier J, Kingham JD, Stein E | Ocular and Ocular Adnexal Injuries Treated by United States Military Ophthalmologists During Operations Desert Shield and Desert Storm. Ophthalmology 100(10): 1462-1467, 93. |
| Taravella MJ, Stulting RD, Mader TH, Weisentahl RW, Forstot SL, Underwood LD | Calcific Band Keratopathy Associated With the Use of Topical Steroid-Phosphate Preparations. Arch Ophthalmol 112: 608-613, 1994. |

**DEPARTMENT OF SURGERY, ORTHOPEDIC SERVICE**

| | |
|---|---|
| Dietz J | Cervical Spine Injuries IN Handbook of Sports Medicine, 1993. |
| Jones DE | Ligament Injuries Associated with Diatal Radius Fractures. Orthopaedic Transactions, 1994. |
| Schofield TD, Pitcher JD, Youngberg R | Synovial Chondromatosis Simulating Neoplastic Degeneration of Osteochondroma: Findings on MRI and CT. Skeletal Radiol 23(2): 99-102, 1994. |
| Taylor G | Thoracic and Lumbar Injuries IN Handbook of Sports Medicine, 1993. |

**DEPARTMENT OF SURGERY, PODIATRY SERVICE**

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|---|---|
| Chen JB, Youngberg RA, Jones RO | Enhanced Magnetic Resonance Imaging of the First Metatarsal After a Bunionectomy. J Amer Podiatric Med Assoc 84(9): 406-408, 1994. |
| Neary MT, Jones RO, Sunshein K, VanManen W, Youngberg R | Avascular Necrosis of the First Metatarsal Head Following Austin Osteotomy: A Follow-Up Study. Journal of Foot & Ankle Surg 32(5): 530-535, 1993. |
| Wilkinson SV, Neary MT, Jones RO, Sunshein KF | The Neuroanatomy of Pain. Clin Podiatric Med & Surg 11(1): 1-13, 1994. |

**DEPARTMENT OF SURGERY, UROLOGY SERVICE**

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| Fox CW, Vaccaro JA, Kiesling VJ, Brown SL, Belville WD | Determination of Indwelling Ureteral Stent Patency: Comparison of Standard Contrast and Nuclear Cystography, and Lasix Renography. Urology 43(4): 442-445, 1994. |
| Schwartz BF, Wettlaufer JN, Bagg MD, Thrasher JB | The Normal Flora of the Human Epididymis. Infections Urology 7(6): 168, 1994. |

# PRESENTATIONS

## FISCAL YEAR 94

### I CORP SURGEON

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| Lombardi WM, Grediagin A, Lancaster A | Prenatal Programs for Pregnant Soldiers. | Health Promotion Conference, Baltimore, MD, June 94. |

### BEHAVIORAL HEALTH SCIENCE DIVISION, CLINICAL PSYCHOLOGY SERVICE

| | | |
|---|---|---|
| Sorenson RC, Luzio RC, Mangione-Lambie MG | Perceived Seriousness, Recommended and Expected Organizational Response, and Effects of "Bystander" and "Direct" Sexual Harassment. | 23rd International Congress of Applied Psychology, Madrid, Spain, July 94. |

### DEPARTMENT OF CLINICAL INVESTIGATION

| | | |
|---|---|---|
| Moore DC | Euthyroid Hashimoto Thyroiditis with elevated TSH - should we treat?. | Annual Uniformed Services Meeting, Seattle, USA, March 94. |
| Stewart RS, Shoemaker L, Watling DA | Use of Direct Digoxigenin-duTP Incororation to Increase Detection Sensitivity of PCR Assays for Common Sexually Transmitted Disease. | 93rd General Meeting, American Society of Microbiology, Las Vegas, NV, May 94. |

### DEPARTMENT OF EMERGENCY MEDICINE

| | | |
|---|---|---|
| Brantner RD | The Randomized Use of Helium-Oxygen Mixture for the Administration of Bronchodilator Therapy in the Treatment of Bronchial Asthma. | Society for Academic Emergency Medicine, Washington, DC, May 94. |
| Burke TF, Pace SA, Mack SR, Coward B, Carter Pl | The Use of Intravenous Morphine for Early Pain Relief in Patients with Acute Abdominal Pain. | Society for Academic Emergency Medicine, Washington, DC, May 94. |
| Noonburg GE | The Utility of Sinus Tenderness As A Diagnostic Sign of Acute Sinusitis. | The American Academy of Otolaryngology-Head and Neck Surgery, Minneapolis, MN, October 93. |
| Rudman NT | Clinicopathologic Case Conference on Cocaine Induced Rhabdomyolysis. | Society for Academic Emergency Medicien Annual Meeting, Washington, DC, May 94. |

### DEPARTMENT OF FAMILY PRACTICE

| | | |
|---|---|---|
| Adams RA | Severe Post-partum Preeclampsia, presenting five days after a term delivery. | Uniformed Services Academy of Family Physicians Conference, Norfolk, USA, March 94. |
| Bradshaw D, MacDonald D, Ellis D, Runkle G, Kugler JP | USAFP Research Workshop. | XIX Annual Scientific Assemply of USAFP, Norfolk, USA, March 94. |
| Marlowe S | Response to Low Back Pain/Exercises in Basic Trainees. | Uniformed Services Academy of Family Physicians Conference, Norfolk, USA, March 94. |

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| Murray M | Toxic shock-like syndrome in a patient with systemic lupus erythematosis. | Uniformed Services Academy of Family Physicians Conference, Norfolk, USA, March 94. |
| Rubel E | Changing Physician Prescribing Patterns. | Uniformed Services Academy of Family Physicians Conference, Norfolk, USA, March 94. |
| Tuggy M | Uterine-vesicular rupture during trial of labor. | Uniformed Services Academy of Family Physicians Conference, Norfolk, USA, March 94. |

**DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE**

| | | |
|---|---|---|
| Cambier P, Stajduhar K, Powell D, Gomez R, Moore J | Improved Safety of Transcatheter Vascular Occlusion Utilizing A New Retrievable Coil Device. | 1993 Army College of Physicians, Orlando, FL, November 93. |
| Cambier PA, Stajduhar KC, Powell DA, Gomez RR, Virmani R, Farb AJ, Moore JW | Improved Safety of Transcatheter Vascular Occlusion Utilizing a New Retrievable Coil Device. | American College of Cardiology, 43rd Annual Scientific Session, Atlanta, GA, March 94. |
| Mascette AM, Stajduhar KC, Cambier PA, Paris JA | Cardiac Dimensions in Female Athletes. | Army Chapter, American College of Physicians Meeting, Orlando, FL, November 93. |
| Mullin J | Localizing Accessory Pathways Using the Pre-excitation Index: A Useful Tool for the Radiofrequency Era. | Army Chapter, American College of Physicians, Orlando, FL, November 93. |
| Mullin JC, Klein LS, Zipes DP, Miles WM | Localizing the Ventricular Insertion Site of Accessory Pathways Using the Preexcitation Index. | 15th Annual Sci Session of the North Amer Soc of Pacing and Electrophysiology, Nashville, TN, May 94. |
| Peele M, et al | c-Myc Proto-oncogene Expression in Human Carotid Atheroma: Analysis by Expression PCR (RT-PCR). | Army Chapter, American College of Physicians, Orlando, FL, November 93. |

**DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE**

| | | |
|---|---|---|
| Chapin BL, Case B, Lemar HJ, Ng JD, Knodel D, Carter P | Vitamin D Malabsorption and Secondary Hyperparathyroidism Following Biliopancreatic Diversion. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Gibson CA | Hyperinsulinemia, Ovarian, and Adrenal Anrogens in Obese Patients With Disorders of Ovulation. | 1993 Army College of Physician's Meeting, Orlando, FL, November 93. |
| Lemar HJ, Tuttle RM, Mazzaferri EL | The Role of Clinical Assessment in the Management of Indeterminant Fine Needle Aspirations of Thyroid Nodules. | 1993 Army College of Physicians' Meeting, Orlando, FL, November 93. |
| Reed HL, Gisbson CA, Bunner DL, Lance J, Moon MR, Jones RE | Time-Course of Changes in Thyroxine and Thyrotropin Following 131I Therapy for Thyrotoxicosis: Predictors of Metabolic Hypothyroidism. | 1993 Army College of Physician's Meeting, Orlando, FL, November 93. |
| Tuttle RM, Budd S, Patience TH | Effects of Pretreatment With PTU on Efficacy of 131I Treatment in Patients With Graves Disease. | American Thyroid Asspcoation, Tampa, FL, November 93. |

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| Tuttle RM, Jhiang SM, Gomez RR, Peele ME, Mazzaferri EL | Detection of the Papillary Thyroid Cancer (PTC) Oncogene Transcript in Paraffin Embedded Papillary Thyroid Cancer. | 1993 Army Chapter of the American College of Physician's Meeting, Tampa, FL, November 93. |
| Weber SE, Timmons J, Tuttle RM | The Effect of Thyroid Hormone Supporession on Thyroid Nodules Found to be Indeterminate by Fine Needle Aspiration. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |

**DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE**

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| Small EJ, Srinivas S, Rearden TP | Effect of Prior Radiotherapy on Response and Survival in Hormone-Refractory Prostate Cancer Patients. | Proceeding of the American Society of Clinical Oncology, March 94. |
| Small EJ, Srinivas S, Rearden TP | Doxorubicin and Dose-Escalated Cyclophosphamide With Granulocyte Colony Stimulating Factor (G-CSF) Support for Hormone-Refractory Prostate Cancer. | Proceedings of the American Society of Clinical Oncology, March 94. |

**DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE**

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| Place RJ, Cavanaugh D | Thoracoplasty for Giant Bullous Emphysema. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Place RJ, Cavanaugh D | Computed Tomography to Diagnosis Percardial Rupture. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Place RJ, Simmang CL | Preoperative Computed Tomography from Primary Colorectal Carcinoma. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Place RJ, Simmang CL | Non-Hereditary Multiple Polyposis Syndrome. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |

**DEPARTMENT OF MEDICINE, INTENSIVE CARE UNIT**

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|---|---|---|
| Low LL | The Effect of Arterial Lines on Blood Drawing Practices and Costs in Intensive Care Units. | Army Annual American College of Physicians Meeting, Orlando, USA, November 93. |
| Low LL | The Ethics of Costs in the ICU. | Army Annual American College of Physicians Meeting, Orlando, USA, November 93. |

**DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE**

| | | |
|---|---|---|
| Clayton WL | Gogi Aphasia Following a Right Occipital. | 13th Annual Neurology AMEDD Conference, Tacoma, USA, November 93. |
| Clayton WL | Pharmacologic Therapy of Headache. | Washington State Society of Hospital Pharmacists, USA, November 93. |
| Clayton WL | Treatment in Headache. | Grand Rounds, Bremerton Naval Hospital, Bremerton, USA, October 93. |

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| Elliot MA | Case Report: Familial Hemiplegic Migraine. | 118th Annual Meeting of the Neurological Association, Baltimore, MD, October 93. |
| Elliott MA | Ocular Motility Findings in a Familial Syndrome of Hemiplegic Migraine and Nystagmus. | 13th Annual Neurology AMEDD Conference, Tacoma, USA, November 93. |
| Elliott MA, Peroutka SJ, Welch S, May EF | A Familial Syndrome of Hemiplegic Migraine and Nystagmus: Chromosomal Defect Localization and Ocular Motility Characteristics. | North American Neuro-Opthalmology Society Meeting, Durango, CO, February 94. |
| Flynn FG | The Neurology of Attention Deficit Disorder in Children and Adults. | 13th Annual AMEDD Neurology Conference, Tacoma, USA, November 93. |
| Flynn FG | Non-Cognitive Neurobehavioral Changes in Dementia. | Neurology Grand Rounds, Texas Tech University, Lubbock, USA, October 93. |
| Flynn FG | The Neurology of ADD. | Psychiatry Grand Rounds, Walter Reed Army Medical Center, Washington, USA, December 93. |
| Hassid EI | A Case of Language Dysfunction Associated with Cerebellar Infarction. | American Society of Neurorehabilitation Annual Meeting, Minneapolis, MN, June 94. |
| Kesting L | Abulic State Associated With Caudate Stroke. | 14th Annual AMEDD Conference, Bethesda, MD, November 94. |

**DEPARTMENT OF MEDICINE, PULMONARY SERVICE**

| | | |
|---|---|---|
| Keenan LM, Ficke RF, Walsh ES, Young-McCaughan S, Kirk LC, Mueller JP, Cragun WH | Do Not Resuscitate: Do Not Provide Care?. | 59th Annual International Scientific Assembly, Orlando, FL, October 93. |
| Keenan LM, Willadsen D, Roth B | Malignant Fibrous Tumor of the Pleura With Unusual Metastasis. | ACCP International Meeting, October 93. |
| Murray TR, Kidd P, Rhagu G, Crawford S | Diagnosis of Recurrent B-cell Lymphoma Using Immunocytometric Analysis of Bronchoalveolar Lavage Fluid. | ACCP International Meeting, October 93. |
| Pike J, Zacher L | Bronchoalveolar Lavage in the Evaluation of Leukemia in Prolymphocytic Transformation. | ACCP International Meeting, October 93. |
| Pina J, Meyer C, Clagett C, Horan M | Does Sampling of the Lung With the Guidance of High Resolution Computed Tomography Improve the Yield of Bronchoalveolar Lavage?. | ACP Army Regional Meeting, November 93. |
| Roth BJ, Meyer C, Smith D, Cragun WH | Computed Chest Radiography at Madigan Army Medical Center. | Army ACP Regional Meeting, November 93. |
| Zacher L, Keenan LM, Pike J, Meyer C | Computed Tomography in the Evaluation of Hemoptysis. | ACP Army Regional Meeting, November 93. |

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| Zacher LL, Bryceland P, Smith D, Cragun WH | Total Lung Capacity Measured by a Medical Diagnostic Imaging Support System Planimetric Method. | American Lung Association/American Thoracic Society International Conference, Boston, MA, May 94. |
| Zacher LL, Keenan LM, Pike JD, Meyer CA | HRCT in the Evaluation of Hemoptysis. | ACP Army Regional Meeting, Orlando, USA, November 93. |
| Zacher LL, Pike JD | Diagnosis of Leukemia Infiltrates by Bronchial Lavage in Prolymphocytic Leukemia. | ACCP, Orlando, USA, October 93. |

**DEPARTMENT OF NURSING**

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| DePaul D | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Western Perinatal Research Meeting, Banff, Alberta, Canada, February 94. |
| DePaul D | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | 8th Annual Nursing Research Conference, Oahu, USA, September 94. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Perinatal Care Conference, Vancouver, Canada, November 93. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | 6th Annual Karen A Reider Nursing Research Poster Session, San Antonio, USA, November 93. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Pacific Lutheran University, Tacoma, USA, February 94. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Pacific Northwest Association of Neonatal Nurses Membership Meeting, Seattle, USA, February 94. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | University of Washington, Seattle, USA, March 94. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Phyllis J. Verhonick Army Nursing Research Conference, Denver, USA, June 94. |
| Renaud MT | The Effects of a Modified Care Environment on the growth and Development of High Risk Infants. | Pacific Northwest Association of Neonatal Nurses, Seatac, USA, July 94. |
| Renaud MT | The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants. | Research in Women's Health & Perinatal Nursing, Seattle, USA, July 94. |
| Webb S | Physiologic Responses to Exogenous Surfactant: Nursing Interventions. | Washington State Nurses Association Annual Meeting, Spokane, WA, June 93. |

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| **NUTRITION CARE DIVISION** | | |
| Grediagin A | The Effect of Exercise Intensity on Body Composition Change in Untrained Moderately Overfat Women. | The American Dietetic Association Meeting, Anaheim, Obesity, October 93. |
| **DEPARTMENT OF OBSTETRICS/GYNECOLOGY** | | |
| Armstrong AY | Hyperinsulinemia, Ovarian, and Adrenal Androgens in Obese Patients with Disorders of Ovulation. | Conference on Ovulation Induction: Basic Science and Clinical Advances, Palm Beach, FL, January 94. |
| Armstrong AY | Hyperinsulinemia, Ovarian, and Adrenal Androgens in Obese Patients With Disorders of Ovulation. | Armed Forces District of the American College of Obstetricians and Gynecologists, November 93. |
| Armstrong AY | Weight and Reproductive Function. | National Medical Association, Orlando, FL, July 94. |
| Foos CC | A Strategy to Decrease the Time and Cost of Diagnosis of Ectopic Pregnancy. | Armed Forces District, Seattle, USA, November 93. |
| Letterie GS, Morgenstern LL | Training Residents to Critically Evaluate Clinical Literature: The Journal Club. | Annual Meeting of the Council on Resident Education in Obstetrics and Gynecology, Nashville, USA, March 94. |
| Macedonia C, Maslow AS, Rasband W | Three-Dimensional Ultrasonographic Imaging Using a Continuous Acquisition Process. | American College of OB/GYN, Armed Forces District, Seattle, USA, October 93. |
| Magelssen DJ | Women's Health Maintenance Examination in the 21st Century. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Magelssen DJ | The Role of the Gynecologist in Women's Health Promotion. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Magelssen DJ, Teague G, Rodzak J | A Case Report of Hysteroscopic Resection of Placenta Increta. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Markenson GR | Use of Color Flow Doppler in Obstetrics. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Markenson GR, Bayliss PM, Boley TS, Maslow AJ | The Dual Perfusion Cotyledon Model; Is a Control Needed?. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Markenson GR, Boley TJ, Maslow AS | Optimizing the Dual Perfusion Cotyledon Model: Is Estradiol and Progesterone Necessary?. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Markenson GR, Gilliam L | A Case Report of a Bilateral Tubal Gestation. | American College of OB/GYN, Armed Forces District, Seattle, USA, November 93. |
| Maslow AS | Diagnostic Uses of Perinatal Ultrasound. | 28th Annual Uniformed Services Pediatric Seminar, Seattle, USA, March 94. |

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| Maslow AS, Joseph R, West P | The Effect of Intravenous Magnesium Sulfate on Maternal/Serum Calcium and Parathyroid Levels in Premature Labor and Preeclampsia. | American College of OB/GYN, Armed Forces District, Seattle, USA, October 93. |
| Maslow AS, Kopelman J | Maternal-Fetal Medicine Quiz. | American College of OB/GYN, Armed Forces District, Seattle, USA, October 93. |
| Maslow AS, Rearden K, Gatlin BD | Anti-Parietal Cell Antibody Induced Macrocytic Anemia in a Pregnant Patient. | American College of OB/GYN, Armed Forces District, Seattle, USA, October 93. |
| Morgenstern LL | A History of the Armed Forces District of the American College of Obstetricians and Gynecologists. | American College of OB/GYN, Seattle, USA, October 93. |
| Napolitano PG, Soisson AP | Vaginal 5-Fluorouracil Therapy in the Management of Human Papilloma Virus Infections of the Cervix Uteri: A preliminary report. | 32nd Annual Armed Forces District Meeting of the American College of OB/GYN, Seattle, USA, November 93. |

**DEPARTMENT OF PATHOLOGY, BLOOD BANK**

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| Gomez R | From the Pathologist: Specimen Processing, PIN, and Gleason's Grading. | Symposium on Prostate Cancer, Madigan AMC and American Cancer Society, Tacoma, USA, March 94. |
| Gomez R | Improved Safety of Transcatheter Vascular Occlusion Utilizing a New Retrievable Coil Device. | American College of Cardiology, Orlando, USA, March 94. |
| Gomez R, Crothers B | Screening for Cervical Human Papillomavirus among College Women. | Society for Adolescent Medicine, Los Angeles, USA, March 94. |

**DEPARTMENT OF PEDIATRICS**

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| Leander DJ, Stephan MJ | Facilitating Parental Grief: Practical Principles for Physicians and Nurses. | Presented at the USPS, Seattle, USA, March 94. |
| Rawlings JB, Rawlings VB, Read JA, Adams MM | Race-Specific Occurrence of Low Birth Weight in Relation to Interpregnancy Interval. | American Academy of Pediatrics Annual Meeting, Washington, DC, November 93. |
| Stafford EM, Stewart RS, Teague G, Michel TJ, Crothers BA, Patience TH, Moore DC | Screening for cervical human papilloma virus among college women. | Annual Meeting of Society for Adolescent Medicine, Boston, USA, March 94. |
| Stafford EM, Stewart RS, Teague G, Michel TJ, Crothers BA, Patience TH, Moore DC | Screening for Cervical Human Papillomavirus Among College Women. | Society of Adolescent Medicine, Los Angeles, CA, March 94. |
| Walker WO, Kelly PC, Clingan T, Peterson WR, Amstutz K, Greefkens S | So many children, so little time. | Workshop at 28th Annual Uniformed Services Pediatric Seminar, Seattle, USA, March 94. |

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| Winkler T, Perkins J, Jensen R, Stephan MJ | Severe Subglottic and Distal Tracheal Deviation in Mucolipidosis type II (I-Cell disease). | American Academy of Otolaryngology/Head and Neck Surgery Meeting, Minneapolis, USA, October 93. |

**DEPARTMENT OF RADIOLOGY**

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| Carter J, Parsons DM, Kim Y | Quality Control Assessment for a Medical Diagnostic Imaging Support System. | Radiological Society North America, 79th Scientific Assembly and Annual Meeting, Chicago, USA, November 93. |
| Carter MS, Weiser JC, Frederick MD, Donnelly MS, Tucker JE | Relationship Between Entrance Exposure and S Number for Chest Radiographs Acquired with Computed Radiography. | Radiological Society of North America, 79th Scientific Assembly and Annual Meet, Chicago, USA, November 93. |
| Crocker J | Correlation of Antral Nodularity with H. Pylori Gastritis. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Do-Dai DD | MR Imaging of the Hip with a Shoulder Surface Coil in the Offcoronal Plane. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Do-Dai DD, Bender GN | Decompression of Acute Colonic Pseudo-Obstruction With A Tricomponent Coaxial System Under Fluoroscopy. | Radiologyucal Society of North America, 79th Annual Meeting, Chicago, IL, November 93. |
| Dorsay T | Cine MR in Temporomandibular Joint Evaluation. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Ho VB | Soft Tissue Technetium Methylene Diphosphonate Uptake: Frequency and Clinical Significance. | 79th Annual Meeting of the Radiological Society of North America, Chicago, IL, November 93. |
| Ho VB, Chuang SH | A Modern Approach to Congenital Metabolic and Neurodegenerative Diseases of Childhood. | Singapore, January 94. |
| Ho VB, McGuckin JF, Smergel EM, Kubachi J, Villafana T | Diagnostic Dilemma: MR Imaging versus CT for Evaluation of an Intraorbital Wooden Foreign Body in the Setting of Acute Penetrating Trauma. | Radiological Society North American, 79th Scientific Assembly and Annual Meeting, Chicago, USA, November 93. |
| Ho VB, McGuckin JF, Villafana T | MR Imaging of the Orbits in Penetrating Gunshot Injury. | Radiological Society North America, 79th Scientific Assembly and Annual Meeting, Chicago, USA, November 93. |
| Ho VB, Rovira MJ | MR Imaging and MR Venography of the Posterior Fossa Dural Sinuses: Normal Anatomy and Variants. | Radiological Society North America, 79th Scientific Assembly and Annual Meeting, Chicago, USA, November 93. |
| Mansfield LT | Utility of the Knee MRI Examinations: Comparing Orthopedic and Non-orthopedic Referrals. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Morissette J | The Podiatric Foot: The Digital Imaging Approach. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |

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| Parker JES | Computer Based system for Tracking of Vascular and Interventional Procedures. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Parker JES | Computer Program for Documentation of Vascular and Interventional Procedures and Biopsies. | Society of Cardiovascular and Interventional Radiology, 19th Annual Meeting, San Diego, CA, March 94. |
| Reichle J | Nasogastric Biopsy Augmenting Double Contrast UGI Studies. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Smith DV | PACS Refresher Course: PACS in a New Hospital: Madigan Experience. Foreign Body in the Setting of Acute Penetrating Trauma. | Radiological Society North America, 79th Scientific Assembly and Annual Meeting, Chicago, USA, November 93. |
| Timmons JH | Radiologic Imaging in the Staging of Prostate Cancer: Current Appraisal, Diagnosis and Management of Prostate Cancer, An Update. | ACS/Madigan/Multicare Combined Conference, Tacoma, USA, January 94. |
| Wade L | MR Evaluation of Silicone Breast Implants. | Washington-Oregon Radiology Residents Research Symposium, USA, April 94. |
| Yackovich FH, Ho VB | Von Hippel Lindau-Disease: A Radiologic-Pathologic Spectrum. | Radiological Society of North American, 79th Annual Meeting, Chicago, IL, November 93. |

**DEPARTMENT OF SURGERY, ANESTHESIA SERVICE**

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| Bolt SL, Bettencourt J, Gordon J | Long 1: Use of Laser Doppler Flowmetry to Measure Variation in Hippocampal Blood Flow During Fluid-Percussion Brain Injury in the Rat. | Neuroscience Meeting, Washington, USA, October 93. |
| Burgess FW, Plyman ML, Helman JD | The Ideal Epidural Bupivacaine Concentration for Postoperative Analgesia. | Annual Meeting of the American Society of Anesthesiologists, Washington, DC, October 93. |
| Gridley GD, Mancuso JJ, Caldwell S | Does Terbutaline Affect the Epinephrine Epidural Test Dose?. | Society for Obstetric and Perinatology Annual Meeting, Philadelphia, PA, May 94. |
| Polaner DM | Pediatric fiberoptic laryngoscopy. | American Society of Anesthesiologists Annual Meeting, New Orleans, USA, October 93. |

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| Armstrong PL, Kim D | Data Management Systems in Surgery: Surgical Information System. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Chismire KJ | I Had Laser But I Don't Know What It Was For. | Summer Seminar, JCAHPO and The American Academy of Ophthalmology, Seattle, USA, August 94. |

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| Chismire KJ | Glaucoma 2001, Update on AAO's Newest Public Service Project. | Washington State Medical Annual Meeting, Wenatchee, USA, September 94. |
| Gutfreund CA | Dermatomyositis: An Otolaryngologic Presentation. | American Academy of Otolaryngology - Head and Neck Surgery, San Diego, CA, September 94. |
| Schwartz RE, Wong ML, Moore DW, Larson TL | Facial Nerve Schwannoma Extending From the Geniculate Ganglion to the Parotid Gland: A Case Report. | American Academy of Otolaryngology - Head and Neck Surgery, San Diego, CA, September 94. |

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| Bevill K, Andersen CA, Tollefson D | Primary Aortoenteric Fistula. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Carter PL | Gastroduodenal Artery Aneurysms: An Experience with Four Cases. | Annual Clinical Congress, ACS, San Francisco, USA, October 93. |
| Case B, Deaconson T | Gastroduodenal Artery Aneurysmal Disease: Experience with Five Cases. | Washington State Chapter Meeting Annual Clinical Congress, American College Surg, San Francisco, USA, October 93. |
| Chung M, Offner PJ | The effects of inhaled nitric oxide on right heart function in sepsis. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Holland RM | Biliary Atresia. | Presented to Pediatrics Department, Madigan AMC, Tacoma, USA, October 93. |
| Holland RM | Thoracoscopic Resection of an Esophageal Duplication Cyst. | American College of Surgeons, 79th Clinical Congress, San Francisco, USA, October 93. |
| Place RJ, Simmang CL | Laparoscopic Right Colectomy is Safe and Cost Effective in a Military Teaching Center. | Gary Wratten Surgical Symposium, Tacoma, USA, April 94. |
| Simmang CL | Laparoscopic Right Colectomy: Is It Safe and Cost Effective in a Miliatry Medical Teaching Center? | Northwest Society of Colon and Rectal Surgeons, Sun Valley, ID, August 94. |

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| Fannin LA, Mazzoli RA | Ocular Injuries from Merchandise Display Hooks. | Current Concepts in Ocular Trauma, USUHS Walter Reed Army Med Center, Bethesda, USA, March 94. |
| Fannin LA, Parmley VC, Gee BT, Mader TH, Truxal AR, Varga JH, Hansen CS, Powell DA | Efficacy of Gram Negative Endotoxin Monoclonal Antibody as Adjunctive Therapy for Gram Negative Endophthalmitis in Rabbits. | Association for Research in Vision and Ophthalmology, Sarasota, FL, May 94. |

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| Gee BT, Mazzoli RA | Management of Massive Orbital Trauma. | Current Concepts in Ocular Trauma, USUHS Walter Reed Army Med Center, Bethesda, USA, March 94. |
| Hadley S, Mazzoli RA | Point Blank Facial Gunshot Wounds. | Current Concepts in Ocular Trauma, USUHS Walter Reed Army Med Center, Bethesda, USA, March 94. |
| Mader TH, Bagian JP, Charles J, Taylor G, Gibson CR, Caputo M, Meeham RT | Intraocular Pressure In Astronauts During Space Shuttle Operations. | American Academy of Ophthalmology, Chicago, IL, November 93. |
| Mazzoli RA | Orbital Trauma. | USUHS Tri-Service Ophthalmic Trauma Course, Bethesda, USA, May 94. |
| Ng JD, Mazzoli RA | Combined Hydroxyapatite/Dermis-Fat Graft in Complex Socket Reconstruction. | Current Concepts in Ocular Trauma, USUHS Walter Reed Army Med Center, Bethesda, USA, March 94. |
| Ng JD, Nekola M, Parmley VC, Richardson M, Mader TH | Comparison of Three Corneal Trephines for Use in Therapeutic Penetrating Keratoplasties for Large Corneal Perforations. | Association for Research in Vision and Ophthalmology, Sarasota, FL, May 94. |

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| Schwartz BJ | Small cell carcinoma of the prostate. | AUA Western Section, Seattle, USA, August 94. |
| Schwartz BJ, Thrasher JB, Bagg MD, Wettlaufer JN | The Normal Flora of the Human Epididymis. | Western Section of the American Urological Association, Palm Desert, CA, November 93. |
| Thrasher JB, Gingrich JR, Paulson DF | Surgery for Renal Cell Carcinoma: A Contemporary Review of Presentation, Complications, and Outcome of 356 Cases. | Western Section American Urological Association, 69th Annual Meeting, Palm Desert, CA, November 93. |
| Thrasher JB, Kreder KJ | Suprapubic Tube Tract Dilation Using the Otis Urethrotome. | Western Section American Urological Associatioin, 69th Annual Meeting, Palm Desert, CA, November 93. |

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| Rearden TP #94/058 | O | SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary | 566 |
| Ellis RB #94/120 | O | SWOG 9332: Phase III Trial of Adriamycin Versus Taxol Versus Taxol Plus Adriamycin Plus G-CSF in Metatastatic Breast Cancer, Intergroup | 567 |
| Vallion RD #94/121 | O | SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell... | 568 |
| Rearden TP #94/122 | O | SWOG 9339: Evaluation of Topotecan in Esophageal Carcinoma, Phase II | 569 |
| Hu JSD #94/123 | O | SWOG 9348: Evaluation of the Standard DCNU/DTIC/Cisplatin/Tamoxifen Regiment in Disseminated Malignant Melanoma, Phase II | 570 |
| Ellis RB #94/163 | O | SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study | 571 |
| **University of Washington Neuro-Oncology Group** | | | **572** |
| Davidson H #88/017 | C | UWNG 87-01: Phase II Study of TPDCFH for Recurrent Malignant Brain Tumor | 573 |
| Davidson H #89/013 | O | UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System | 574 |

# DETAIL SHEETS FOR PROTOCOLS

# ACTIVE DUTY STUDENT DETACHMENT, HSC

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/126 | **Status:** Completed |
| **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 Cost:** | $0.00 | **OMA 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: Thirty subjects were studied. Statistical analysis showed no statistically significant difference in the effect of body position in ventricular arrhythmia in coronary artery patients in the CCU.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/136 | **Status:** On-going |
| **Title:** Electrical Stimulation and Diabetic Foot Skin Perfusion | | |
| **Start Date:** 08/05/94 | **Est. Completion Date:** | |
| **Department:** Student Detachment, HSC | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Darlene M. Gilcreast, AN | | |
| **Associate Investigators:** | Nancy A. Stotts, RN, Ed.D. | |
| **Key Words:** diabetes, foot, electrical stimulation | | |

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

Study Objective: To examine the effect of electrical stimulation on skin perfusion of the feet in persons with diabetes who either have or are at risk for developing foot ulcers.

Technical Approach: Persons attending the Diabetic Foot Clinic at the California College of Podiatry Medicine will be invited to participate in the study. Persons consenting and meeting the entry criteria will have their oral temperature taken to rule out systemic infection.

For those in Wagner Grade 0 (intact skin), a table of random numbers will be used to select the study extremity. For those in Wagner Grades 1 and 2, the foot with the ulcer will be utilized. After baseline measurements is recorded, the electrical stimulation treatment will be initiated for a duration of 30 minutes. During the treatment, the nurse will monitor the patient and transcutaneous oxygen level readings will be taken and recorded at baseline, 15 minutes, 30 minutes and (end of treatment), and 60 minutes (30 minutes after the end of electrical stimulation). At the conclusion of the treatment, electrodes will be removed, wounds will be redressed as they were when the subject came in for study.

Double data entry will be used for computer analysis. A repeated measures, one-way analysis of variance will be performed to answer he primary hypothesis. Alpha is preset at 0.05. For each secondary hypothesis, a repeated measures, two-way analysis of variance will be performed. If significant, post-hoc analyses will be performed to examine the nature of the difference using the Scheffe test.

Progress: No subjects have been enrolled yet.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/082 | **Status:** On-going |
| **Title:** The Effects of Rotating Shifts on Nurses in Military Hospitals | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Jun 94 | |
| **Department:** Student Detachment, HSC | **Facility:** MAMC | |
| **Principal Investigator:** Poso ML | | |
| **Associate Investigators:** | Diane D. Stajduhar, RN | |
| **Key Words:** nurses:military, rotating shifts | | |

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

Study Objective: Describe the effects of shift work on nursing related to self reported accidents/medication errors in military hospitals.

Technical Approach: This study will use a survey to sample 300 nurse from 3 military medical centers. The relationship between rotating shifts and accidents/near accidents will be described through a self reported questionnaire.

Relationships between rotating shifts, sleep, and accidents will be computed using coerrelational formulas. The SPSS/PC+ statistical software will be used to compute data. A decision tree by Knapp will be sued to determine data analysis. Chi square analysis of the associations of nominal data and T-test analysis of interval data is planned. Since some questions have multiple parts, more than one analysis may be used for a single question.

Progress: The survey has not yet been done at MAMC.

# DETAIL SHEETS FOR PROTOCOLS

# FORT LEWIS, SPECIAL FORCES

# Detail Summary Sheet

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

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

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

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

Progress: Three animals were used in one session.

# DETAIL SHEETS FOR PROTOCOLS

# FORT ORD MEDDAC

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/055 **Status:** Completed

**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: 350 infant breast-feeding surveys sent out and collected over the last 18 months. PI left the service. No further information available.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/170 | **Status:** Terminated |
| **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 | | |

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|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative 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.

Progress: PI was reassigned before protocol was implemented.

# DETAIL SHEETS FOR PROTOCOLS

# I CORP SURGEON

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/047 **Status:** Completed

**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 Corps 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 subject'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. To date, all testing and analysis have been completed. Data was presented at the 6th Annual Health Promotion Conference.

# DETAIL SHEETS FOR PROTOCOLS

# MADIGAN CANCER INSITITUTE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/043 **Status:** Suspended

**Title:** An Integrated Breast Cancer Information System

**Start Date:** 12/17/93 **Est. Completion Date:** Mar 98

**Department:** MCI **Facility:** MAMC

**Principal Investigator:** Charlene P. Holt, M.D.

**Associate Investigators:**
Anne Schur
MAJ James H. Timmons, MC
MAJ Richard R. Gomez, MC
MAJ Steven S. Wilson, MC
Mark Hinchee
COL Sankaran S. Babu, MC
COL Preston L. Carter, MC
MAJ Donald V. Smith, MC
MAJ Mark E. Robson, MC
Sam Stevens, Ph.D.
Barbara Fecht

**Key Words:** Cancer:breast, information systems

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

Study Objective: To develop an integrated breast cancer information and education system.

Technical Approach: System components developed under this proposal include: an integrated breast cancer information model and demographic database; an interactive, multi-media kiosk for gathering and maintaining patient demographics and educating the patient about risk factors, diagnosis and treatment approaches; standards-based reporting tools for radiology, pathology, surgery, oncology and radiation therapy that oriented specifically to breast cancer; and a breast cancer data retrieval tool for researchers. The system will be developed over a four year period in a site-independent fashion, enabling it to be acquired and used by other medical centers and hospitals throughout the United States.

Progress: Project on hold pending funding.

# DETAIL SHEETS FOR PROTOCOLS

# SIERRA ARMY DEPOT

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/173 | **Status:** Completed |
| **Title:** Experiencing the Phenomenon of Fatigue | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** Feb 94 | |
| **Department:** Sierra Army Depot | **Facility:** MAMC | |
| **Principal Investigator**: Bingham MO | | |
| **Associate Investigators:** None | | |
| **Key Words:** fatigue, soldiers | | |

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

Study Objective: The primary objective of this research of lived experiences is to gain a greater understanding of fatigue as it is perceived by individuals.

Technical Approach: This descriptive study consists of engaging discussions with individual active duty soldiers to gain personal descriptions reflecting the meaning of the situation of experiencing fatigue. Volunteer soldiers will be interviewed individually and asked questions to explore their feelings and perceptions of fatigue. The interviews will be approximately 45 minutes to 2 hours long and will be taped. These tapes will be transcribed at a later time and studies to determine and identify patterns of the responses. There are no proposed conclusions.

Progress: Protocol completed. No other information could be obtained because PI could not be located.

# DETAIL SHEETS FOR PROTOCOLS

# U. S. DEPARTMENT OF AGRICULTURE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **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:** USDA | **Facility:** MAMC | |
| **Principal Investigator:** Betty Jo Burri, Ph.D. | | |
| **Associate Investigators:** | Andrew J. Clifford, Ph.D. | |
| **Key Words:** liver,vitamin A,isotope technique | | |

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|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | **OMA** $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 retinol acetate) of the study. In a pilot study to test the time course of equilibration and elimination of the analogs, three volunteers from each group will be given the cocktails as stated and blood samples taken a 5, 8, and 30 hr, and at 2, 3, 4, 5, 15 days and every 30 days thereafter. This blood would be collected in addition to the blood required for the regular study (pre ingestion, 5 hr, and days 8, 29, and 30). The study will compare three promising new methods for assessing vitamin A status to serum retinol, and to vitamin A liver stores measured by deuterated analogs and by vitamin A2. The new methods tested will be free- and transthyretin-bound holo-retinol binding protein as determined by HPLC, erythrocyte transglutaminase levels, and goblet cell abnormalities. Addendum (Oct 91): All of the testing was done except for tests of the vitamin A2. Vitamin A2 proved to be very difficult to purify, so it was never actually given to the subjects. Then two significant things happened a supply of high quality vitamin A2, approved for human use, was obtained, and it was found that the tetradeuterated analog may interfere with the vitamin A2 test, even when these analogs are given 8 days apart. It is now recommended that the doses of vitamin A2 and other analogs be separated by at least 30 days. Therefore in this study, the vitamin cocktails will be given on day 1 and day 30, with blood draws added as appropriate.

Progress: Study not able to proceed due to delay in construction of metabolic research unit and need to complete a previous metabolic study. Enrollment stands at 54 subjects.

# DETAIL SHEETS FOR PROTOCOLS

# BEHAVIORAL SCIENCES DIVISION, CLINICAL PSYCHOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/108 **Status:** On-going

**Title:** Medical Cost Offset and Clinical Effectiveness of a Behavioral Treatment Program for Medical Resource Overutilizers

**Start Date:** 05/06/94 **Est. Completion Date:** Jan 96

**Department:** BSD, Clin Psychology Svc **Facility:** MAMC

**Principal Investigator:** LTC John B. Powell, MS

**Associate Investigators:**
Ellsworth C
Brencick M
Thorndyke Am

**Key Words:** medical resources, overuse, treatment program

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

Study Objective: This study will identify patients with few physical findings and whose presenting complaints are produced or aggravated by psychological, rather than organic, factors, and to provide a brief, effective behavioral intervention designed to ameliorate these psychological factors.

Technical Approach: This study will follow 100 patients referred from the Adult Primary Care Center, and compare them to 100 non-treatment controls. Patients will complete a four week behavioral program consisting of four weekly classes and four individual biofeedback sessions. medical usage for the six months prior to treatment (including outpatient visits, inpatient treatment, laboratory procedures, and pharmacy costs) will be compared to usage for the six months post treatment.

Progress: A treatment program has been initiate and a system for handling referrals from APCC worked out. To date, 15 patients have completed treatment and 7 are in a no-treatment (6 month delay) category.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/025 | **Status:** Completed |
| **Title:** Sexual Harassment: Attitudes and Actions | | |
| **Start Date:** 12/04/92 | **Est. Completion Date:** Mar 93 | |
| **Department:** BSD, Clinical Psychology Svc | **Facility:** MAMC | |
| **Principal Investigator:** CPT Mary G. Lambie, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Sexual Harrassment, attitudes, actions | | |

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|---|---|---|---|---|
| **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 were collected from 410 active duty soldiers attending sexual harassment training. The results indicate that perceptions of sexual harassment vary based on the attitudes, gender, rank, and race of the perceiver. In turn, these differing perceptions influence the actions that are recommended for sexual harassment incidents.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF CLINICAL INVESTIGATION

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/005 | **Status:** Completed |
| **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:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** CPT Stephen Caldwell, VC | | |
| **Associate Investigators:** None | | |
| **Key Words:** cancer,alimentary tract,nasogastaric 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 , 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: No training was performed on this protocol in FY 94.

It was replaced in February 94 by MAMC #94/084.

# Detail Summary Sheet

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

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

**Start Date:** 02/09/94 **Est. Completion Date:** Feb 97

**Department:** DCI **Facility:** MAMC

**Principal Investigator:** CPT Stephen Caldwell, VC

**Associate Investigators:** None

**Key Words:** Training:vet techs,Animal Study

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $200.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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

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

Progress: This protocol updates and replaces MAMC 92/005. One animal was used during FY 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/079 **Status:** On-going

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

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

**Department:** DCI **Facility:** MAMC

**Principal Investigator:** CPT Rodger K. Martin, MS

**Associate Investigators:**
MAJ Katherine S. Foley, MC
MAJ Jerome N. Kopelman, MC
CPT Rodger K. Martin, MS
LTC Arthur S. Maslow, MC
MAJ Glenn R. Markenson, MC

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

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

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

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

Progress: Total RNA has been isolated from three different sites (amnion, chorion, and decidual plate) from 3 normal and 4 pre-eclamptic placentas. DNA primers and probes have been developed for the detection of atrial natriuretic factor (ANF) and neutral endopeptidase (NEP) by the polymerase chain reaction (PCR). From total RNA isolated from pre-eclamptic placentas and subsequently treated with RNase-free, DNase I, a correctly-sized beta-2 microglobulin product has been amplified by RNA-PCR as a control for the quality and the integrity of the RNA. A NEP product of 534 base pairs has been amplified from these same samples. Preliminary data by two rounds of RNA-PCR for ANF suggested that it may be expressed in chorion but at low levels. Total RNA from normal and pre-eclamptic samples analyzed by hybridization with a digoxigenin-labeled probe for ANF was negative. These preliminary studies will be repeated and extended to additional samples.

# Detail Summary Sheet

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

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

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

**Department:** DCI **Facility:** MAMC

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

**Associate Investigators:** None

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

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

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

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

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

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

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

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

Progress: All equipment required to commence this protocol has not been received. Preliminary work on cell lines is being done.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** COL Dan C. Moore, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** thyroid size,adolescents | | |

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | **OMA** $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=365). No data analysis has occurred.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 90/091 **Status:** On-going

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

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

**Department:** DCI **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:** 07/01/94 |
|---|---|---|---|---|

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

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

Progress: Two patients have been studied One of the patients has died of the underlying disease. The other patient is responding well to treatment.

# Detail Summary Sheet

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

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $1200.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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

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

Progress: Original attempts to immortalize cell line from subjects failed. Work is being done on improving this technique before requesting more patient blood. RFLP analysis is underway in normal controls for the PTH gene.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** DCI **Facility:** MAMC

**Principal Investigator:** COL Dan C. Moore, MC

**Associate Investigators:** CPT Katherine H. Moore, MS
MAJ Jim Hansen, MC

**Key Words:** precocious puberty,LH:isoforms

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $1843.00 | **Periodic Review:** | // |
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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 has been completed. Further work has been delayed due to the inability to find a reproducible LH bioassay.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/048 | **Status:** On-going |

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

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| **Start Date:** 04/03/92 | **Est. Completion Date:** |
| **Department:** DCI | **Facility:** MAMC |
| **Principal Investigator:** COL Dan C. Moore, MC | |
| **Associate Investigators:** | MAJ Robert A. Newman, MC |
| **Key Words:** delayed maturation and growth, boys, oxandrin | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 08/05/94 |

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 94 **Protocol No.:** 94/048 **Status:** Suspended

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

**Start Date:** 12/06/93 **Est. Completion Date:** Sep 97

**Department:** DCI **Facility:** MAMC

**Principal Investigator:** CPT Katherine H. Moore, MS

**Associate Investigators:** MAJ Kenneth A. Bertram, MC
MAJ Richard R. Gomez, MC

**Key Words:** Cancer: breast, SHBG, mRNA,Animal Study

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 05/26/95 |
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Study Objective: The goal of this study is to further examine paraffin embedded breast tumor tissue for the expression of SHBG mRNA and to determine if breast cancer cells are producing alternate transcripts of SHBG, and begin characterizing those transcripts.

Technical Approach: The relatively new technique of polymerase chain reaction (PCR) *in-situ* hybridization will be modified for the study of breast tissue sections attached to glass slides. This technique will allow the determination of the association between cells expressing SHBG and tumor cells.

We will construct a cDNA library from ZR-75-1 mRNA, and sequence the clones containing SHBG and related inserts. Peptides will be synthesized based on the predicted amino acid sequence of the SHBG clones, and monoclonal antibodies produced. These monoclonal antibodies will be used for immunoprecipitation to determine if the alternate transcripts of SHBG in breast cancer cells are producing protein.

Progress: Study has not been implemented. The initial request for funding for this protocol was not approved. The protocol will be submitted for other funding at a later date.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** CPT Katherine H. Moore, MS | | |
| **Associate Investigators:** Louis A. Matej, B.S. | MAJ Kenneth A. Bertram, MC | |
| **Key Words:** SHBG, breast cancer | | |

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

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: The goal of this study is to determine if mRNA for SHBG is expressed in breast cancer cell lines and tumor tissue. Two estrogen receptor positive cell lines were used, ZR-75-1 and MCF-7; and one estrogen negative cell line, MDA-MB-231. SHBG mRNA was detected by Northern blot analysis in ZR-75-1 cells using a 500 bp 3' SHBG cDNA probe. Using the polymerase chain (PCR), SHBG mRNA was detected in ZR-75-1, MCF-7, and MDA-MB-231 cells. In addition, SHBG protein production from these 3 breast cancer cell lines was detected by the method of immunoprecipitation using an affinity purified SHBG antibody. Evidence of alternative splicing of the SHBG mRNA in breast cancer cells was found. This was confirmed by DNA sequencing. In the alternate transcripts, exon 7 is deleted, accompanied by a point deletion in the beginning of exon 8, which results in a new stop codon and a shortened transcript Amplification of RNA extracted from breast tissue by PCR revealed the presence of SHBG mRNA in breast tumor tissue and in tissue from women who have had cancer.

SHBG mRNA was not detected in histologically normal tissue. In addition, 18 of 30 tumor samples analyzed did not contain detectable SHBG mRNA (by PCR). The presence of functional steroid receptors does not seem to be associated with SHBG mRNA expression.

Presented at the 19th Army Science Conference, Jun 94.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/127 | **Status:** On-going |
| **Title:** Biofeed back for Pain: A Multipractitioner Outcome Study | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Jun 96 | |
| **Department:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** LTC Richard A. Sherman, MS | | |
| **Associate Investigators:** | Antje F. W. Goeken, Psy.D. | |
| **Key Words:** Pain:biofeedback, low back pain, orofacial pain | | |

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

Study Objective: 1) To determine the short term effectiveness of biofeedback interventions for chronic musculoskeletal low back pain and muscle related orofacial pain through a multipractitioner outcome study.;2) To test the proposed design, data gathering techniques, and scientist-practitioner interactions.

Technical Approach: Licensed clinicians who are members of the AAPB and meet its practice criteria will sequentially enter all patients who meet the diagnostic and other entrance requirements. The providers will fill out one form which details their usual treatment for the disorder. Very careful diagnostic categorization for each patient according to specified, standard criteria will be required. After treatment, each practitioner will send a form for each patient indicating deviations of the individual subject's treatment from their usual practice, number of sessions, objective outcome measures, and details of how the diagnosis was made. Each patient will keep a home log of pain and other factors for two weeks during the pre-treatment evaluation period, at the end of treatment, three-month after treatment, and six months after treatment. The patients will send their logs directly to the investigators. One thousand subjects with each disorder will be enrolled.

Progress: Nineteen subjects have been enrolled at MAMC

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/109 | **Status:** Terminated |
| **Title:** Effect of Presurgical Pain Control Training on Recovery | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Jun 96 | |
| **Department:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** LTC Richard A. Sherman, MS | | |
| **Associate Investigators:** | Antje F. W. Goeken, Psy.D. | |
| **Key Words:** Pain:presurgical control | | |

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

Study Objective: a. The overall objective of the study is to determine the impact on the recoveries of typical patients about to receive a typical mix of surgical procedures who will be housed on typical surgical wards of (1) pre-surgical training in the use of biofeedback and relaxation techniques to control stress and pain and (2) additional education about surgical procedures beyond that normally provided on a typical surgical ward.

Technical Approach: The effects of pre-surgical education (beyond that normally provided) combined with relaxation - stress/pain control training on post-surgical recovery among adult patients receiving specified surgical procedures will be evaluated. The effects of this intervention on several types of surgical procedures including cervical and lumbar fusion, laminectomy, external fixators, scoliosis correction, hip replacement, amputation, wrist and ankle fusion, ACL reconstruction, colon resection, aortic aneurysm repair, and knee replacement will be evaluated on soldiers and adult dependent/retired subjects at several facilities. ; Baseline levels for each outcome measure will be established for each procedure for each type of patient prior to initiation of the training intervention program. Objective outcome measures will include number of days in the hospital; time to each stage of recovery (e.g. ambulation, self-care); amount of pain medication; and number, type and severity of complications. Pre and post surgical measures of anxiety, knowledge of the procedure and recovery, focus of control, and psychological profile will also be established. The pain control program will consist of individual training in the standard muscle tension-awareness training procedures including muscle tension biofeedback and relaxation-pain avoidance procedures commonly used prior to painful dental and surgical procedures combined with individualized education about the procedure and recovery process.; A placebo group will be run after the intervention group has been completed in order to determine the effects attention and beliefs have on the outcomes. The ward staff evaluating the patients will not know when the placebo intervention have replaced the active ones. Three power analyses indicate that approximately 200 people will be required per group.

Progress: This protocol originated at FAMC. The pilot phase of the study is being completed at FAMC The protocol was not funded, and, therefore, is being terminated at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/001 **Status:** Terminated

**Title:** Comparison of Two PCR-based Detection Methods for Chlamydia trachomatis With the Standard EIA Method in Symptomatic and Asymptomatic Males

**Start Date:** 11/05/93 **Est. Completion Date:** Nov 93

**Department:** DCI **Facility:** MAMC

**Principal Investigator:** MAJ Robert S. Stewart, MS

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

**Key Words:** Chlamydia trachomatis, polymerase chain reaction, enzyme immunoassay

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $600.00 | **Periodic Review:** | // |
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Study Objective: To determine the relative sensitivity and specificity levels of three different in vitro methods used for the detection of the presence of Chlamydia trachomatis.

Technical Approach: Sixty to 90 males presenting to the troop medical clinic for NGU will be tested for evidence of Chlamydia trachomatis infection. Urethral swabs will be collected from all volunteers and submitted in the standard manner to the Microbiology Service, Department of Pathology, for enzyme immunoassay (EIA) analysis. Urine will be collected from all volunteers and submitted to the Department of Clinical Investigation for genetic analysis. Cells will be collected from the urine by centrifugation and processed according to manufacturer's directions. Chlamydia DNA will be extracted and amplified by polymerase chain reaction (PCR). PCR product will be analyzed by two techniques: as commercial solid phase detection system (Amplicor by Roche Diagnostic Systems) and a research grade Southern blot analysis system utilizing direct incorporation of digoxigenin-dUTP and chemiluminescence. The "gold standard" will be a consensus of two of the three assays. Discrepant results for the Amplicor method will be reanalyzed by the manufacturer utilizing amplification of another Chlamydia gene region.

Progress: This study was put in a suspended status when Dr. Stewart departed MAMC, with the thought that a new microbiologist might want to pursue the study. The protocol has been reviewed by the staff at MAMC. A decision was made to terminate the study since several very similar studies have been done that elucidated the information that the investigators sought.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/074 **Status:** Suspended

**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:** DCI **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:** | // |
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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 Urea plasma urealyticum and the remaining fraction was stored frozen at -20 degrees Centigrade. These stored samples will be thawed, processed for DNA extraction, and analyzed by PCR for organisms not previously suspected, including HPV, HSV, HIV, C. trachomatis, T. vaginalis, and M. genitalium.

Progress: PI has departed. His replacement has not decided whether to resume study.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/075 | **Status:** Terminated |
| **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:** DCI | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Robert S. Stewart, MS | | |
| **Associate Investigators:** | Troy H. Patience, B.S. | |
| **Key Words:** breast biopsy, DNA, hormone receptors | | |

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| **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: Funding for this study was not approved..

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/073 | **Status:** Suspended |
| **Title:** Molecular Microbiology Assay Development | | |
| **Start Date:** 06/05/92 | **Est. Completion Date:** Indef. | |
| **Department:** DCI | **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 Cost:** | **OMA** $0.00 | **Periodic Review:** // |
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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 original PI has departed. His replacement will decide whether to continue.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 92/034 | **Status:** Completed |

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

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| **Start Date:** 01/03/92 | **Est. Completion Date:** |
| **Department:** DCI | **Facility:** MAMC |

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

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

**Key Words:** protein, growth factor, prostate carcinoma

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| **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: In the previous year, the principal investigator attempted to gain data using Western blot analysis and specific IGFBP antibody probes, labeled with a biotinylated fluorescing. This process was used on protein extracted from conditioned media collected from prostate cancer cell lines and stored frozen at -70° C. It proved to be a very finicky procedure and yielded no reliable results after 6 months. The conditioned media that were prepared were exhausted and the stored frozen cells were found to contain mycoplasma and could not be used. The results yielded by the ligand blot procedure were sufficient to complete this project. Northern analysis revealed that IGFBP 1, 2, 3, 4, and 5 are produced by the four cell lines studied (Du-145, AL 141, AL 101, and HEP G2). IGFBP at 25 kDa and 30 kDa was detected with ligand blots using $^{125}I$ labeled IGF-1. A paper is being written for submission for publication.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/166 | **Status:** On-going |

**Title:** Effects of Gravity and Microgravity on Growth and Differentiation in Mus musculus Long Term Bone Marrow Culture

| | |
|---|---|
| **Start Date:** 09/21/94 | **Est. Completion Date:** |
| **Department:** DCI | **Facility:** MAMC |
| **Principal Investigator:** Mary C. Tillotson-Criss, BS | |
| **Associate Investigators:** Davis DJ | Lilly MB<br>CPT Rodger K. Martin, MS |

**Key Words:** bone marrow, Mus musculus, growth, gravity, microgravity,Animal Study

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

Study Objective: To assess (1) the effects of microgravity on growth and differentiation of bone marrow cells; (2) to determine if bone marrow cells will grow in stimulated microgravity using collagen microspheres as a substrate; (3) to study the 3-D architecture of bone marrow to assist in determining tissue ultra-structure; (4) to develop and test normal murine bone marrow through infusion of in vitro grown cell culture marrow into syngenic mice in vivo.

Technical Approach: The mouse will be euthanized and both femurs removed to obtain bone marrow. The marrow will be placed into supplemented nutrient media, manual cell counts performed, and then placed into tissue culture flasks. Bone marrow cells will be grown in two different environments: gravity and simulated microgravity. Gravity's environment will be represented by using a tissue culture flask containing marrow cells, nutrient media, and special collagen beads that assist in cell adherence, then placed in an undisturbed horizontal position in 5% $CO_2$ incubator. Microgravity will be represented by using a tissue culture vessel containing equal amounts of marrow cells, nutrient media, and collagen beads. This vessel will continuously rotate about a horizontal axis. After obtaining optimal growing conditions for bone marrow cells by measuring glucose, $CO_2$, $O_2$, and pH levels, cell types will be determined by using special antibodies and stains. The investigator will be looking for these cells to change from immature to mature forms and will use antibodies to recognize surface antigen markers which are expressed as these cells mature (differentiate). In the microgravity environment it is anticipated that cells will have attached to the small collagen beads and developed so that a 3-D structure results. The investigator will examine the beads with an electron microscope in order to visualize cellular structure and their relationship to each other. To demonstrate functioning cells, male murine marrow cells grown from the two environments (gravity and microgravity) will be infused into immunologically compatible female mice which have had their bone marrow removed by irradiation. The mice will be observed daily for signs of becoming ill and then by the 30th day if the mice have survived the infusion and appear to be doing well, they will be euthanized and bone marrow from their femurs will be collected and examined for the presence of male hematopoietic cells.

Progress: This protocol is awaiting a decision for funding by NASA It has not been started.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF DENTISTRY

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/016 **Status:** Terminated

**Title:** Comparison of Digital Panoramic Radiographs With Conventional Panoramic Radiographs for Use in Oral and Maxillofacial Surgery

**Start Date:** 02/04/94 **Est. Completion Date:** Aug 94

**Department:** Dentistry **Facility:** MAMC

**Principal Investigator:** LTC Frank E. Orr, DC

**Associate Investigators:** CPT Theodore A. Dorsay, MC
COL Jerre M. Griffin, DE

**Key Words:** radiographs:digital, oral and maxillofacial surgery

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $45.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: 1) To demonstrate that digitized panoramic radiographs are as accurate as conventional panoramic radiographs in detecting mandibular hard tissue defects. 2) To demonstrate that digitized panoramic radiographs are as effective as conventional panoramic radiographs in visualizing mandibular anatomic structures.

Technical Approach: Fifty conventional panoramic radiographs will be collected from dental treatment records maintained at Ft. Lewis DENTAC clinics. The makeup of these films will be approximately 15-20 with previously diagnosed mandibular fractures, 20-25 with previously diagnosed mandibular bone lesions, and 10 previously diagnosed as clinically normal. Each of these conventional panoramic radiographs will be digitized and then loaded onto MDIS with a random number for viewing. The PI and AI will evaluate each of the 50 conventional radiographs and compare their diagnosis with the original diagnosis documented in the dental chart. If a discrepancy exists between the PI and AI over the diagnosis of a particular film, it will be deleted from the study and a similar film will be selected for entry into the study. A panel of 5 observers from the Oral and Maxillofacial Surgery Service will then evaluate 50 randomly numbered conventional panoramic radiographs using 2 different rating questionnaires developed for this study. The first questionnaire with have viewers evaluating images and looking specifically for mandibular fractures or bone lesions. The second questionnaire will direct viewers to examine specified anatomic structures and rate the image quality of these structures. Additionally, the viewer will rate the image quality of any hard tissue defects identified in the first questionnaire. The conventional panoramic radiographs will then be digitized and logged onto MAMC's MDIS. The observers will then evaluate the digitized panoragraphs on MDIS using the same 2 questionnaires. Data from the questionnaires will then be used to compare the two imaging modalities for significance.

Progress: This protocol was terminated because the MDIS was not installed in the Dental Clinic before the reassignment of the PI.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF EMERGENCY MEDICINE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/100 **Status:** Completed

**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: Seventy-two patients were entered. Albuterol nebulized by Heliox failed to significantly improve airway obstruction more rapidly than albuterol nebulized by air. Patients with severe airway obstruction showed a trend toward more rapid reversal with albuterol nebulized by Heliox, but this difference was not statistically significant.

A poster presentation was made at the Society for Academic Emergency Medicine, May 1994,

# Detail Summary Sheet

**Date:** 30 Sep 94 **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. By the end of FY 94, 30 patients were enrolled. Data will be analyzed when all information has been collected.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/074 **Status:** On-going

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

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

**Department:** Emergency Medicine **Facility:** MAMC

**Principal Investigator:** CPT Thomas F. Burke, MC

**Associate Investigators:** CPT Jack K. Handley, MC
Evans W

**Key Words:**

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

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

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

Progress: Seven patients have been entered in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/135 **Status:** On-going

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

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

**Department:** Emergency Medicine **Facility:** MAMC

**Principal Investigator:** CPT Thomas F. Burke, MC

**Associate Investigators:**
MAJ Jonathon Newmark, MC
Schwartz RB
Hobbs JL
MAJ John W. McBurney, MC
CPT Leo W. Kesting, MC
MAJ William T. Hurley, MC

**Key Words:** stroke:ischemic, Selfotel, plac ebo

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

Study Objective: To evaluate the efficacy and safety of a single 1.5 mg/kg dose of selfotel relative to placebo in improving the 90-day functional outcome of acute ischemic stroke patients.

To determine whether selfotel improves the 30-day and 90-day outcome compared with placebo.

To determine whether selfotel reduces mortality from acute ischemic stroke compared with placebo.

Technical Approach: There will be three periods to this trial: Screening/Treatment, Acute Monitoring, and Follow-up.

Screening/Treatment Period: The Screening/Treatment period begins when the patient is admitted to the Emergency Room. This trial will enroll patients 40-85 years with a clinical diagnosis of paretic hemispheric acute ischemic stroke. Baseline neurologic symptoms will be documented with the Scandinavian stroke Scale and the National Institutes of Health (NIH) Stroke Scale. Screening procedures and treatment must be accomplished as soon as possible and no longer than six hours from the onset of the patient's stroke symptoms.

Patients will be randomized to 1.5 mg/kg selfotel or placebo. A single dose of trial drug will be given.

Acute Monitoring Period: The Acute Monitoring period begins immediately after trial drug administration and ends on Day 8 or hospital discharge (if earlier). During this acute period, the patients will be monitored for safety and neurologic function.

Follow-up Period: The Follow-up period begins after Day 8 or when the patient is discharged from the hospital (if earlier). Clinic visits will be made on Trial Days 30 and 90 when efficacy will be determined using the Barthel Index, NIH and Scandinavian Stroke Scales.

Progress: No patients entered. This study is awaiting CIRO approval.

# Detail Summary Sheet

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

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

**Start Date:** 06/03/94 **Est. Completion Date:** Jul 95

**Department:** Emergency Medicine **Facility:** MAMC

**Principal Investigator:** CPT Thomas F. Burke, MC

**Associate Investigators:**
Etzkorn EU
LTC Ronald H. Cooper, MC
MAJ Joseph T. Morris III, MC

**Key Words:** pyelonephritis, ciprofloxacin

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To compare the treatment effects of ciprofloxacin (IV single dose/PO or PO) versus standard therapy (IV single dose/PO or PO) as outpatient management in premenopausal females with acute uncomplicated pyelonephritris. The efficacy and tolerability of a seven day treatment of ciprofloxacin will be compared with a fourteen day treatment with standard therapy. In addition, healthcare resource utilization will be evaluated related to treatment drop-outs, failures/relapses, as well as adverse events between both treatment arms (direct costs). Patient perception will be collected by recording patient's speed of recovery and return to normal activity.

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

Progress: Seven subjects have been entered, with headache in one patient reported as the only side effect.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/051 **Status:** Completed

**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:** | // |
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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-one patients (35/MS and 36/NS) were entered into the study. There were no cases of study drug reaction.

A paper was presented at the Society for Academic Medicine, May 1994 and a manuscript is being written. The results of the study indicate that the administration of morphine to patients with acute abdominal pain effectively relieved pain and did not alter the ability of physicians to accurately evaluate and treat patients when compared with saline placebo.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/039 **Status:** Completed

**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:** | // |
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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: Ninety-two (92) adults were enrolled in the study. The results indicate that patching does not significantly affect the rate of healing nor the pain profile of corneal abrasions. Patients that were not patched had significantly less pain at 24 hours. The value of routine eye patching should be further studied

Accepted for presentation at the Triservice Course in Emergency Medicine, Jan 95.

# Detail Summary Sheet

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

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

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

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

Progress: No sessions held. New protocol.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/152 | **Status:** On-going |
| **Title:** Pediatric Intubation Training Utilizing the Ferret Model | | |
| **Start Date:** 08/16/94 | **Est. Completion Date:** | |
| **Department:** Emergency Medicine | **Facility:** MAMC | |
| **Principal Investigator:** Steven A. Pace, MD | | |
| **Associate Investigators:** MAJ Lawrence A. Wilson, MC | CPT Thomas F. Burke, MC | |
| **Key Words:** Intubation:training, animal model, ferret,Animal Study | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

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

Technical Approach: Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure.

Progress: No training sessions held. New protocol.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/007 **Status:** Completed

**Title:** A Randomized, Double-Blind, Multicenter Trial Comparing 10 Days of Oral Therapy with CP-99,219 or Ofloxacin for the Treatment of Acute Exacerbation of Chronic Bronchitis

**Start Date:** 10/01/93 **Est. Completion Date:** Apr 94

**Department:** Emergency Medicine **Facility:** MAMC

**Principal Investigator:** Steven A. Pace, MD

**Associate Investigators:**
MAJ William J. Frohna, MC
LTC Lawrence Lavine, MC
MAJ Peter P. Taillac, MC

**Key Words:** chronic bronchitis, CP-99,219, ofloxacin

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

Study Objective: To compare the safety and efficacy of CP-99,219 and ofloxacin in the treatment of patients with acute exacerbations of chronic bronchitis.

Technical Approach: Patients 18 to 72 years of age who meet the inclusion criteria and agree to participate will have baseline labs drawn. A satisfactory sputum specimen will be examined microscopically for consistency and color and a Gram stain will be performed. If the sputum is adequate it will be cultured and the patients will be randomly assigned to study drug (CP-99,219 100 mg or 300 mg qd x 10 days) or ofloxacin (400 mg bid x 10 days). Patients will be seen on days 6, 11, 18 and 25. Lab hematology and chemistry studies will be performed at on days 6 and 11 and clinical assessment will be performed at all visits. Sputum specimens will be collected for gram stain and culture at each visit if the patient has a productive cough. Serum trough levels will be collected on day 6. Bacterial and clinical response will be evaluated by the sponsor.

Progress: 13 subjects were enrolled at MAMC with no serious adverse effects.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/008 **Status:** Completed

**Title:** A Randomized, Double-Blind, Multicenter Trial Comparing 10 Days of Oral Therapy with CP-99,219 or Cefaclor for the Treatment of Uncomplicated Community Acquired Pneumonia

**Start Date:** 10/01/93 **Est. Completion Date:** Nov 94

**Department:** Emergency Medicine **Facility:** MAMC

**Principal Investigator:** Steven A. Pace, MD

**Associate Investigators:**
MAJ William J. Frohna, MC
LTC Lawrence Lavine, MC
MAJ Peter P. Taillac, MC

**Key Words:** pneumonia:community acquired, CP-99,219, cefaclor

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

Study Objective: To compare the safety and efficacy of CP-99,219 and cefaclor in the treatment of patients with uncomplicated community acquired pneumonia.

Technical Approach: Subjects between the ages of 18 and 72 with a medical history, clinical, and radiological findings consistent with community-acquired bronchopneumonia or lobar pneumonia will be invited to participate. Laboratory studies of the patient's hematological and blood chemistry status will be performed. A sputum specimen will be collected, examined microscopically, cultured, and a gram stain made. If the sputum is "adequate" the patient will be randomized to receive CP-99,219 (200 mg or 300 mg daily) or cefaclor (1500 mg qd). The patient will be followed on day 4 and 11 with clinical assessment and a laboratory evaluation to include sputum culture. On days 18 and 25 the patient will receive a clinical evaluation and a sputum culture. Data analysis will be performed by the sponsor.

Progress: 11 patients were enrolled at MAMC with no adverse events.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 82/025 **Status:** Completed

**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:** 06/10/94 |
|---|---|---|---|---|

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: No training sessions in FY 94. Replaced by 94/165.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 90/016 **Status:** Completed

**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:** 06/10/94 |
|---|---|---|---|---|

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: Two training sessions were held. 7 animals were entered. Protocol was rewritten and approved as 94/152.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/052 | **Status:** On-going |
| **Title:** Comparison of the Esophageal-Tracheal Combitube and Endotracheal Intubation in the Prehospital Management of Cardiac Arrest | | |
| **Start Date:** 02/04/94 | **Est. Completion Date:** Jun 94 | |
| **Department:** Emergency Medicine | **Facility:** MAMC | |
| **Principal Investigator:** CPT Tracey Shirk, MC | | |
| **Associate Investigators:** MAJ Peter P. Taillac, MC | Fuller F<br>Marc McIlrath, R.E.M.T.-P. | |
| **Key Words:** Combitube, cardiac arrest | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** 01/20/95 |

Study Objective: To determine, using subjective and objective criteria, whether the Esophageal-Tracheal Combitube is an effective alternative to endotracheal intubation in the prehospital airway management of cardiac arrest patients.

Technical Approach: Patients in full cardiac arrest who are treated by EMS personnel will, on even numbered days, will be intubated with and endotracheal tube. On odd numbered days, the patient will be intubated with the Esophageal-Tracheal Combitube (ETC). The hypopharynx will first be visualized with a laryngoscope to insure no foreign body is present. An End-Tidal Carbon Dioxide Detection device will be used on all patients. Resuscitation will then proceed according to ACLS standards and Pierce County protocols until the patient is transferred to the receiving facility. If intubation attempts with either device fail, the patient may be intubated with the opposite device. Data from these intubation failures will be analyzed separately.

After transport to the receiving facility, EMS personnel and Emergency Department physicians will complete a data collection form on which they will describe their impressions of the effectiveness of airway management. They will comment on ease of intubation, adequacy of intubation, oxygenation, and ventilation, and any complications encountered. They will also document any available objective data (end-tidal CO2 detection, pulse oximetry, and ABG results), and the patient outcome.

Data will be compiles and analyzed at frequent intervals by a physician medical monitor. If a statistically significant increase in complications or mortality rates is observed with ETC usage, the study will be immediately terminated. Data analysis will include chi-square for complication rates, subjective ease of use, and the number of attempts. Paired t-test will be used for arterial blood gas data.

Progress: Seven patients have been entered in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/169 **Status:** Completed

**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: Ten subjects were entered. No significant trend was noted.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF FAMILY PRACTICE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/151 | **Status:** On-going |
| **Title:** Factors Associated With Physician's Marriage Satisfaction | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** | |
| **Department:** Family Practice | **Facility:** MAMC | |
| **Principal Investigator:** CPT Kevin DeWeber, MC | | |
| **Associate Investigators:** | MAJ David C. MacDonald, MC | |
| **Key Words:** marriage:physicians, satisfaction | | |

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

Study Objective: To find those factors that are associated with high marital satisfaction among marriages comprised of at least one physician. This includes male and female physicians with a nonphysician spouse and dual physician marriages.

Technical Approach: Two questionnaires will be sent to both the husband and the wife. The first will be the Marital Assessment Questionnaire, a five item list that is a brief highly reliable assessment of marital satisfaction. The second is a 43 item questionnaire consisting of 9 demographic items and 34 items related to marriage and family life. Subjects dealt with include children, finances, medical practice, communication, and interpersonal relationships Regression analysis will be used to analyze the data.

Progress: Questionnaire packets have been mailed to 300 individuals

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/076 **Status:** Completed

**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:**

| **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: 260 residents were included in the data analysis, 54 GMO residents and 206 continuous family practice residents (CFP) The only statistically significant difference seen between the GMO and CFP groups was in the psychiatry section scores between the PGY1 and PGY3 where the scores dropped for the GMO group. A paper was submitted for consideration for the Fellow's Research Award.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/084 **Status:** Completed

**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: 244 questionnaires were analyzed, yielding a 40% response rate. With 88% of the aviators experiencing back pain and 40 % experiencing activity limitation, this study demonstrates the significance of back pain in military aviation. Aviators sought care from sanctioned and non-sanctioned providers. Those aviators who experienced pain and sought care outside of the system or avoided care differed from those aviators who did not experience pain. The only significant provider differences occurred with chiropractors and medical doctors being the most common providers seen. Patients with activity limiting pain sought care outside or avoided care for their back pain more frequently No difference existed in avoidance of care for any reason. Patients with activity limiting pain differed significantly in their use of chiropractors, medical doctors, osteopathic physicians, and physical therapists. Aviators with activity limiting pain sought manipulation care. Medical doctors, physical therapists, and osteopathic physicians provided more care to those with activity limiting pain, at a statistically significant level. Of interest is that no difference existed between those who sought chiropractic care based on the nature/intensity of the pain.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Craig Meier, MC

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

**Key Words:** preeclampsia, exercise, heart rate

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

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

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

Progress: Approximately 200 volunteers have been studied. Pregnancy outcome records have been obtained on 80 subjects. Review of the records shows that the incidence of preeclampsia may be as low as 6% Therefore, the initial power analysis, based on a 10% incidence rate which indicated a minimal number of 200, has been revised to a number of 300. A grant has been received under the Defense Women's Health Initiative system to continue this protocol.

The principal investigator has been changed from CPT Harrington to CPT Meier due to the PCS of CPT Harrington.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/143 | **Status:** On-going |
| **Title:** Adolescent Risk Behavior and the Influence of Parents and Education | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** | |
| **Department:** Family Practice | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Brent V. Nelson, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** risk behavior:adolescents, parents, education | | |

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

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

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

Survey results will be entered into a Data Base for calculation of responses. Chi square distribution will be used to compare parent and student paired responses, with statistical significance accepted at .05. General knowledge questions will be tabulated for parent and student in a percentage correct format.

Progress: This is a recently approved study which has not been started.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/002 | **Status:** Completed |
| **Title:** Non-steroidal Anti-inflammatory Drug (NSAID) Prescribing Patterns | | |
| **Start Date:** 11/05/93 | **Est. Completion Date:** Apr 94 | |
| **Department:** Family Practice | **Facility:** MAMC | |
| **Principal Investigator:** Rubel EJ | | |
| **Associate Investigators:** None | | |
| **Key Words:** NSAID, prescribing patterns | | |

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

Study Objective: a. To describe individual and department level physician NSAID prescribing patterns.

b. To examine the impact of new algorithms and policies on physician prescribing patterns. One of the objective of these policies was to decrease the number of second generation NSAIDS prescribed by asking prescribers to first try first generation NSAIDS.

Technical Approach: The Pharmacy computer system records will be queried to obtain a listing of all NSAIDS prescriptions written by Family Practice Physicians during the initial study period. Individual prescriptions will be sorted and subtotaled by physician and medicine. Summary data will then be compiled for each three month period (pre and post-intervention), to include the number of first and second generation NSAID scripts and pills by physician. Basic physician demographics such as age, sex, level of training, years in practice, and degree will be collected to determine their association with prescribing behavior. T-test for paired values to compare proportion of second generation NSAIDS prescribed by each provider before and after the intervention. Chi-Square test will be utilized to compare first and second generation prescriptions and total pills before and after intervention.

Progress: The average % of SG NSAIDS scripts decreased from 31% (pre-intervention) to 25% (post). Age, sex, MD/DO status, and years since residency had no significant effect on SG NSAID use. An administrative and educational intervention can significantly reduce SG NSAID use.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/123 | **Status:** Completed |
| **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: Nine men who had recently undergone vasovasostomy were interviewed using life histories. None of these men felt that regret was significant in their decision. It seemed that rather than an attempt to escape from remorse, vasectomy reversal was seen as something that was "worth a shot."

Despite the fears of some men about the potential adverse effects of vasectomy on their sexuality, none reported any adverse effects and some experienced improvement. Social situations such as marital discord or financial situations or number of children, which changed over time, influenced some men to opt for vasectomy. Also, the fact that male fertility potentially lasts a life time while the female fertility ends with menopause seems to be a factor.

A thesis for an MA degree in Social Sciences has been written from this protocol.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/053 | **Status:** On-going |
| **Title:** Does Treatment of Subclinical Hypothyroidism Improve Glycemic Control in Type II Diabetics | | |
| **Start Date:** 02/04/94 | **Est. Completion Date:** Jun 94 | |
| **Department:** Family Practice | **Facility:** MAMC | |
| **Principal Investigator:** CPT Jon K. Van Valkenberg, MC | | |
| **Associate Investigators:** MAJ Robert M. Tuttle, MC | Tuggy ML | |
| **Key Words:** diabetes, obesity, levo-thyroxine | | |

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

Study Objective: To determine if glycemic control can be improved by treating subclinical hypothyroidism in Type II diabetic patients.

Technical Approach: Fifty patients from the Endocrinology and Family Practice clinics with subclinical hypothyroidism and Type II diabetes will be identified. Patients may be on oral agents or insulin. These patients will have serum TSH values between 5 and 20 mIU/ml and have no clinical symptoms of hypothyroidism. The patients will be randomly assigned to one of two groups. The first group is the treatment group in which the TSH will be normalized with levothyroxine. Patients randomized to the second group will serve as the control or observation patients (no attempt will be made to normalize their TSH). Once randomized, the patients will be followed for 6 months with measures of glycemic control and thyroid hormone assessed at entry, 3, and 6 months. At the completion of the study we will compare the glycemic control measurements (fasting glucose, glycosylated hemoglobin) between the levothyroxine treatment group and the observation group using repeated measures ANOVA.

Progress: No subjects entered yet due to reassignment of PI and assignment of new PI.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, ALLERGY AND IMMUNIZATION SERVICE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/087 | **Status:** Terminated |
| **Title:** Immunoglobulin Response To Tuberculin Skin Testing | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Feb 94 | |
| **Department:** Med, Allergy/Immun. Svc | **Facility:** MAMC | |
| **Principal Investigator:** COL James S. Brown, MC | | |
| **Associate Investigators:** CPT Paul A. Brundage, MC | MAJ Danny M. Douglas, MC | |
| **Key Words:** tuberculosis, immunoglobulin | | |

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

Study Objective: To determine whether or not frequent IPPD injections for the purpose of TB surveillance may induce IgG or other immunoglobulin classes to PPD (purified protein derivative of mycobacterium tuberculosis.)

Technical Approach: Eight to ten medical personnel who had experienced repeated IPPD testing but remain negative would be recruited. They would donate 507 ml of serum for a PPD-ELISA. A similar number of PPD positive patients would also be asked to donate 5-7 ml of serum. The sera would then be assayed for immunoglobulin ELISA technology. Subjects with active TB would also be asked to donate sera for this assay as potential positive controls. Any showing positively for IgG would also be interviewed for reactivity occurring within 4-8 hours after the IPPD. Study subjects will have a repeat IPPD and be observed at four, eight, twenty-four, forty-eight, and seventy-two hours later. Evaluation will consist of examination of the skin for erythema or induration.

Progress: Eight subjects were entered. Terminated when serum samples lost.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/124 **Status:** Completed

**Title:** Pulmonary Function Test Parameters Corrected for Thoracic Height in Noncausians

**Start Date:** 06/03/94 **Est. Completion Date:** Apr 95

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

**Principal Investigator:** COL James S. Brown, MC

**Associate Investigators:**
MAJ Danny M. Douglas, MC
Moore J
MAJ Sarah S. Marlowe, MC
CPT Eric T. Fajardo, MC

**Key Words:** pulmonary function test:thoracic height

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $385.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: 1) Obtain pulmonary function tests from normal adult active duty men and women presenting to the consolidated troop medical clinic for routine physicals. The parameters to be studied include $FEV_1$, FVC, MMEF, and PEFR.

2) Show that the racial differences in $FEV_1$, FVC, MMEF, and PEFR are eliminated when these parameters are expressed as a function of thoracic height.

Technical Approach: Soldiers presenting to the consolidated troop medical clinic for routine exams will be asked to participate in this study. Individuals that have clinical symptoms referable to the sinuses or lungs will be excluded along with those who have a history of smoking or any lung disease. Test subjects will be asked to perform a forced vital capacity into the spirometer. The spirometer will calculate the $FEV_1$, MMEF, and PEFR. By comparing the data from white soldiers with well accepted normal values, we will show the validity of our control population. The data from the Asians, Hispanic and black subjects will be put through an analysis for variance to show that those racial groups have different PFT parameters than whites. This data will then be corrected for thoracic height and again be subjected to an analysis for variance. This time we expect to see no difference in the data between races.

Progress: Seventy subjects have been entered. Data is being analyzed. PI has been reassigned.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/074 **Status:** Completed

**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 Svc **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:** 06/10/94 |
|---|---|---|---|---|

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: 11 animals underwent embolization of either a patent ductus arteriosus or collateralized peripheral artery. Each coil was retracted into the guide and subsequently reinserted prior to final deployment. Successful delivery was achieved in 11 of 11 attempts. There were no incidents of acute coil migration or vascular

complication. Microscopic examination of the short-term implants revealed organized thrombus. Late specimens demonstrated endothelialization and fibrous consolidation.

**Conclusion.** The retrievable coil occlusion system represents a significant improvement regarding the precision and safety of transcatheter vascular embolization. Presented at the annual meeting of the American College of Cardiology, 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Svc **Facility:** MAMC

**Principal Investigator:** COL Roger F. Chamusco, MC

**Associate Investigators:**
COL Joseph A. Paris, 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:** 09/02/94 |
|---|---|---|---|---|

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: 23 patients were entered. There was one serious adverse event (death), associated with coronary angiography which was done to evaluate additional unstable angina.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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 Service | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Alice M. Mascette, MC | | |
| **Associate Investigators:** MAJ Karl C. Stajduhar, MC | MAJ Patrick A. Cambier, MC | |
| **Key Words:** cardiac dimensions, female athletes | | |

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| **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: Fifty subjects have been enrolled to date but attempts are still being made to enroll more weight lifters. This study provides evidence for significant increases in echocardiographic left ventricular diastolic and systolic internal dimensions and left ventricular mass in female athletes engaged in aerobic and power sports as compared to control women similar in age and body habitus. This is the first description of such parameters in female weight lifters. The study showed a statistically significant increase in left ventricular wall thickness for women engaged in power sports compared to controls; this difference was not significant for the aerobic athletes. The maximum wall thickness measured in these women was 12 mm. Increases in wall thickness much in excess of this level should not be attributed to training alone in the casual female athlete.

# Detail Summary Sheet

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

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

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

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

Progress: No subjects have been entered due to time restraints of the principal investigator

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/126 | **Status:** On-going |

**Title:** Potassium Channel Gene Expression in States of Thyroid Dysfunction and Amiodarone Treatment

| | |
|---|---|
| **Start Date:** 06/10/94 | **Est. Completion Date:** |
| **Department:** Medicine, Cardiology Service | **Facility:** MAMC |

**Principal Investigator:** MAJ Mark E. Peele, MC

**Associate Investigators:** None

**Key Words:** Thyroid, potassium, amiodarone,Animal Study

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

Study Objective: To study the expression of the potassium channels RK3(Kv1.5) in rat heart. The effects of amiodarone, thyroid hormone deficiency, and thyroid hormone excess upon steady state messenger RNA levels as determined by northern analysis.

Technical Approach: Sixteen adult male rats will be divided into four equal experimental groups. T3 group will receive daily intraperitoneal (IP) injections of T3 200 mcg/kg for 2 weeks prior to sacrifice. Hypothyroid group will receive a 0.1% merthimazole solution ad lib in their drinking water supply for 4 weeks prior to sacrifice. Amiodarone group will receive daily IP injections of amiodarone 20 mg/kg for 4 weeks prior to sacrifice. Control animals will receive standard rat chow. Animals will be euthanized by standard lab practice with collection of sera for determination of thyroid stimulating hormone levels and harvesting of myocardium. Total cellular RNA will be collected by standard methodology. Size fractionated by electrophoresis on 1% agarose denaturing formaldehyde gels. RNA will be capillary transferred to charged nylon membranes and UV light fixed after formaldehyde neutralization.; Samples of rat heart total cellular RNA will serve as template for first strand synthesis of cDNA. Restriction fragment analysis of amplified RK3 (Kv1.4) and RK4 (Kv1.5) DNA will be performed on 1% agarose gels to confirm cDNA identity. Statistical significance of study variables between experimental groups will be determined by ANOVA.

Progress: Experimental animal phase is completed. Laboratory phase is in progress.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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: 10 subjects have been entered. Specificity for adenosine for detection of coronary artery disease was 100% compared with 22.2% in exercise thallium ($p = 0.1$). These results are consistent with previously published data and argue against use of exercise in conjunction with radionuclide imaging in patients with left bundle branch block. Abstract presented at Army American College of Physicians meeting, 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/041 **Status:** Terminated

**Title:** A Double-Blind, Randomized, Parallel, Sotalol-Controlled, Dose-Confirmation Study to Investigate The Safety and Electrophysiologic Effects of MK-499 in Patients With Sustained Ventricular....

**Start Date:** 12/17/93 **Est. Completion Date:** Feb 95

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

**Principal Investigator:** MAJ Karl C. Stajduhar, MC

**Associate Investigators:** MAJ James C. Mullin, MC

**Key Words:** Tachyarrhythmias, MK-499, sotalol

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

Study Objective: 1.) To determine the safety and tolerability of two oral doses of MK-499 in the patients with sustained ventricular tachyarrhythmias (VT). 2.) To determine an oral dose or a dose range of MK-499 which suppresses induction of sustained VT during electrophysiological testing (EP) in >30% of patients with sustained ventricular tachyarrhythmias. 3.) To compare the safety, efficacy and EP effects of MK-499 to sotalol.

Technical Approach: This Phase IIB study will evaluate the safety, electrophysiologic activity and antiarrhythmic effect of oral dosing with MK-499 or sotalol in patients with sustained ventricular tachyarrythmias. The primary endpoint is: Suppression of induction of sustained ventricular tachyarrhythmias by prespecified EP techniques. The safety profile will be based on clinical and laboratory evaluations.

Patients with a history of syncope, presyncope, or symptomatic VT and inducible monomorphic VT by EP testing will be evaluated. Qualified patients will be randomized to one of the following double-blind treatment groups:

Group A: MK-499 1.0 mg b.i.d.

Group B: MK-499 1.5 mg b.i.d.

Group C: Sotalol 80 mg b.i.d. x 2 days, then force-titrated to 160 mg b.i.d.

On the sixth day a repeat EP study will be performed and if the patient is determined to have responded an optional out-patient extension period is available.

Progress: 1 subject was entered. Protocol was terminated by sponsor.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/040 **Status:** On-going

**Title:** The Effect of Oral D-Sotalol on Mortality in Patients With Atherosclerotic Coronary Heart Disease and Left Ventricular Dysfunction

**Start Date:** 12/17/93 **Est. Completion Date:** Jul 95

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

**Principal Investigator:** MAJ Karl C. Stajduhar, 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
MAJ James P. Olson, MC
MAJ Alice M. Mascette, MC
COL Joseph A. Paris, MC
MAJ Patrick A. Cambier, MC
CPT Michael A. Rave, MC

**Key Words:** coronary disease, oral d-Sotalol, mortality

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

Study Objective: To determine whether d-sotalol, a Class III antiarrhythmic agent, will reduce total (all-cause) mortality compared to placebo in patients with left ventricular dysfunction (resting LV ejection fraction ≤ 40% and CHD.

Technical Approach: This is a multicenter, randomized, double-blind, placebo-controlled trial in patients with LV dysfunction and athersclorotic coronary heart disease (CHD). This study will consist of a screening and double blind phase. The screening phase will determine if the volunteers meet the enrollment criteria. Those qualifying for the double-blind phase will receive either d-sotalol or placebo for eighteen months and be monitored clinically as well as by standard laboratory methods. Data will be analyzed by the sponsor.

Progress: No subjects have been entered.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, CRITICAL CARE SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/029 **Status:** On-going

**Title:** A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation

**Start Date:** 12/17/93 **Est. Completion Date:** May 94

**Department:** Medicine, Critical Care Svc **Facility:** MAMC

**Principal Investigator:** MAJ Lewis L. Low, MC

**Associate Investigators:**
MAJ George N. Giacoppe Jr., MC
CPT Jeremy R. Blanchard, MC
MAJ James D. Pike, MC
MAJ Francis J. Landry, MC

**Key Words:** ventilation, airway occlusion pressure

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

Study Objective: The main objective of this study is to ascertain the usefulness of the PO.1 as a weaning parameter in predicting success or failure of patients upon extubation. The secondary objective is to validate the Rapid Shallow Breathing Index as described by Yang and Tobin.

Technical Approach: Weaning parameters will be obtained and documented by a Respiratory Care Practioner (RCP) on patients in the surgical and medical ICU at MAMC. Individual progress toward weaning and extubation will be determined by the primary physician/team. When it is determined the patient is ready for extubation, a second set of weaning parameters will be obtained immediately prior to extubation. Weaning parameters will only be collected on patients at rest and who have not been stimulated within the prior 10 minutes. The parameters will be obtained by utilizing the Respiratory Mechanics Package on the Infrasonics Adult Star as required by MAMC policy. Only the data obtained from patients on the Infrasonic Adult STAR mechanical ventilator will be used so that our results are reproducible since other available ventilators do not easily measure the PO.1. The first 50 patient's will be used to form ROC curves to develop threshold values for the prediction of success or failure of extubation which can then be prospectively applied. A successful weaning/extubation will be defined as one in which the patient does not have to be reintubated within 24 hours.

Progress: 65 subjects were entered. The data were found to be skewed and not analyzable. It was decided to recollect data. To date 6 new subjects have been entered.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/005 | **Status:** On-going |
| **Title:** Effect of Empiric Low-Dose Amphotericin B or Fluconazole on the Development of disseminated Candidiasis in an Intensive Care Unit | | |
| **Start Date:** 10/01/93 | **Est. Completion Date:** Jul 95 | |
| **Department:** Medicine, Critical Care Svc | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Lewis L. Low, MC | | |
| **Associate Investigators:** | CPT Gregory S. Witkop, MC | |
| **Key Words:** Candidiasis, amphotericin B, Fluconazole | | |

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

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

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

Progress: 9 subjects have been enrolled. No adverse reactions have been noted. No data has been analyzed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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, Critical Care Svc **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: No patients entered. PI has had difficulty finding patients who can consent.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/131 | **Status:** Terminated |

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

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| **Start Date:** 07/02/93 | **Est. Completion Date:** Jan 94 |
| **Department:** Medicine, Critical Care Svc | **Facility:** MAMC |
| **Principal Investigator:** MAJ Kathleen M. Sheehan, MC | |
| **Associate Investigators:** MAJ Doreen Saltiel, MC | |
| **Key Words:** myocardial infarction, magnesium, thromboelastograph | |

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

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

Technical Approach: Acute myocardial infarction patients ordered to receive IV 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. PI has departed. No new PI has been found.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/046 **Status:** On-going

**Title:** A Randomized, Double-Blind, Placebo-Controlled, Parallel Titration Which Explores the Safety and Efficacy of Glipizide GITS Tablets in A Broad Range of Patients With NIDD

**Start Date:** 12/17/93 **Est. Completion Date:** Jul 95

**Department:** Medicine, Endocrinology Service **Facility:** MAMC

**Principal Investigator:** COL David L. Bunner, MC

**Associate Investigators:**
LTC Daniel H. Knodel, MC
CPT Barrett L. Chapin, MC
LTC (P) Robert E. Jones, MS
MAJ Robert M. Tuttle, MC
CPT Lloyd D. Hancock, MC

**Key Words:** Diabetes, NICC, glipizide

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

Study Objective: 1) To evaluate the safety and efficacy of the Glipizide GITS tablet, a once-a-day formulation of Glipizide, in a broad spectrum of Non-Insulin Dependent Diabetes Mellitus patients. In addition, an evaluation of hypoglycemia and hyperglycemia will be made via questionnaires in association with documented home glucose measurements.

Technical Approach: Fifteen patients from MAMC will be evaluated for a maximum of 16 weeks. The study will consist of a 1-week washout from current oral sulfonylureas (if applicable); a 3 week, single-blind placebo phase; a 4-week, double-blind titration phase; and an 8-week, double-blind efficacy phase. Patients who have been on diet alone for at least 3 months and are considered to be dietary failures may enter the placebo phase directly. Following participation in this study, patients may be eligible for entry into a long-term, open-label extension study.

Progress: 19 subjects have been entered. There was one adverse event (angina) in a patient who had completed the study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/101 **Status:** Terminated

**Title:** Androgen Effects on Glucose Metabolism in Men

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

**Department:** Medicine, Endocrinology Service **Facility:** MAMC

**Principal Investigator:** CPT Barrett L. Chapin, MC

**Associate Investigators:** LTC (P) Robert E. Jones, MS
COL Stephen R. Plymate, MC

**Key Words:** metabolism, androgen

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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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 IM 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 subjects entered. Terminated due to lack of personnel support.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/102 | **Status:** Completed |
| **Title:** Evaluation of Calcium Metabolism After Biliopancreatic Bypass Surgery | | |
| **Start Date:** 05/07/93 | **Est. Completion Date:** Oct 93 | |
| **Department:** Medicine, Endocrinology Service | **Facility:** MAMC | |
| **Principal Investigator:** CPT Barrett L. Chapin, MC | | |
| **Associate Investigators:**<br>LTC Daniel H. Knodel, MC<br>MAJ John D. Ng, MC | LTC Homer J. Lemar Jr., MC<br>COL Preston L. Carter, MC | |
| **Key Words:** metabolism, calcium, biliopancreatic bypass | | |

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

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

Technical Approach: Patients who have had biliopancreatic bypass surgery within the previous three years will be invited to participate in this study. The control will be an equal number of patients who have had a different surgical procedure for obesity called vertical banded gastroplasty. These populations will be matched for age, sex, and amount of weight loss. It is assumed that the surgery of vertical banded gastroplasty does not cause calcium abnormalities. If the control group population has significant abnormalities in the biochemical evaluation of calcium metabolism, the protocol will be revised to add an additional control group. That group would consist of an equal number 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 performed in each group. Tests performed to evaluate calcium metabolism will be serum calcium, albumin, alkaline phosphatase (a marker for bone turnover), magnesium, phosphorus, parathyroid hormone, 25-hydroxyvitamin D, 1.25-dihydroxy vitamin D, and a 24 hour urine collection for calcium and hydroxyproline (a marker for bone turnover). Evaluation of other fat soluble vitamins will be performed by checking prothrombin time (vitamin K) and serum carotene (vitamin A). Confirmation of normal liver function will be obtained with serum gamma glutamic aminotransferase. Confirmation of normal renal function will be obtained with serum creatinine and 24 hour urine creatinine. If the serum carotene level is below normal, the patient will be referred to the Ophthalmology Service for formal testing for night blindness.

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

Progress: 22 subjects were entered. The biliopancreatic diversion group had significantly lower seru calcium, 25-hydroxyvitamin D, serum carotene and 24 hour urine calcium excretion, compared to the vertical banded gastroplasty group. The BPD group also had higher 1,25 dihydroxyvitamin D levels, PTH levels, alkaline phosphatase and urine hydroxyproline/creatinine. This represents vitamin D deficiency, hypocalcemia, and secondary hypoparathyroidism following BPD surgery. Abstract presented at the 1994 Endocrine Society meeting and won the 1994 Fellow research award at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/132 **Status:** On-going

**Title:** Does Pretreatment with Propylthiouracil or Methimazole Decrease the Effectiveness of Radioactive Iodine Therapy in Graves Disease?

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

**Department:** Medicine, Endocrinology Service **Facility:** MAMC

**Principal Investigator:** CPT Lloyd D. Hancock, MC

**Associate Investigators:**
LTC Homer J. Lemar Jr., MC
Troy H. Patience, B.S.
MAJ Robert M. Tuttle, MC
LTC John M. Bauman, MC

**Key Words:** Graves disease, propylthiouracil, methimazole, radioactive iodine

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

Study Objective: Our objective is to determine whether pretreatment with antithyroidal medications significantly effects the therapeutic efficacy of radioactive iodine used in the treatment of Graves disease.

Technical Approach: We plan to review all cases of RAI administered at MAMC between 1960 and 1994 to identify all cases of Graves disease treated with RAI. Using the clinical records we will determine which patients received antithyroidal agents. In all patients in whom at least one year follow-up data is available, we will compare treatment failure rates in those receiving RAI alone with those receiving RAI after pretreatment with PTU or methimazole. Demographic parameters will be evaluated in an effort to find any selection bias in those patients receiving antithyroidal drug pretreatment. It is hoped that this retrospective study will clarify whether pretreatment with antithyroidal drugs has an effect on the therapeutic efficacy of RAI.

Progress: 70 subjects have been entered. Pre-treatment with anti-thyroidal medications appears to be associated with a significantly higher single dose RAI failure rate (24%) than RAI therapy not preceded by antithyroidal therapy.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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 Service | **Facility:** MAMC | |
| **Principal Investigator:** LTC (P) Robert E. Jones, MS | | |
| **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 patients studied in FY 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** LTC (P) Robert E. Jones, MS

**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: No new subjects studied in FY 94. Manuscript in preparation.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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:** Medicine, Endocrinology Service | **Facility:** MAMC |

**Principal Investigator:** LTC (P) Robert E. Jones, MS

| | |
|---|---|
| **Associate Investigators:** | LTC (P) Robert E. Jones, MS |
| CPT M. Ahmed, MC | CPT J. Olson, MC |
| CPT Wilma I. Larsen, MC | CPT Colleen C. Foos, MC |
| CPT David H. Harrison, MC | Jones AY A. Y. Jones |

**Key Words:** spermatozoa, cyropresavation, hyperactivation

| | | | | |
|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | **OMA** $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: No subjects studied in FY 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** LTC (P) Robert E. Jones, MS

**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: No subjects studied in FY 94. Manuscript in preparation.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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 Service | **Facility:** MAMC | |
| **Principal Investigator:** LTC (P) Robert E. Jones, MS | | |
| **Associate Investigators:** COL Bruce L. Fariss, MC | COL Stephen R. Plymate, 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 mC 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: No additional subjects studied in FY 94. Publication in J Andrology in Dec. 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** LTC (P) Robert E. Jones, MS

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

**Key Words:** spermatozoa,lipids,morphology

| Accumulative MEDCASE Cost: | Est. Accumulative OMA Cost: | Periodic Review: |
|---|---|---|
| $40000.00 | $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 subjects studied in FY 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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 Cost:** | **OMA** $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 complete (30 subjects). Preliminary data analysis reveals a clear correlation 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 associated with changing thyroid function. Manuscript in preparation.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 92/010 | **Status:** Completed |

**Title:** Predictors of Response to Ovulation Induction with Clomiphene Citrate in the Overweight Patient

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|---|---|
| **Start Date:** 12/06/91 | **Est. Completion Date:** |
| **Department:** Med, Endocrinology Svc | **Facility:** MAMC |
| **Principal Investigator:** MAJ Robert M. Tuttle, MC | |
| **Associate Investigators:** CPT Carl A. Gibson, MC | CPT Nathan J. Hoeldtke, MC<br>MAJ Alicia Y. Armstrong |
| **Key Words:** ovulation induction, clomiphene citrate, overweight | |

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|---|---|---|---|---|
| **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: 7 subjects have been entered. The mean BMI for the group was 31.7. Total insulin, androstenedione, total testosterone, free testosterone and SHBG all correlated weakly with BMI. The fasting glucose/insulin (G/I) ratio correlates poorly with BMI. Three patients had a G/I > 6, suggesting a lack of insulin resistance. Two of these became pregnant. Patients who appear to be less insulin resistant may respond best to ovulation induction with clomiphene citrate.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** MAJ 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 170 papillary thyroid cancers have been examined for the presence of the activated PTC/ret oncogene.- 100 FNA samples, 20 fresh frozen samples and 50 paraffin imbedded samples from Marshall islanders exposed to radiation. Laboratory analysis of the latter continues, and a comparison will be made.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/080 **Status:** Terminated

**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 Service **Facility:** MAMC

**Principal Investigator:** MAJ Robert M. Tuttle, MC

**Associate Investigators:**
COL Stephen R. Plymate, MC
LTC (P) Robert E. Jones, MS
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 MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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: One subject enrolled. Subjects have been difficult to enter due to a lack of patients who meet the criteria.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, GASTROENTEROLOGY SERVICE

# Detail Summary Sheet

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

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

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

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

**Principal Investigator:** MAJ Amy M. Tsuchida, MC

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

**Key Words:** dysphagia, esophageal lesion

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $31.65 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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

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

Progress: Eighteen subjects have been enrolled. Patient accrual continues.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, HEMATOLOGY/ONCOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/080 **Status:** On-going

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

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

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

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

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

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

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 10/21/94 |
|---|---|---|---|---|

Study Objective: 1.) To compare the anti-tumor efficacy, as evaluated by the primary variable of objective response rate, and the secondary variables of duration of response, time to treatment failure (TTF), time to progression (TTP) and time to death among the three treatment arms (daily) doses of 0.5 mg letrozole, 2.5 mg letrozole, or 50 mg megestrol acetate (q.i.d.);2.) To compare tolerability and toxicity of daily doses of 0.5 mg letrozole, 2.5 mg letrozole and 40 mg megestrol acetate q.i.d.;3.) To assess information on population pharmacokinetics, including evaluation of trough estrogen levels during treatment, with daily doses of 0.5 mg and 2.5 mg letrozole.

Technical Approach: This is a multicenter, multinational, randomized, parallel-group, double-blind trial in postmenopausal women with advanced breast cancer who have failed on antiestrogen as an adjuvant or advanced disease therapy. Patients will receive either one tablet letrozole 0.5 mg or 2.5 mg once daily in the morning plus one placebo capsule matching megestrol acetate q.i.d. or one 40 mg capsule megestrol acetate q.i.d. plus one placebo tablet matching letrozole once daily in the morning. Patient evaluations will be done at baseline (prior to treatment), after 2 weeks, 1, 2, 3, 4, 5 and 6 months and every 3 months thereafter until the code is broken to the participating investigators which will occur after the last patient has been enrolled for 18 months. In addition any patient who manifests an objective tumor response will have her full tumor evaluations repeated at least 4 weeks but no later than the next scheduled tumor assessment after the initial observation of response to confirm the presence of the response.

Patients who respond to treatment (complete response, partial response or stable disease) will continue the treatment until the double-blind code is broken or there is disease progression, whichever comes first. After this period, the patients will be followed periodically for the purpose of collecting survival data for a total period of 5 years after initiation of treatment of the first patient on trial.

Progress: 1 subject has been entered. Patient accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/057 **Status:** On-going

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

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

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

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:** CPT John R. Caton, MC

**Key Words:** herpes simplex, immunocompromised, penciclovir, intravenous

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

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

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

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

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

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

Progress: No subjects entered. Awaiting approval of CRDA.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/070 **Status:** On-going

**Title:** A Dose Ranging, Efficacy, Safety, and Pharmacokinetic Study of Single Oral Doses of RS-25259 for Prevention of Nausea and Vomiting in Chemotherapy-Naive Cancer Patients Receiving Highly Emetogenic ...

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

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

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:** LTC Howard Davidson, MC

**Key Words:** antiemetic:RS-25259

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 10/21/94 |
|---|---|---|---|---|

Study Objective: 1.) To determine the dose-response relationship among single oral doses of RS-25259 over the dose range of 3-30 mcg/kg. 2.) To assess the safety of single oral doses of RS-25259 administered through the range of doses tested in this patient population. 3.) To assess the pharmacokinetics of single oral doses of RS-25259 through the range of doses tested in this patient population.;

Technical Approach: Patients 18 years of age and older with a proven diagnosis of cancer who are chemotherapy-naive will be invited to participate in this study. After informed consent is obtained they will give a full medical history and undergo a full physical exam including a 12-lead ECG, and submit blood and urine for laboratory examination.

On Dosing Day, patients will be assigned a patient number. At -90 minutes (1 1/2 hours before the start of chemotherapy) the patient will have sitting blood pressure and heart rate recorded and complete the predose nausea assessment. At -60 minutes, RS-25259 will be given orally. Sitting blood pressure and heart rate will be recorded again at -20 minutes, then at 30 minutes, 1.5, 3.5, 7.5, and 23.5 hours after the commencement of chemotherapy. At 24 hours a limited physical and 12-lead ECG will be done.

Diary cards will be provided to record the number of emetic episodes and to record the degree of nausea at various timepoints. At follow-up, 2 week after dosing, patients will have a limited physical, and submit blood and urine samples for laboratory evaluation. 12-lead ECG will be repeated for those patients who had an abnormal ECG at 24 hours. At 14 days patients will be contacted either by telephone or during a visit and questioned regarding adverse events and concomitant medications.

Progress: 10 subjects have been entered. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/100 **Status:** Completed

**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, Hem/Oncology Service **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, 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: Six subjects were entered. Two died of underlying disease. Kapanol was found to be as effective and safe as MS Contin.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/099 **Status:** Completed

**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, Hem/Oncology Service **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, 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 opioid 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: Six patients were entered. All patients completed treatment and progressed to the long term study (93/100). Kapanol was as safe and effective as MS Contin.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/009 **Status:** Terminated

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

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

**Department:** Medicine, Hem/Oncology Service **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. 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: No additional subjects entered. Terminated due to stringency of inclusion criteria.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/001 **Status:** Completed

**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, Hem/Oncology Service **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: 11 subjects enrolled (17 total). None had true evidence of micrometastatic disease. No conclusions could be made.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/017 **Status:** On-going

**Title:** Evaluation of Immunity to Breast Cancer

**Start Date:** 02/04/94 **Est. Completion Date:** Nov 94

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

**Principal Investigator:** MAJ Kenneth A. Bertram, MC

**Associate Investigators:**
LTC Howard Davidson, MC
MAJ Robert B. Ellis, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC
CPT John R. Caton, MC
MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC
MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Mark E. Robson, MC
MAJ Richard F. Williams, MC

**Key Words:** Cancer:breast, immunity

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $18.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To determine the significance/relationship of CD4 helper/inducer T cell response in the presence of H2N positive/negative cancers in an attempt to determine how the immune system responds to breast cancer.

Technical Approach: Patients with breast cancer will have samples of tumor tissue obtained at the time of surgery for Her-2/neu. Blood will be obtained at the same time to evaluate for an anti-Her-2/neu T-lymphocyte response. Further venipunctures will be performed monthly during the 5 year follow-up period to continue evaluation for an anti-Her-2/neu T-lymphocyte response.

Progress: 33 subjects have been entered. 5 had a response to HER2/neu protein. The data are being analyzed for a relationship between patients' clinical history and laboratory response.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/130 **Status:** Terminated

**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, Hem/Oncology Service **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: No subjects entered. Not funded by MRMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/081 **Status:** Terminated

**Title:** Development of a Non-Radioactive Method for Evaluating bck-2 Gene Rearrangement and Expression in Follicular Non-Hodgkin's Lymphoma

**Start Date:** 05/06/94 **Est. Completion Date:** Dec 94

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

**Principal Investigator:** CPT John R. Caton, MC

**Associate Investigators:**
CPT John R. Caton, MC
MAJ Mark D. Brissette, MC
MAJ Mark E. Robson, MC
MAJ Richard F. Williams, MC
CPT Dale T. Waldner, MC
Martin KR

**Key Words:** Cancer:non-Hodgkin's, gene:bcl2, gene:rearrangement, gene:expression

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To develop a non-radioisotopic in-situ reverse transcriptase polymerase chain reaction (IS-RT-PCR) technique suitable for the analysis of gene expression in formalin-fixed, paraffin-embedded (FFPE) lymphoid tissue, in particular in follicular non-Hodgkin's lymphoma (NHL).

Technical Approach: This project will identify, through review of pathology records, cases of follicular non-Hodgkin's lymphoma. DNA will be extracted from tissue blocks and examined by the polymerase chain reaction for the presence of bcl-2 gene arrangement. After positive cases are identified, a protocol will be devised to amplify the DNA rearrangement in situ using non-radiographic methodology. Once this protocol is established, a reverse transcription step will be incorporated to allow the identification of bcl-2/lg fusion mRNA. Comparison will be made between the sensitivity of conventional PCR, in situ PCR, and RT-in situ PCR in the detection of the bcl-2 rearrangement.

Progress: PI could not find time to begin protocol. Alternate PI could not be found.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/103 **Status:** Completed

**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, Hem/Oncology Service **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: 14 subjects were enrolled. Data has been forwarded to the sponsor.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/072 **Status:** Completed

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

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

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

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:**
MAJ 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, carcinoma 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 Automated Central Tumor Registry (ACTUR) database was searched for cases of males breast carcinoma. Between 1947 and 1992, 109 males with breast cancer were identified and 94 had sufficient data for review. The patients were followed for a median of 38.5 months (range, 1 to 497). The median age at presentation was 63 years (range 14 to 85), which is 10-12 years higher than that of women. Analysis of the frequency distribution by stage revealed that 74 (79%) were Stage I or II and 20 (21%) were Stage III or IV. The 5 year overall survival was 70% and dropped to 45% for those patients with axillary node-positive disease. Further data regarding survival by stage, recurrence patterns, and treatment will be presented and compared to other recently reported series.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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, Hem/Oncology Service **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 Cost:** | **OMA** $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: No patients were entered this FY. One patient was enrolled prior to FY 94 with complete remission to single agent adriamycin. The patient was taken off the agent due to cardiac toxicity.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/117 **Status:** On-going

**Title:** A Randomized, Parallel Group, Double-Blind, Placebo-Controlled Phase II Study of Glycosylated Recombinant Human Interleukin-6 (Sigosix) in Patients Undergoing Combination Chemotherapy....breast cancer

**Start Date:** 06/03/94 **Est. Completion Date:** Jul 95

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

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:** MAJ Richard F. Williams, MC

**Key Words:** Cancer:breast, interleukin-6, Sigosix TM

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

Study Objective: 1) To evaluate the rate of hematopoietic recovery after myelosupressive chemotherapy, and to determine any evidence of efficacy from r-hIL-6 which may be apparent in terms of attenuated thrombocytopenia or accelerated platelet count recovery. 2) To assess the safety and tolerance of administering repetitive daily subcutaneous doses of r-hIL-6 to patients with solid tumors after myelosuppressive chemotherapy. 3) To perform study-associated laboratory based investigations which will provide insight into the biologic actions of r-hIL-6 in vivo.

Technical Approach: Patients with advanced breast cancer who conform to the protocol eligibility criteria will be assigned to the study which consists of four treatment cycles of 21 days each. At the beginning of each cycle, all patients will receive CAF combination chemotherapy (Cyclophosphamide 3,000 mg/M2 IV on day 1, doxorubicin (Adriamycin) 37.5 mg/M2 IV on days 1 & 2; and Fluorouracil 600 mg/M2 IV on day 1). All patients will receive G-CSF (Filgrastim, r-metHuG-CSF, 5 mcg/kg/day) daily SC days 3-14 and until the post nadir ANC count exceeds 10,000/MM3. They will also receive study drug (placebo or r-hIL-6, 10 mcg/kg/day SC) daily, starting on day 3 until the post nadir platelet count exceeds 10,000 platelets/MM3 or for 23 days, whichever comes first. Patients will be prospectively randomized into two groups: Group 1 will receive placebo during cycles 1 & 2 and will receive r-hIL-6 during cycles 3 & 4; Group 2 will receive r-hIL-6 during cycles 1 & 2 and will receive placebo during cycles 3 & 4.

The primary parameter for analysis will be the percentage of patients who do not require platelet transfusions and the number of days each patient is dependent on platelet transfusions during cycles 1 or during cycle 2. A second primary efficacy variable will be the number of platelet transfusions required during cycle 1 or during cycle 2.

Progress: Awaiting MEDCOM approval.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/121 | **Status:** Completed |
| **Title:** Clinical Significance of Lymphoid Aggregates in Bone Marrow | | |
| **Start Date:** 05/07/93 | **Est. Completion Date:** Oct 93 | |
| **Department:** Medicine, Hem/Oncology Service | **Facility:** MAMC | |
| **Principal Investigator:** CPT James S. D. Hu, MC | | |
| **Associate Investigators:** MAJ George F. Hodeges, MC | MAJ Luke M. Stapleton, MC<br>Brisette MD | |
| **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: 178 subjects have been entered. Several univariate variables were associated with malignancy in bone marrow. Multivariate independent variable, paratrabecular lymphoid aggregates, transverse abutment and high density index all correlate with malignant lymphoid aggregate. Manuscript in preparation.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/118 **Status:** On-going

**Title:** Phase II Study of Single Agent Thiotepa for Advanced, Hormone-Refractory Prostate Carcinoma

**Start Date:** 06/03/94 **Est. Completion Date:** Dec 96

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

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**
MAJ James B. Thrasher, MC
MAJ Richard C. Tenglin, MC
Celestia S. Higano, MD
MAJ Robert B. Ellis, MC

**Key Words:** Cancer:prostate, thiotepa

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

Study Objective: The purpose of this study is to evaluate the efficacy and toxicities of single agent thiotepa for advanced hormone-refractory prostate carcinoma.

Technical Approach: This is a non-randomized phase II study. All eligible patients with metastatic, hormone-refractory prostate cancer who are considered by their physicians to have a chance to benefit and also agree to participate will be entered. Patients will be initially staged with abdominal/pelvic C.T. scans, bone scans, chest radiographs, serum PSA, serum PAP, BUN, creatinine, liver function tests and complete blood count. All patients will receive thiotepa 50 mg/M2 by intravenous administration at 28 - day intervals. Patients will be continued on therapy until: 1. disease progression is documented; 2. Unacceptable toxicities occur; or 3. the patient refuses further treatment for any reason. Any patient obtaining a complete response will receive two (2) additional courses of thiotepa past CR, and then be followed off therapy.

Progress: 1 subject entered. No adverse effects. PSA reduced by > 50%.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/055 | **Status:** On-going |
| **Title:** Agrelin (Anagrelide) for Patients With Thrombocythemia | | |
| **Start Date:** 02/04/94 | **Est. Completion Date:** Jan 97 | |
| **Department:** Medicine, Hem/Oncology Service | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Luke M. Stapleton, MC | | |
| **Associate Investigators:**<br>MAJ Kenneth A. Bertram, MC<br>MAJ Timothy P. Rearden, MC<br>MAJ Robert B. Ellis, MC<br>Hu JS<br>CPT Diana S. Willadsen, MC | LTC Howard Davidson, MC<br>MAJ Patrick L. Gomez, MC<br>MAJ Mark E. Robson, MC<br>MAJ Richard C. Tenglin, MC<br>LTC Robert D. Vallion, MC<br>MAJ Richard F. Williams, MC | |
| **Key Words:** thrombocythemia, Agrelin, safety, efficacy | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** 01/20/95 |

Study Objective: To assess the safety and efficacy of Anagrelide in patients suffering from thrombocythemia of various etiologies.

Technical Approach: Patients who are 18 years or older, free of infection and have thrombocythemia due to a myeloproliferative disorder will be asked to participate. Those consenting will have a physical examination, complete blood count and serum chemistry and then be dispensed a three-month supply of drug. During treatment with Anagrelide, blood counts should be determined as often as needed to assure patient safety. Other test will be done as clinically indicated. Any patient whose thrombocythemia is unchanged (± 20%) after two weeks of treatment will be removed from the study. Those patients receiving benefit may remain on the study until the drug is released by the FDA or all trials are terminated. The data derived from the study will be analyzed by the sponsor.

Progress: Originally approved because a patient was being given the drug on a one-time use basis approved through MEDCOM. No further patients have been entered.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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, Hem/Oncology Service **Facility:** MAMC

**Principal Investigator:** CPT Diana S. Willadsen, MC

**Associate Investigators:**
CPT Steven E. Brilliant, MC
MAJ Mark E. Robson, 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 $1000/mm^3$) 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: 15 subjects entered. 3 had mild side effects of myalgia, relieved with Tylenol. Due to unequal accrual in the two arms, statistical analysis is not meaningful yet. G-CSF appears to be safe and well tolerated. Both immediate and delayed G-CSF seem to decrease the days of fever, IV antibiotics and maybe hospital days.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, INFECTIOUS DISEASE SERVICE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/158 | **Status:** Terminated |
| **Title:** Study of Pyelonephritis in Women | | |
| **Start Date:** 08/06/93 | **Est. Completion Date:** Aug 95 | |
| **Department:** Medicine, Infectious Disease Service | **Facility:** MAMC | |
| **Principal Investigator:** LTC Ronald H. Cooper, MC | | |
| **Associate Investigators:** | MAJ Joseph T. Morris III, MC | |
| **Key Words:** pyelonephritis, women, ofloxacin, trimethoprim-sulfamethoxazole | | |

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|---|---|---|---|---|
| **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: No subjects entered. A better study became available and was substituted.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/042 | **Status:** Terminated |
| **Title:** Ketoconazole Absorption in HIV Infected Patients | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** | |
| **Department:** Medicine, Infectious Disease Service | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Joseph T. Morris III, MC | | |
| **Associate Investigators:** Etzkorn ET | LTC Ronald H. Cooper, MC | |
| **Key Words:** HIV, ketoconazole | | |

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|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $120.00 | **Periodic Review:** // |

Study Objective: To determine if the absorption of ketoconazole is normal in HIV positive individuals with a past history of an opportunistic infection.

Technical Approach: Approximately 30 subject, consisting of 15 healthy individuals as controls and 15 patients with HIV infection will be drawn from the Infectious Disease Outpatient Clinic. The Walter Reed Staging System will be used to subdivide the patients with HIV-1 infection into "early infection" (WR Stages 1 and 2) and "late infections" (WR Stages 3, 4, and 5).

Following an overnight fast and obtaining Informed Consent, ten milliliters of venous blood will be obtained from both patients and volunteer controls prior to the ingestion of a single 200 milligram tablet of Ketaconazole. Ten milliliters of venous blood will subsequently be obtained from patients and volunteer controls at 1, 1 1/2, 2, 2 1/2, and 3 hours after ingestion of the Ketaconazole tablet.

Ketaconazole quantitation will be determined by high-performance liquid chromatography (HPLC) with fluorescence detection. The simple T-test will be done to assess for a statistical difference between the control and study groups.

Progress: No subjects enrolled in FY 94. Study terminated due to insufficient potential study subjects.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/151 **Status:** Terminated

**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, Internal Med Svc **Facility:** MAMC

**Principal Investigator:** CPT Cynthia L. Clagett, MC

**Associate Investigators:** MAJ Patrick A. Cambier, MC
Prewitt K

**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. Study has been duplicated by elsewhere and published.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/054 **Status:** Completed

**Title:** The Effects of Saline Infusion on Hematocrit in healthy Euvolemic Patients: Hemodilution or Not?

**Start Date:** 02/04/94 **Est. Completion Date:** May 94

**Department:** Med /IM **Facility:** MAMC

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

**Associate Investigators:**
MAJ Howard M. Cushner, MC
Burns BJ
MAJ Agnes K. Ohno, MC

**Key Words:** hematocrit, euvolemia, hemodilution

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

Study Objective: This study will determine if there is a significant decrease in the hematocrit (HCT) and/or hemoglobin (HGB) after infusing normal saline into healthy subjects.

Technical Approach: Ten healthy volunteers will be examined, assessed clinically and with laboratory data to ensure euvolemia, as well as to rule out confounding medical problems that might interfere with the study and/or participation. On admission, their vital signs will be determined as will their weights and I/O's. A baseline HCT/HGB will be obtained and they will be placed in Fowlers position. They will be randomized to one of three study groups: 1) Control group - lying in Fowlers position for 8 hours. 2) Maintenance infusion group to receive 40 cc hour plus 1 cc/kg/hr. or 3) Bolus 2 liter bolus followed by maintenance infusion as above. The groups will have HCT/HGB measurements at 1, 4, and 8 hours. In addition they will be asked to come back at 24 hours for a final HCT/HGB. The same 10 subjects will be employed to return in 1 - 3 weeks to be randomly crossed over to one of the two remaining groups and the procedures will be repeated exactly. Finally, the 10 subjects will return a third time in 1 - 3 weeks after the last trial to complete the final group. ANOVA will be used to compare the control groups to the study groups. Repeated measures ANOVA will be used to determine any statistically significant difference between the groups.

Progress: 9 subjects entered. Abstract presented at 1994 Army American College of Physicians meeting.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/057 **Status:** Terminated

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

**Start Date:** 03/05/93 **Est. Completion Date:** Jan 94

**Department:** Medicine, Internal Medicine Service **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: Twenty-five patients have been entered. Data was uninterpretable due to poor data collection.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/066 **Status:** On-going

**Title:** Using Systems Methodology to Model and Deploy Ambulatory Care Resources

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

**Department:** Medicine, Internal Medicine Service **Facility:** MAMC

**Principal Investigator:** MAJ Duane J. Jeffers, MC

**Associate Investigators:** Tesfai Gabre-Kidan, MD
Kenric W. Hammond, MD
Scott Iverson, MD

**Key Words:**

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

Study Objective: To: 1) Modify and validate two computer simulation models of ambulatory care resource allocation nearing completion at the Seattle VA Medical Center (SVAMC) ambulatory care clinic; and 2) adapt these "source" models for the ambulatory care clinics at the Madigan Army Medical Center (MAMC) and American Lake VA Medical Center (ALVAMC), as well as 3) perform sensitivity analysis and preliminary validation.

Technical Approach: Existing computer simulation models of the Ambulatory Care Service at SVAMC will be further refined and adapted to the MAMC and ALVAMC Ambulatory Care Services over a period of two and one-half years. The adaptation process includes surveying interested parties at the two sites, collecting the necessary data, and changing the "source" model. Sensitivity analysis, which assesses how the models respond to parameter changes, will be performed on all three models using the data to construct the models as well as data collected subsequently. Preliminary validation of the model with the aim of determining how well the model represents the system in question will also take place. Surveys will be conducted to investigate the impact of the model development process on organizational behavior. The models will be used, in a future project, to suggest intervention(s) to reconfigure one or more of the ambulatory care clinics, whereupon the intervention will be implemented and assessed.

Progress: Computer models are being developed in conjunction with Seattle VA. Initial funding has been received through the VA. Initial equipment purchases have been made.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/018 **Status:** On-going

**Title:** Impact of Adult Primary Care Clinic (APCC) on the Health Status of Patients and the Resource Utilization of MAMC

**Start Date:** 11/05/93 **Est. Completion Date:** Oct 95

**Department:** Medicine, Internal Medicine Service **Facility:** MAMC

**Principal Investigator:** MAJ Duane J. Jeffers, MC

**Associate Investigators:**
MAJ Sabrina A. Benjamin, MC
CPT Robert V. Gibbons, MC
LTC Jackie W. Saye, AN
COL Eric B. Schoomaker, MC
MAJ Francis J. Landry, MC
Lupo M
Rhonda J. McColpin, DAC

**Key Words:** resource utilization, adult primary care clinic

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $1600.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To determine the impact of a primary care clinic operating with managed care principles (the Adult Primary Care Clinic), on the health status of patients and overall resource utilization by enrolled clinic patients within a tertiary care medical center.

Technical Approach: Approximately 100 patients from a pool of 14,500 being enrolled into the Adult Primary Care Clinic will be selected by random number table to provide the sample. The study will measure two main outcomes: 1. The health status of patients and 2. Hospital Resource Utilization using predetermined yardsticks. A 12 month retrospective and prospective chart review will be used to determine resource utilization.

Comparison of before and after rates of compliance will be analyzed by Chi-square analysis for categorical variables. Analysis of Resource utilization will be done by paired T-test and multiple linear regression.

Progress: 100 patients have been enrolled. Initial data collection has begun. Chart reviews have commenced. No data yet available for review.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/083 **Status:** On-going

**Title:** Converting Patients From One Anti-hypertensive to Another: Drug Usage Study on Felodipine: Cost Savings and Patient Outcomes

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

**Department:** Medicine, Internal Medicine Service **Facility:** MAMC

**Principal Investigator:** MAJ Francis J. Landry, MC

**Associate Investigators:**
CPT James D. Horwhat, MC
COL Richard J. Ferrell, MC
David Tomich, DAC
Lisa Pinski, DAC

**Key Words:** Anti-hypertensives:conversion, Felodipine, cost savings

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

Study Objective: This study will determine outcomes of switching patients from more expensive calcium channel antagonists to a less expensive alternative. Such a change will 1) decrease antihypertensive therapy cost 2) cause no adverse effect on blood pressure control.

Technical Approach: Patients enrolled in the Adult Primary Care Clinic and referred by their physician will be eligible for entry if they are currently on either Nifedipine XL or Cardizem CD for hypertension. Physicians will be prompted to refer potential patients via an information sheet provided by the pharmacy after record review. Referred patients will be seen in the newly designated "hypertension clinic". The following information will be collected on initial referral: 1) Patient demographics to include age, race, major medical problems, previous HTN meds, and current hypertensive meds 2) Baseline in office blood pressure recording 3) Subjective symptom assessment profile (SSAP).

Patients will be continued on current medication until 5 day self determination BPs are obtained. Patients or family members will be versed on the used of standardized and calibrated semiautomatic aneroid cuff (taken at 6-8 am, prior to medication and 6-8 pm).

On return to clinic patients will be started on Felodipine 5 mg PO qd and titrated to achieve desired blood pressure control as determined by mean systolic and diastolic home BP evaluations and set by either 1) primary physicians goal BP for specific patients or 2) BP less than 140/90. Upon each visit to clinic (minimum 3--initial, one at one week then q 2 weeks and final visit at 1 month post optimal titration) results of 5 day self measured BP will be reviewed, repeat in office BP measurement recorded, review of side effects obtained, post questionnaires (SSA)) completed.

Descriptive statistics will be used to describe the number of patients achieving targeted BP at each level of dose titration, number and type of adverse side effects and number of patients discontinued from felodipine. Total cost of antihypertensive therapy, number of antihypertensives used and mean change in systolic and diastolic blood pressured will be compared pre and post medicine change using the student t-test.

Progress: 15 subjects have been enrolled. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/037 **Status:** On-going

**Title:** A New Method of Diagnosing and Treating Patients With Dyspepsia and Antibodies to Helicobacter pylori

**Start Date:** 12/17/93 **Est. Completion Date:** Jan 95

**Department:** Medicine, Internal Medicine Service **Facility:** MAMC

**Principal Investigator:** CPT Eric J. Ormseth, MC

**Associate Investigators:**
MAJ Amy M. Tsuchida, MC
Peller T
Lyons FM
MAJ Kazunori Yamamoto, MC
LTC Gregory N. Bender, MC

**Key Words:** dyspepsia, H. pylori, diagnosis, treatment

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

Study Objective: To develop a cost effective algorithmic approach (ie. clinical pathway) that will predict which patients can be safely diagnosed and treated in a single outpatient visit for Helicobacter pylori induced symptoms of dyspepsia.

Technical Approach: Patients (300) with symptoms consistent with dyspepsia will be enrolled in the protocol. Patients will fill out a questionnaire designed to screen for those patients with symptoms consistent with dyspepsia. Those enrolled will all go through an esophagealgastroduodenoscopy (EGD). Those patients with evidence of peptic ulcer disease will be so identified. Biopsies of gastric mucosa will be taken from all patients and sent to the lab for analysis of gastritis as well as for the presence of H. pylori using histologic methods. At endoscopy, biopsy material will also be tested for H. pylori using the CLO test. In addition, the ELISA and Flex Sure antibody tests for H. pylori will be performed. The patients will then be routed through radiology where they will receive an UGI barium study while at the same time a nasogastric tube (NGT) intubation of the esophagus and stomach and biopsies for H. pylori will be taken. Patients who do not have evidence of PUD, but with a positive diagnosis for H. pylori, will be randomized to four treatment arms each lasting two weeks. In the first, patients will be treated with the current standard at MAMC Gastroenterology Service, that being a two week course of amoxicillin and omeprazole. The second group of patients will be treated with a combination of metronidazole, peptobismal, and tetracycline plus omeprazole. Patients will be treated with omeprazole alone in the third arm, and in the fourth arm patients will be treated with a placebo. All patients will be treated for two weeks. Patients with evidence of PUD and with a positive diagnosis for H. pylori will be randomized to one of the first three treatment arms mentioned above. They will not be given a placebo. At the completion of the two week treatment all patients will then be given 28 days of ranitidine 150 mg twice daily, then 14 days of once daily treatment. Patients will then be followed at 2, 4, 8, 12, 20, 24, 28 and 32 weeks after treatment. A follow-up worksheet will be updated by the study coordinator. Follow-up serological blood test using the same H. Pylori antibody test will be performed. They will have a repeat EGD at 12 weeks after day #1 of treatment at which time they will have repeat biopsies for H. pylori and to assess ulcer healing if they originally had PUD. Data will be analyzed using Kappa test to determine sensitivities, specificities, and positive and negative predictive values.

Progress: Approximately 45 subjects have been entered, however, only 14 have met criteria to advance to drug treatment.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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
Gilman MD

**Key Words:**

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

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: Fourteen patients have been enrolled since approval. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/179 **Status:** On-going

**Title:** Impact of Serial Neuroimaging Studies in Changing the TOAST Classification of Acute Stroke Patients

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

**Department:** Medicine, Internal Medicine Service **Facility:** MAMC

**Principal Investigator:** CPT Stephen M. Salerno

**Associate Investigators:** MAJ Francis J. Landry, MC Schoomaker

**Key Words:** TOAST classification, acute stroke, neuroimaging

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

Study Objective: (1) Determine how often a second neuroimaging study is done in a patient with a new, but stable or improving neurologic deficit, (2) Determine whether more than one neuroimaging study in a stable patient with a new neurologic deficit has any impact on the patient's TOAST classification system or medical management.

Technical Approach: 200 inpatient charts with the discharge diagnosis of acute stroke and two neuroimaging studies will be examined retrospectively. The results of the initial neurologic exam, stroke risk factors, initial neuroimaging study and all ancillary studies to include carotid duplex, electro and echocardiograms, chest radiographs, and other blood and DSF tests will be recorded. These results along with the official radiology report of the initial neurologic imaging exam will be classified using the TOAST system.

The number of patients receiving a second neuroimaging study will be recorded. The indication for the study will be documented. In the cases where a second study was obtained for diagnostic purposes, the TOAST classification will be reviewed a second time and any changes recorded. The PI will perform the initial and final TOAST classification.

The amount of times the second neuroimaging study changed clinical management, defined as a change in medication or ordering of another diagnostic test documented in the physicians progress notes, will be recorded. Days of hospitalization of patients getting two or more neuroimaging studies will be compared to those who receive only one.

Progress: Newly approved study. Chart review has just begun.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/066 | **Status:** Completed |
| **Title:** A Prospective Study of Headache in Pregnancy | | |
| **Start Date:** 05/01/92 | **Est. Completion Date:** | |
| **Department:** Medicine, Neurology Service | **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 Cost:** | **OMA** $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: All patients were entered and data collected. However, data was transferred to a disk and PI has been unable to retrieve it. PI has transferred to WRAMC. Will continue to attempt to access data and give us a report if she is able to.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** LTC William L. Clayton III, MC

**Associate Investigators:** Leininger M
CPT Curtis S. Hansen, RPH, MSC

**Key Words:**

| **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 benefited 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: No subjects entered yet due to change of associate investigators and need to appoint new ones.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 92/050 | **Status:** Terminated |
| **Title:** Effects of Valproic Acid on Semen Parameters in Male Epileptics | | |
| **Start Date:** 04/03/92 | **Est. Completion Date:** | |
| **Department:** Medicine, Neurology Service | **Facility:** MAMC | |
| **Principal Investigator:** LTC William L. Clayton III, MC | | |
| **Associate Investigators:**<br>LTC (P) Robert E. Jones, MS<br>James R. Wright, M.T. | COL Lawrence A. Marden, MC<br>CPT Katherine H. Moore, MS<br>Louis A. Matej, B.S. | |
| **Key Words:** epilepsy, semen parameters, valproic acid | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative Cost:** $0.00 | **OMA 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 interpretation 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: This project was terminated due to low enrollment. Only one subject had consented for sperm analysis. He showed a 30 % drop in motility.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/067 **Status:** Completed

**Title:** A Familial Syndrome of Hemiplegic Migraine and Nystagmus: Chromosomal Defect Localiztion and Ocular Motility Characteristics

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

**Department:** Medicine, Neurology Service **Facility:** MAMC

**Principal Investigator:** CPT Mark A. Elliott, MC

**Associate Investigators:**
S. J. Peroutka
MAJ Eugene F. May, MC
S. Welch

**Key Words:** Migraine, nystsgmus, chromosomes

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

Study Objective: To correlate the clinical histories of a pedigree with familial hemiplegic migraine with their ocular motility findings and genetic linkage analysis.

Technical Approach: This study analyzes the ocular motility characteristics and genetic linkage of a three generation family with familial hemiplegic migraine (FHM). Nine family members will examined, seven with a history of FHM, and two without. Examinations will include evaluations of saccades, smooth pursuits, vestibulo-ocular reflex (VOR), vestibulo-ocular reflex suppression, primary position nystagmus, and optokinetic nystagmus. DNA linkage analysis will be performed on affected and unaffected family members using blood samples. The clinical histories, ocular motility findings, and DNA linkage analysis will be correlated.

Progress: 9 subjects were entered. Abstract presented at 20th Annual Meeting of North American Neuro-ophthalmology Society and 13th Annual Neurology AMEDD meeting. Manuscript in preparation.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/129 | **Status:** On-going |
| **Title:** The Assessment of Motor Recovery After Stroke Induced Hemiplegia | | |
| **Start Date:** 08/05/94 | **Est. Completion Date:** Aug 94 | |
| **Department:** Medicine, Neurology Service | **Facility:** MAMC | |
| **Principal Investigator:** CPT Eric I. Hassid, MC | | |
| **Associate Investigators:** | MAJ Jonathon Newmark, MC | |
| **Key Words:** hemiplegia, stroke, motor recovery | | |

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

Study Objective: We hope to determine whether or not there exist certain consistent patterns of motor recovery after stroke. We also hope to be able to prognosticate about extent of motor recovery with relation to lesion site and size.

Technical Approach: Select patients from the neurology service who have sustained their first non-hemorrhagic stroke affecting motor function will obtain an MRI of the brain at about the 7 day post event mark for purposes of accurate neuroanatomical localization. These patients will be evaluated weekly to assess motor recovery. No additional studies which would not be part of good stroke care will be done. Clinical and statistical significance will be done by a statistician. The initial data analysis will be longitudinal, modeled upon that of Twitchell. Should trends develop of statistical significance, standard tests including ANOVA will be used as data points.

Progress: 25 subjects have been entered. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/039 **Status:** Terminated

**Title:** Felbamate Monotherapy in Newly Diagnosed Partial Epilepsy

**Start Date:** 12/17/93 **Est. Completion Date:** Jan 95

**Department:** Medicine, Neurology Service **Facility:** MAMC

**Principal Investigator:** MAJ John W. McBurney, MC

**Associate Investigators:** LTC William L. Clayton III, MC
Michele D. Leininger, RN

**Key Words:** epilepsy, Felbamate

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

Study Objective: To determine the efficacy of felbamate monotherapy in preventing recurrent seizures in subjects with newly diagnosed partial onset epileptic seizures.

Technical Approach: This is an outpatient, multi-center, parallel, double-blind, randomized placebo-controlled clinical trial of 200 subjects between 14 and 65 years of age with newly diagnosed partial onset epilepsy. Subjects will be randomized to one of the three groups: felbamate monotherapy at 1200 mg/day, felbamate monotherapy at 2400 mg/day, or placebo. Study drug will be administered in a B.I.D. regimen. In addition to regular and frequent clinic visits where blood chemistry, hematology and urinalysis will be monitored, each participant will maintain a daily seizure log. Weekly telephone contacts will be accomplished to monitor the seizure status of each subject in order to allow early detection and treatment of breakthrough seizure activity. The study endpoint is seizure recurrence.

Progress: No patients were enrolled. PI discontinued study due serious adverse events in national study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/153 **Status:** On-going

**Title:** Use of Proton Magnetic Resonance Spectroscopy (MRS) to Determine the Anatomic Location of a Pathologic Lesion in a Patient with Post-traumatic Movement Disorder

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

**Department:** Medicine, Neurology Service **Facility:** MAMC

**Principal Investigator:** MAJ Jonathon Newmark, MC

**Associate Investigators:** None

**Key Words:** PET, focal dystonic syndrome

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

Study Objective: To use magnetic resonance spectroscopy (MRS) technology to verify and refine the anatomic localization of a lesion suspected on single proton emitted computed tomography (SPECT) in a unique patient.

Technical Approach: The patient will have 2 MRS sessions one week apart at the University of Washington Medical Center, Seattle. Each procedure will take approximately 60 minutes; no injections of dye will be used during either procedure. The patient will be required to go off anticholinergic medication during this one week period between the two examinations.

Progress: New protocol. Enrollment has not begun.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/019 **Status:** On-going

**Title:** Use of CSF D-dimer Assay to Differentiate Subarachnoid Hemorrhage From Traumatic Lumbar Puncture

**Start Date:** 11/05/93 **Est. Completion Date:** Jun 94

**Department:** Medicine, Neurology Service **Facility:** MAMC

**Principal Investigator:** CPT David J. Wilke, MC

**Associate Investigators:**
LTC William L. Clayton III, MC
Larson RR
Elliott MA
Lipps DC
MAJ Mark D. Brissette, MC
CPT Dale T. Waldner, MC

**Key Words:** Assay:D-dimer, subarachnoid hemorrhage, lumbar puncture

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $100.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To prospectively determine the sensitivity and specificity of the CSF D-dimer assay in differentiating subarachnoid hemorrhage from traumatic lumbar puncture.

Technical Approach: This study will analyze cerebrospinal fluid (CSF) and plasma samples from 100 patients with a clinical history suggestive of subarachnoid hemorrhage (SAH). A lumbar puncture is done as part of the standard diagnostic workup. The fluid will be tested for D-dimer, xanthochromia and cell counts in addition to routine chemistries. A D-dimer will be obtained simultaneously from a peripheral blood sample that is routinely obtained for PT/PTT. The diagnosis of SAH will be determined by a combination of results from CT, LP, neuroimaging, and autopsy, which will serve as our "gold standard". Traumatic LP will be determined by the findings as noted above, plus the absence of SAH by standard diagnostic means.

Progress: 3 subjects entered. Change of PI late in FY resulted in delay of further enrollment until FY 95.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, PULMONARY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/024 **Status:** Completed

**Title:** Relationship of Airway Occlusion Pressure (Po.1) and Lung Compliance

**Start Date:** 11/05/93 **Est. Completion Date:** Jun 94

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** MAJ George N. Giacoppe Jr., MC

**Associate Investigators:**
MAJ James D. Pike, MC
CPT Jeremy R. Blanchard, MC
LTC Anthony S. Sado, MC

**Key Words:** airway occlusion pressure, lung compliance

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $100.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To assess the relationship between P0.1 and lung compliance.

Technical Approach: Weaning parameters, including lung compliance, will be obtained on all patients undergoing mechanical ventilation in the surgical and medical ICUs. Stepwise multiple regression on these parameters will be performed to determine which correlates most closely with the P0.1.

Progress: 75 subjects were entered. No relationship of PO.1 to lung compliance was detected. Lack of relationship suggests use of both variables as independent predictors of weaning from mechanical ventilation.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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: Fourteen of thirty patients needed have been enrolled at this time, and will be followed for one year. Currently analyzing pre- and 3 month (post) studies.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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: Thirty patients have been evaluated for possible enrollment; however, only four patients have meet all the eligibility requirements. The tests performed on each patient include pulmonary function testing, fiberoptic bronchoscopy with bronchoalveollar lavage (BAL), transbronchial biopsies (TBBx), and high-resolution CT scanning of the chest. So far, the presence or absence of "ground glass" by CT scan has not correlated with alveolitis by BAL or TBBx on any of the patients. The small number of subjects so far makes drawing valid conclusions from the data impossible.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/178 **Status:** On-going

**Title:** The Sensitivity and Specificity of High Resolution CT Scanning in the Detection of Alveolitis in Interstitial Lung Disease

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

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** CPT Joseph S. Pina, MC

**Associate Investigators:** CPT Bernard J. Roth, MC
CPT Cristopher A. Meyer, MC

**Key Words:**

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

Study Objective: To determine the sensitivity and specificity of the ground glass opacification on high resolution CT scanning of the chest in detecting alveolitis in the evaluation of interstitial lung disease

Technical Approach: Records of all high resolution CT scans of the chest over the past year will be reviewed in the Department of Radiology. The cases with no ground glass opacification seen on the scan will be checked to see if a bronchoscopy with bronchoalveolar lavage and transbronchial biopsy was done as part of the evaluation in the pulmonary clinic. If a diagnosis was obtained by transbronchial biopsy, open lung biopsy, or other modality, it will be noted. The subject's outpatient record, chest X-ray, etc., will also be reviewed to assess the stage and clinical extent of the disease process. The data obtained then will be analyzed to determine if any trends exist, such as diagnoses more likely to present with the lack of ground glass opacification.

Progress: New study. No patients entered.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/059 **Status:** Terminated

**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 Service **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. The study has been terminated due to difficulty in obtaining appropriate patients. There were no adverse events associated with this protocol.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 90/099 **Status:** On-going

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

**Start Date:** 08/17/90 **Est. Completion Date:**

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** CPT 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. Three additional patients are needed. Data analysis will occur after completion of the project.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/015 **Status:** On-going

**Title:** Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure

**Start Date:** 12/07/90 **Est. Completion Date:**

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** 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-oculogram, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous capnograpny. At this time the patient will be tested to determine if he tolerates intermittent positive pressure ventilation through a nose mask (nIPPV). Patients who tolerate nIPPV will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAP and nIPPV patients using Student's T test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or $PaCO_2$ will be considered a positive result of nIPPV.

Progress: Seven patients have been enrolled. The protocol was placed on hold during most of FY 94 due to lack of adequate support staff. Increased staffing in FY 95 will allow continuation of the protocol.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 89/043 **Status:** Terminated

**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 Service **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, energy 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. The analysis of the collected data will be used to design a future protocol.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/024 **Status:** On-going

**Title:** Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging

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

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** 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: 30 patients have entered the study. Protocol has been started at Wm Beaumont Army Medical Center. An additional study site at Walter Reed Army Medical Center is being negotiated. No conclusion can be made at this time.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/023 **Status:** On-going

**Title:** The Effect of Using A Standard Mouthpiece vs Facemask on the Exercise Tolerance of Patients With Severe Chronic Obstructive Pulmonary Disease (COPD)

**Start Date:** 11/05/93 **Est. Completion Date:** Mar 94

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** CPT Jeffrey S. Strong, MC

**Associate Investigators:** CPT Bernard J. Roth, MC
CPT James D. Horwhat, MC

**Key Words:** COPD, exercise, facemask

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $430.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To evaluate the possible effect of standard apparatus used to measure exercise parameters on the maximal exercise tolerance of patients with severe COPD. A secondary objective is to determine if pursed-lip breathing improves exercise capacity by decreasing oxygen demand or by improving ventilation-perfusion (VQ) relationships.

Technical Approach: We plan to perform 3 consecutive standard exercise tests on 15 patients with severe COPD. The three exercise trials will consist of one performed with a mouthpiece and noseclip, one with a facemask, and one without either. A one hour break will be provided between each trial, and the order of the trials will be randomly assigned for each individual. Multiple non-invasive parameters will be assessed. The data will be analyzed to evaluate for the presence of statistically and clinically significant differences in exercise tolerance between each technique of assessment.

Progress: 10 subjects have been entered. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/139 **Status:** On-going

**Title:** Total Lung Capacity Measured by a Medical Diagnostic Imaging Support System Planimetry Technique, Part II

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

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** CPT Lisa L. Zacher, MC

**Associate Investigators:**
MAJ Donald V. Smith, MC
CPT Daniel Walsh, MC
LTC William H. Cragun, MC
Bryceland P

**Key Words:** Lung:capacity, MDIS, planimetry

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

Study Objective: To prospectively compare a planimetry method to calculate total lung capacity from a medical diagnostic imaging support (MDIS) system posteroanterior (PA) and lateral chest roentgenogram with total lung capacities derived from body plethysmography.

Technical Approach: This study will compare the planimetry technique outlined by Harris on a MDIS system posteroranterior and lateral chest roentgenograms with total lung capacities measured directly by body plethysmography in 100 patients being referred for pulmonary function testing that include measurement of lung volumes by body plethysmography. Each subject will undergo a chest roentgenogram and body plethysmography. Results from the two methods will be compared to obtain a correlation coefficient. In addition, regression equations will be obtained based on plethysmography values to determine if a new equation is necessary.

Progress: Thirty nine subjects were studied. A correlation coefficient of 0.91 was obtained for BPTLC versus PTLC. Similar to other studies, PTLC was greater than BPTLC. A regression equation derived from a pilot study of normal subjects on the MDIS system improved estimation of TLC. All patients with less than 80% predicted BPTLC had less than 80% predicted PTLC. The simplicity, speed, reliability, economy, storage and transmission properties of the MDIS system planimetry method are reasons to encourage its further clinical use.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **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 discriminate analysis method to determine risk factors associated with lung cancer.

Progress: This study is on-going with 24 subjects entered in FY94 (30 total at MAMC). Study has been expanded to WBAMC, with enrollment of 8 subjects. Data analysis should begin within 6 months.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/006 **Status:** Completed

**Title:** Total Lung Capacity Measured by a Medical Diagnostic Imaging Support System Planimetry Technique, Part 1

**Start Date:** 10/01/93 **Est. Completion Date:** May 94

**Department:** Medicine, Pulmonary Service **Facility:** MAMC

**Principal Investigator:** CPT Lisa L. Zacher, MC

**Associate Investigators:** Mueller JP
MAJ Donald V. Smith, MC

**Key Words:** lung capacity, MDIS, planimetry

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $200.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To prospectively compare a planimetry method to calculate total lung capacity from a medical diagnostic imaging support (MDIS) system posteroanterior (PA) and lateral chest roentgenogram with total lung capacities derived from body plethysmography.

Technical Approach: We propose a pilot study comparing the planimetry technique outlined by Harris et al (1) on a MDIS system posteroanterior and lateral chest roentgenograms with total lung capacities measured directly by body plethysmography in 20 normal subjects. Each study subject would undergo a chest roentgenogram and body plethysmography values to determine if a new equation is necessary. A sample population would be obtained by picking subjects who would represent a broad range of predicted total lung capacities.

Progress: 13 subjects have been studied. Correlation coefficients for BPTLC versus PTLC and BPTLC versus PSA were 0.95 and 0.80 respectively. The average time required to calculate the 3 PSA's was 3 minutes. This pilot study showed the efficacy of this method. A prospective study looking at the role of planimetry in a random sample of pulmonary patients is planned.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF MEDICINE, RHEUMATOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/168 **Status:** Completed

**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 Service **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: 18 subjects were screened. 13 were randomized to be in the study. There were no adverse outcomes. Data were forwarded to the sponsor.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF NURSING

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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:** | Maniaci PA | |
| **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: 141 subjects have been entered. Data is being analyzed statistically.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/175 | **Status:** On-going |
| **Title:** Planning for Pregnancy: The Experience of Women With Diabetes | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** | |
| **Department:** Nursing | **Facility:** MAMC | |
| **Principal Investigator:** Gwendolyn M. Brown, RN, BSN | | |
| **Associate Investigators:** None | | |
| **Key Words:** pregnancy, diabetes | | |

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

Study Objective: (1) To determine the percent of women who have knowledge and understanding about the relationship between poor glycemic control and birth defects prior to becoming pregnant, (2) To assess the frequency and quality of pregnancy planning information women with diabetes receive from providers, (3) To determine the percent of women with diabetes who plan their pregnancies and who optimize their glycemic control prior to pregnancy, (4) To identify barriers and motivators associated with pregnancy planning and preconception glycemic control, across a broad socioeconomic population base, (5) To determine the rate of birth defects associated with diabetes and pregnancy in Washington State.

Technical Approach: Patients enrolled will be mailed a set of questionnaires designed to assess a variety of factors related to their experiences with diabetes. The study also involves home interviews by a member of the study interview team. This informal interview will last about 1 to 1 1/2 hours. Brief notes will be taken and if agreed to, the interview will be tape recorded to that the information given can be recorded accurately. Patients will also be asked to sign a release of information form to obtain selected information from their hospital records: blood sugar and glycosylated hemoglobin values, complications during pregnancy, and newborn assessment of their babies.

Progress: PI is only referring subjects to University. Accrual is continuing.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/110 | **Status:** On-going |
| **Title:** Psychology of Pregnancy: Peace and War-time | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Sep 94 | |
| **Department:** Nursing | **Facility:** MAMC | |
| **Principal Investigator:** LTC Susan L. Burroughs, AN | | |
| **Associate Investigators:** None | | |
| **Key Words:** pregnancy, peace,war-time psychology | | |

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

Study Objective: To explore peace and war-time differences in the psychological experience of pregnancy.

Technical Approach: Three questionnaires will be used in the research. 1) A newly developed pregnancy questionnaire, the R-PAAS, will be used to look at feelings that women have about the experience of pregnancy, and how these feelings vary over a one week period. 2) A questionnaire called the SCL-90-R will be used to look at symptoms women have experienced over the past week. 3) Background information about occupation, education, and medical history will be obtained using a demographic information sheet.

Progress: Still entering subjects.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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: 42 subjects were entered. Data analysis will commence in the next few months to determine final N.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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<br>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 administration, and the resulting neonatal physiologic responses and outcomes. A secondary aim will be to determine the relationships between type of surfactant and administration technique, nursing assessed neonatal clinical cues of a hemodynamically significant patent ductus arteriosus, and neonatal outcomes.

Technical Approach: This is a prospective, quasi-experimental study, in which selected physiologic parameters will be monitored during exogenous surfactant administration in a convenience sample of 24 premature infants. Subjects will be randomly divided into one of three administration groups. A control group receiving no surfactant would not be appropriate as it would mean the infants would receive less than the standard of care.

The convenience sample will consist of 24 neonates, with the diagnosis of RDS, who will receive exogenous surfactant using rescue therapy. The three groups will be: 1) n=12, Exosurf administered by sideport adapter. 2) n=6, Survanta administered by feeding tube through endotracheal tube. 3) n=6, Survanta administered through double lumen ET tube. After consent is obtained and electronic monitors applied, baseline data will be collected for 10 minutes after which either Survanta or Exosurf will be administered by the predetermined route. The infant will be ventilated during the procedure using NICU SOPs. At completion of the surfactant administration, data collection will continue for 2 hours. Nurses will be free to make whatever adjustments they deem necessary in response to the lung compliance changes using their own judgment or in consultation with the physician.

Descriptive statistics obtained from the data will be categorized into critical ranges for each of the data collection periods. Demographic data will be coded and analyzed.

Progress: 16 patients entered. 2 deaths occurred within 48 hours of entry and were deemed not to be protocol related. Enrollment and data collection continue.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/157 **Status:** Completed

**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, blooc 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: Five subjects were entered into the study. Recruitment of subjects was limited due to low census in the NICU during the period of rental for the Capillary Blood Flow equipment. Data from the subjects continues to be analyzed. Preliminary results show no clinically significant changes in temperature gradients over time. Although measurement of dorsal foot and abdominal skin temperature gradients works well in the clinical arena, this study was not able to validate this method of measuring thermal compensation due to the difficulty of obtaining accurate measures of capillary blood flow both during and following nursing care. Presented at the Western Society for Research in Nursing, April 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 89/028 **Status:** Completed

**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: Data collection is complete. Data analysis is complete. At this time, work continues in interpretation of results and final report preparation. Results indicate no clinically significant differences in CO2 either by treatment group or by level of FiO2. There were statistically significant changes in oxygen saturation over time; however, when the two treatment modes were compared, there was no statistically significant difference between treatment groups. The provision of 20% increase in FiO2 prevented suction-induced oxygen desaturation. Intracranial pressure changes were not clinically significantly different; of interest were the trends of ICP during ETS by treatment mode. Presented at AACN Endotracheal Study Group Meeting and Pacific Northwest ANN Conference, 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/003 **Status:** Terminated

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

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 problem could not be resolved, and as a result, the protocol was terminated.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/100 **Status:** On-going

**Title:** Postoperative Wound Healing: Hydration and Oxygenation

**Start Date:** 05/06/94 **Est. Completion Date:** Oct 96

**Department:** Nursing **Facility:** MAMC

**Principal Investigator:** LTC Brenda I. Mygrant, AN

**Associate Investigators:**
Lori A. Loan, AN
Diane M. Pierson, BS, BA, CCRN
JoAnne D. Whitney, Ph.D., RN
COL Daniel G. Cavanaugh, MC

**Key Words:** wound healing:hydration, wound healing:oxygenation

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 02/17/95 |
|---|---|---|---|---|

Study Objective: 1) Compare an augmented fluid replacement protocol to a conventional fluid replacement protocol after open-heart surgery for its effects on:

a. subcutaneous tissue oxygen levels ($pSCO_2$), using a subcutaneous tonometer/optode system, measured on the day of surgery and on postoperative day 1 and day 2

b. subcutaneous tissue perfusion, based on a perfusion score measured on the day of surgery and on postoperative day 1 and 2

c. wound healing indicators in wound tissue samples including: 1) hydroxyproline accumulation measured by high pressure liquid chromatography; and 2) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation on postoperative day 7.

2) Determine the relationships between subcutaneous tissue oxygen levels and wound healing indicators and incidence of wound complications/infections.

Technical Approach: This is a randomized 2 group (80 subjects per group) experimental design. Forty subjects per group will be collected in the first year, with a proposed additional 40 subjects compiled in the second year pending funding of the competitive continuation application next year. The control group will receive the standard protocol for postoperative intravenous fluid. The experimental group will receive fluid augmentation with an additional intravenous infusion of 20 cc/hr of 5% Dextrose in water (D5W). The random group assignments will be placed in envelopes that will be opened after the patient returns to the ICU from surgery, prior to the first oxygen measurement. The biochemical and cellular markers of healing will be measured 7 days postoperatively. The tissue indicators of oxygen and perfusion will be measured on the day of surgery and for the next 2 postoperative days. Sternal and leg wound assessments will be made for the first five days during hospitalization. For subjects discharged before the 7th postoperative day the ePTFE implant will be removed on the 7th postoperative day during a clinic visit. Descriptive statistics (means, standard deviation) will be used to summarize sample description variables. Student's t tests or Chi-Square analysis will be performed on the variables measured pre-intervention to ensure randomization of the two groups.

Progress: Funding received Oct 94. No patients entered yet.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/154 | **Status:** On-going |
| **Title:** Wellness Intervention With Pregnant Soldiers | | |
| **Start Date:** 09/21/94 | **Est. Completion Date:** Sep 95 | |
| **Department:** Nursing | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Judy B. Peniston, MC | | |
| **Associate Investigators:** Lancaster KA | Wendy M. Lombardi, DAC | |
| **Key Words:** pregnancy, female soldiers, wellness | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: The objectives of this investigation is to determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcome indexes: 1) homologous transfusion requirements 2) post-op hours until extubation 3) post-op hours until SICU discharge 4) post-op days until hospital discharge.

Technical Approach: Cardiopulmonary bypass patients will be prospectively randomized into one of two groups. The test group will utilize cardiopulmonary bypass circuits treated with Duraflo II (surface bound USP heparin). The control group will utilize precisely the same assortment of perfusion components, but they will not have been treated with Duraflo II.

During the post-operative period the patient will have routine blood work done. Complications during the intra-operative and post-operative periods will be documented. Higgins scores will be used during the analysis of data.

Progress: New study. No subjects entered.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/125 **Status:** Completed

**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. Rea, AN

**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 surgical 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: Final data analysis showed that while nursing staff did not significantly alter their nursing activities as operationally defined by 13 care categories, it is thought that this finding is reflective of system immaturity. With planned computer system enhancements, nursing staff may find less time is needed for documentation activities. A third data collection period after integration of system enhancements is planned. In contrast this study provides clear evidence that a computerized CIS improves documentation completeness. It is believed that this completeness is closely linked with the on-screen cueing of required responses. If true, the development of screens that match the desired documentation outputs is important. Additionally, it is thought that the one cluster of standards that received a JCAHO score of 4 could be improved by linking specified nursing interventions with a time-delayed screen cue to alert the nursing staff to document the effects of their interventions, a form of artificial intelligence. While the quality of documentation was not specifically evaluated, the JCAHO standards are used as a proxy measure of overall quality in the current voluntary accreditation process. Presented at the TAMC Nursing Research Conference, 1994.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **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<br>Karen A. Thomas, Ph.D. | |
| **Key Words:** neonates,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 repeated measures ANOVA will be used to test group differences in the BNBAS, NCAFS, PSI and Transition from NICU to Home Questionnaire. The 24-hour recordings of sleep obtained by the NCASA will be summarized and differences in total sleep and wake time, number of awakenings, and synchrony to day-night pattern will be tested using ANOVA and repeated measures ANOVA. Cyclicity of NCASA data will be determined within subject using cosinor analysis.

Progress: Data collection continued to include weight gain, length of stay, transition to oral feeding, sleep/wake time, diurnal cycling of sleep/wake states, heart rate and body temperature, incidence of stress cues, neurobehavioral assessment, neurological examination, hearing screen, parental stress and physiologic stability. Added to the study during FY 94 was a home visit to assess the impact of a modified NICU environment on parents in the period of transition from hospital to home and post discharge. Approximately 8 home visits remain. Data entry is continuing. Anticipated completion of data entry is the second week of December. Analysis of the environmental data (i.e., light and sound recordings) has been started. Anticipated completion of analysis is the end of December 1994.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/101 **Status:** On-going

**Title:** Fatigue Following Childbirth: Military Family Outcomes

**Start Date:** 05/06/94 **Est. Completion Date:** Sep 95

**Department:** Nursing **Facility:** MAMC

**Principal Investigator:** LTC Michelle T. Renaud, AN

**Associate Investigators:**
Killien MG
Karen A. Thomas, Ph.D.
Debra DePaul, RN
Blackburn ST
Lori A. Loan, AN

**Key Words:** childbirth:fatigue, childbirth:military

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

Study Objective: To determine if an advanced practice nursing intervention to reduce fatigue will promote job well-being, parenting ability, and infant outcomes among military active duty personnel and their spouses/partners following the birth of an infant.

Technical Approach: Pregnant females and their spouses/partners (if applicable) will be recruited during weeks 28-32 of gestation in the prenatal clinic at MAMC. Data will be collected at six time points: prenatally at time of enrollment and post birth when the infant is 24-48 hours, 2 weeks, 2 months, 4 months, 6 months or age. Time measures correspond to typical timing of clinic visits. During the clinic visit, parents will complete a packet of questionnaires specific to each time of measure and active military status. If only one parent attends the clinic visit, the other parent will complete their part of the questionnaire packet at home and return it by mail. Following birth, infant neurobehavioral status will be assessed by trained study personnel at 24-48 hours of age. At 4 and 6 months of age parent-infant interaction will be assessed during the clinic visit using the NCATS observational tool. At 6 months of age infant development will be assessed by trained study personnel using the CAT/CLAMS-r and Denver II assessment instruments.

Experimental subjects will begin the fatigue modulating intervention following the initial assessment at Time 1. Throughout the study experimental subjects will receive care from the project's advanced nurse practitioners. Continuing monitoring of the intervention's integrity and effectiveness will allow the nurse practitioner to reinforce and modify the intervention as appropriate.

Progress: Funding received. Official start date is 1 Oct 94.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **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:** 1LT Barbara Wall, RN | | |
| **Associate Investigators:**<br>Frances M. Lewis, RN, Ph.D.<br>MAJ Stacey B. Young-McCaughan, AN | Diane D. Stajduhar, RN<br>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-metastatic breast cancer in the mother; (2) to test a causal model of nurses' coaching behavior underlying the intervention; (3) to test the cost-effectiveness of the intervention.

Technical Approach: Subjects will be recruited whose mothers were recently diagnosed (6 months or less) with early stage breast cancer and have had either breast conserving surgery or simple modified mastectomy. Subjects will be living in a partnered relationship and have 1 or more school-age children living at home. A total of 100 families will be recruited and randomly assigned to either the Experimental or Control group.

The Experimental Group will receive home visits and the Control or Evaluation Group will receive "treatment as usual" from physicians and clinic nurses. The initial visits (by the Nurse Coach Team) will last one to one and one half hours, on 3 occasions, during which time experienced nurses will talk about the breast cancer, the concerns or issues related to it, and ways which might prove helpful in managing the experience. Each visit will include a joint session, individual sessions and a concluding joint session with the mother and partner.

The Couples' Evaluation Team Visits are made on four occasions. Each visit from that team will involve the completion of questionnaires and an interview about their experiences as a result of the breast cancer. After permission is granted the school aged children living at home will be asked to complete several questionnaires about self esteem and their relationships with their parents and friends.

The outcome analysis will employ multivariate analysis and which can detect differences between the Experimental and the Control groups.

This study will be conducted in conjunction with the University of Washington.

Progress: Two patients have been entered. 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 Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/078 **Status:** On-going

**Title:** The Relationship Between Skin Temperature Changes and Level of Sensory Blockade in Subarachnoid Block with Bupivacaine

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

**Department:** Nursing **Facility:** MAMC

**Principal Investigator:** MAJ Linda A. Webster, AN

**Associate Investigators:**
MAJ Jeffrey W. Albritton, AN
CPT Hyelan Kim, AN
CPT Michael R. Lamparelli, AN
CPT Kyu OK Simpson, AN

**Key Words:** sensory blockade, skin temperature, bupivacaine

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

Study Objective: To determine if skin temperature change can be used to predict the level of sensory blockade following the injection of bupivacaine into the subarachnoid space.

Technical Approach: This observational (n=30) study will examine changes in skin temperature as displayed on a skin temperature monitoring device concurrently with a response to a standardized "pin prick" test at dermatome levels T1 thru T10. These concurrent observations will be recorded every 2 minutes for the first ten minutes and again at fifteen minutes after the injection of bupivacaine into the subarachnoid space.

An analysis of distributions of sensory blockade lag from sympathetic blockade will be examined and numeric summary statistics will be computed. In addition to numeric techniques, graphical displays of the data will be examined to assess the individual variability and predictive usefulness of any blockade relationships found (e.g. Can skin temperature predict sensory blockade level, thereby reducing the need for repeated "pin prick" assays).

Progress: Approximately 20 subjects have been entered.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/145 | **Status:** On-going |

**Title:** A Comparison of Smoking Cessation Behaviors Between Patients Who Have Experienced A Documented Acute Myocardial Infarction (MI) and Patients Admitted for Suspected MI

| | |
|---|---|
| **Start Date:** 07/01/94 | **Est. Completion Date:** Dec 94 |
| **Department:** Nursing | **Facility:** MAMC |
| **Principal Investigator:** Williams ME | |
| **Associate Investigators:** | Saptunzoff |
| **Key Words:** smoking:cessation, myocardial infarction | |

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

Study Objective: To examine the differences in smoking cessation attitudes and behaviors between patients who have experienced a documented acute myocardial infarction (AMI) and patients who have been admitted to a hospital for a suspected myocardial infarction ("cardiac scare").

Technical Approach: A sample of 40 patients admitted with a first AMI and a sample of 40 patients admitted with suspected MI will be studied to compare the differences in smoking cessation attitudes and behaviors between the two groups. The study will be conducted using a questionnaire containing demographic questions as well as questions which seek to identify the attitudes patients have about smoking and the attitudes they have about smoking cessation. To complete the study, each participant will receive a telephone call from the investigator six weeks after his/her discharge from the hospital asking about his/her smoking status.

Demographic data will be analyzed using an unpaired t-test and chi-square analysis. A Hollingshead Four-Factor Index for socioeconomic status will be computed and correlated with reported smoking status. Mann-Whitney U test will be utilized to analyze the non-parametric data from the questionnaire and provide the statistical data to address each research question.

Progress: No subjects entered yet.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/020 | **Status:** Completed |
| **Title:** Weaning: The Transition of the Preterm Infant to an Open Crib | | |
| **Start Date:** 11/05/93 | **Est. Completion Date:** Dec 93 | |
| **Department:** Nursing | **Facility:** MAMC | |
| **Principal Investigator:** Sue Wilson, RN | | |
| **Associate Investigators:** Lori A. Loan, AN | LTC Barbara S. Turner, AN | |
| **Key Words:** preterm infant:open crib, transition | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: To determine the effect of the intervention of weaning, from an incubator to an open crib, on the preterm infant's skin temperature, weight, and feeding tolerance.

Technical Approach: This retrospective study will use the convenience sample of the thirty-five premature infants requiring double walled incubator thermoregulatory support who were enrolled into a previous protocol. The following data will be collected from the patient records: 1. Abdominal skin temperature, 2. total daily caloric intake, 3. Feeding tolerance as identified as change in method of feeding as in total number of nipple feedings and gavage feedings per day and number of residuals. Measurement of these parameters will be for the period 48 hours before weaning until 48 hours after weaning.

The data will be analyzed for trends during the measurement period for each subject and among subjects. Repeated measures of analysis of variance will be used to analyze the body temperature and weights before and after weaning. Results from this study will provide data to further the understanding of the intervention of weaning on the preterm infant.

Progress: Thirty subjects were entered. All subjects were weaned to the open crib. Clinically, the number of subjects with temperatures below the normal range decreased during the weaning process; however, there were infants who continued to have below normal temperatures at 48 hours after weaning. On the average, subjects gained weight during weaning; however, some subjects gained weight during weaning, but no infant had a weight loss at 48 hours after weaning. The criteria of feeding tolerances as a whole was inconclusive; however, the percentage of nipple feedings and the number of changes in method of feeding were supported as criteria for thermal stability based on the data collected. Utilizing the number of residuals as a criterion was not supported; however, an increased or unchanged number of residuals may be a subtle behavioral cue to thermal instability and requires further research. The combination of the subtle behavioral cues of feeding tolerances along with temperature and weight gain may give a more accurate picture of weaning and thermal stability.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF OBSTETRICS/GYNECOLOGY

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/011 | **Status:** On-going |
| **Title:** The Incidence of Spontaneous Abortion in Obese Patients: A Retrospective Chart Review | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** Jun 94 | |
| **Department:** OB/GYN | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Alicia Y. Armstrong | | |
| **Associate Investigators:** | CPT David H. Harrison, MC | |
| **Key Words:** abortion, obesity | | |

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

Study Objective: To determine the response rates of metastatic or locally advanced breast cancer with administration of four cycles of high doses of Taxol as a three hour infusion with Rhu-G-CSF support. 2) To evaluate the feasibility of administering this regimen for at least four cycles.

Technical Approach: Women with metastatic Stage IV or locally advanced Stage IIIb breast cancer, with measurable disease, will be eligible for this study. Although patients may have received adjuvant chemotherapy, they should not have received any chemotherapy for metastatic disease. All patients will receive a premedication regimen prior to taxol administration. Taxol will be administered as a three hour continuous infusion at a dose of 250 mg/M2; the infusion will be repeated every 3 weeks. Rhu-G-CSF will be given at 5 ug/kg subcutaneously from day 2 of every cycle. After completion of the four cycles, further treatment, including continuation of Taxol will be at the discretion of the investigator.

Progress: Data collection in progress.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/156 | **Status:** Completed |
| **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:** C.C. Engel, Jr. | MAJ Alicia Y. Armstrong<br>Walker E | |
| **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: Thirty one patients were entered; 28 completed the protocol Final data are being analyzed. Abstract submitted to Armed Forces District meeting of ACOG.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Katherine S. Foley, 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 Glenn R. Markenson, 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 chronic 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: Thirty patients have been entered into the study. Only one patient has delivered preterm and one has developed pre-eclampsia. A higher rate of complications was expected. To assure only the highest risk patients are enrolled, women with AFP values of 2.0 - 2.4 will be limited to 50. That will assure 50 women with values of 2.5 and greater will be entered (these are the patients at highest risk). This study will begin at TAMC and continue at MAMC with hopes of completion within 1 year.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/043 **Status:** Terminated

**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: Two subjects were entered. PI was reassigned. Subsequent accrual was not successful.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/041 **Status:** Terminated

**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 Cost:** | $0.00 | **OMA 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: 2 subjects entered (9 total). Data insufficient to evaluate. PI departed. No replacement found.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/002 | **Status:** Terminated |

**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:** Edward Illions, M.D. | MAJ Alicia Y. Armstrong |
| **Key Words:** cervical dysplasia, cerivcal mucus, LEEP | |

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|---|---|---|---|---|
| **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.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/155 | **Status:** On-going |
| **Title:** Pregnancy Outcomes Comparison Between Active Duty Military Women and Working and Non-working Family Members | | |
| **Start Date:** 09/21/94 | **Est. Completion Date:** Sep 95 | |
| **Department:** OB/GYN | **Facility:** MAMC | |
| **Principal Investigator:** LTC Roderick T. Hume JR, MC | | |
| **Associate Investigators:** | Lombardi W | |
| **Key Words:** Pregnancy:outcomes, female soldiers | | |

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

Study Objective: To evaluate the differences between the pregnancy outcomes of active duty soldiers, working family members, and non-working family members.

Technical Approach: This study entails tracking pregnancy outcomes at MAMC and comparing those outcomes between active duty soldiers and working family members and non-working family members. Data will be gathered from an initial questionnaire, mid-pregnancy questionnaire (5 1/2 - 6 1/2 months gestation), and obstetric and delivery records. Through this series of questionnaires and surveys demographic information will be obtained. Additionally, information will be collected regarding an individuals' type and quantity of work, stress levels at work, other kinds of physical activity in which they engage, lifestyle and social habits, and self esteem and morale. These can be considered variables which may affect pregnancy outcomes and/or complications.

Data collection from obstetric and delivery records will include types of complications, method of delivery, labor duration, gestational age and infant weight at birth, NICU stay (if applicable), and the costs related to the delivery and/or neonatal care. Dependent variables will be pregnancy outcomes (birth weight, gestational age at delivery, Apgar score) and complications; Independent variables will be type and quantity of work, perceived stress levels, lifestyle and social habits and self esteem.

Progress: New protocol. Awaiting MRMC funding.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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:** LTC Glenn C. Tripp, MC | Millie Herd, AN | |
| **Key Words:** herpes simplex virus, pregnancy | | |

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| **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 56 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 94 **Protocol No.:** 92/060 **Status:** Terminated

**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, 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 subjects have been entered. The collection of cases is slower than anticipated and the technical quality of the ultrasounds is poor. The data was examined and it was determined that the study should be terminated.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/010 | **Status:** Terminated |
| **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<br>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. Data insufficient to evaluate prior to reassignment. No replacement PI.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/112 **Status:** Completed

**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

| **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: Five subjects were entered. Data was forwarded to the sponsor.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/004 **Status:** Completed

**Title:** The Effects of Atrial Natriuretic Factor Infusion on Perfusion Pressure in the Isolated Perfused Human Placental Cotyledon

**Start Date:** 11/05/93 **Est. Completion Date:** Mar 4

**Department:** OB/GYN **Facility:** MAMC

**Principal Investigator:** MAJ Glenn R. Markenson, MC

**Associate Investigators:**
MAJ Timothy J. Boley, MC
MAJ Jerome N. Kopelman, MC
MAJ Katherine S. Foley, MC
LTC Arthur S. Maslow, MC

**Key Words:** Atrial natriuretic factor, cotyledon

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $4110.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: To investigate the effect of atrial natriuretic factor (ANF) on the maternal and fetal components of the human placenta, via the dually perfused isolated human cotyledon. The properties investigated will include changes in perfusion pressure, intravascular electrolytes, and the production of endothelial derived vasoactive substances, after preconstriction of the chorionic vessels with angiotensin II.

Technical Approach: All experiments will utilize the dually perfused cotyledon model. Two cotyledons from the same placenta will be perfused. The influence of physiologic and pharmacologic doses of ANF on the placental model will be studies. Both cotyledons will receive infusions of angiotensin II into the chorionic artery. Then one cotyledon will receive increasing doses of ANF. A total of 10 placentas will be perfused. In the first five of the perfusion studies, ANF will be injected into the intervillous space, in the next five ANF will be injected into the chorionic artery. The effects, if any on the chorionic perfusion pressure will be measured. After each injection of ANF, effluent samples from both the intervillous and chorionic circulation will be assayed for sodium, chloride, nitric oxide, thromboxane and prostacyclin.

Progress: Fifteen placentas were studied. Pharmacologic doses of ANF decreased the pressor responses to AT II, which confirms the presence of ANF receptors in the fetoplacental vasculature. Physiologic doses of ANF did not change the pressor response to AT II. The role of ANF in placentas from normal term pregnancies appears to be limited in uncomplicated placentas.

# Detail Summary Sheet

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

**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 ANOVA.

Progress: This protocol was listed as completed in FY 93. However, while sorting through the data, it became evident to the investigators that the assays could be performed in a more optimal manner. The previous samples were not duplicated. Therefore, the investigators requested that this study be reactivated to assay more samples for thromboxane and 6-keto prostaglandin F1-alpha.

This request was approved and the investigators are now obtaining appropriate samples as they become available.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/022 **Status:** Terminated

**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 Cost:** | **OMA** $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, posthydration, 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: This protocol has been terminated due to clinic work loads of the investigators. No patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 89/017 **Status:** Terminated

**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: Protocol terminated to be rewritten in updated format. One animal was used.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/085 **Status:** On-going

**Title:** Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig (Sus scrofa) and Goat (Capri hircus)

**Start Date:** 02/09/94 **Est. Completion Date:** Feb 97

**Department:** OB/GYN **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:**
LTC David J. Magelssen, MC
MAJ Alicia Y. Armstrong
COL Paul N. Smith, MC
MAJ Rosemary L. Casey, MC
MAJ Mary C. Nace, MC

**Key Words:** surgical management:gynecology, endoscopy, pig, goat,animal Study

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

Study Objective: 1) To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. 2) To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. 3) To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans.

Technical Approach: With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

Progress: No animals were used during FY 94.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/138 | **Status:** On-going |
| **Title:** Once vs Thrice Daily Gentamicin Dosing in Postpartum Endomyometritis | | |
| **Start Date:** 08/05/94 | **Est. Completion Date:** | |
| **Department:** OB/GYN | **Facility:** MAMC | |
| **Principal Investigator:** CPT Anne B. Shrout, MC | | |
| **Associate Investigators:** | MAJ Jerome N. Kopelman, MC | |
| **Key Words:** endomyometritis, gentamicin, dosing | | |

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

Study Objective: To evaluate the once-daily dosing of gentamicin compared to the usual thrice-daily regimen of gentamicin in the treatment of postpartum endomyometritis and in patients with chorioamnionitis that undergo cesarean section.

Technical Approach: Patients will be enrolled from the patient population at Madigan. They must be diagnosed with postpartum endomyometritis or with chorioamnionitis and subsequent cesarean section. Patients will be randomized into two arms. Group 1 will receive the standard gentamycin 1.75 mg/kg every 8 hours IVPB with clindamycin 900 mg every eight hours. Group 2 will receive gentamycin 5.25 mg/kg every 24 hours IVPB and clincamycin 900 mg every eight hours IVPB. Both groups will have frequent drug levels obtained from a heplock in the opposite arm. All patients will remain on antibiotics until afebrile X 48 hours. Clinical response and failure will be determined by Chi Square.

Progress: Eight subjects have been entered. No adverse reactions or unusual outcomes.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/157 **Status:** On-going

**Title:** The Effect of Pregnancy on the Performance, Health, and Nutritional Status of Postpartum Soldiers

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 95

**Department:** OB/GYN **Facility:** MAMC

**Principal Investigator:** COL Paul N. Smith, MC

**Associate Investigators:**
LTC Kathleen A. Westphal, MC
CPT Anthony Pusateri, MS
LTC Joseph R. Dettori, MC
LTC Alana D. Cline, MS
CPT Teresa M. Vanderlinde, MC

**Key Words:** female soldiers:pregnancy, health

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

Study Objective: (1) To determine the proportion of soldiers who return to their preconception fitness level at their first postpartum APFT, and to compare; (2) distribution, incidence and risk of injury and illness between postpartum soldiers and nonpregnant, non-postpartum soldiers; (3) changes in weight and body composition between soldiers and family members in the postpartum period; (4) bone mineral status between late pregnant and postpartum soldiers and their family members; (5) nutritional status between late pregnant and postpartum soldiers and family members; (6) iron and folate status among late pregnant and postpartum soldiers, late pregnant and postpartum family members, and nonpregnant, non-postpartum soldiers.

Technical Approach: Women in their third trimester of pregnancy will be identified through the OB-GYN clinics at their respective hospitals and asked to volunteer for the study. Non-pregnant soldiers will be solicited through the unit chain of command.

Full-time health personnel hired for the study at each site will measure the dependent variables and collect the data. Study health personnel will be supervised by an Army obstetrician. Study subjects will undergo blood draws to assess iron, folate and calcium status; anthropometric measurements to determine body composition, dual energy x-ray absorptiometry to measure bone mineral density and to validate body fat evaluations. Fitness will be assessed using the last pre-pregnancy Army Physical Fitness Test scores and the first postpartum APFT scores for all soldiers in the study. Medical records of all soldiers will be reviewed monthly to record all injuries and illnesses. Demographics, health habits and diet history, and exercise before, during and following pregnancy will be obtained through questionnaires.

Progress: Awaiting funding. No subjects entered.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF PEDIATRICS

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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. '94 (n=16,893). 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.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/095 **Status:** Terminated

**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. Four sets of twins were studied. Complete cardiac data were obtained (pressure & output) in all cases. Magnesium sulfate-treated animals had ductal patency. Due to uncontrollable differences in lamb age at delivery, data variables could not be appropriately analyzed.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 90/058 | **Status:** Suspended |
| **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:** 06/10/94 |
|---|---|---|---|---|

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 id 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: No animals used this FY. Suspended pending rewrite.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/055 **Status:** Suspended

**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,children:7 - 18 YO

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

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 follow-up 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 follow-up evaluation. All diagnoses and medical problems will be determined at follow-up 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 follow-up clinical interviews.

Progress: No subjects were enrolled into this study during FY 94. Dr. Kelley is in the process of assigning new PI.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/098 | **Status:** On-going |
| **Title:** Is the Use of Nose Clips Necessary in Children Performing Routine Spirometry? | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** Sep 94 | |
| **Department:** Pediatrics | **Facility:** MAMC | |
| **Principal Investigator:** LTC Edward R. Carter, MC | | |
| **Associate Investigators:** Berhens M | COL Donald R. Moffitt, MC | |
| **Key Words:** Spirometry:children, nose clips | | |

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

Study Objective: To determine whether the use of nose clips significantly affects spirometric values in children performing routine spirometry.

Technical Approach: This is a randomized, investigator-blinded, prospective, crossover study that will involve 100 subjects. Each subject will be asked to perform spirometry without nose clips and then again with nose clips. Half will be randomized to perform spirometry without nose clips first and the other half will perform spirometry first with nose clips. The investigator involved with the pulmonary function testing will not know when the nose clips are being used. Each subject will perform a minimum of three acceptable spirometric maneuvers with and without nose clips. Standard pulmonary function values will be obtained.

Patients will be placed into 4 groups of children: ≤ 10 years-old and who have never performed spirometry (Group 1); ≤ 10 years-old who have performed spirometry in the past (Group 2); > 10 years-old have never performed spirometry (Group 3); and > 10 years-old who have performed spirometry before. Groups were chosen because both experience with the test and the age of the patient may influence the affect of nose clips on spirometry.

Progress: Sixty seven subjects have been entered. We have so far found no difference between NC and no NC. We did not have very many patients with airways obstruction, so to strengthen our results we wish to enroll 10-20 patients with cystic fibrosis and airways obstruction.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/040 **Status:** Completed

**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 Student's t test, and difference in clinical score (median) will be assessed with the Wilcoxon rank sum test.

Progress: The protocol worked very well.. Blinding was achieved. Excellent data was collected on 11 children with acute, severe asthma. No patient asked to participate in the study declined. We found no significant difference in PFTs or clinical score with Heliox vs. air/ox. However, no patient got worse with Heliox. Abstract submitted for 1995 USPS meeting and ATS meeting.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/041 | **Status:** On-going |
| **Title:** The Short-Term Use of a Helium-Oxygen Mixture in Infants Hospitalized 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:** CPT Anthony R. Neri, MC | COL Donald R. Moffitt, MC | |
| **Key Words:** bronchiolitis: helium-oxygen, infants | | |

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| **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: 3 subjects entered. We may terminate the study. We find that our primary outcome - clinical score, is too variable to pick up any small difference between heliox and air/ox. It may not be worth our while to continue. However, we do not plan to terminate the study until the next RSV season (Jan-Mar 95) is done. There may be some sick infants with RSV who would be ideal for the study and we may evaluate them.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/129 **Status:** On-going

**Title:** Randomized Trial of Nerbulized vs Instilled Cromolyn Sodium (Intal) in the Preventin of Airway Inflammation in Ventillated Premature Neonates

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

**Department:** Pediatrics **Facility:** MAMC

**Principal Investigator:** 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 MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $4379.00 | **Periodic Review:** 10/21/94 |
|---|---|---|---|---|

Study Objective: To evaluate the efficacy of direct intra-tracheal instillation of Cromolyn Sodium (Intal) vs traditional Cromolyn Sodium nebulization in preventing airway inflammation in a high risk group of intubated premature neonates.

Technical Approach: The study population will consist of premature infants born at 32 weeks gestation and less, who are placed on mechanical ventilation. Those infants for which informed parental consent has been obtained will be randomized to receive either 3 mg Cromolyn via direct intra-tracheal instillation every 6 hours for 16 doses or 20 mg by nebulization every 6 hours for 16 doses. The doses will be started within 12 hours of being placed on a ventilator. At 48, 72, and 96 hours after the first dose is given, the infant will undergo tracheobronchiolar lavage. The lavage fluid will be analyzed for number and type of inflammatory cells as well as for the presence of chemical mediators of inflammation. Analysis of data will be by CHI-square and Student's t-test. Variables that will be considered in the analysis will be use of antenatal steroids, surfactants, antibiotics, indomethacin, diuretics and bronchodilators.

Progress: Seven patients have been enrolled. Four have been randomized to the nebulized Cromolyn (control) group and three into the instilled Cromolyn (study) group. The samples collected for cell count have been run and data entered into the flow sheet. The samples collected for LTB4 analysis are being held in a -70 C freezer. There is not enough data to run a statistical comparison at this time. Patient enrollment has been slower than anticipated, secondary to lower numbers of eligible infants in the NICU. Approximately 50% of those parents approached for consent have enrolled their infants into the study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/025 **Status:** On-going

**Title:** Fetal Development: Are Undiagnosed Maternal Inborn Errors of Metabolism Associated With Poor Intrauterine Growth and Congenital Malformations in the Developing Fetus

**Start Date:** 12/17/93 **Est. Completion Date:** May 95

**Department:** Pediatrics **Facility:** MAMC

**Principal Investigator:** MAJ Thomas D. Carver, MC

**Associate Investigators:**
James R. Wright, M.T.
LTC Arthur S. Maslow, MC
CPT Andrew J. Bauer, MC
CPT Katherine H. Moore, MS
MAJ Jerome N. Kopelman, MC
MAJ Katherine S. Foley, MC

**Key Words:** metabolism, fetal development, malformations, fetal death

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

Study Objective: To determine if previously undiagnosed maternal inborn errors of metabolism (amino acidemias or organic acidurias) are a significant cause of fetal growth retardation, fetal malformations and fetal demise.

Technical Approach: In this controlled prospective study, the serum amino acid and urine organic acid contents will be evaluated in 3 groups of pregnant women. Group 1 will consist of women who have had 2 or more spontaneous abortions, a stillbirth, or have delivered a child identified as growth retarded, microcephalic, mentally retarded or with congenital anomalies. Group 2 will be the control group and consist of women who have had no more than 1 spontaneous abortion, or have delivered children with no known anomalies or are pregnant for the first time. Group 3 will consist of women not previously enrolled who are found during the pregnancy to have a fetus which is growth retarded (≤ 3rd percentile on two ultrasounds 3-4 weeks apart), is microcephalic (≤ 3 percentile on 2 ultrasounds 3-4 weeks apart), or has congenital anomalies.

The study questionnaire will be filled out at the time of entrance into the study and will consist of information pertaining to maternal educational and health history.

All samples will be sent to clinical investigation for storage until they can be analyzed. The blood samples will be frozen at -70 C until analyzed for quantitative amino acid content. The urine sample will be analyzed by GD Mass Spectroscopy for organic acid content. If both are normal then no further investigation will be done. If both are abnormal compared to published standards, the appropriate diagnostic work-up will be done to further identify the abnormality. All samples will be collected after an 8-12 hour fast to avoid post-prandial fluctuations in amino-acid concentrations. The study participants will be notified of their individual results (if abnormal) as they become known.

Progress: One hundred four women have been enrolled. Biographical data has been entered into the database for 80 subjects thus far. The chromatogram for about 50 of the amino acid samples have been run. The glycine conjugate standards have arrived and the organic acid library is being established for the GC-mass spectrometer.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/022 **Status:** Terminated

**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 were entered into this study because of the difficulties in obtaining the necessary placebo medication.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/137 **Status:** On-going

**Title:** A Phase III Multiple Dose Use Study of APAP Extended Release Pediatric Suspension Compared to Children's Tylenol Elixir in the Treatment of Febrile Children

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

**Department:** Pediatrics **Facility:** MAMC

**Principal Investigator:** COL Marvin S. Krober, MC

**Associate Investigators:**
CPT Kevin M. Creamer, MC
Jung C
CPT Katherine M. Hermann, MC

**Key Words:** fever, APAP, Tylenol

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

Study Objective: To compare the antipyretic effect, side effects, and overall product acceptability of acetaminophen extended release pediatric suspension (320 mg/5 ml) compared to acetaminophen elixir 160 mg/5 ml, in the treatment of febrile children at home in a multiple dose use study.

Technical Approach: Patients entering this study will have two consecutive temperatures taken at least 15 minutes apart. The baseline temperature must be ≥ 102.0°F to 105.5°F rectally or ≥ 101.0°F to 104.5°F orally. Patients will then receive acetaminophen elixir 10-15 mg/kg or acetaminophen extended release pediatric suspension at 20-30 mg/kg. The Extended Release treated group will have temperatures taken at 0, 1, 2, 4, 6, 8, and 10 hours after the initial dose. After the initial dose, subsequent identical doses should be given every 8 hours thereafter as needed for temperature of >101.0°F up to a maximum of 3 doses/day. The Elixir treated group will have their temperature taken at the same interval and subsequent doses should be given every 4 hours thereafter for temperatures of > 101.0°F up to a total daily maximum of 5 doses. Daily telephone follow-up will be performed by the nurse and a follow-up evaluation will be made in the clinic on day 4.

Progress: No patients entered. Just received CIRO approval.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Cost:** | **OMA** $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: 2 subjects have been enrolled. 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

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/046 | **Status:** Terminated |

**Title:** Single Dose Cefixime Therapy for the Treatment of Uncomplicated Urinary Tract Infections in Female Children and Adolescents

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| **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<br>MAJ Elisabeth M. Stafford, MC |

**Key Words:** urinary tract infections:female children, cefixime

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative 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. 2 subjects were entered. Terminated due to insufficient subjects and departure of PI.

# DETAIL SHEETS FOR PROTOCOLS

# PREVENTIVE MEDICINE SERVICE

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/090 | **Status:** On-going |
| **Title:** Clinical Trial to Compare Two Smokeless Tobacco Cessation Programs | | |
| **Start Date:** 04/01/94 | **Est. Completion Date:** Jul 95 | |
| **Department:** Preventive Medicine | **Facility:** MAMC | |
| **Principal Investigator:** Kathie J. Brendemuhl, RN | | |
| **Associate Investigators:** VanBeuge SS | MAJ Jeffrey D. Gunzenhauser, MC | |
| **Key Words:** smoking cessation:smokeless tobacco | | |

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

Study Objective: The objective is to ascertain whether either of two treatment regimens is more effective in assisting individuals in cessation from use of smokeless tobacco products.

Technical Approach: This is a clinical trial which will compare the effectiveness of two regimens on smokeless tobacco cessation rates. Users of smokeless tobacco products in the Fort Lewis and McChord Air Force Base communities will be recruited to participate in a tobacco cessation program designed specifically for smokeless tobacco users. Potential volunteers will be screened through the use of a questionnaire and a limited history and physical examination. After obtaining informed consent, participants will be randomized to receive one of two treatment regimens. Both treatment groups will receive physician advice to quit using tobacco products and will be prescribed nicotine replacement therapy in accordance with the Madigan Army Medical Center (MAMC) prescribing protocol. In addition, the first treatment group (phone counseling) will receive an initial face-to-face counseling session with the study nurse during which time a quit date will be selected, standardized written materials will be provided, and follow-up procedures will be reviewed; subsequently each participant in this treatment group will receive four (4) phone follow-up consultations at 48 hours, 1 week, 3 weeks, and 6 weeks after the preselected quit date. The second treatment group (Freshbreath) will participate in the FRESHBREATH smokeless tobacco behavior change therapy course, a 6-hour course, meeting as a group twice a week (1.5 hours each session) for two weeks. During the course of the trial (1 year), participants in both groups will have access to the study nurse or physician to address specific needs or problems. Cessation rates will be monitored by self-report during phone interviews at 3 months, 6 months, and 1 year. Differences in cessation rates will be assessed through multivariate analysis. Determinants (confounders) of cessation other than treatment group will be included in the analytic model. Statistically significant results will be interpreted at the .05 level of significance.

Progress: Funding continues to be sought.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/076 **Status:** Terminated

**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: Data was transferred to disk which was lost when PI was reassigned - no other persons at MAMC wanted to continue study.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/045 | **Status:** Terminated |
| **Title:** Analysis of the Impact of A Mammography Health Care Finder on the Utilization of Breast Cancer Screening Activities in a Military Community | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Jul 97 | |
| **Department:** Preventive Medicine | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Jeffrey D. Gunzenhauser, MC | | |
| **Associate Investigators:** | LTC John P. Kugler, MC | |
| **Key Words:** Cancer:breast, mammography, military | | |

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

Study Objective: The technical objective of this study is to assess the effect of a minimal-cost intervention designed to reduce barriers to mammography utilization in a military community. Component objectives include training and utilizing a mid-level clerk to: 1) schedule and monitor mammography utilization, 2) provide breast cancer screening education to targeted high risk groups, and 3) educate providers on current screening guidelines. A final objective is to conduct baseline and follow-up population-based surveys to assess profiles and changes of mammography determinants.

Technical Approach: This study is designed to perform an intervention which targets specific barriers to mammography utilization and to monitor the effect of this intervention on a population basis. The study will be conducted over a 3-year period. Military health care beneficiaries in the Madigan catchment area will receive a specific intervention, while those living in the Ft. Belvoir catchment area will receive normal care. The intervention consists of the employment of a single individual dedicated to improving access to mammography in the MAMC catchment area. This employee will be a mid-level clerk who will be trained and used as a mammography health care finder and breast cancer screening education coordinator. In order to reduce logistical barriers within the medical center, this individual will monitor, facilitate and coordinate all requests for mammography. To minimize the effect of behavioral determinants of mammography under-utilization, the clerk will coordinate an educational outreach program targeted at high-risk, low-utilization beneficiary groups. Aspects of mammography utilization will be measured through population-based surveys conducted at baseline, 12, 24, and 36 months. The primary measure of effect of the study will be the adjusted proportion of women in the MAMC catchment area who comply with national guidelines for breast cancer screening.

Progress: Study was never funded and will not be resubmitted.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 being done in conjunction with WRAIR. No subjects entered in FY 94 at MAMC. A revised protocol is being prepared and will be submitted in FY 95.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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 | | |

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

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: No subjects have been enrolled.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/059 | **Status:** Completed |
| **Title:** Cervical Cancer in the US Army | | |
| **Start Date:** 02/04/94 | **Est. Completion Date:** May 94 | |
| **Department:** Preventive Medicine | **Facility:** MAMC | |
| **Principal Investigator:** CPT John A. Pavlin, MC | | |
| **Associate Investigators:** | MAJ Margot R. Krauss, MC | |
| **Key Words:** Cancer:cervical, Army | | |

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

Study Objective: 1) Determine the number of women in the US Army who have developed cervical cancer, to include carcinoma in situ (CIS). Compare this rate with the national average. 2) Determine the prevalence of cervical cancer risk factors in young enlisted soldiers, and the self reported utilization of preventive services (Pap smears and pelvic exams). 3) Determine the actual rate of screening Pap smears in an active duty population. 4) Describe the rate of abnormal Pap smears (dysplasia to CIS) in an active duty population.

Technical Approach: A descriptive study will be employed to determine the need for more aggressive Pap smear screening in the US Army. The presence of risk factors and behavior in the active duty population of 18-29 year old enlisted women will be documented. Active duty enlisted women who are currently stationed at Fort Lewis will be picked by choosing alternate social security numbers. Approximately 600 questionnaires will be sent utilizing three mailings to increase return. The questionnaires will be used to determine risks and date of last Pap smear, if they were informed of the results, and demographic data. The data will be analyzed for self-reporting of Pap smears, knowledge of results, and the presence of risk factors. Demographic data will then be calculated to determine if race, age, marital status and home of record are predictive of risk factors for use and knowledge of Pap smears.

Progress: 776 subjects were studied. 90% of USA women get an annual PAP smear. Risk factors are about the same as civilians. However, abnormal smears are about twice as frequent as civilian women. Manuscript in preparation.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/158 | **Status:** On-going |
| **Title:** Risk Factors for Lead Poisoning in Children of Ft Lewis Personnel | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** Apr 94 | |
| **Department:** Preventive Medicine | **Facility:** MAMC | |
| **Principal Investigator:** CPT Ann A. Yackovich, MC | | |
| **Associate Investigators:** | MAJ Margot R. Krauss, MC | |
| **Key Words:** lead poisoning, children, Ft Lewis | | |

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

Study Objective: To assess the risk factors for lead poisoning in children of Ft. Lewis active duty personnel.

Technical Approach: A self-administered questionnaire will be mailed to a sample of Ft. Lewis personnel with children under six years of age. The survey will include questions on housing (peeling paint, age, location), use of various ethnic remedies (which will be specifically named in the survey question so that there is no confusion on the part of the respondent), and any hobbies or occupations of the adult members of the household which could increase the children's exposure to lead. The hobbies/occupations question will be in two parts: part will include a listing of specific hobbies and occupations and the other part will be short answer, allowing the respondent to add any pertinent information or suggest something that is not specifically listed.

The survey will also include several additional questions on other childhood risk factors such as use of bicycle helmets, childproofing in the home, and use of car safety seats. Analysis of variance and logistic regression will be performed; variables will include race, sex, location of housing, use of ethnic remedies, hobbies, and occupation.

Progress: Approximately 1000 questionnaires have been mailed to potential participants.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF RADIOLOGY

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/056 | **Status:** Terminated |

**Title:** Protocol for the Compassionate Use of Indium In-111 Pentetreotide in Patients with Known or Suspected Neuroendocrine Tumors Containing Somatostatin Receptors

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| **Start Date:** 02/04/94 | **Est. Completion Date:** Jan 95 |
| **Department:** Radiology | **Facility:** MAMC |

**Principal Investigator:** LTC John M. Bauman, MC

**Associate Investigators:** None

**Key Words:** Cancer:neuroendocrine, Indium In-111 pentetreotide, somatostatin

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

Study Objective: To allow the compassionate use of indium In-111 pentetreotide in patients with a known or suspected neuroendocrine tumor containing somatostatin receptors, in whom conventional imaging methods are ineffective or insufficient.

Technical Approach: For planar imaging, patients will receive 3.0 mCi of indium ;In-111 pentetreotide and 3.0 mCi of Indium In-111 Chloride Sterile Solution. For SPECT imaging, patients will receive 6.0 mCi of indium In-111 pentetreotide and 6.0 mCi of Indium In-111 Chloride Sterile Solution.

Patients will drink two 8-ounce glasses of water immediately prior to administration of indium In-111 pentetreotide. All patients will be observed for one hour following drug administration and will be evaluated at 24-hours post-procedure.

Anterior and posterior whole body imaged will be performed approximately 4, 24 and optionally 48 hours after intravenous administration of indium In-111 pentetreotide. In addition, each patient will undergo SPECT imaging as clinically indicated.

Progress: This was a compassionate treatment protocol. No patients were entered before the drug was approved and released by the FDA.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/119 **Status:** On-going

**Title:** Gallbladder Ejection Fractions

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

**Department:** Radiology **Facility:** MAMC

**Principal Investigator:** LTC John M. Bauman, MC

**Associate Investigators:**
MAJ Michael F. Lyons II, MC
MAJ Richard R. Gomez, MC
Jerome Billingsley, M.D.
LTC Clifford L. Simmang, MC

**Key Words:** gallbladder, ejection fractions

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $6166.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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: Seven subjects have been entered. Accrual continues.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/077 | **Status:** On-going |

**Title:** Determination of Normal Regional Myocardial Thallium Distribution and Development of a New Display Technique

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| **Start Date:** 05/06/94 | **Est. Completion Date:** Jul 94 |
| **Department:** Radiology | **Facility:** MAMC |

**Principal Investigator:** LTC John M. Bauman, MC

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| **Associate Investigators:** | COL Stanton R. Brown, MC |
| Jerome Billingsley, M.D. | MAJ James H. Timmons, MC |

**Key Words:** thallium, myocardial distaribution, new technique

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

Study Objective: (1) To determine the normal regional variation in the myocardial distribution of 201T1. (2) To use this information to create a color translation table for semiquantitative analysis of Thallium images. (3) To evaluate the ability of the new translation table to predict the presence or absence of significant coronary artery lesions at cardiac catheterization.

Technical Approach: We intend to pull all Thallium studies and cardiac catheterization data on patients who have had both studies at MAMC since 1 August, 1992. Results of Thallium and catheterization studies will be entered on worksheets and from there into a computerized database.

We will review a minimum of 10 data sets where both the Thallium study and catheterization data are normal. The relative distribution of Thallium on the stress studies will be quantitated using a circumferential image profile on the short axis slices using 8 mid-ventricular slices which demonstrate a complete left ventricular chamber.

Sixty values will be calculated for each of eight central stress slices. The maximum and minimum count values for all slices will give us the range of normal Thallium variation for each patient's stress study. This value, will be expressed as a percent of the maximum uptake. Finally the mean, range and standard deviation for the 10 patients' percent normal variations will be calculated.

The color map will be created using the information from phase I. All images are limited to a maximum of 256 gray levels. We will divide these 156 levels into only 5 colors for our map. As a result, individual pixels will be colored according to their relative count value with respect to the maximum in the image. Break points for color levels will be determined by the mean percent normal variation and standard deviation.

The new color translation will then be used to reinterpret a minimum of 50 Thallium studies for which cardiac catheterization data is available. Studies will be read separately by 2 board certified nuclear medicine physicians without knowledge of the clinical history, previous Thallium result, exercise data or catheterization result. Using only the new color table, results will be annotated as normal or abnormal. If abnormal, location and extent of abnormality will be recorded. Actual colors of defects will be recorded and subsequent data analysis for correlation with the bull's eye plots, prior image interpretations and cardiac cath data will be made for each color level of defect.

Progress: Data has been collected. Awaiting image review and analysis.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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:** | // |
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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: Three subjects have been entered. Accrual continues.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/098 | **Status:** Terminated |
| **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 | | |

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| **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 sulfur 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: Could not obtain normal volunteers.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/038 **Status:** On-going

**Title:** Digitally Acquired Radiographic Air Contrast Barium Enema vs. Colonoscopy in Polyp Detection, Cancer Detection, and cost in a Federal Tertiary Care Center

**Start Date:** 12/17/93 **Est. Completion Date:** Jan 95

**Department:** Radiology **Facility:** MAMC

**Principal Investigator:** LTC Gregory N. Bender, MC

**Associate Investigators:**
Lyons FM
MAJ Amy M. Tsuchida, MC
CPT Thomas P. Peller, MC

**Key Words:** polyps, barium enema, colonoscopy

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To determine if digitally acquired radiographic air contrast barium enema (DAR-ACBE) examinations of the colon might serve as a cost effective surrogate to colonoscopy in the MAMC colon cancer screening program.

Technical Approach: By obtaining DAR-ACBE and colonoscopy on the same patient a test of diagnostic equality for these two examinations will be performed. The diagnostic equality of these examinations will be tested by assessing their ability to find polyps >5mm in size and in finding cancers of any size.

Progress: No subjects entered yet.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/167 | **Status:** Completed |

**Title:** A Descriptive Study of Antral Nodularity, Fold Thickening, and Narrowing: Upper GI Series Findings That May Indicate Chronic Gastritis Secondary to Helicobacter pylori (A Pilot Study)

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| **Start Date:** 09/21/94 | **Est. Completion Date:** Mar 95 |
| **Department:** Radiology | **Facility:** MAMC |
| **Principal Investigator:** CPT John D. Crocker, MC | |
| **Associate Investigators:** | LTC Gregory N. Bender, MC |
| **Key Words:** gastritic, Helicobacter pylori, upper GI | |

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

Study Objective: To establish a preliminary descriptive correlation of the upper GI series findings of antral nodularity, fold thickening, and narrowing with the histologic diagnosis of gastritis secondary to Helicobacter pylori.

Technical Approach: All UGI reports during the time frame of 1 June 1993 to 31 March 1994 (and for a longer period if necessary) are to be reviewed for the findings of antral nodularity, fold thickening, or narrowing. Those patients who were biopsied by either esophagogastroduodenoscopy (EGD) or by nasogastric technique are to be included. The pathologic diagnoses are to be tabulated and correlated to the UGI series findings. The sample population was derived from the general patient population of MAMC presenting to the Radiology Department for an upper GI series from various clinical services. Those patients with a history of gastric surgery will not be included.

Progress: Thirty-one subjects have been entered. 19 were found to have chronic active gastritis and be positive for H. pylori, 5 were normal, 5 had inflammation but were negative for H. pylori, 1 had a superficial biopsy with organisms suspicious for H. pylori, and 1 had an insufficient amount of tissue. Abstract submitted to Radiological Society of North America

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/030 **Status:** On-going

**Title:** Decompression of Acute Colonic Pseudo-obstruction With A Tricomponent Coaxial System Under Fluorosscopy

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

**Department:** Radiology **Facility:** MAMC

**Principal Investigator:** Do-Dai DD

**Associate Investigators:** LTC Gregory N. Bender, MC

**Key Words:** colonic obstruction decompression, fluoroscopy

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To respectively review all the colonic decompression of pseudo-obstruction with a tricomponent coaxial system (TAS) under fluoroscopy performed between 1 March 1992 and 1 August 1993 to determine the related morbidity and mortality. The study will also attempt to introduce methods or techniques that can prevent the risks of bleeding and colonic perforation.

Technical Approach: This study will retrospectively review the following information: indication, procedure time, indwelling decompression catheter time, complications of bleeding and colonic perforation and rate of recurrence of pseudo-obstruction after removal of decompression catheter.

Progress: Colonic decompression with TAS was successfully performed in 5 patients without associated complications of bowel perforation or bleeding. Patient comfort was enhanced immediately after placement of the TAS. Complete decompression was observed in all patients within 6-18 hours. There was no recurrence after removal of the TAS. Presented at the Radiological Society of North America.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/124 | **Status:** On-going |
| **Title:** Measurement Accuracy of Reformatted MR Images in Cardiac Imaging Usign A Pig Cadaveric Model | | |
| **Start Date:** 06/09/93 | **Est. Completion Date:** Jul 93 | |
| **Department:** Radiology | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Vincent B. Ho, MC | | |
| **Associate Investigators:** | SSG James Adams, NCOIC | |
| **Key Words:** MRI, cardiac imaging, pig model | | |
| **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, pending acquisition of specialized 3D software.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/044 | **Status:** Terminated |
| **Title:** Magnetic Resonance Mammography (MRM): A New Age Imaging Tool | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Mar 98 | |
| **Department:** Radiology | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Vincent B. Ho, MC | | |
| **Associate Investigators:** Charlene P. Holt, M.D. | COL Sankaran S. Babu, MC | |
| **Key Words:** Cancer:breast, MRI | | |

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

Study Objective: To incorporate Magnetic Resonance Mammography (MRM) into the clinical pathway of breast cancer detection.

Technical Approach: Non-pregnant female with a high-risk history of breast cancer will be invited to participate in this study. After consenting, an intravenous line will be placed into a peripheral vein. The patient's breast will be examine and if specific lesions are palpable, the "lumps' will be marked with a MR-compatible marker on the skin surface. After being placed in the proper position for imaging, Sagittal and Axial T1-weighted images of the breast in question will be obtained. Next, pre-contrast fast SPGR images of the breast will be performed in either the axial or sagittal plane. Image plane will be chosen to best visualize the suspicious mass(s) on supplied clinical and radiologic data and/or the appearance of suspicious lesions on STIR and T1-weighted images. A 0.1 mmol/kg dose of Gadolinium-chelate (Gd) will be hand-injected over a 10 second period using the previously placed intravenous line. The Gd bolus will be immediately followed by a 20 ml hand-injected bolus of normal saline to assure that all the contrast has been administered.

Following the administration of the contrast, continuous dynamic fast SPGR images of the mass will be performed over the first 8 minutes. Post-contrast sagittal and axial T1-weighted images will then be obtained.

Images will be evaluated and suspicious lesions will be evaluated for their signal intensity prior to and dynamically following GD administration. The enhancement rate and pattern will then be calculated as compared with the baseline pre-Gd values.

Breast masses with > 90% change in signal intensity within the first minute of enhancement or with peak enhancement less than 1-2 minutes will be considered criteria for "suspicious" lesions. "Suspicious" masses by MRM will be removed surgically or be biopsied with MRI-guided localization. Patients with an enhancing lesion on their initial MRM will be followed by serial annual MRM over the course of the study and patients without enhancing lesions will undergo routine traditional follow-up with FSM ultrasound as per recommendations of the initial FSM ultrasound and clinical suspicion. Repeat MRM will be performed two years following the initial MRM to confirm stability of the initial MRM findings.

Progress: 4 subjects entered. Project terminated secondary to insufficient funding to continue.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/122 | **Status:** Completed |

**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 | |

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| **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 100 patients with known congenital metabolic and neurodegenerative diseases of childhood were retrospectively reviewed. Based on review of neuroimaging data, an algorithm approach to diagnosis was formulated.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/016 | **Status:** Terminated |
| **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: Project terminated secondary to lack of support and time.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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. Review of 50 autopsy specimens by Dr. Rosemary Borke, Dept of Anatomy, USUHS, has been completed.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/014 | **Status:** Terminated |
| **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:** | // |
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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: Project terminated secondary to lack of support and time.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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 | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | **OMA** $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: 20 subjects were studied. Stones and x-ray films on conventional x-rays and computed radiographs have been acquired. Region of interest analysis for stone density is ongoing.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/159 **Status:** On-going

**Title:** Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method

**Start Date:** 09/21/94 **Est. Completion Date:** Apr 96

**Department:** Radiology **Facility:** MAMC

**Principal Investigator:** MAJ Vincent B. Ho, MC

**Associate Investigators:** Youngberg RA
Szumowski J

**Key Words:** Magnetic Resonance Mammography: fat suppression, Dixon method

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: The objective of this study is to further refine a promising new MRI technique for fat suppression (phase unwrapping in a 3-point-Dixon method) for application in magnetic resonance mammography (MRM).

Technical Approach: Phase unwrapping in the 3-point-Dixon method is a recently described method for fat suppression which promises to bridge the difficulties encountered with fat signal on post-contrast MRM images. This new fat suppression technique promises to provide the reproducible homogeneous fat suppression necessary for the efficient performance of MRM and the accurate rendering of diagnoses.

This new technique, by increasing the conspicuousness for areas of Gd-enhancement, will dramatically improve the overall accuracy of MRM for breast cancer and make the identification of even very small cancers possible. MR with its reported high sensitivity will potentially identify lesions not otherwise detected by film screen mammography, ultrasound or physical exam at MAMC, MRM has already discovered lesions which were otherwise not detected by these other conventional means. Because the success of any breast imaging modality relies on its ability to diagnose cancer early to effect cure and increase survival, this technique will represent a major advance in breast cancer screening.

Progress: New study. Awaiting funding.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/075 | **Status:** On-going |
| **Title:** Cost Effectiveness of Screening MRIs of the Knee Prior to all Knee Arthroscopies | | |
| **Start Date:** 03/04/94 | **Est. Completion Date:** Aug 94 | |
| **Department:** Radiology | **Facility:** MAMC | |
| **Principal Investigator:** CPT Liem T. Mansfield, MC | | |
| **Associate Investigators:** LTC Gregg W. Taylor, MC | Youngberg RA<br>MAJ Winston J. Warme, MC | |
| **Key Words:** MRI, knee, arthroscopy | | |

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

Study Objective: 1. To determine the sensitivity (SN), specificity (SP), negative predictive value (NPV), positive predictive value (PPV), and accuracy of knee MRIs in predicting internal derangement of the knee.;2. To determine the percentage of negative diagnostic knee arthroscopies.;3. To determine whether screening MRIs can reduce the number of negative arthroscopies resulting in institutional cost savings and a reduction in patient morbidity.

Technical Approach: This is a prospective, single-blinded study of MRI versus diagnostic arthroscopy, comparing their abilities to diagnose internal derangement(s) of the knee. Patients selected for this study will have met the surgical indications monitoring for appropriateness (SIM-A) suggested criteria for selected orthopedic surgery procedures.

Patients (100) will have an MRI of the knee prior to arthroscopy which is to be within 2 weeks after the MRI. MRIs will be interpreted by Drs. Youngblood and Mansfield. Arthroscopies will be performed by Dr. Taylor and other orthopedic senior staff. MRI interpretation will be in the form of a radiological report and a diagram showing the location of meniscal tears. The arthroscopists performing the arthroscopy will record his findings both before and after review of the radiologic findings.

Using diagnostic arthroscopy as the gold standard, after 100 arthroscopies the data will be reviewed to determine the SN, SP, NPV, PPV, accuracy of MRI, and the frequency of avoidable arthroscopy. Avoidable diagnostic arthroscopy will be defined as arthroscopy performed on a patient whose MRI and arthroscopic findings demonstrate non-surgical pathology.

Progress: Twenty five patients underwent MRI. 17 had arthroscopy. The sensitivity and specificity of the knee MRI for the detection of anterior cruciate ligament interruption are 100% and 83%, respectively; PCL tear, 100% and 63%; medial meniscal tear, 67% and 82%; lateral meniscal tear, 67% and 82%; and composite injury, 93% and 50%. There were 4 avoidable diagnostic arthroscopies. (24%) MRI may be cost effective.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** | // |
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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, 100 patients have been enrolled in the protocol. Fifty five of the image sets have been processed for viewing, and have been reviewed by four observers. Two additional sets are pending completion. Statistical analysis is in progress

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/022 **Status:** On-going

**Title:** Free Receiver Operating Characteristic Analysis of Alveolar Consolidation Detection: Conventional Chest Radiography vs. Digital Radiography vs. Digital Advanced Multiple Beam Equalization Radiography

**Start Date:** 11/05/93 **Est. Completion Date:**

**Department:** Radiology **Facility:** MAMC

**Principal Investigator:** CPT Cristopher A. Meyer, MC

**Associate Investigators:**
MAJ Robert G. Leckie, MC
MAJ James H. Timmons, MC
Dev P. Chakraborty, Ph.D.
CPT Bernard J. Roth, MC
CPT Kyle L. Colvin, MC
MAJ Donald V. Smith, MC
Jon R. Carter, M.S.

**Key Words:** AMBER, SPDR, chext x-ray, alveoli pulmonis

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

Study Objective: To determine the relative sensitivity of AMBER-Storage Phosphor Digital Radiography (SPDR) in the detection of alveolar consolidation by comparing AMBER-SPDR with conventional radiography using a free response receiver-operating characteristic curve.

Technical Approach: BAL will be performed using a flexible fiberoptic bronchoscope. Each lobe subjected to lavage will have 100 ml of saline solution instilled, followed immediately by aspiration of the infused fluid. Twenty-five patients will have one lobe lavaged, 25 patients two lobes lavages and 25 patients three separate areas lavaged. The patients will then have three follow-up posteranterior chest radiographs: a conventional radiograph, SPDR and AMBER-SPDR. Conventional chest radiographs will be performed using standard radiographic technique. Digital film will be provided in a masked, hard copy 2/3 format. Digital-AMBER films will be obtained with normal equalization and provided in a masked, hard copy 2/3 format. All digital films will be uncompressed. The films will be randomized and number. All films will be reviewed in sets of 25/session to prevent viewer fatigue and image recall. Data will be evaluated for four lung zones and a 0-4 grading system assigned for subjective level of certainty/quantification of alveolar consolidation. Analysis will be performed utilizing a free-response methodology. Spearman rank correlation will be used to determine correlation between retained lavage fluid volume and lung opacification grade.

Progress: Thus far, this study has been on hold pending contract negotiations for funding between Odelft, Phillips and Henry M. Jackson Foundation.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/060 | **Status:** Completed |
| **Title:** Computer Program for Documentation of Vascular and Interventional Procedures and Biopsies | | |
| **Start Date:** 03/04/94 | **Est. Completion Date:** Mar 94 | |
| **Department:** Radiology | **Facility:** MAMC | |
| **Principal Investigator:** Parker ES | | |
| **Associate Investigators:** | MAJ Michael F. Haggerty, MC | |
| **Key Words:** | | |

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To evaluate the performance and general acceptability of a new database program designed for simple, low-error rate data entry for documentation and quality assurance of invasive radiologic procedures including biopsies.

Technical Approach: All staff and resident radiologists will be given a brief orientation to the operation of the program which will be installed on a centrally located personal computer. Access to the computer will be restricted by location in a non-patient area and by password to protect patient privacy. After performing an invasive procedure, the resident or staff radiologist is responsible for entering the following information: date of procedure, patients name, the prefix and last four digits of the FMP, age, sex, inpatient/outpatient status, ASA category, brief history, department section, procedure name, biopsy results (if any), complications, staff radiologist's name, first and second assistants' names, flag, and finally a comment/results. The investigators will act as "system operators," intermittently reviewing entries for correctness, creating archival copies of data in case of hardware or software failure, and printing reports. At the end of a three month trial period, radiologist will be surveyed regarding aspects of the program.

The opinion and comment survey contained six multiple choice questions. Responses to each question will be tallied and percentages of each response will be calculated.

Progress: Compliance with logging of procedures was approximately 85% the first month, then rose to 97%. Acceptance was enthusiastic. The program simplified and centralized documentation of all procedures performed in the department. Availability of accurate printed reports was cited as the main advantage of the program by physicians and other quality assurance personnel.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/039 | **Status:**Completed |
| **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 | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | $0.00 | **OMA 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: MR venograms have been performed on 100 different patients. Data on anatomical variants correspond to previously reported angio data. Data being analyzed for final presentation.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, ANESTHESIA SERVICE

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/031 | **Status:** Completed |
| **Title:** Spinal Anesthesia/Analgesia in Laboring Obstetric Patients: Comparison of 22-Gauge, 25-Gauge, and 27-Gauge Whitacre Needles | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Dec 93 | |
| **Department:** Surgery, Anesthesia Service | **Facility:** MAMC | |
| **Principal Investigator:** Tess G. Boylon, MD | | |
| **Associate Investigators:** Gridley G | LTC Joseph J. Mancuso Jr., MC | |
| **Key Words:** anesthesia, needles, OB patients | | |

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

Study Objective: To assess the incidence of post-dural puncture headache (P.D.P.H.), backache, technical ease of use, and incidence of successful dural puncture for spinal analgesia between gauges 22, 25, and 27 Whitacre pencil point needles.

Technical Approach: Collection of data on existing usual spinal anesthesia/analgesia technic already performed on obstetrical patients admitted to labor and delivery by OB-Anesthesia investigators. Post-op anesthesia follow-up and data will be collected by Anesthesia providers other than the anesthesia provider who performed the spinal anesthesia/analgesia to double blind the study. Each patient is allocated by computerized random number selection to one of the three different spinal needle groups. Data to be collected are: post-spinal backache, P.D.P.H., number of needle insertion attempts before successful spinal analgesia/anesthesia; quality of spinal analgesia/anesthesia based on onset duration; denseness of analgesia/anesthesia provided; and level of patient satisfaction with the procedure.

Progress: One hundred twenty subjects were studied. The 22 gauge Whitacre needle did not offer any advantage over the smaller gauge needles when evaluated for ease of use, time to accessing the subarachnoid space, or success of analgesia. The 22 gauge Whitacre had a greater incidence of PDPH within the first 48 hours postpartum but this difference was not statistically significant beyond this time period.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/046 **Status:** Terminated

**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 Service **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:** | // |
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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: Principal Investigator has been reassigned to Ft. Hood. PI was unable to recruit patients for this study before he was reassigned because the patients were being entered on another study.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/032 | **Status:** Completed |
| **Title:** The Effect of Epinephrine on Terbutaline Treated Goats | | |
| **Start Date:** 11/05/93 | **Est. Completion Date:** Jan 94 | |
| **Department:** Surgery, Anesthesia Service | **Facility:** MAMC | |
| **Principal Investigator:** CPT Gary D. Gridley, MC | | |
| **Associate Investigators:** | LTC Joseph J. Mancuso Jr., MC | |
| **Key Words:** terbutaline, epinephrine, goat model,Animal Study | | |

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 06/10/94 |
|---|---|---|---|---|

Study Objective: To investigate the heart rate and blood pressure response to epinephrine administration in the goat treated with terbutaline.

Technical Approach: Five adult goats will be used for this study. On day 0, after fasting for 48 hours the animals will be sedated with xylozine, and anesthesia will be induced with ketamine 4 mg/kg. The animal will breath oxygen enriched room air throughout the procedure of placing intravenous and intraarterial catheters. On day 1 the goat will be placed in a quiet, dark room, and the catheters will be accessed and connected to a pressure transducer. After a 15 minute period of stable baseline measurements, the goat will be given intravenous epinephrine, 15 micrograms, and continuously monitored for heart rate and blood pressure response for five minutes. When the animal has returned to a stable baseline, it will then be given intravenous terbutaline, 250 micrograms. A 15 minute stable baseline will again be established. The animal will again receive intravenous epinephrine, 15 micrograms, and be continuously monitored for hemodynamic response for five minutes. On days 2 and 3 the experiment will be repeated as day 1. Statistical analysis will be performed using the t-test.

Progress: The heart rate and blood pressure response of the goat to epinephrine was similar to that observed in humans. In the presence of terbutaline, a beta agonist commonly used in obstetrics, epinephrine did not produce an increase in heart rate, but rather a decrease. The blood pressure response to epinephrine was similar with or without terbutaline. Further research in humans will be needed to ascertain if indeed this same response is manifested in both obstetric and nonobstetric populations.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/021 **Status:** Terminated

**Title:** The Effect of Magnesium on Bupivacaine Transfer Across the Dually Perfused Cotyledon Model

**Start Date:** 12/17/93 **Est. Completion Date:** Dec 93

**Department:** Surgery, Anesthesia Service **Facility:** MAMC

**Principal Investigator:** CPT Gary D. Gridley, MC

**Associate Investigators:** LTC Joseph J. Mancuso Jr., MC

**Key Words:** cotyledon, bupivacaine, magnesium

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: This research will investigate the placental transfer of bupivacaine, with and without magnesium administration, across the dually perfused cotyledon model.

Technical Approach: Ten placentas from uncomplicated term deliveries will be reperfused. After a 30 minute equilibration period, bupivacaine and antipyrine will be added to the perfusates. Bupivacaine, 1 mcg/ml final concentration will be added to the maternal perfusate. Antipyrine, 100 mcg/ml in the fetal perfusate, will act as a reference diffusion compound. Magnesium, 4 mcg/ml final concentration, will be added to the maternal perfusate during the equilibration period of five of the study cotyledons. Maternal and fetal perfusate will be sampled 1, 3, 5, 10, 15, 30 and 60 minutes after initiation of the bupivacaine and antipyrine via HPLC. Each placenta cotyledon will be run as a pair with another cotyledon from the same placenta. The second perfused cotyledon will serve as a control, receiving only the baseline balanced salt solution as a perfusate.

Progress: Principal Investigator was to work on project in conjunction with a study done by the Perinatal Service. They were unable to coordinate with Perinatal and protocol was terminated.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/087 **Status:** Terminated

**Title:** Patient-Controlled Analgesia and the Risk of Postoperative Myocardial Ischemia

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

**Department:** Surgery, Anesthesia Service **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:** | // |
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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. The project was terminated due to inability to obtain equipment and technical support.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Service **Facility:** MAMC

**Principal Investigator:** MAJ James D. Helman, MC

**Associate Investigators:**
LTC Douglas M. Anderson, MC
COL Daniel G. Cavanaugh, MC
MAJ Edward J. Walz Jr., 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:** | // |
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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 pneumonectoperformed. Six more patients will be needed prior to data analysis.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/047 **Status:** Completed

**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 Service **Facility:** MAMC

**Principal Investigator:** MAJ James D. Helman, MC

**Associate Investigators:**
CPT David J. Bower, MC
MAJ Edward J. Walz Jr., 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:** | // |
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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 Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/130 **Status:** On-going

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

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

**Department:** Surgery, Anesthesia Service **Facility:** MAMC

**Principal Investigator:** CPT John D. Hermann, MC

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

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

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To determine if the periarterial infiltration of lidocaine and/or hydralazine near the radial artery at the wrist will either decrease the velocity of flow and/or increase the diameter of the radial artery at the wrist as measured by a duplex/doppler instrument.

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

Progress: Nine patients have been entered in this study.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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 Service | **Facility:** MAMC | |
| **Principal Investigator:** MAJ William A. Hughes, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Mivacurium neuromuscular blockade:steroidal nondepolarizers | | |

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| **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 proceed until funding is received for a neuromuscular blockade monitor.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/035 | **Status:** Terminated |
| **Title:** Bacterial Colonization of Epidural Catheters As a Function of Time | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Apr 94 | |
| **Department:** Surgery, Anesthesia Service | **Facility:** MAMC | |
| **Principal Investigator:** COL Michael Robert Moon, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** catheters, bacterial colonization, function of time | | |

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

Study Objective: This study will determine the risk of bacterial colonization of epidural catheters placed by the anesthesiology service in elective operative patients as a function of the time of placement.

Technical Approach: A polyethylene epidural catheters will be inserted using standard of care procedures and the site covered by a sterile occlusive translucent dressing. Porous tape will be used to reinforce the edges of the plastic dressing and secure the catheter. The catheter will be inspected on a daily basis. The catheter will be discontinued when the acute pain service anesthesiologist deems it appropriate. When the criteria for catheter removal have been met, two cultures will be obtained using aseptic technique. The first specimen, intended to indicate skin colonization, will be the catheter tip which will be bathed in 0.5 cc NS to prevent desiccation prior to plating. The catheter tip will be wiped with alcohol to sterilize the outside of the tip. The second specimen will be a NS irrigation 0.5 cc injected through the catheter in an attempt to assess colonization from sources outside the skin. Duration of epidural catheterization in hours will be recorded. The incidence of colonization as a function of time will be recorded.

Progress: Approximately 100 patients were entered. There were no infections. Study discontinued with loss of residency.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/073 **Status:** Suspended

**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 Service **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:** | // |
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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. It remains suspended pending available research time.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/028 **Status:** Completed

**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 Service **Facility:** MAMC

**Principal Investigator:** CPT Michael L. Pylman, 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:** | // |
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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: Sixty-five patients have been entered into this study. There was an increase invasopressure with preloading with both solutions. There seemed to be decreased urinary retention with colloid preload, but this was not statistically significant. Manuscript in preparation

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, CARDIOTHORACIC SURGERY SERVICE

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/156 | **Status:** On-going |
| **Title:** North American Duraflo II Working Group | | |
| **Start Date:** 09/21/94 | **Est. Completion Date:** | |
| **Department:** Surgery, Cardiothroacic Surgery Svc | **Facility:** MAMC | |
| **Principal Investigator:** LTC Blaine R. Heric, MC | | |
| **Associate Investigators:** | LTC Maceo Braxton Jr, MC | |
| **Key Words:** Duroflo II, heparin, cardiopulmonary bypass circuits | | |

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

Study Objective: To determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcomes indices: (1) homologous transfusion requirements (2) post-op hours until extubation (3) post-op hours until SICU discharge (4) post-op days until hospital discharge.

Technical Approach: The deleterious effects of cardiopulmonary bypass on hematologic parameters have been will established in cardiac surgery. In particular, the systemic inflammatory response is a well recognized entity which occasionally may create severe clinical problems including ARDS (Adult Respiratory Distress Syndrome), neurologic dysfunction, myocardial edema and myocardial dysfunction, and postoperative weight gain.

Heparin coating all blood containing surfaces of the extracorporeal circuit creates a "pseudo endothelium". Early studies, in a relatively small number of patient in Europe, have indicated that platelet function and numbers are preserved. Bleeding is decreased. Levels of complement activation are reduced and, therefore, postoperative pulmonary function is improved. The number of patients studied in a randomized blinded fashion, however, has been very small and, therefore, improved clinical outcome using this new technology has not been documented.

The Duraflo tubing is one of several heparin coated or "biocompatible" surfaces which have been the focus of active research by many of the industries in the past several years. No U.S. center has reported a clinical evaluation of the product, despite the fact that the FDA has approved the majority of the components for use in routine clinical practice. Adding the heparin coating to the tubing increases the expense of open-heart surgery and no study has yet been able to justify its use. This will be the first study to address this question in a scientific fashion.

Progress: New study. No subjects entered yet.

# DETAIL SHEETS FOR PROTOCOLS

## DEPARTMENT OF SURGERY, OTOLARYNGOLOGY
## SURGERY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/026 **Status:** Terminated

**Title:** Atrial Natriuretic Factor as a Mediator of Airway Obstruction Induced Enuresis

**Start Date:** 12/04/92 **Est. Completion Date:** Jun 93

**Department:** Surgery, Otolaryngology Surg Svc **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:** | // |
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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 technician and has been unable to hire another due to budget constraints.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/160 | **Status:** Suspended |

**Title:** Analyzing the Dynamic Behavior of the Eustachian Tube Through A Sonometric Monitor

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| **Start Date:** 08/06/93 | **Est. Completion Date:** |
| **Department:** Surgery, Otolaryngology Surg Svc | **Facility:** MAMC |

**Principal Investigator:** MAJ Charles V. Edmond Jr, MC

**Associate Investigators:** None

**Key Words:** eustachian tube, sonometric monitor

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

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 through the VA-DOD initiative denied. Will resubmit for other funding.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/177 **Status:** On-going

**Title:** ENT Surgical Simulator Project

**Start Date:** 09/02/94 **Est. Completion Date:** Jun 96

**Department:** Surgery, Otolaryngology Surg Svc **Facility:** MAMC

**Principal Investigator:** MAJ Charles V. Edmond Jr, MC

**Associate Investigators:**
Doug Sluis, Ph.D.
Bill Winn, Ph.D.
Don Stredney
Gregory J. Wiet, MD
Dale Fawcett
Weghorst W
Blake Hanaford, Ph.D.
Roni Yagel, Ph.D.
Bill Bolger, MD

**Key Words:** Simulator:surgical, Simulator:ENT

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To develop and evaluate a minimally invasive prototype surgical simulator to establish real time fidelity requirements for tactile feedback and computer image synthesis.

Technical Approach: This project is a two phase program with the goal of Phase I to construct a simulator prototype to serve as a platform for further enhancement and evaluation. This includes the development of the geometric and virtual database of the human sinus anatomy, the development of a system to track the surgical instruments, and the system software to implement sinuscope camera emulation and tissue dissection. The prototype will provide the novice with the ability to perform a limited sinus surgery procedure on a virtual patient using sinuscope and surgical tools similar to those used in the operating room. Visual recognition skills and psychomotor skills specific to the surgical context are improved through the experience of the simulated surgery.

In Phase II, development will continue by enhancing the simulator to include changes and enhancements suggested by surgeons in the Phase I evaluation. Additional features such as tactile feedback and tissue deformation will be integrated into the prototype as time and budget permit. During Phase II further analysis will determine the simulators training effectiveness in operation.

Progress: Awaiting funding

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/128 **Status:** On-going

**Title:** Utility of Transtympanic Ultrasound in the Diagnosis of Middle Ear Pathology

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

**Department:** Surgery, Otolaryngology Surg Svc **Facility:** MAMC

**Principal Investigator:** MAJ Ronald E. Schwartz, MC

**Associate Investigators:** Welle GJ
MAJ Charles V. Edmond Jr, MC

**Key Words:** ear:pathology, ultrasound

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: To evaluate the efficacy of transtympanic ultrasound in evaluating middle ear pathology in the human cadaver.

Technical Approach: The first part of the study will involve obtaining normative date from ten unaltered temporal bones. This data will then be compared with already established normative middle ear anatomic data to insure reliability of transtympanic ultrasound. Data obtained will include: size, position and relationship of middle ear ossicles, distance from tympanic membrane to the promontory, signal characteristic of disease free middle ear cavity and extent of the middle ear that is able to be evaluated by ultrasound.;;The second part of the study will use the normative data obtained in the first part of the study and compare it to surgically altered temporal bones. The bones will be altered to mimic middle ear pathology seen in clinical practice. Middle ear disease that will be looked at include soft tissue masses, ossicular chain abnormalities, and surgically altered middle ear clefts.;;The final part of the study will involve true transtympanic evaluation of the middle ear space by placing the probe within the middle ear cavity and then obtaining both normative data and data obtained from pathologic specimens. This will allow us to assess whether areas inaccessible to transtympanic ultrasound are better assessed from within the middle ear cavity.

Progress: Eight temporal bones have been obtained and prepared for use in the study. The cost of borrowing the hardware with which to do the study was prohibitive. The department of Cardiology is purchasing a machine that should arrive in the December time frame. Therefore, actual ultrasound evaluation will probably not occur until Jan-Feb 1995.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/068 **Status:** Completed

**Title:** The Effect of Radial vs Circumferential Myringotomy on Ventilatory Tube Retention

**Start Date:** 03/05/93 **Est. Completion Date:** Dec 93

**Department:** Surgery, Otolaryngology Surg Svc **Facility:** MAMC

**Principal Investigator:** CPT Jeffrey L. Silveira, MC

**Associate Investigators:** CPT Philemon L. Anderson, MC
MAJ Charles R. Souliere, MC

**Key Words:** myringotomy:tube retention

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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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: Follow-up has been completed on 50 participants. All data has been collected. Data requires analysis. To be presented at AAOHNS Annual Meeting.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/050 | **Status:** On-going |
| **Title:** Supine Cephalometrics in the Evaluatin of Obstructive Sleep Apnea Syndrome | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Dec 94 | |
| **Department:** Surgery, Otolaryngology Surg Svc | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Thomas P. Winkler, MC | | |
| **Associate Investigators:** | MAJ Ray E. Jensen, MC | |
| **Key Words:** sleep apnea, cephalometrics | | |

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|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $1800.00 | **Periodic Review:** // |

Study Objective: To evaluate the upper airways of patients with obstructive sleep apnea syndrome by comparing lateral roentgenographic cephalometrics in patients in the upright position with patients in the supine, relaxed position.

Technical Approach: This study will assess the difference in evaluating the upper airway while the patient is lying down vs. standing. A population of 20 patients with diagnosed obstructive sleep apnea along with 20 controls will be studied. The study requires that three X-rays be obtained instead of the usual one X-ray. One film will be taken standing, one will be taken lying down with the teeth closed and one while lying down with the jaw open and relaxed. Specific measurement the cephalometrics will include: 1) the posterior airway space, 2) sell-nasion-supramentale angle, 3) soft palate length and 4) distance from the hyoid to the mandibular plane. Analysis will be by the student t-test.

Progress: No patients entered due to non-functioning cephalometiric X-ray.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/161 **Status:** Completed

**Title:** 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

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

**Department:** Surg, General Surgery Svc **Facility:** MAMC

**Principal Investigator:** COL Charles A. Andersen, MC

**Associate Investigators:** LTC David F. J. Tollefson, MC

**Key Words:**

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

Study Objective: To establish the safety and efficacy of Dermagraft in the promotion of healing chronic venous insufficiency ulcers.

Technical Approach: This multicenter study will be stratified by medical center and by ulcer size. Two ulcer size strata are defined: ulcers $\leq 50$ $cm^2$ and ulcers $>50$ $cm^2$. The purpose of this stratification is to ensure approximately equal allocation of patients between treatments within each stratum. Dermagraft will be applied to the wound bed under a paste boot and elastic bandage. Control treatment wounds will receive a conventional paste boot and elastic bandage only. All patients will be followed at weekly intervals for 12 weeks or until one week after the wound achieves complete closure. Thereafter, all patients will be seen at 16, 20, and 24 weeks. Patients will also complete a short series of health status questionnaires that will assess overall health, quality of life, activity level, pain and discomfort, and labor force participation.

Progress: Enrollment in the trial was closed in FY93. A total of 5 patients were entered in the protocol A final summary has not yet been issued by the study sponsor.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 85/021 **Status:** Suspended

**Title:** Advanced Trauma Life Support Course

**Start Date:** 01/18/85 **Est. Completion Date:** Indef.

**Department:** Surg, General Surgery Svc **Facility:** MAMC

**Principal Investigator:** LTC Patrick J. Offner, MC

**Associate Investigators:**
COL Stanley C. Harris, MC
MAJ Christopher R. Kaufmann, 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:** 06/10/94 |
|---|---|---|---|---|

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: No animals were used this fiscal year. Suspended pending rewrite.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/079 **Status:** Terminated

**Title:** Serum Levels of Tumor Necrosis Factor in Postoperative Patients

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

**Department:** Surg, General Surgery Svc **Facility:** MAMC

**Principal Investigator:** CPT Ronald J. Place, MC

**Associate Investigators:**
MAJ Robert M. Tuttle, MC
LTC Anthony S. Sado, MC
CPT Robert A. Avery, MC
CPT Ronald L. Hurst, MC

**Key Words:** Tumor necrosis factor:serum levles, postop patients

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $2865.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: 1. To determine whether tumor necrosis factor (cachectin) can be detected in the serum of postoperative patients. 2. To determine whether post-op Tumor Necrosis Factor (TNF) levels differ according to the operation performed. 3. To determine if TNF can be used to predict post-op course.

Technical Approach: Patients admitted to the vascular surgery service who are greater than 18 years of age, undergoing either abdominal aortic aneurysm or carotid endarterectomy will be invited to participate. Pregnant females and patients with evidence of sepsis, malignancy, shock or hemodynamic instability prior to the study will be excluded.

A standard history and physical along with standard preoperative laboratories will be done. A baseline serum TNF will be drawn on the day of admission and serve as the control TNF measurement. Intraoperatively, a serum TNF level will be drawn at induction of anesthesia at 30, 60 and 120 minutes after incision. In addition, a serum TNF level will be drawn at cross clamp placement and 30 minutes after the cross clamp is released from the aorta or the carotid artery. In the event of a hypotensive episode, defined as a systolic BP less than 90 lasting greater than one minute, a serum TNF level will be drawn. Daily laboratories to include a serum TNF will be drawn for the first 72 hours after surgery.

Other data to be evaluated include fluid status monitored by input and output, daily weights, and IV fluid intake including the amount of crystalloid, albumin, other colloids, and packed red blood cells. Serial blood pressure following admission to ICU will be reviewed for any episode of hypotension. Daily Apache scores will be obtained for the day of surgery and for the first 72 hours postoperatively. Patients will also be monitored for temperatures of greater than 101.6°F, evidence of positive blood cultures, infection, myocardial event, congestive heart failure, and fluid overload.

Repeated measurements of TNF will be analyzed by ANOVA analysis.

Progress: CPT Avery, who has been reassigned, was the original PI. A new P.I. (Dr. Place) was named in July 93, but he was unaware of this and the protocol was suspended in Sept 93. The Associate Investigators were reassigned and left MAMC, therefore, the protocol has been terminated.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 87/007 **Status:** Terminated

**Title:** General Surgery Stapling Familiarization Lab (Swine Model)

**Start Date:** 10/17/86 **Est. Completion Date:** Oct 87

**Department:** Surg, General Surgery Svc **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:** 06/10/94 |
|---|---|---|---|---|

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: 6 animals were used in FY 94. Protocol terminated to be rewritten new format.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/029 | **Status:** Completed |
| **Title:** Laparoscopic Assisted Colon and Rectal Operations | | |
| **Start Date:** 12/04/92 | **Est. Completion Date:** May 93 | |
| **Department:** Surg, General Surgery Svc | **Facility:** MAMC | |
| **Principal Investigator:** LTC Clifford L. Simmang, MC | | |
| **Associate Investigators:** MAJ Timothy F. Deaconson, MC | MAJ William C. Williard, III, MC<br>MAJ Daniel Jorgenson, MC | |
| **Key Words:** laparoscopy:colon, rectal | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: The determine the feasibility of performing laproscopic-assisted colon and rectal surgical procedures at MAMC.

Technical Approach: Laparoscopic-assisted colon and rectal surgery have been performed in both medical centers and community hospitals throughout the country. These procedures have been demonstrated to often reduce postoperative pain, ileus, and hospital stay, and to have an earlier return to regular activities. Our procedure will not differ from those previously done.

Laproscopic-assisted colon and rectal resection differs from standard open procedures in that the dissection and mobilization is performed with laparoscopic techniques using endoscissors and endocautery. Vascular structures are divided between endoclips instead of clamps and ligatures. A small (average 7 cm) incision is made to deliver the specimen. Standard open techniques through the small incision are used to complete the bowel resection and anastomosis. The patients will be followed in the hospital with usual postoperative until normal bowel function has returned and the patient can tolerate self care. A review of the procedure, complications, hospital course, and patient's level and rate of return to normal activity will be assessed. Because these techniques will be new to MAMC, it is felt that review of the initial procedures should be monitored to determine the impact on our facility.

Progress: Studied in this protocol were 89 colon and rectal resections of which 10 were performed by laparoscopic-assisted technique. Of these, there were 6 right colectomies which form the study population. Standard open technique was used to perform 79 colon and rectal resections, of which 17 were right colectomies. To provide similar patients for comparison, 12 were excluded (6 for acute inflammation, 3 for ischemia, 1 for trauma, and 2 for comorbid existing conditions), and the remaining 5 form the control population.

There were no major complications in either group. Additional cost in the laparoscopic group included approximately $600.00 for equipment and an increased operating time with a mean average of 186 min for the laparoscopic group vs 155 min for the open group. Postoperative hospital stay was significantly reduced from an average of 7 days in the open group compared to only 4.5 days in the laparoscopic group, reducing the cost of hospitalization.

We conclude that laparoscopic-assisted colectomy is safe, cost effective, and should be employed in selected patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/069 **Status:** Terminated

**Title:** Hemodynamic Consequences of Pneumoperitoneum in Patients with Cardiopulmonary Disease

**Start Date:** 03/05/93 **Est. Completion Date:** Jan 93

**Department:** Surg, General Surgery Svc **Facility:** MAMC

**Principal Investigator:** CPT Steven E. Weber, MC

**Associate Investigators:**
MAJ Daniel Jorgenson, MC
CPT Michael J. Decker, 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 terminated because the Principal Investigator was unable to obtain the equipment.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/049 **Status:** On-going

**Title:** A Multiple-dose, Double-masked, Active Treatment Controlled, 2 Period, Crossover Multiclinic Study of 0.5% Preservative-Free Timolol-in-GELRITE.... in Patients With Elevated Intraocular Pressure

**Start Date:** 12/17/93 **Est. Completion Date:** Dec 94

**Department:** Surg, Ophthalmology Svc **Facility:** MAMC

**Principal Investigator:** COL Kevin J. Chismire, MC

**Associate Investigators:** MAJ Vernon C. Parmley, MC
CPT Benjamin N. Gilbert, MC

**Key Words:** Intraocular pressure, Timolol-in-Gerlite, with and without preservative

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

Study Objective: 1. To compare the relative ocular hypotensive effect of 0.5% preservative-free Timolol-in-Gelrite administered one daily to that of 0.5% Timolol in-Gelrite with preservative administered once daily.

2. To compare the safety and tolerability of both preservative-free timolol-in-Gelrite and timolol-in-Gelrite with preservative.

Technical Approach: Ten to twelve patients who are twenty-one years and older with glaucoma or ocular hypertension will be invited to participate at MAMC. Between 2 and 21 days prior to entry into the study all patients will have a prestudy evaluation to include, visual acuity, external and slit lamp examination, intra-ocular pressure, dilated ophthalmoscopy, visual fields and physical examination. At 1 day prior to study the patient will be examined at 0830. If the IOP (this measurement is baseline) is > 22 mgHG the patient will be able to continue. The patient will return the next day at 0830 hours, external and slit lamp examinations will be performed. The first administration of Period 1 study drug will be administered at 0900 hrs. External and slit lamp examination will be performed at 0930 hours. Goldmann applanation IOP will be performed at 1100 hrs. This same process will be repeated on days 15, 42, 77, and 84 plus all other evaluation performed at 1 day prior to study will be repeated. Period 2 will begin on Day 85 and patients will be crossed-over. The dosing and evaluation schedule remain the same and additional study days are 99, 126, 161, and 168. On days 84 and 168, a visual field exam and ophthalmoscopy will also be conducted. Data from this study will be evaluated by the sponsor.

Progress: 10 subjects entered. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/125 **Status:** On-going

**Title:** Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by Magnetic Resonance (MR) and Computed Tomography (CT) Imaging in the Goat

**Start Date:** 06/10/94 **Est. Completion Date:** Apr 95

**Department:** Surg, Ophthalmalogy Svc **Facility:** MAMC

**Principal Investigator:** CPT Lilia A. Fannin, MC

**Associate Investigators:**
COL Thomas H. Mader, MC
D. P. George
MAJ Miquel J. Rovira, MC
R. A. Mazzoli
MAJ Vernon C. Parmley, MC
MAJ Vincent B. Ho, MC
W. F. Coughlin

**Key Words:** Foreign bodies:intraocular, Foreign bodies:intraorbital, Foreign bodies:plastic, MRI, CT scan,Animal Study

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

Study Objective: 1. To determine the efficacy of CT and MR imaging in detecting intraocular or intraorbital plastic foreign bodies in the goat.;2. To determine if intravenous contrast during CT and MR imaging improves the detection of intraocular or intraorbital plastic foreign bodies.

Technical Approach: Twelve goats will be used to evaluate the efficacy of CT and MR imaging in detecting plastic foreign bodies in the eye and around the eye. The goats will be sedated, anesthetized, and intubated prior to the surgical placement of 1 to 6 plastic foreign bodies (sizes ranging from 1/32 - 1/4 inch) in the eye. The wound will not be closed so as to simulate an eye injury. Plain film x-ray, CT and MR images will be obtained. Intravenous dye will be given for the imaging studies. The fellow eye will be the control. After the CT and MR studies are completed, the goats will be sacrificed. Plain films, CT and MR images will be evaluated by four masked physicians (two radiologist and two opthalmologists). These doctors will not know which eye has the plastic foreign bodies. From these evaluations, we will determine if CT or MR are equally effective in detecting the foreign bodies and we will determine if the intravenous dye improved the detection of the plastic foreign bodies.

Progress: Awaiting funding from MRMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/088 **Status:** Completed

**Title:** Refractive Changes During Prolonged Exposure to Altitude Following Radial Keratotomy Surgery

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

**Department:** Surg, Ophthalmalogy Svc **Facility:** MAMC

**Principal Investigator:** COL Thomas H. Mader, MC

**Associate Investigators:**
MAJ John D. Ng, MC
E. Sieck
Walter Hubickey, M.D.
R. Enzenauer
MAJ Lawrence J. White, MC
C. Blanton
MAJ Vernon C. Parmley, MC
Michael Caputo

**Key Words:** Keratotomy, refractive changes, altitude

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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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 prolonged high altitude.

Technical Approach: The first of two study groups will consist of 20 Navy volunteers who have had radial keratotomies one to two years prior to this study. We will record and examine several ocular parameters, at sea level and at 12,000 feet elevation, including cycloplegic refraction, intraocular pressure, corneal keratometry, corneal computer topographic analysis and central corneal thickness. Oxygen saturation will be monitored and recorded using a pulse oximeter. Barometric pressure will also be recorded. All subjects will be taken to the research facility at 12,000 feet elevation at Pike's Peak. ;;The second study group will consist of 10 active duty normals. In these individuals, we will measure the above listed parameters at sea level and 12,000 feet. We will then compare data to see if a significant difference exists between the two groups.

Progress: Six radial keratotomy patients(11 eyes), 6 photorefractive keratectomy patients (12 eyes) and 9 control myopes (17 eyes) had the following measured at sea level: cycloplegic and manifest refraction, keratometry, and pachymetry, both central and peripheral. Patients also had videokeratography performed prior to being taken to altitude. Subjects then had these same parameters measured daily at 14,110 feet on Pike's Peak for 3 days. Radial keratotomy patients demonstrated a significant hyperopic shift and corneal flattening during exposure to altitude when compared to control myopic eyes. Patients who had undergone photorefractive keratectomy did not demonstrate a statistically significant shift in refraction or keratotomy when compared with control myopes. This study strongly suggests that radial keratotomy surgery on active duty military may be inappropriate.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/111 | **Status:** Completed |
| **Title:** Refractive Changes at Altitude Following Radial Keratotomy Surgery | | |
| **Start Date:** 06/09/93 | **Est. Completion Date:** Jul 93 | |
| **Department:** Surg, Ophthalmalogy Svc | **Facility:** MAMC | |
| **Principal Investigator:** COL Thomas H. Mader, MC | | |
| **Associate Investigators:** | | |
| MAJ John D. Ng, MC | MAJ Lawrence J. White, MC | |
| CPT Carl A. Gibson, MC | Jon R. Carter, M.S. | |
| Walter Hubickey, M.D. | 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: 20 subjects entered. Study showed no statistically significant change in cycloplegic refraction or keratotomy in radial keratometry eyes during a 6 hour exposure to a simulated altitude of 12,000 feet. The study suggests that the corneal changes that lead to a hyperopic shift during altitude exposure require more than 6 hours to produce measurable effects. Since we observed no significant change over 6 hours, it is unlikely that the purely mechanical effects of decreasing barometric pressure alone are responsible for refractive changes noted at altitude. Our study supports the hypothesis that a slow metabolic process is responsible for the hyperopic shift reported at high altitude. Although the specific origin of the hyperopic shift is open to question, the theory of hypoxic corneal expansion at the RK incision appears most consistent with our altitude chamber findings. Manuscript in preparation.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/112 **Status:** On-going

**Title:** Clinical Utility and Reliability of Afferent Pupillary Defect Testing

**Start Date:** 06/03/94 **Est. Completion Date:** Jun 94

**Department:** Surg, Ophthalmalogy Svc **Facility:** MAMC

**Principal Investigator:** MAJ Eugene F. May, MC

**Associate Investigators:** Undefined investigator
CPT Benjamin N. Gilbert, MC

**Key Words:** afferent pupillary defect, visual acuity, color vision, contrast sentivity, visual field defect

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: The goal of the study is to determine the clinical utility of a recently described method of quantification of the afferent pupillary defect (APD), by comparing the amplitude of the APD with other standardized measures of optic nerve function. In addition, individual physician's measurements of APD amplitude will be compared to other physicians' measurements to assess interrater variability.

Technical Approach: This study will measure the amplitude of the APD in a series of 60 outpatients with optic neuropathies using the technique of Bell et al. The amplitude of the APD measured as such in each patient will be compared to a similar measurement using the neutral density filter technique. Each patient will also undergo visual acuity, color sensitivity, contrast sensitivity, and visual field testing. The following examiners will perform APD testing on each patient without knowledge of the others' results: a neuro-ophthalmologist, a general ophthalmologist, and an ophthalmology resident. Only the neuro-ophthalmologist will be familiar with each patient's history. For each examiner, a regression analysis will be performed between the APD amplitude using the neutral density filter and the APD grade using the technique of Bell et al to determine the accuracy of the new technique compared to the "gold standard". In addition, regression analysis will be performed between the visual function tests and the APD grade and amplitude for each examiner, in all patients, to assess the relationship of each measurement to the more standard tests of vision. The results from each examiner using each technique will be compared to the results from the other examiners (using kappa statistic and repeated measures ANOVA) to assess reliability of the measurement.

Progress: A total of 44 patients and controls have been studied to date. No analysis of the data has been performed to date. The study will run until the end of November, at which time one of the examiners will no longer be available for participation. I anticipate that 10 more patient or control subjects will be enrolled before the conclusion of the study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/091 **Status:** Terminated

**Title:** Refractive Changes During Exposure to the Hyperbaric Environment Following Radial Keratotomy Surgery

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

**Department:** Surg, Ophthalmalogy Svc **Facility:** MAMC

**Principal Investigator:** MAJ John D. Ng, MC

**Associate Investigators:**
COL Thomas H. Mader, MC
MAJ Vernon C. Parmley, MC
Hampson NB
White L
MAJ Steven C. Hadley, MC

**Key Words:** eratotomy, hyperbaric refractive changes

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

Study Objective: Our objective is to document significant changes in corneal shape and visual acuity, refraction and intraocular pressure that may take place in subjects one year following radial keratotomy when these individuals are exposed to the hyperbaric environment.

Technical Approach: Two groups will be selected for our experiment. The first study group will consist of 5 civilian volunteers who have had radial keratotomies one to two years prior to this study. We will record and examine several ocular parameters, at sea level and at depth (i.e. 50 feet of sea water (50fsw): 1) cycloplegic refraction, 2) intraocular pressure, 3) corneal keratometry and 4) central corneal thickness. Oxygen saturation will be monitored and recorded using a pulse oximeter. Barometric pressure will also be recorded. We will take all subjects to 50fsw. This depth was chosen because military divers carry out most of their missions at or above this depth and this is an average depth for recreational diving. Also a deeper depth would be prohibitive due to time constraints imposed by tissue nitrogen saturation.;;The second study group will consist of 5 active duty normals. In these individuals, we will measure the above listed parameters at sea level and at 50fsw. We will then compare data to see if a significant difference exists between the two groups.

Progress:Protocol was not funded by MRMC. PI has departed so it will not be continued.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/114 **Status:** Completed

**Title:** Clinical and Microbiological Study Comparing Ciprofloxacin Opthalmic Ointment to TOBREX Ophthalmic Ointment for Treating Bacterial Conjunctivitis in Children

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

**Department:** Surg, Ophthalmalogy Svc **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

| **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: 3 subjects were entered. Data were forwarded to the sponsor. There were no adverse events. Study was discontinued by sponsor.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/171 | **Status:** On-going |

**Title:** A Comparison of the Ability of Extracapsular Cataract Extraction Versus Phacoemulsification to Assist in the Control of Glaucoma

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|---|---|
| **Start Date:** 09/02/94 | **Est. Completion Date:** |
| **Department:** Surg, Ophthalmalogy Svc | **Facility:** MAMC |

**Principal Investigator:** CPT Gregory S. Witkop, MC

**Associate Investigators:** None

**Key Words:** glaucoma, cataract extractiion, phacoemulsification

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

Study Objective: A retrospective comparison of the ability of phacoemulsification versus standard extracapsular cataract extraction (ECCE) to lower intraocular pressure in glaucoma patients.

Technical Approach: This study is a retrospective chart review from a private practitioner's office to compare the effects of two types of cataract surgery on the control of glaucoma. Inclusion criteria included, 1) well controlled glaucoma defined as minimal visual field and optic nerve head damage and an intraocular pressure considered adequate to prevent further damage, 2) having the cataract extraction performed by the same surgeon, 3) no pre- or post-cataract extraction glaucoma surgery of any kind, 4) a minimum of one year follow-up.

Progress: Data has been collected. Analysis in progress.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, ORTHOPEDIC SURGERY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/089 **Status:** On-going

**Title:** A Randomized Open-label, Parallel Group Comparison of the Safety and Efficacy of Lovenox (Enoxaparin) Injection versus Coumadin (Adjusted Dose Warfarin) in the Prevention of Thromboembolic Disease....

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

**Department:** Surg, Orthopedic Surg Svc **Facility:** MAMC

**Principal Investigator:** CPT Barry T. Bickley, MC

**Associate Investigators:**
MAJ John D. Pitcher Jr., MC
LTC Gregg W. Taylor, MC
Steedman JT

**Key Words:** thromboembolisis, hip replacement, Lovenox, Coumadin

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

Study Objective: 1) To evaluate the safety and efficacy of Lovenox Injection versus adjusted dose Coumadin in the prevention of clinically significant thromboembolic disease following elective total hip replacement during hospitalization.

2) To determine the medium term incidence (three months post-hospital discharge) of morbidity and mortality resulting from thromboembolic disease following elective total hip replacement surgery in patients treated with Lovenox Injection vs. adjusted dose Coumadin.

Technical Approach: This study is divided into two phases; an inpatient period following surgery, not to exceed 14 days, and an outpatient follow-up period of three months.

This is a randomized, open-label, parallel group, multicenter study conducted in patients 18 years of age or older undergoing elective unilateral primary hip replacement. When the surgeon is satisfied that hemostasis has been achieved, and within 24 hours postoperatively, patients will begin their randomly assigned treatment of either Lovenox Injection 30 mg b.i.d. or adjusted dose Coumadin until hospital discharge, but not to exceed a maximum of fourteen (14) days. (Coumadin may be started up to 48 hours preoperatively at the discretion of the investigator.) Thereafter, all patients will return to the investigator for follow-up examinations at approximately six weeks and twelve weeks post hospital discharge.

The primary efficacy parameter will be the incidence of symptomatic thromboembolic disease during hospitalization and over the subsequent three month period.

Progress: Twelve subjects have been entered. Accrual continues.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** Surg, Orthopedic Surg Svc **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

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $21.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

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 5 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: Fifteen 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. Accrual is very slow.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/176 | **Status:** On-going |

**Title:** Computer Assisted Measurement of Scoliosis from Digitized Radiographs versus Traditional Cobb Angle Measurement

| | |
|---|---|
| **Start Date:** 11/05/93 | **Est. Completion Date:** Sep 93 |
| **Department:** Surg, Orthopedic Surg Svc | **Facility:** MAMC |

**Principal Investigator:** MAJ John W. Dietz, MC

**Associate Investigators:** LTC Richard W. Kruse, MC
MAJ Donald V. Smith, MC

**Key Words:** scoliosis, computer assisted meaurements

| | | | | |
|---|---|---|---|---|
| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $500.00 | **Periodic Review:** // |

Study Objective: The purpose of this study is to determine the interobserver and intraobserver error and accuracy of measurement in determining Cobb angle measurements of scoliosis and kyphosis using the digitized radiographs and measuring techniques available in the Medical Diagnostic Imaging System.

Technical Approach: In the first phase fifty anterior-posterior or posterior-anterior spine radiographs will be collected in the Orthopaedic Clinic by two of the Investigators. These radiographs must demonstrate coronal plane deformity of 10 degrees or more. During this the radiographs will be modified to obscure the patients' names and copy the radiographs into the MDIS system. Each radiograph MDIS image will be assigned a random number. The MDIS image and its corresponding radiograph will have different numbers and a log will be created showing which random numbers have been assigned to corresponding images. The examiners will be blinded to this information.

The images will be measured in random order. All measurements will be made using the Cobb method. A line will be drawn along the superior end plate of the upper vertebra to the inferior end plate of the lower vertebra. Some radiographs will have 2 measurable curves. Only one curve from the thoracic and one from the lumbar area will be measured. Measurements on radiographs will be done with pencil and protractors usually employed in the Orthopaedic Clinic. Measurements on MDIS images will be done by choosing lines along end plates with the mouse and indicator. Actual measurements will be made by each of four observers. Measurements will be recorded on a data sheet.

Progress: Protocol just approved. Collection of films is beginning.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/096 **Status:** Completed

**Title:** Thumb Flexor Retinaculum and Tendon Sheath Pulley Study

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

**Department:** Surg, Orthopedic Surg Svc **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: There were no significant differences in excursion of the tendon, or ROM of the thumb in intact specimens across groups, nor did position of the hand have an effect. There was a significant increase in excursion with all pulleys cut. With proximal to distal injury, the largest change in tendon excursion occurred when the oblique was sectioned after the flexor retinaculum and first annular pulleys had been cut. Sectioning distal to proximal, the greatest increase in excursion occurred fro second annular + oblique on. There was no effect of pulley sectioning on total ROM of the thumb.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/142 | **Status:** On-going |
| **Title:** Cost Effectiveness of Screening MRIs of the Shoulder Prior to Neer Acromioplasties | | |
| **Start Date:** 08/05/94 | **Est. Completion Date:** | |
| **Department:** Surg, Orthopedic Surg Svc | **Facility:** MAMC | |
| **Principal Investigator:** CPT Randall K. Hildebrand, MC | | |
| **Associate Investigators:** | MAJ John D. Pitcher Jr., MC | |
| **Key Words:** acromioplasty, MRI, cost effectiveness | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: 1. To determine the sensitivity (SN), negative predictive value (NPV), and positive predictive value (PPV) and accuracy of shoulder MRIs in predicting rotator cuff tears of the shoulder. 2. To determine whether screening shoulder MRIs in patients with impingement syndrome is helpful and cost effective in the surgical management of preoperative management of those cases that are refractory to non-operative treatment.

Technical Approach: This is a prospective, single-blinded study of MRI vs operative evaluation, comparing their abilities to diagnose rotator cuff tears and other pathology about the shoulder. Patients selected for this study will have met the surgical indications for a modified Neer Acromioplasty for impingement syndrome with or without a suspected rotator cuff tear.

One hundred patients will have an MRI of the affected shoulder within two weeks of the anticipated subacromial decompression. MRI interpretation will be in the form of a radiological report documenting the presence or absence of rotator cuff tears or tendonitis, glenohumeral labral pathology, or other pathology about the shoulder. Intraoperatively the surgeon will record his findings both before and after review of the MRI and the MRI report. However, he will remain blinded to the MRI results until a surgical course has been decided intraoperatively. In other words, the surgery will begin as if no MRI had been performed. After an operative diagnosis and treatment course planned, the MRI and its report will be reviewed. If indicated by the MRI, the planned treatment course will be altered intraoperatively. Any and all treatment alterations based on the MRI will be recorded, and correlations will be made between pathology on surgical observation and those seen on the MRI.

Using open acromioplasty as the gold standard, after 100 surgeries the data will be reviewed to determine the SN, SP, NPV, and PPV, and accuracy of MRI. The need for preoperative MRI will be assessed by determining whether and how many operative plans are affected by the MRI and its interpretation.

Progress: No subjects have been entered.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/113 | **Status:** Completed |
| **Title:** Partial Sacretomy Through A Posterior Midline Incision | | |
| **Start Date:** 06/03/94 | **Est. Completion Date:** Jun 94 | |
| **Department:** Surg, Orthopedic Surg Svc | **Facility:** MAMC | |
| **Principal Investigator:** CPT Randall K. Hildebrand, MC | | |
| **Associate Investigators:** MAJ William C. Williard, III, MC | MAJ John D. Pitcher Jr., MC | |
| **Key Words:** sacretomy:technique | | |

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

Study Objective: To describe, by using a chart review of surgical cases, a technique for partial surgical sacrectomy that is not well documented in the literature.

Technical Approach: A retrospective chart review of all patients undergoing a partial sacrectomy, using a posterior midline approach, at MAMC in the past two years will be conducted. Advantages, disadvantages, and complication of this uncommon approach will be described and discussed and compared to those of the more commonly used approaches.

Progress: A new method of sacral resection was presented and compared with other techniques. A retrospective review of cases presenting to Madigan Orthopedic Clinic over 3 years was performed and cases were reviewed for benefits and complications of this procedure. When data analysis is complete, an abstract will be sent to Society of Military Orthopedic Surgeons.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 86/016 **Status:** Suspended

**Title:** Teaching Program for Practical Microsurgery

**Start Date:** 11/15/85 **Est. Completion Date:** Indef.

**Department:** Surg, Orthopedic Surg Svc **Facility:** MAMC

**Principal Investigator:** LTC Frederick Johnstone, MC

**Associate Investigators:**
COL Jackie L. Finney, MC
LTC Donald B. Blakeslee, MC
MAJ Stephen D. Clift, MC
LTC Bruce R. Wheeler, MC
MAJ Michael Q. Cosio, 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
MAJ Stephen M. Davis, MC

**Key Words:** training protocol,microsurgery,Animal Study

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $690.00 | **Periodic Review:** 06/10/94 |
|---|---|---|---|---|

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: Seven sessions were held with one animal used at each session. Suspended pending rewrite.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/160 **Status:** On-going

**Title:** Use of Pulsing Electromagnetic Fields for the Treatment of Pelvic Stress Fractures

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 95

**Department:** Surg, Orthopedic Surg Svc **Facility:** MAMC

**Principal Investigator:** Jones DEC

**Associate Investigators:**
LTC David J. Magelssen, MC
Goeken A
LTC Richard A. Sherman, MS
Kungys A

**Key Words:** Stress fractures:pelvic, electromagnetic fields

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

Study Objective: To determine whether application of Pulsing Electromagnetic Fields (PEMFs) over the stress fracture site, used in conjunction with standard therapeutic approaches, reduces the time to return to full duty in relation to those receiving the standard treatments and placebo PEMFs.

Technical Approach: Subjects diagnosed as having pelvic area stress fractures will receive one hour of PEMF or placebo PEMF therapy five days per week in addition to the standard treatment (sharply reduced activity and minimized walking) from the time the diagnosis is made until return to full duty. Subjects will be randomly assigned to groups and evaluated.

The patient will lay on an exam table with the head of the PEMF generator positioned several millimeters above the stress fracture site. The patient will be exposed to the fields for 15 minutes while on their backs and an additional 15 minutes while on their fronts. Each subject will have a total of 30 exposure to the field every day until they return to duty. The machine makes the same humming sound regardless of whether or not it is generating a field and subjects can not feel the field. Thus, subjects should not be aware of whether they are in the exposure or placebo group. The technician who turns on the device will know which group the subject is in so the machine can be set for either actual or placebo functioning but the technician and physicians doing the evaluations will have no idea which group the patients are in.

Progress: New study. Awaiting funding.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/180 | **Status:** On-going |
| **Title:** Lateral Ankle Reconstruction Study | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** Apr 95 | |
| **Department:** Surg, Orthopedic Surg Svc | **Facility:** MAMC | |
| **Principal Investigator:** CPT James D. Swenson, MC | | |
| **Associate Investigators:** CPT Mark C. Weston, MC | MAJ John D. Pitcher Jr., MC | |
| **Key Words:** ankel reconstruction | | |

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

Study Objective: Evaluate functional (subjective) and mechanical (objective) improvement in patients undergoing reconstruction of lateral ankle ligaments.

Technical Approach: Patients found to have unstable lateral ankle ligaments will undergo surgery to reconstruct these ligaments. They will be evaluated before surgery with radiographs and a physical examination of the ankle to determine the amount of pre-operative laxity. Patients will be followed after surgery for at least 6 months at which time repeat radiographs and physical examination of the ankle will be done to determine the amount of post-operative ankle laxity. Patients will also be asked to fill out a questionnaire regarding the functional status of their ankle.

Progress: 30 subjects entered, have been seen for first time, and are to return for 6 month evaluations.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, PLASTIC SURGERY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/099 **Status:** On-going

**Title:** The Implantation of Bone Morphogenic Protein Using Vascularized Omentum in a Predetermined Size and Shape in Swine

**Start Date:** 09/04/92 **Est. Completion Date:** Dec 92

**Department:** Surg/Plas **Facility:** MAMC

**Principal Investigator:** MAJ Stephen M. Davis, MC

**Associate Investigators:**
MAJ Robert J. Wygonski, DC
MAJ Cecil R. Dorsett, DC
MAJ Richard R. Gomez, MC

**Key Words:** bone protein, omentum, animal study,Animal Study

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $600.00 | **Periodic Review:** 06/07/93 |
|---|---|---|---|---|

Study Objective: To determine if a vascularized graft utilizing omentum with bone morphogenetic protein can induce bone formation in a three dimensional shape; and to determine bone produced in this manner can survive transplantation to a different location.

Technical Approach: Bone grafting is a commonly performed procedure. The best bone graft is a vascular autogenous graft (one obtained from the patient complete with its own blood supply). However, this is not always possible and does have certain risks, even when properly performed. Bone morphogenetic protein (BMP) is a substance which induces new bone to form in intra- or extra-skeletal sites and has recently been cloned by recombinant DNA techniques. Six pigs will be used for this study. Each pig will undergo a laparotomy with the placement of six tubular molds around individual omental pedicles. Two molds will contain only omentum, two will contain omentum and autogenous bone, and two will contain omentum and bone morphogenetic protein. Forty five days after being implanted, each mold will be opened and visually examined. The two molds containing bone morphogenetic protein will have their vascular supply switched by microsurgical techniques. After an additional 45 days, all molds will be harvested and examined to determine if bone has been produced in a three dimensional shape with its own blood supply. If present, an attempt will be made to determine if it is cortical, cancellous, or corticocancellous bone.

Progress: Cell cultures are proceeding as planned and pig implantation will proceed on schedule.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, PODIATRY SERVICE

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/034 | **Status:** Completed |

**Title:** A Retrospective Study of the Surgical Correction in Patients with Multiple Hammertoe Deformities by Digital Arthrodesis, Modified Hibbs Tenosuspension and Flexor Tendon Transfers

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|---|---|
| **Start Date:** 12/17/93 | **Est. Completion Date:** Nov 93 |
| **Department:** Surgery, Podiatry Service | **Facility:** MAMC |
| **Principal Investigator:** DeBorja JA | |
| **Associate Investigators:** | MAJ Richard O. Jones, MC |
| **Key Words:** hammertoe, arthrodesis, Hibbs Tenosuspension, flexor tendon transfers | |

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

Study Objective: To question and examine post-operative patients, and review their X-rays, inpatient records, and outpatient records to determine efficacy of the modified Hibbs Tenosuspension with flexor tendon transfer for correction of hammertoes.

Technical Approach: Ten patients that fit the criteria and have had a Modified Hibbs Tenosuspension and Flexor Tendon Transfer performed at MAMC will be examined and complete a questionnaire. The operative reports, x-rays, questionnaire and pre and post-operative records will be reviewed to determine if the patient will be examined. Subjective findings will include patient satisfaction (better or worse off than before surgery), patient complaints of pain (joint, metatarsalgia, digital), and activity. The objective finding will examine the recurrence of hammertoes and complications.

By using a scoring system for patient satisfaction comparisons can then be made with t-test. Similarly, pain level can be compared preoperatively vs. postoperatively using the t-test. Changes in pain location as a result of surgery will be compared using chi-square.

Progress: Completed. No other information available.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/068 **Status:** Completed

**Title:** Technical Protocol for the Evaluation of Podiatric Neoplasms of the Foot and Ankle

**Start Date:** 05/06/94 **Est. Completion Date:** Oct 94

**Department:** Surgery, Podiatry Service **Facility:** MAMC

**Principal Investigator:** CPT Stephen V. Wilkinson, MC

**Associate Investigators:** MAJ John D. Pitcher Jr., MC
MAJ Richard O. Jones, MC

**Key Words:** neoplasms, foot and ankle

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

Study Objective:

Technical Approach:

Progress: Presented at American College of Foot and Ankle Surgeons. Won first place poster award.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, UROLOGY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/098 **Status:** Completed

**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 Service **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

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/144 | **Status:** On-going |
| **Title:** Evaluation of the Safety and Efficacy of Transurethral Resection of the Prostate Using the Contatct Laser System vs Electrosurgery | | |
| **Start Date:** 09/02/94 | **Est. Completion Date:** | |
| **Department:** Surgery, Urology Service | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Kurt L. Hansberry, MC | | |
| **Associate Investigators:** MAJ James B. Thrasher, MC | COL John N. Wettlaufer, MC | |
| **Key Words:** prostate:resection, laser, electrosurgery | | |

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

Study Objective: 1. To evaluate the effectiveness (resection and coagulation) of the Contact Laser System in comparison to that of electrosurgery for transurethral resection of the prostate (TURP).

2. To evaluate the relative cost effectiveness of the Contract Laser in comparison to that of electrosurgery for transurethral resection of the prostate.

Technical Approach: Male patients who have been diagnosed with symptomatic benign prostatic hypertrophy (BPH) will be enrolled into this study once all of the entrance criteria have been fulfilled. After all baseline evaluations have been performed, each patient will undergo TURP using either electrosurgery or the Contact Laser System. All patients will be monitored closely through discharge, and will undergo follow-up evaluation a one and six months, and one year following surgery. Follow-up evaluation will be encouraged (optional) annually for five (5) years thereafter.

Progress: Awaiting MEDCOM approval. No patients entered.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** Surgery, Urology Service **Facility:** MAMC

**Principal Investigator:** CPT Bradley F. Schwartz, MC

**Associate Investigators:** MAJ James B. Thrasher, MC
MAJ Kurt L. Hansberry, MC

**Key Words:** penile prosthesis, fluoroguinolones, prophylaxis

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 10/21/94 |
|---|---|---|---|---|

Study Objective: To determine if oral Fluoroquinolones afford efficacious alternatives to the current regimens in penile prosthetic surgery prophylaxis.

Technical Approach: 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: Ten patients have been entered. Patient entry continues. One adverse reaction of nausea and vomiting, which resolved itself has been reported.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 93/045 | **Status:** Completed |
| **Title:** The Normal Flora of the Human Epididymis | | |
| **Start Date:** 02/05/93 | **Est. Completion Date:** Jul 96 | |
| **Department:** Surgery, Urology Service | **Facility:** MAMC | |
| **Principal Investigator:** CPT Bradley F. Schwartz, MC | | |
| **Associate Investigators:** COL John N. Wettlaufer, MC | MAJ James B. Thrasher, MC | |
| **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: Thirty-four men undergoing orchiectomy for androgen deprivation, trauma, cancer, torsion, or other noninfectious causes were entered in the study. The data from the study indicate that there are no normal (or endemic) flora of the human epididymis. There were 3 positive cultures. These were grown on aerobic media and numbered fewer than 10,000 colonies of gram-positive organisms. In each of these cases, the patient had no symptoms and preoperative and postoperative cultures showed no growth. In all cases, these were believed to be contaminants, based on the organisms and colony counts reported.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/133 **Status:** On-going

**Title:** Comparison of Self-Injection versus External Vacuum Devices in the Treatment of Erectile Dysfunction

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

**Department:** Surgery, Urology Service **Facility:** MAMC

**Principal Investigator:** CPT Douglas W. Soderdahl, MC

**Associate Investigators:** MAJ James B. Thrasher, MC
Hansberry K

**Key Words:** erectile dysfunction, self-injection devise, external vacuum devise

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

Study Objective: To directly compare two non-surgical treatments of erectile dysfunction: self-injection vs. external vacuum devices.

Technical Approach: Patients actively undergoing either self-injection pharmacotherapy or external vacuum device (EVD) therapy will be invited to participate in this study. Each patient enrolled will receive a detailed questionnaire which covers satisfaction, effectiveness, and side effect issues of their currently employed treatment modality. The self-injection group will then be given instruction and necessary equipment to employ the EVD. Likewise, the EVD group will receive instructions for injection treatment. After four months, the participants will be asked to complete the same questionnaire to evaluate the alternate modality. The participants will also be asked to comment on their comparison of the two therapies. Sexual partners of the patients will also be asked to attend a follow-up visit and fill out a confidential questionnaire comparing the two different treatments. At the end of the study, the patient and his physician will make an informed decision about which modality to continue with.

Progress: No patients entered yet.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/164 **Status:** On-going

**Title:** Prostate Cancer Intervention vs Observation Trial (PIVOT): A Randomized Trial Comparing Radical Prostatectomy vs Palliative Expectant Management for the Treatment of Clinically Localized Prostate ...

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 04

**Department:** Surgery, Urology Service **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:** Hansbury KL

**Key Words:** Cancer:prostate, prostatectomy, palliative management

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

Study Objective: To determine which of 2 treatment strategies is superior in reducing all-cause mortality in patients with clinically localized prostate cancer (1) radical prostatectomy and early intervention of subsequent disease persistence or recurrence or (2) expectant management with reservation of therapy for palliative treatment of symptomatic or metastatic disease progression.

Technical Approach: Patients will be randomized to one of the two groups listed (1) will have a radical prostatectomy; (2) will be assigned to Watchful Waiting Management.

Patients in group 1 will have 2 surgical procedures; removal of the lymph nodes from near the prostate gland (pelvic lymph node surgery); and then proceed with the prostatectomy.

Patients in group 2 will not have their cancer removed. Patients will be closely observed; if the cancer causes symptoms, treatment will be aimed at providing relief of these symptoms.

Progress: New study. No subjects entered.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/051 **Status:** On-going

**Title:** Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer

**Start Date:** 05/06/94 **Est. Completion Date:** Jan 95

**Department:** Surgery, Urology Service **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:**
Romez RR
CPT Patrick A. Twomey, MC
COL Stephen R. Plymate, MC
CPT Michael D. Bagg, MC

**Key Words:** cancer:prostate, IGF

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

Study Objective: The purpose of this study is to localize IGFBP's -2.-3,-4, and -6 in regions of histologically proven prostate cancer. Additionally, these same techniques will be used to identify these binding proteins in areas of prostatic intraepithelial neoplasia (PIN) and benign prostatic hyperplasia (BPH). The information gleaned from this study will help better understand IGFBP expression in both malignant, premalignant, and benign prostatic tissue.

Technical Approach: Radical prostatectomy specimens will be obtained by the Urology Service and taken to Pathology for histologic sectioning. Prostate adenocarcinoma will be identified in sections (as well as areas of PIN or BPH) with an adjacent section taken for immunohistochemical staining. Immunohistochemical staining will be performed for identification of IGFBP's-4, -2, -3, and -6 in regions of associated neoplasm, PIN or BPH. Approximately 10 patients will be studied with comparisons to be made between neoplastic premalignant, and benign prostatic tissue.

Progress: Fifteen subjects were entered. We have noted the presence of IGFBP-5 in the stomal component of the prostate tissue with absence of this BP in the glandular component. We will need to study more PIN to make definitive statements about changes in IGFBP-2, 3, and 4 as prostate tissue progresses from a normal to a neoplastic state.

# DETAIL SHEETS FOR PROTOCOLS

# DEPARTMENT OF SURGERY, VASCULAR SURGERY SERVICE

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/174 **Status:** On-going

**Title:** Assessing Quality of Life of Patients With Lower Extremity Arterial Occlusive Disease

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

**Department:** Surgery, Vascular Surgery Service **Facility:** MAMC

**Principal Investigator:** LTC Jon Charles Bowersox, MC

**Associate Investigators:** None

**Key Words:** Quality of Life:lower extremity arterial occlusive disease

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

Study Objective: The goal of this study is to use a questionnaire to longitudinally assess the health related quality of life in patients with lower extremity arterial occlusive disease.

Technical Approach: Patients will be required to fill out a questionnaire titled "Assessing Quality of Life of Patients with Leg Circulatory Problems" upon initial enrollment, one week later, 6 months, 12 months, 18 months and 24 months.

Physicians will complete the questionnaires titled "Physician's Expectations of Patient Outcomes" and "Longitudinal Patient Data Form" during initial enrollment of the patient. Physicians will complete the "Physician's Expectations" questionnaire again at 6 months, 12 months, 18 months, and 24 months.

The Principal Investigator will complete the "Comorbidity Score Sheet" after reviewing the patient's chart following initial enrollment and then the "Longitudinal Patient Data Form". The Principal Investigator will also complete "Comorbidity Score Sheet" and "longitudinal Patient Data Form" at the 6 month, 12 month, 18 month and 24 month intervals.

After completion, coded forms will be sent to the study coordinator center in White River Junction, VT.

Progress: New study. No patients entered yet.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/168 **Status:** On-going

**Title:** Efficacy of an Oxygen Delivery Solution in Preventing Tissue Ischemia During Hypotensive Resuscitation From Hemorrhagic Shock in Guinea Pigs

**Start Date:** 09/21/94 **Est. Completion Date:** Jun 95

**Department:** Surgery, Vascular Surgery Service **Facility:** MAMC

**Principal Investigator:** LTC Jon Charles Bowersox, MC

**Associate Investigators:** Cornum RLS
CPT Stefan M. Pettine, MC

**Key Words:** Ischemia, hemorrhagic shock, resuscitation, guinea pig,Animal Study

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative Cost:** | **OMA** $0.00 | **Periodic Review:** // |
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Study Objective: The objective of the proposed research is to determine if an oxygen delivery solution can prevent tissue ischemia during hypotensive resuscitation from hemorrhagic shock.

Technical Approach: The investigator will simulate hemorrhagic shock in anesthetized guinea pigs (cavia porcellue) by removing blood and maintaining the mean arterial blood pressure at 35 mm Hg. Animals will receive HBOC-201, a polymerized solution of bovine hemoglobin, and tissue oxygen levels will be measured. Control animals will receive either standard electrolyte solutions, hypertonic saline solutions or blood. At the end of the experiment, the anesthetized animals will be euthanized.

Progress: Study awaiting funding.

# DETAIL SHEETS FOR PROTOCOLS

# GYNECOLOGY ONCOLOGY GROUP

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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 William L. Benson, MC | COL Roger B. Lee, MC | |
| **Key Words:** | | |

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| **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 94. GOG protocols 26 DD, KK, LL, Q, and U were terminated due to sufficient data collection.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 William L. Benson, MC
COL Roger B. Lee, MC

**Key Words:** cancer:pelvic,cisplatinum

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

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 have been entered in this study.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 88/067 | **Status:** On-going |

**Title:** GOG 0026DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies

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|---|---|
| **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

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| **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 94 **Protocol No.:** 90/023 **Status:** Terminated

**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: This study was terminated 23 Mar 94. No patients were entered at MAMC.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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:** Id 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 have been entered in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/085 **Status:** Completed

**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.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 93/153 | **Status:** Terminated |
| **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: This study has been terminated due to sufficient data collection. One patient was entered at MAMC and is still living.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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

**Date:** 30 Sep 94 **Protocol No.:** 83/026 **Status:** Terminated

**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: This protocol was terminated 20 May 94. No patients were entered in FY 94. One patient was entered in FY 85 and died of the disease.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 85/087 **Status:** Terminated

**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: This study was terminated 20 May 94. No patients were entered in this study at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 81/079 | **Status:** Terminated |
| **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 William L. Benson, MC | COL Roger B. Lee, 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: This study has been terminated by GOG due to sufficient data. One patient was entered at MAMC and is still surviving.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: This study was closed to patient entry 12 Feb 87. Thirteen patients were enrolled, 2 have been lost to follow up, 2 have died, and 9 are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 81/105 **Status:** On-going

**Title:** GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma

**Start Date:** 08/21/81 **Est. Completion Date:** Mar 98

**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: This study was closed to patient entry, 20 Jul 85. Six patients were entered in the study and one is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 and 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: This study was closed to patient entry 25 Feb 92. Ten patients were enrolled; 1 has died and 9 are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: Closed to patient entry 10 Feb 92. One patient was enrolled in FY 92 and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 86/089 **Status:** On-going

**Title:** GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and...

**Start Date:** 08/15/86 **Est. Completion Date:** 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 (at a different institution). After further review it was discovered that this was a mistake and the protocol was reopened in Feb 93. Two patients were entered at MAMC and are still being followed.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/093 | **Status:** On-going |
| **Title:** GOG 0087G: A Phase II Trial of Paclitaxel (Taxol) in Patients With Advanced or Recurrent Uterine Sarcomas | | |
| **Start Date:** 04/01/94 | **Est. Completion Date:** Apr 97 | |
| **Department:** GOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Mark E. Potter, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Cancer:uterine, sarcoma, Paclitaxel | | |

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

Study Objective: To compare the efficacy of Paclitaxel (Taxol) in patients with advanced or recurrent uterine sarcomas.

Technical Approach: Patients eligible to participate in this study will be treated with Paclitaxel at 175 mg/m$^2$ given as a three hour infusion every three weeks. Infusion is administered intravenously after premidication with decadron, and H1 and H2 blockers. Weekly CBC's are monitored and patients will be subseqauently treated with granulocyte-colony stimulator factor (G-CSF) support for prolonged neutropenia or febrile neutropenia. In the event of persistent neutropenia despite G-CSF support, dose reductions will occur. Patients who have received previous pelvic radiation therapy will be treated at a decreased dose of 135 mg/m$^2$. In the event that tumor measurements are obtainable by either physical examination or routine radiographs, tumor measurement will be obtained every three weeks prior to therpay. If CT or ultrasound imaging is required for tumor measurements, tumor measurements will be obtained every six weeks. Patients will remain on study until disease progression or evidence of significant toxicity.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 have been enrolled in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **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 have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: This protocol was closed to patient entry 14 Mar 94. Five patients have been entered and 1 remains in follow-up.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** | $0.00 | **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 94. The two patients enrolled in previous years are both in follow-up.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 87/106 | **Status:** Completed |

**Title:** GOG 0101: A Phase II Evaluation of Preoperative Chemoradiation for Advanced Vulvar Cancer

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| **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<br>COL Donald H. Kull, MC |
| **Key Words:** cancer:vulva,chemoradiotherapy | |

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| **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 l 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: This study was closd to patient entry 14 Feb 94. No patients were entered in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/065 **Status:** Completed

**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: This study was closed to patient entry 14 Mar 94. No patients were enrolled at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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

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| **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

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| **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 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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-Fluorouracil,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: This study was closed to patient entry 20 May 94. No patients were enrolled at MAMC during FY 94. The one patient enrolled in previous years is still in follow-up.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/009 **Status:** Completed

**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: This study has been closed to patient entry. No patients were entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 91/010 **Status:** Completed

**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: This study was closed to patient entry, 2 March 92. .Two patients were enrolled in previous years and both are deceased.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 91/011 | **Status:** Completed |

**Title:** GOG 0112: A Randomized Comparison of Chemoprophylaxis Using Methotrexate versus Routine Surveillance in the Management of the High Risk Molar Pregnancy

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|---|---|
| **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: This protocol was closed to patient entry, 5 Nov 93. No patients were entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: This study was closed to patient entry, 15 Oct 91. Two patients were enrolled in FY 92 and still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: One patient was enrolled in this study in FY 94 and one patient was enrolled in FY 84. Both are still being followed.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/013 | **Status:** On-going |
| **Title:** GOG 0116: Evaluation of Adjuvant VP-16 and Carboplatin Therapy in Totally Resected Ovarian Dysgerminoma | | |
| **Start Date:** 10/01/93 | **Est. Completion Date:** Apr 96 | |
| **Department:** GOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Mark E. Potter, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Cancer:ovarian, VP-16, carboplatin | | |

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

Study Objective: To evaluate the efficacy and toxicity of adjuvant VP-16 and carboplatin in patients with totally resected ovarian dysgerminoma.

Technical Approach: Patients who have had totally resected Stage Ib-III ovarian dysgerminoma will be eligible for this study. Those patients will undergo chemotherapy utilizing VP-16 10 mg/m$^2$ on days 1-3 carboplatin 400 mg/m$^2$ on day 1. After completion of the chemotherapy, patients will be evaluated in follow-up every two months for one year, every three months for the second year, then every four to six months thereafter for a total of five years. At the completion of the five year follow-up annual evaluations will then be performed. At the time of each follow-up, physical examination, liver function tests, and tumor markers of Beta-HCG and Alpha-fetoprotein will be obtained.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/014 | **Status:** On-going |

**Title:** GOG 0122: Whole Abdominal Radiotherapy Versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

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| **Start Date:** 10/01/93 | **Est. Completion Date:** Jan 97 |
| **Department:** GOG | **Facility:** MAMC |

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:endometrial, radiotherapy, doxorubicin, cisplatin

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

Study Objective: 1) To compare the effectiveness of chemotherapy to whole abdominal radiation therapy in patients with advanced endometrial cancer which has been resected to less than 2 cm residual tumor. 2) To compare the relative toxicity of these two treatment strategies.

Technical Approach: Patients who have had surgical intervention for advanced (Stage III or IV) endometrial carcinoma confined to the abdominal cavity will be randomized either to whole abdominal radiation therapy or chemotherapy utilizing Doxorubicin at 60 $mg/m^2$ and Cisplatin at 50 $mg/m^2$ given every three weeks for eight cycles. After the completion of therapy patients will be seen and evaluated every three months for two years and six months thereafter for five years after treatment. Nationally 240 patients will be enrolled over 4 years. Patients will be evaluated for length of survival, disease-free survival and toxicity.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/064 **Status:** Completed

**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: This study was closed to patient entry, 5 Nov 93. No patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/152 **Status:** Completed

**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: This study was closed to patient entry, 30 Dec 94. There were no patients entered at MAMC.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **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: This study was closed to patient entry 21 Nov 94. No patients entered this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/071 **Status:** Completed

**Title:** GOG 0127D: Evaluation of Altretamine (Hexamethylmelamine) in Advanced or Recurrent Squamous Cell Carcinoma of the Cervix

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

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** cancer:cervix, Altretamine

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

Study Objective: To evaluate the potential efficacy and toxicity profile of patients with cisplatin refractory squamous cell carcdinoma of the cervix.

Technical Approach: Patients who have advanced or recurrent squamous cell carcinoma of trhe cervix and fail treatment with cisplatin therapy or combination therapy which uses cisplatin can be entered into this study. Patients so entered will take altretamine orally at 260 $mg/m^2/d$ for three continuous weeks. The fourth week will result in no therapy. If significant toxicity or disease progression is not apparent after the fourth week, chemotherapy will be reinitiated. Therapy will be continued at this schedule as long as significant toxicity or progression of the tumor does not occur. Weekly CBC's will be obtained to evaluate hemopoietic toxicity. Serial renal and hepatic profiles will be obtained prior to each cycle of chmeotherapy to insure absence of toxicity. Physical examination will be performed prior to every cycle to insure response. If radiologic techniques in particular CT, are required they will be repeated every two cycles.

Progress: This study was closed to patient entry, 6 Jun 93.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/141 | **Status:** Terminated |

**Title:** GOG 0127E: Evaluation of CPT 11 (Irinotecan) (NSC #616348) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix

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|---|---|
| **Start Date:** 08/05/94 | **Est. Completion Date:** |
| **Department:** GOG | **Facility:** MAMC |

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:cervix, irinotecan

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

Study Objective: 1. To determine whether CPT-11 (Irinotecan) demonstrates significant clinical efficacy in the treatment of squamous cell carcinoma of the cervix. 2. To evaluate toxicity for treatment with CPT-11 in this disease.

Technical Approach: Patients will receive weekly infusions of CPT-11 at a dose of 125 $mg/m^2$ over a 90 minute period for four consecutive weeks. A two two week rest with then ensue and subsequent courses will be repeated at six week intervals. Treatment will continue until significant toxicity or disease progression precludes further therapy. All patients will be followed until their death.

Progress: This study was withdrawn by GOG, 23 Sep 94 until further data analysis could be completed and a decision made as to whether to perform the protocol.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/102 | **Status:** On-going |
| **Title:** GOG 0128B: Evaluation of Paclitaxel (Taxol) in Persistent or Recurrent Non-Squamous Cell Carcinoma of the Cervix and Vagina | | |
| **Start Date:** 05/06/94 | **Est. Completion Date:** May 95 | |
| **Department:** GOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Mark E. Potter, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Cancer:cervix, Cancer:vagina, paclitaxel | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: To evaluate efficacy of Paclitaxel (Taxol) in the treatment of patients wil persistent or recurrent non-squamous cell carcinoma of the cervix or vagina.

Technical Approach: Patients with incurable recurrent or persistent non-squamous cell carcinoma of the cervix and vagina are eligible to participate in this study. All patients will receive a 24 hour infusion of Paclitaxel at 170 mg/m$^2$ everry three weeks. Patients who have received previous radiation therapy to the pelvis will be treated at a dose of 135 mg/m$^2$ every three weeks. Routine weekly CBCs will be obtained to monitor for significant neutropenia. Should significant neutropenia develop resulting in fever or prolonged neutropenia, dose reduction will occur. If a dose of 110 mg/m$^2$ still results in significant neutropenia, granulocyte colony stimulating factor (G-CSF) will be used. On subsequent treatment cycles, 5 microgram/kg will be administered subcutaneously starting 24 hours after therapy and continuing until absolute granulocyte count is sufficient. Patients will continue to receive Taxol every three weeks until tumor progression occurs or severe side effects prevent further therapy. Tumor measurements will be obtained prior to every cycle if detectable on physical examination. Measurements determined by x-rays or imaging studies will be obtained every 6 weeks.

Progress: No patients were enrolled at MAMC.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/015 | **Status:** Completed |
| **Title:** GOG 0129B: A Phase II Trial of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Endometrial Carcinoma | | |
| **Start Date:** 10/01/93 | **Est. Completion Date:** Oct 94 | |
| **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 determine if the utilization of semi-continuous low dose oral etoposide has significant activity with an acceptable level of toxicity in patients with advanced or recurrent endometrial carcinoma who have failed standard therapy.

Technical Approach: Patients with histologically documented recurrent or advanced endometrial carcinoma with clinically measurable disease who have failed standard therapy and are not curable by surgery or radiation therapy will be given VP-16 by mouth for three (3) out of four (4) weeks at a dose of 50 $mg/m^2$. Clinical and laboratory evaluations will be performed at prescribed intervals. Treatment will continue until disease progression or significant toxicity precludes further therapy.

Progress: This study was closed to patient entry 6 Jun 94. No patients were entered at MAM

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/062 **Status:** On-going

**Title:** GOG 0131B: Evaluation of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus

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

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:uterus, leiomyosarcoma, etoposide

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

Study Objective: To determine if the utilization of semi-continuous low dose oral etoposide has significant activity with an acceptable level of toxicity in patients with advanced or recurrent Leiomysosarcoma of the uterus who have failed standard therpy.

Technical Approach: Patients with histologically confirmed recurrent or metastatic leiomyosarcoma that have failed local therapeutic measures and have adequeate bone marrow, renal, and hepatic function will be invited to participate in this study. Etosposide (VP-16) will be administered at a dosage of 50 mng/$m^2$/day, day 1-21 every 4 weeks. If side effects are not severe, a patient may remain on the study agent indefinately at the investigator's discretion. Likewise, patients with evidence of progressive disease or those with significant side effects or deterioration of performance status may be removed from study at the investigator's discretion. All patients will be followed until death.

Progress: No patients have been entered at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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

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|---|---|
| **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

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| **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 have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 have been enrolled in this study at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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

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| **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

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| **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 94 **Protocol No.:** 93/086 **Status:** Completed

**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: This study was closed to patient entry, 15 Oct 93. No patients entered this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** // |
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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.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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 | | |

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| **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.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/140 **Status:** On-going

**Title:** GOG 0145: A Randomized Study of Surgery vs Surgery + Vulvar Radiation in the Management of Poor Prognosis Primary Vulvar Cancer and of Radiation vs Radiation & Chemotherapyt for Positive Inguinal Node

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

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:vulvar, positive inguinal nodes

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: 1. To determine whether he additional radiation therapy to the area of vulvar resection decreases the risk of recurrent cancer in high risk patients. 2. Whether the addition of chemotherapy along with radiation improves the effect of radiation therapy in decreasing the risk of tumor recurrence in the areas treated by radiation therapy. 3. To evaluate the impact of these therapeutic interventions on the overall quality of life both during and subsequent to treatment. 4. To determine if HPV status alters the risk of local recurrence and/or survival.

Technical Approach: Patients with invasive squamous cell carcinoma of the vulva who meet the eligibility criteria will have initial surgery on the vulva and groins. After pathological examination of the specimen, patients will be eligible for randomization to observation or to additional therapy to the vulva. Patients with positive nodes will be randomized to receive radiation alone or radiation and chemotherapy to the inguinal and pelvic nodes. Patient treated with chemotherapy will receive Cisplatin day one, followed by four days of continuous infusion of 5 FU. In addition, patients will complete quality of life questionnaires prior to receiving radiation or chemotherapy, then at three, six, twelve, eighteen, and twenty-four months. All patients will be followed in the OB-GYN Oncology Clinic subsequent to treatment. Initial frequency of follow-up will be at three month intervals for one year, followed by four month intervals for one additional year and then every six months for an additional three years. The patient's disease status will be correlated with the presence or absence of HPV in the tumor and surrounding tissue.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/103 **Status:** On-going

**Title:** GOG 0146B: Evaluation of Tomudex (ZD1694) (NSC #639186) in Recurrent, Platinum-Sensitive Ovarian Cancer

**Start Date:** 05/06/94 **Est. Completion Date:** May 96

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:ovarian, Tomudex

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: To identify effective agents for the treatment of epithelial ovarian cancers.

Technical Approach: Patients who agree to participate in this study will be treated with Tomudex, an ivnestigational chemotherapeutic agent. Tomudex is a specific Thymidylate Synthase inhibitor. This treatment, administered every three weeks, is given as intravenous infusions over 15-30 minutes. Toxicity will be monitored with serial history and physical examinations, CBCs, liver function tests, and tumor measurements. Diagnostic imaging studies will be performed every six weeks, if necessary, to evaluate tumor response and then three weeks after treatment. Upon evidence of progressive disease or significant toxicity, treatment will be discontinued and an alternative treatment plan will be determined.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/076 **Status:** On-going

**Title:** GOG 0147: A Quality of Life Companion Study to GOG 122 - Whole Abdominal Radiotherapy versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

**Start Date:** 05/06/94 **Est. Completion Date:** Jan 97

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:endometrial, quality of life

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: To evaluate the quality of life of patients entered into protocol GOG #122, Whole Abdomen Radiotherapy versus Combination Doxorubicin-Cisplatin Chemotherapy in advanced Endometrial Carcinoma.

Technical Approach: This is a quality of life protocol which evaluates patients already entered into protocol therapy on GOG protocol #122. Questionnaires will be administered pre treatment, post treatment, at 3, 6, and 12 month intervals and then yearly thereafter for three additional years. Data interpretation will be performed by the sponsor.

Progress: No patients have been entered at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/094 | **Status:** On-going |

**Title:** GOG 0148: The Clinical Utility of Soluable TNF/LT Membrane Receptors in the Serum of Patients With All Stages of Primary Epithelial Ovarian Cancer

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| **Start Date:** 04/01/94 | **Est. Completion Date:** May 95 |
| **Department:** GOG | **Facility:** MAMC |

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:ovarian, membrane receptors, tumor necrosis factor, lymphotoxin

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

Study Objective: To evaluate the clinical utility of TNF/LT membrance receptor levels in the serum of patients with epithelial ovarian cancers as both a screening test and marker of therapeutic effect.

Technical Approach: This investigaton will follow serum TNF/LT membrane receptors in the serum of patients who are undergoing treatment for primary epithelial ovarian cancer under other GOG protocols. Serum will be obtained prior to the first cycle of chemotherapy and then every other cycle thereafter. After the completion of chemotherapy, serum will be obtained every six months for two additional years. In the event that recurrent disease is suspected, serum will be obtained for investigation. The serum samples will be obtained at the time of routine laboratory studies utilized in the monitoring of ovarian cancer patients. No additional phlebotomy is therefore required.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/061 **Status:** On-going

**Title:** GOG 0150: A Phase III Randomized Study of Acclerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) vs Combination Ifosfamide-Mesna With Cisplatin ... Carcinosarcoma (CS) of the Uterus

**Start Date:** 02/04/94 **Est. Completion Date:** Feb 00

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:uterine, ifosfamide,mesna, cisplatin, abdominal radiotherapy

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: To compasre the use of combination Ifosfamide with Mesna and Cisplatin to hyperfractionated whole abdomen radiation therapy with regard to tolerance and efficacy in patients with carcinosarcomas of the uterus.

Technical Approach: Patients entering this study will have undergone surgical staging, TAH/BSO, and resection of gross intra-abdominal/pelvic disease. They will then be randomized to receive either radiation therapy (given as a hyperfractionated technique) or chemotherapy (utilizing ifosfamide with mesna and cisplatin). The chemotherapy will be administered over a four day period, at three week intervals. Ratients treated with radiation therapy will receive twice a day treatments of 3000 cGy to the whole abdomen with a boost to the pelvis to 5000 cGy. Subsequent to therapy, patients will be seen in the clinic at three month intervals for two years and then six month intervals for the remainder of their follow-up, until completion of their analysis. Routine blood work evaluating renal and hepatic status will be obtained throughout therapy and in post-treatment follow-up.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 94/134 | **Status:** On-going |

**Title:** GOG 0151: Phase II Trial of Intraperitoneal Paclitaxel (Taxol) as Salvage Therapy in Patients with Small Volume Residual Ovarian Cancer Following Initial Systemic Chemotherapy

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| **Start Date:** 08/05/94 | **Est. Completion Date:** Jul 96 |
| **Department:** GOG | **Facility:** MAMC |

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:ovarian, paclitaxel, salvage therapy

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

Study Objective: To evaluate the efficacy of Paclitaxel (Taxol) when administered intraperitoneally to patients with recurrent, small volume (< ml residual disease) ovarian disease.

Technical Approach: To be eligible for this study patients must have residual tumor nodules not in excess of 5 mm which were assessedd at surgery. They will also have have either had a peritoneal catheter placed prior to entry or agree to have a catheter placed prior to treatment. Therapy will then be delivered by giving Paclitaxel (Taxol) at 60 mg/m$^2$ dissolved in 2 liters of normal saline through the peritoneal catheter on a weekly basis. Patients will be assessed hematologically on a weekly basis and a history and physical, routine liver function test, renal function test and tumor measurements will be obtained every four weeks. If tumor progression is noted therapy will be discontinued. If, at the completion of chemotherapy, imaging studies or physical examination dones not demonstrate further evidence of disease the patient will undergo a reassessment operation to determine the response to therapy.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/150 **Status:** On-going

**Title:** GOG 0152: A Phase III Randomized Study of Cisplatin & Taxol (Paclitaxel) With Interval Secondary Cytoreduction vs Cisplatin and Paclitaxel in Patients with Suboptimal Stage III & V....ovarian carcinom

**Start Date:** 07/01/94 **Est. Completion Date:** Mar 96

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:ovarian, cisplatin paclitaxel, cytoreduction

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $23500.00 | **Periodic Review:** // |
|---|---|---|---|---|

Study Objective: To determine the impact of interval cytoreductive surgery on the progression free interval, survival and quality of life of patients with subnoptimal debulked Stage III & IV epithelial ovarian cancer.

Technical Approach: All patients will have undergone maximal cytoreductive surgery for their cancer prior to entrance into the study. Subsequently, all patients will receive three treatments at three week intervals of Paclitaxel and Cisplatin by intravenous infusion. After three treatment cycles, patients will be re-evaluated to determine tumor response. Patients with stable disease or tumor response will then be randomized to secondary cytoreductive surgery followed by or three more courses of chemotherapy. Those receiving secondary cytoreductive surgery will receive three more couses of chemotherapy after surgery. Quality of life questionnaire will be completed at intervals during and after therapy.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/149 **Status:** On-going

**Title:** GOG 0153: A Phase II Study of Recurrent and "Advanced Endometrial Adenocarcinoma Treated With Alternating Courses of Megestrol Acetate (Megace) and Tamoxifen Citrate (Nolvadex)

**Start Date:** 07/01/94 **Est. Completion Date:** Sep 95

**Department:** GOG **Facility:** MAMC

**Principal Investigator:** LTC Mark E. Potter, MC

**Associate Investigators:** None

**Key Words:** Cancer:endometrial, adenocarcinoma, megestrol acetate, tamoxifen

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

Study Objective: To evaluate the potential up-regulating of progesterone receptors by Tamoxifen to enhance progesterone induced cell kill initiated by Megace therapy for recurrent or advanced endometrial carcinoma.

Technical Approach: Patients eligible for this study will be given megestrol acetate 160 mg/day x 3 weeks followed by tamoxifen citrate 40 mg/day for the next three weeks. This alternate sequence will continue until there is evidence of disease progression or grade 3 or 4 toxicity occurs. Patients will have a physical examination tynir measurements, documentation of major symptoms at six week intervals and HGB, HCT, CBC, Diff, and platelets will be determined every 3 months.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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.

# DETAIL SHEETS FOR PROTOCOLS

# NATIONAL SURGICAL ADJUVANT BREAST & BOWEL PROJECT

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/171 **Status:** Completed

**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
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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: This study was closed to patient entry, Jan 94. No patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/012 **Status:** Completed

**Title:** NSABP B-25: A Clinical Trial to Evaluate the Effect of Dose Intensification and Increased Cumulative Dose of Postoperative Adriamycin-Cyclophosphamide (AC) Therapy With G-CSF on the Disease-Free Survival and Survival of Patients with Primary Breast Cancer and Positive Axillary Nodes

**Start Date:** 10/01/93 **Est. Completion Date:** Oct 98

**Department:** NSABP **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
MAJ Richard F. Williams, MC

**Key Words:** Cancer:breast, adriamycin, cyclophosphamide, G-CSF

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

Study Objective: 1) To determine whether giving larger but fewer doses of cyclophosphamide ((CY) dose intensification) in an AC combination with G-CSF will more effectively prolong disease-free survival than does the same cumulative dose of CY given over a more prolonged period of time. 2) To determine whether increasing the dose intensity as well as cumulative dose of CY (longer administration of a higher dose) will more effectively prolong disease-free survfival and survival than does the same dose intensity but for a shorter period of time longer cumulative dose).

Technical Approach: Patients who have histologically proven primary operable breast cancer with one or more positive axillary nodes and no evidence of metastatic disease will be randomly assigned to one of three treatment groups. Patients in all groups will receive irradiation after chemotherapy, or total mastectomy plus axillary dissection. Following operation, patients in Groups I will be treated with AC therapy, i.e. four cycles Adriamycin (60 mg/m$^2$) and cyclophosphamide (CY 1200 mg/m$^2$) with a 21 day interval between courses. G-CSF will be given in each of four cycles. As in Group I, patients in Group II will receive the same dose of adriamycin, at 21 day cycles X 4, but will receive CY 2400 mg/m$^2$ for two cycles, day 1 and 22. No CY will be given cycles 3 and 4. Patients in Group III will receive the same dose of adriamycin as Group I and II but CY will be given at 2400 mg/m$^2$ for a total of 4 cycles. In all three groups, patients who are >= 50 years of age will receive Tamoxifen 10 mg p.o. b.i.d. on day 1 of cycle 1 and will continue this treatment regimen for 5 years.

Progress: This study has been closed to patient entry. No patients were entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/036 **Status:** Completed

**Title:** NSABP BP-55: A Phase II Study in Patients With Metastatic or Locally Advanced Breast Cancer To Evaluate the Worth of High-Dose Taxol Administration As A 3-Hour Infusion With RHu G-CSF Support

**Start Date:** 10/01/93 **Est. Completion Date:** Oct 98

**Department:** NSABP **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
MAJ Richard F. Williams, MC

**Key Words:** Cancer:breast, taxol, RHu G-CSF

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: To determine the response rates of metastatic or locally advanced breast cancer with administration of four cycles of high dose Taxol as a three hour infusion with Rhu G-CSF support; and to evaluate the feasibility of administering this regimen for at least four cycles.

Technical Approach: Women with metastatic Stage IV or locally advanced Stage IIIb breast cancer, with measurable disease, will be eligible for this study. Although patients may have received adjuvant chemotherapy, they should not receive any chemotherapy for metastatic disease. All patients will receive a premedication regimen prior to Taxol administration. Taxol will be administered as a three hour continuous infusion at a dose of 250 mg/m$^2$; the infusion will be repeated every 3 weeks. Rhu-GCF will be given at 5 ug/kg subcutaneously from day 2 of every cycle. After completion of the four cycles, further treatment, including continuation of Taxol will be at the discretion of the investigator.

Progress: This study has been closed to patient entry. No patients were entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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

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| **Date:** 30 Sep 94 | **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' | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 12/17/93 |

Study Objective: To compare 1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D; (2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy; (3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy; and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

Technical Approach: All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

Progress: This protocol was closed to patient entry, 1 Sep 94. One patient enrolled at MAMC in FY93 is being followed.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **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 | | |

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| **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 94 **Protocol No.:** 94/033 **Status:** On-going

**Title:** POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study

**Start Date:** 11/05/93 **Est. Completion Date:** Jun 96

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** COL Stephen R. Stephenson, MC

**Key Words:** Cancer:non-Hodgkin's, cyclophosphamide, adriamycin, prednisone, methotrexate, 6-mercaptopurine, ARA-C, hydrocortisone

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** | // |
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Study Objective: 1. To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites. 2. To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

Technical Approach: After staging, subjects that qualify will receive Vincristine 1.5 $mg/m^2$ (max 2 mg) IV q wk x 6 weeks, prednisone 40 $mg/m^2$/day in 3 divided doses x 28 days, Adriamycin 40 $mg/m^2$/day IV days 1 & 22, and Cyclophosphamide 750 $mg/m^2$/day IV days 1 & 22. Fluid intake is to be > 3000 $ml/m^2$ on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries. On day 43, or when blood counts recover, the patient will receive Adriamycin 40 $mg/m^2$ IV, Cyclophosphamide 750 $mg/m^2$ IV, Vincristine 1.5 $mg/m^2$ (max 2 mg) IV, and Prednisone 50 $mg/m^2$ in 3 divided doses x 5 days. On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/147 **Status:** On-going

**Title:** POG 9220: Phase II 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:** 07/01/94 **Est. Completion Date:** Jul 96

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:leukemia, Cancer:children, all-trans retinoic acid, ARA-C, daunorubicin

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: 1) To compare the complete remission rate and disease-free survival of TRA to that achieved with conventional induction chemotherapy including Cytosine Arabinoside plus Naunorubicin in patients with previously untreated APL. 2) To compare the toxcities of TRA to those of Cytosine Arabinoside plus Naunorubicin as induction therapy in APL. 3) To determine the value of maintenance therapy with TRA.;

Technical Approach: This study inv olves two randomizations. Patients will be initially randomized to either TRA orDaunorubicin plus Cytosine Arabinoside as induction therapy. Consistent with other ECOG studies, 1 or 2 cycles of Daunorubicin plus Cytosine Arabinoside will be permitted to achieve CR since approsimately 20% of patients not achieving CR with 1 cycle do so with a second cycle. Following 2 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: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/135 **Status:** Completed

**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

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| **Date:** 30 Sep 94 | **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

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|---|---|
| **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 | |

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|---|---|---|---|---|
| **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: One patient was enrolled in July 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/146 **Status:** On-going

**Title:** POG 9239: Treatment of Children with Newly-Diagnosed Brain Stem Glioma (BSG) Using Cisplatin as a Radiosensitizer with Either Conventional or Hyperfractionated Radiotherapy. A Phase III Study.

**Start Date:** 07/01/94 **Est. Completion Date:**

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:glioma, cisplatin, radiotherapy

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

Study Objective: To compare the time to neurologic and/or radiographic progression and overall survival in children with newly-diagnosed brain stem glioma (BSG) who are treated with 100mg/$m^2$ of infusional cisplatin combined with conventional vs hyperfractionated radiotherapy; and to determine the toxicities of combining 100mg/$m^2$ of infusional cisplatin as a radiosensitizer with already-tested radiotherapy fractionation regimens.

Technical Approach: This study will evaluate the effectiveness of combining a drug called cisplatin, to be given continuously by vein (IV) over a period of 5 days in combination with either standard radiation treatments given once a day or hyperfractionated (twice daily) radiation treatments. In the first, third, and fifth weeks of radiation therapy, patients will be given a continuous infusion of cisplatin IV over 5 days. The cisplatin infusion will begin at the same time that the radiotherapy begins on that week.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/172 **Status:** On-going

**Title:** POG 9262: A Phase II Study of Taxol in Children with Recurrent/Refractory Soft-Tissue Sarcoma, Rhabdomyosarcoma, Osteosarcoma, Ewing's Sarcoma, Neuroblastoma, Germ Cell Tumors, Wilms' Tumor ...

**Start Date:** 09/02/94 **Est. Completion Date:** Jun 97

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:solid tumors, taxol

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

Study Objective: (1) To determine the response rate of recurrent bone and soft tissue sarcomas, neuroblastoma, germ cell tumors, hepatoblastoma, and hepatocellular carcinoma to taxol in a phase II trial. (2) To further define the spectrum of taxol's toxicity in children and adolescents.

Technical Approach: Patients will be premedicated with dexamethasone and diphenhydramine. Taxol will be given intravenously continuously over a 24 hour period. This course will be repeated every 21 days. This treatment may continue for one year, depending on the progression of the disease.

Progress: One patient has been enrolled at MAMC (FY94).

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/009 **Status:** Completed

**Title:** POG 9310: SIMAL #7: Escalating Rotational Drug Therapy After First Marrow Relapse of Non-T, Non-B ALL - A Pediataric Oncology Group Pilot Study

**Start Date:** 10/01/93 **Est. Completion Date:** Jun 96

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** COL Stephen R. Stephenson, MC

**Key Words:** Cancer:ALL, bone marrow, chemotherapy

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

Study Objective: The major objective of this study is to increase the event-free survival (EFS) of children with acute lymphoblasdtic leukemia following first marrow relapse or first relapse in an extra-medullary site other than CNS. A rotating, escalating, weekly parenteral drug regimen will be used fror continuation therapy. A single arm pilot study is planned.

Technical Approach: After remission induction, patients will receive itensive, weekly, therapy with rotating drug pairs. The drug combinations used are Week 1: vincristine, etoposide; Week 2: doxorubicin, cytarabine; Week 3: TIT, L-asparaginase; Week 4: Cytoxan, Prednisone; Week 5: Methotrexate, mercoptopurine, leucavorin. G-CSF will be given daily during continuation to treat each patient to his or her own maximally tolerated doses. The goal of this dose excalation is not to determine the MTD of the combination of agents, but to determine the impact of intensive, weekly therapy on relapse-free interval and event-free survival.

Progress: This study was closed to patient entry 1 Jul 94. One patient was entered and had transferred to another POG institution where he will be followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/072 **Status:** On-going

**Title:** POG 9317: Chemotherapy for Children with Advanced Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B Cell ALL

**Start Date:** 03/04/94 **Est. Completion Date:** May 99

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:Burkett's lymphoma, ARA-C, cytoxan, Vincristine, Adriamycin, Methotrexate, VP-16, Ifosfamide

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

Study Objective: 1) To evaluate the efficacy of adding VP-16/Ifosfamide intensification to the treatment of patients with advanced-stage B-cell malignancies: Stage III & IV DU NHL and B-cell acute lymphoblastic leukemia (B-ALL). 2) To compare the toxicity and efficacy of high-dose Ara-C given by intermittent bolus (q 12 hour x 4) vs bolus/continuous infusion over 48 hours.

Technical Approach: In this groupwide protocol, we propose to add, in a randomized study, two agents active in the treatment of aggressive NHL: Ifosfamide 2.8 $g/m^2$ with VP-16 100 $mg/m^2$ qd x 5. All patients in this study will be randomized at diagnosis to receive, throughout therapy, high-dose Ara-C by continuous infusion (CI) or by bolus (actually a 3 hour infusion). The CI Ara-C dose is base on the POG pilot study #9190 with a starting dose of 3.8 $g/m^2$/48 hours (80 $mg/m^2$/hr) following 9.5 $g/m^2$ bolus. The bolus Ara-C dose is taken from POG #8617: 3 $g/m^2$ q 12 hr X 4 doses. All patients will receive therapy based on POG #8617/8616, with a reduction in duration. After a common induction with fractionated cyclophosphamide, vincristine, Adriamycin, methotrexate by 24-hour infusion, and Ara-C, patients with Stage III disease will receive these drugs without Adriamycin and patients with Stage IV/B-ALLL will receive these 5 drugs including Adriamycin during consolidation. Patients will also be randomized to receive or not to receive VP-16/ifosfamide intensification, except for patients with CNS involvement who will be assigned to receive VP/16 ifosfamide. The study question is being posed in a randomized 2 X 2 factorial design.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/092 **Status:** On-going

**Title:** POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for .....Osteogenic Sarcoma

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

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:pediatric, cancer:sarcoma, doxorubicin, cisplatin, methotrexate, Ifosfamide, MTP-PE

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: 1) To improve the survival of patients with osteogenic sarcoma.;2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma.;3) To compare the results of a combined chemotherapeutic regimen (high-dost methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide.;4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery.;5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs.;6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma.;7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

Technical Approach: This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherpay alone.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

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|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/047 | **Status:** Completed |
| **Title:** POG 9395: A Pilot Study of Large Cell Lymphomas In Children and Adolescents Evaluating APO + IDMTX/HD ARA-C | | |
| **Start Date:** 12/17/93 | **Est. Completion Date:** Jun 96 | |
| **Department:** POG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Bruce A. Cook, MC | | |
| **Associate Investigators:** | COL Stephen R. Stephenson, MC | |
| **Key Words:** Cancer:lymphoma, chemotherapy, high-dose | | |

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

Study Objective: To accumulate experience with Intermediate Dose MTX/High Dose ARA-C given in addition to APO in the maintenance phase of large cell NHL. Also, to further characterize the immunophenotypic and morphologic correlates of pediatric LCL.

Technical Approach: This is a two phase study, Induction and Maintenance, for children with large call lymphoma. After staging and during the initial phase of treatment (induction), the child will receive vincristine 1.5 mg/m$^2$ (max 2.0 mg) IV on days 1, 8, 15, 22, and 29; Adriamycin 30 mg/m$^2$ IV over 15 minutes on days 1 and 22; Prednisone 120 mg/m$^2$ PO for 5 days in 3 divided doses day 1 - 5; and intrathecal doses of methotrexate 60 mg/m$^2$ on days 1, 8, and 22. Blood chemistry and hematology will be monitored before each treatment. The child will be reevaluated with a repeat of all imaging studies that was positive at diagnosis. Maintenance will be started on day 43 after clinical restaging. All patients who are in complete remission (CR) will proceed to maintenance therapy when ANC >= 500 and platelets >= 75,000. Patients with partial response will be rebiopsied to evaluate residual disease. Those patients with negative biopsies will proceed to maintenance therapy. Patients with less than a CR will start radiation therapy to residual disease sites; if a CR is not achieved 6 weeks after radiation, the patient is off study. Maintenance consist of eight cycles of Intermediate-Dose Methotrexate (MTX) 200 mg/m$^2$ IV push, then 800 mg/m$^2$ over 24 hrs. with Leucovorin rescue for a total of 8 cycles. Upon completion of the 24 hour MTX infusion, ARA-C 500 mg/m$^2$ zib push over 25 minutes followed by Afa-C 60 mg/m$^2$/hr as a continous infusion over 48 hrs. for a total of 8 cycles. Intrathecal doses of MTX will be given on day 1 of maintenance cycles 1, 3, and 5 up to a total of 3 doses. G-CSF 5 mcg/kg SQ daily 24 hours after chemotherapy until ANC >= 10,000.

Progress: Study was closed to patient entry, 30 Sep 94. No patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/148 **Status:** On-going

**Title:** POG 9398: T-4 "D": Efficacy of rhG-CSF in an Intensive Treatment for T-Cell Leukemia and Advanced-Stage Lymphoblastic Lymphoma of Childhood

**Start Date:** 07/01/94 **Est. Completion Date:** May 99

**Department:** POG **Facility:** MAMC

**Principal Investigator:** LTC Bruce A. Cook, MC

**Associate Investigators:** None

**Key Words:** Cancer:lymphoma, Cancer:childhood, rhG-CSF, Cancer:leukemia

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** // |
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Study Objective: (1) To determine if the addition of high-dose Ara-C and IV methotrexate and 6-mercaptopurine will improve the effectiveness of this combination of anticancer medicine against T-cell acute lymphoblastic leukemia and advanced-stage lymphoblastic lymphoma without being too toxic; (2) whether rhG-CSF can reduce the period of neutropenia, and infectious episodes in a cohort of patients receiving multiagent chemotherapy for T-cell leukemia or lymphoblastic lymphoma; (3) whether after different drug combinations, G-CSF reduces delays in chemotherapy.

Technical Approach: Patients will receive vincristine, prednisone, cyclophosphamide and Adriamycin; then cytosine arabinoside with or without cyclophosphamide. All patients will receive a three-drug combination of methotrexate, hydrocortisone, and Ara-C intrathecally to prevent central nervous system disease.

After a disease-free state has been attained, patients will receive a more intense 9-week sequence of drug combinations. This 9-week sequence will be repeated 10 times to complete a total of approximately two years of therapy. Additionally, patients will receive L-asparaginase every week for 20 doses during the 9 week repetitive therapy. Patients will be randomized to receive or not to receive the growth factor G-CSF.

Progress: No patients have been enrolled at MAMC.

# DETAIL SHEETS FOR PROTOCOLS

# PUGET SOUND ONCOLOGY CONSORTIUM

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** // |
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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 94 **Protocol No.:** 77/054 **Status:** On-going

**Title:** SWOG 7406: Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III

**Start Date:** 02/18/77 **Est. Completion Date:** Feb 82

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:** LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC

**Key Words:** Cancer: Hodgkin's, MOPP

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 12/17/93 |
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Study Objective: (1) To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy; (2) To evaluate systematic restaging of patients in apparent complete remission; (3) To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging; (4) To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

Technical Approach: All previously untreated patients with Ann Arbor Stages IIIB or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission (PR) is indicated another 4 courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

Progress: Closed to patient entry, Aug 78, and previously reported as closed. In fact, patients were still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 77/053 | **Status:** On-going |
| **Title:** SWOG 7433: Non-Hodgkin's Lymphomas (Stages I, IE, II, and IIE). A Phase III Study. | | |
| **Start Date:** 02/18/77 | **Est. Completion Date:** Feb 82 | |
| **Department:** SWOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Howard Davidson, MC | | |
| **Associate Investigators:** COL Friedrich H. Stutz, MC | LTC H. Irving Pierce, MC | |
| **Key Words:** Cancer:Non-Hodgkin's lymphoma, radiotherapy, CHOP | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 11/18/94 |

Study Objective: To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, $I_E$, II and $II_E$ treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone or with extended Hydroxyl-daunorubicin (adriamycin), Oncovin (vincristine), and Prednisone.

Technical Approach: Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

Progress: This protocol was closed to patient entry in October 1982 and was previously reported as closed. In fact, patients are still being followed. The protocol was reactivated in December 1993 in order to allow SWOG to continue to collect data on these patients.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 77/024 | **Status:** On-going |
| **Title:** SWOG 7436: Combined Modality Therapy of Breast Cancer | | |
| **Start Date:** 01/21/77 | **Est. Completion Date:** Jan 82 | |
| **Department:** SWOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Howard Davidson, MC | | |
| **Associate Investigators:** LTC H. Irving Pierce, MC | COL Friedrich H. Stutz, MC | |
| **Key Words:** Cancer:breast, 5-FU, vincristine, methotrexate, cyclophosphamide, prednisone | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 11/18/94 |

Study Objective: To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

Technical Approach: Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater that six weeks for entry into the study. All therapy will be discontinued after one year.

Progress: This protocol was closed to patient entry in November 1979 and was previously reported as closed. In fact, patients are still being followed. The protocol was reactivaated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 77/018 **Status:** On-going

**Title:** SWOG 7510: Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel

**Start Date:** 10/15/76 **Est. Completion Date:** Oct 81

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:** LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC

**Key Words:** Cancer:bowel, chemotherapy, BCG immunotherapy

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 11/18/94 |
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Study Objective: To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Suerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

Technical Approach: Patients will be randomly assigned to either of the two following regimens; (1) chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would being every eight weeks; (2) chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

Progress: This protocol was closed to patient entry August 1980 and was previously reported as closed. Pateints were, in fact, still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 78/002 **Status:** On-going

**Title:** SWOG 7713/14: Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance After Remission Induction

**Start Date:** 10/21/77 **Est. Completion Date:** Jun 79

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:** LTC H. Irving Pierce, MC
COL Friedrich H. Stutz, MC

**Key Words:** Cancer:Non-Hodgkin's lymphoma, CHOP, Levamisole, BCG

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 11/18/94 |
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Study Objective: (1) To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma; (2) For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy; (3) For patients with impaired cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole; (4) To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used; (5) To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases; (6) To establish baseline and serial data on immunologic status in bother chemoimmunotherapy groups.

Technical Approach: Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac disease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or impaired bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

Progress: This protocol was closed to patient entry October 1982 and was previously reported as completed. In fact, patients are still being followed. The protocol was reactivated in December 1993 do that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 78/047 | **Status:** On-going |

**Title:** SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6

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| **Start Date:** 07/31/78 | **Est. Completion Date:** Jan 88 |
| **Department:** SWOG | **Facility:** MAMC |

**Principal Investigator:** LTC Howard Davidson, MC

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| **Associate Investigators:** | COL Friedrich H. Stutz, MC |
| LTC H. Irving Pierce, MC | Suresh B. Katakkar, M.D., DAC |

**Key Words:** Hodgkin's disease:Stages III & IV,chemotherapy,modality RX

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| **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. Thirteen patients were enrolled in previous years and 5 are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 |
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Study Objective: To compare the disease-free interval and recurrence rates in: (1) estrogen receptor positive (ER+) premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) ER+ postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative (ER-) patients with Stage II disease using one vs two years of combination chemotherapy; to compare the effect of adjuvant therapy in Stage II breast cancer using partial mastectomy and radiation vs modified radical or radical mastectomy; to compare the effect of the various adjunctive therapy programs upon survival patterns; and to correlate the estrogen receptor status with disease-free interval and survival.

Technical Approach: Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-FU, vincristine, and prednisone): (1) CMFVP for 1yr pre- or postmenopausal ER patients. (2) CMFVP for 2 yr pre- or postmenopausal ER patients. (3) CMFVP for 1 yr premenopausal ER+ patients. (4) Oophorectomy + CMFVP premenopausal ER+ patients. (5) Tamoxifen alone for 1 yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for 1 yr postmenopausal ER+ patients. Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

Progress: Thirty-five patients were enrolled prior to closure of patient enrollment 15 Aug 89. Twenty-two patients are still being followed.

# Detail Summary Sheet

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| **Date:** 30 Sep 94 | **Protocol No.:** 81/064 | **Status:** On-going |
| **Title:** SWOG 8027: The Natural History of Pathological Stage T(1-2) N(O), M(O) ER+ Breast Cancer | | |
| **Start Date:** 03/20/81 | **Est. Completion Date:** Jan 83 | |
| **Department:** SWOG | **Facility:** MAMC | |
| **Principal Investigator:** LTC Howard Davidson, MC | | |
| **Associate Investigators:** A.W. Brown | COL Irwin B. Dabe, MC | |
| **Key Words:** Cancer:breast, natural history | | |

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| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 11/18/94 |

Study Objective: To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative ($T_{1-2}$ $N_0$ $M_0$) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

Technical Approach: Patients having undergone radical, modified radical, or adequate local excision with node dissection for histologically proven breast carcinoma whose axillary nodes are negative for tumor and whose estrogen receptor status is positive are eligible. Patients undergoing local adequate excision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days post-operatively as outlined in the protocol. Only patients with pathologic Stage $T_{1-2}$ $N_0$ $M_0$ with a primary tumor of $\leq$5 cm are eligible. The primary tumor must be movable in relationship to the anterior chest wall and may not be involved with extensive skin ulcerations. This protocol involves no randomization or treatment. It consists only of follow-up and documentation of natural history. Patients will be stratified by primary tumor size, <2 cm bs 2 to 5 cm, and by menopausal status. Patients will be followed until relapse or for 10 years, whichever comes sooner.

Progress: Closed to patient entry Oct 82. Five patients were entered; three are still being followed. This protocol was previously reported as completed. In fact, patients are still being followed and the protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 and are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 85/076 **Status:** On-going

**Title:** SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II

**Start Date:** 08/23/85 **Est. Completion Date:** Jun 87

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**
MAJ Michael D. Stone, MC
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
CPT David R. Bryson, MC

**Key Words:** Cancer:lung, small cell, radiation therapy, adriamycin, cis-platinum, cyclophosphamide, methotrexate, vincristine, VP-16

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

Study Objective: To explore the response rate with the concurrent use of radiation therapy plus chemotherapy utilizing cis-platinum, VP-16, and vincristine in limited small cell carcinoma of the lung and to observe the toxicities of this combined modality program.

Technical Approach: Patients will be started on chemotherapy consisting of cis-platinum, VP-16, and vincristine and concurrent radiation therapy to the primary site. After completion of radiation therapy to the chest, prophylactic cranial radiation therapy will be given. After a brief rest period, the patients will be treated with 12 more weeks of conventional chemotherapy consisting of adriamycin, cytoxan, VP-16, vincristine, and methotrexate. Patients who show a complete response will be followed. Patients with less than a complete response will be taken off study and offered alternative therapy.

Progress: This study was closed to patient entry March 86. It was previously reported as completed. In fact, two patients were entered and one is still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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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 nine continue to be followed. Two have expired.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 84/072 **Status:** On-going

**Title:** SWOG 8312: Megestrol Acetate and Aminoglutethimide/Hydrocortisone in Sequence or in Combination as Second-Line Endocrine Therapy of Estrogen Receptor Positive Metastatic Breast Cancer, Phase III

**Start Date:** 08/17/84 **Est. Completion Date:** Jun 86

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**
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MAJ Timothy J. O'Rourke, MC
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
MAJ Michael D. Stone, MC

**Key Words:** cancer:breast,endocrine therapy,megestrol acetate

| Accumulative MEDCASE Cost: | $0.00 | Est. Accumulative OMA Cost: | $0.00 | Periodic Review: 10/19/90 |
|---|---|---|---|---|

Study Objective: To determine whether combination hormonal therapy with aminoglutethimide and hydrocortisone plus megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased patient survival over the sequential use of each agent in ER+ patients who have progressed after responding to primary hormonal treatment with tamoxifen; to assess the relative toxicities of megestrol acetate and medical adrenalectomy; and to assess the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

Technical Approach: Patients show have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for a minimum of six months with documented disease progression and clear-cut bone scan evidence of cortical bone metastases will be randomized to: Arm I - megestrol acetate, 40 mg PO, 4 times daily given alone until there is documented evidence of disease progression; Arm II -aminoglutethimide, 250 mg PO, twice daily for two weeks, then 250 mg PO, four times daily plus hydrocortisone, 20 mg PO upon rising, 20 mg PO at 1700 hrs, and 60 mg PO at bedtime, daily for two weeks, then 10 mg PO upon rising, 10 mg PO at 1700 hrs, and 20 mg PO at bedtime; or Arm III - megestrol acetate as in Arm I plus aminoglutethimide as in Arm II plus hydrocortisone as in Arm II. An adequate trial of each arm will consist of at least eight weeks of daily therapy in the absence of documented evidence of disease progression. Patients in Arms I and II with documented progressive disease after an adequate trial will be crossed over to the other treatment arm. The only exception to crossover will be patients who develop life threatening brain, liver, or pulmonary metastases who require systemic chemotherapy. Patients randomized to Arm III will go off study at the time of disease progression.

Progress: This protocol was closed to patient entry Nov 90. It was previously reported as closed. However, one patient had been entered and is still in follow-up. The protocol was reactivated in December 1993 so that SWOG could continue to collect data.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **Protocol No.:** 85/009 **Status:** On-going

**Title:** SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II

**Start Date:** 11/16/84 **Est. Completion Date:** Oct 86

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**
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MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC
MAJ Timothy J. O'Rourke, MC
CPT David R. Bryson, MC

**Key Words:** Cancer: Non-Hodgkin's lymphoma, m-BACOD

| Accumulative MEDCASE Cost: | $0.00 | Est. Accumulative OMA Cost: | $0.00 | Periodic Review: 11/18/94 |
|---|---|---|---|---|

Study Objective: To determine an approximate complete remission rate and remission duration for the treatment program of cyclophosphamide, doxorubicin, vincristine, dexamethasone, and bleomycin with intervening moderate dose of methotrexate and leucovorin rescue (m-BACOD) in patients with intermediate and high grade non-Hodgkin's lymphoma and to assess the feasibility of using this regimen in the SWOG with the intent of using m-BACOD in a future Phase III trial.

Technical Approach: Patients will be stratified according to marrow reserve status and creatinine clearance. Treatment will consist of ten 3-week courses. Cytoxan, adriamycin, vincristine, and bleomycin will be given IV on day 1. Dexamethasone will be given by mouth daily for 5 days, and methotrexate will be given on days 8 and 15 at 200 mg/m$^2$. Leucovorin will be given 10 mg/m$^2$ by mouth after each methotrexate injection every 6 hours for eight doses. An adequate trial will be defined as the completion of two complete cycles of m-BACOD. Patients with documented progressive disease or less than complete response after an adequate trial will be taken off study. Those with complete response will continue on study with no further chemotherapy.

Progress: This study was closed to patient entry April 1985 and reported as completed. However, two patients had been enrolled in the study and are still being followed. The study was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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MAJ Thomas M. Baker, MC
CPT David R. Bryson, MC
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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. Seven patinets were enrolled MAMC. All original patients enrolled at MAMC have died but 1 patient has transferred in and is being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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MAJ David M. Dunning, MC
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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 94 **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:**
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LTC Lauren K. Colman, MC
MAJ David M. Dunning, MC
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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 94 **Protocol No.:** 86/080 **Status:** On-going

**Title:** SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma

**Start Date:** 08/15/86 **Est. Completion Date:** Jul 89

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**
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MAJ David M. Dunning, MC
MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC
CPT David R. Bryson, MC

**Key Words:** lymphoma:non-Hodgkin's,chemotherapy,CHOP,m-BACOD,M

| Accumulative MEDCASE Cost: | $0.00 | Est. Accumulative OMA Cost: | $0.00 | Periodic Review: 11/18/94 |
|---|---|---|---|---|

Study Objective: To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

Technical Approach: Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycles): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV) and prednisone (PO). Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV), bleomycin (IV), dexamethasone (PO), methotrexate (IV), and calcium Leucovorin rescue after each MTX dose. Arm III (Pro-MACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide (IV), doxorubicin (IV), VP-16 (IV), Prednisone(PO), Ara-C (IV), bleomycin (IV), vincristine (IV), methotrexate (IV), calcium leucovorin rescue after each MTX dose, and trimetheprim-sulfamethoxazole (PO). Arm IV (MACOP-B will be given over 12 weeks): methotrexate (IV), calcium leucovorin rescue after each MTX bolus, doxorubicin (IV), cyclophosphamide (IV), vincristine (IV), bleomycin (IV), prednisone (PO), and trimethoprimsulfa (PO). Patients with documented progressive disease may be taken off study at any time; however patients will preferably be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

Progress: This study was closed to patient entry, June 1991, and was previously reported as completed. However, two patients were transferred in from another Army medical center and MAMC now follows these patients. It was reactived in December 1993.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 88/003 **Status:** Completed

**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:**
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MAJ David M. Dunning, MC
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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: This study was closed to patient entry, 15 Aug 94. No patients have been entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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
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MAJ Michael D. Stone, MC
LTC Donald B. Blakeslee, MC
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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 and are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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MAJ Jens A. Strand, MC
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MAJ Thomas M. Baker, MC
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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 94 **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:**
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MAJ Ruben D. Sierra, MC
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**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 94 **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:**
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MAJ Everardo E. Cobos Jr., 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 patient 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 94 **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 94 **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:**
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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 94 **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:**
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MAJ Rahul N. Dewan, MC
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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 (1 in FY94) and all continue to be followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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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. Six patients were enrolled at MAMC in previous years and 2 continue to be followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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**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 94 **Protocol No.:** 94/119 **Status:** On-going

**Title:** SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy

**Start Date:** 06/03/94 **Est. Completion Date:** Jun 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:**
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T.O. Taylor
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COL J. N. Wettlaufer, MC
MAJ Kurt L. Hansberry, MC
CPT Michael D. Bagg, MC
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MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC

**Key Words:** Cancer:prostate, radiotherapy

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

Study Objective: 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

Technical Approach: Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

Progress: No patients have been entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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. One patient was enrolled at MAMC (FY88) and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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
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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: This study was closed to patient entry, 15 Nov 93. Approximately 25 patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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MAJ Patrick L. Gomez, MC
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MAJ Robert L. Sheffler, MC

**Key Words:** lymphoma,alpha-interferon,ProMACE-Mopp,chemo

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $0.00 | **Periodic Review:** 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: Four patients have been entered at MAMC (1 in FY94). All patients are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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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 94 **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
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**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: Seven patients have been entered in this study at MAMC (1 in FY94). All are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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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 94 **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:** Aug 95

**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 3 samples have been collected (1 in FY94).

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 in previous years. These patients are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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. Six samples have been studied (1 in FY 94).

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **Protocol No.:** 90/055 **Status:** On-going

**Title:** SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III

**Start Date:** 03/16/90 **Est. Completion Date:** 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 94 **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: This study was closed to patient entry, 15 Sep 94. Three patients were entered in previous years and two are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 and are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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. Five patients have died from their disease and 12 continue to be followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 90/030 **Status:** Completed

**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 FY94. Both are deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **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 in previous years.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **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 94 **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 94 | **Protocol No.:** 94/131 | **Status:** On-going |
| **Title:** SWOG 8994: Evaluation of Quality of Life in Patients with Stage C Adenocarcinoma of the Prostate Enrolled on SWOG 8794 | | |
| **Start Date:** 08/05/94 | **Est. Completion Date:** Jun 01 | |
| **Department:** SWOG | **Facility:** MAMC | |
| **Principal Investigator:** MAJ James B. Thrasher, MC | | |
| **Associate Investigators:** None | | |
| **Key Words:** Cancer:prostate, surgery, radiation therapy | | |

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

Study Objective: To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning

Technical Approach: This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles willb e compared for the two treatment groups at different points in time: baseline, where no differenced are expected six weeks, where the two treatment groups are expected to show maxiumum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key congtinuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurence of specified complications, standard methods of categorical data analysis will be employed.

Progress: New study has not been started.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 94 **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 in FY 93 and are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 were enteredd in this study at MAMC in previous years. Three are deceased and two are being followed.and are being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** | $0.00 | **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: One patient has been enrolled (FY 94) at MAMC .

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 in previous years. One is being followed and the other died of the disease.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/142 **Status:** Completed

**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: This study was closed to patient entry, 15 March 1994. No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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: Two patients have been enrolled in this study in previous years and both are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/040 **Status:** Completed

**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:** Dec 94

**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
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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: This study was closed to patient entry, 15 May 94. No patients have been enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 in previous years. One is deceased and one is being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** Sep 94

**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 94 **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-Cyclophospha-mide 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 was enrolled in this study in FY93 and is now deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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 and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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**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 94 **Protocol No.:** 94/104 **Status:** On-going

**Title:** SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.

**Start Date:** 05/06/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**
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MAJ Kenneth A. Bertram, MC
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LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

**Key Words:** Cancer: colorectal, chemoprevention, calcium carbonate

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

Study Objective: This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.

Technical Approach: Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of ademonas or second primary carcinomas.

Progress: One patient was entered in FY94 and is in the follow-up phase.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/002 **Status:** Completed

**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 both are now deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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CPT Jennifer L. Cadiz, MC
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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 94 **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:**
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**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 and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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**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 t and is still being followed

Progress: One patient was entered in this study in FY94 and is in the follow-up stage.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/095 **Status:** On-going

**Title:** SWOG 9109: Neoadjuvant Zoladex and Flutamide in Bulky and Non-Bulky Clinical Stage C Carcinoma of the Prostate, Phase II

**Start Date:** 04/01/94 **Est. Completion Date:** Apr 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:**
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**Key Words:** Cancer:prostate, Zoladex, Flutamide

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

Study Objective: 1) To evaluate the resectability rate following 16 weks of total androgen blockade therapy. 2) To evaluate the likelihood of clinical response to 16 weeks of total androgen blockade therapy. 3) To assess the feasibility of obtaining flow cytometry specimens for the purpose of evaluating the likelihood of an association between ploidy and clinical response or resectability. 4) To evaluate the qualitative and quantitative toxicities from total androgen blockade therapy and the immediate and long-term morbidity associated with radical prostatectomy and pelvic lymph node dissection following neoadjuvant total androgen blockade therapy. 5) To evaluate time to progression.

Technical Approach: Patients with Stage C, D0, and D1 prostate cancer will begin neoadjuvant total androgen blockade within 24 hours of registration. This treatment will consist of Zoladex 3.6 mg S.Q. every 4 weeks X 16 weeks and Flutamide 250 mg P.O. daily X 16 weeks. Patients will be evaluated by digital rectal exam at weeks 5, 9, 13 and 17, and trans-rectal ultrasound at weeks 9 and 17. After 16 weeks of androgen blockade, patients will be re-evaluated to undergo radical prostatectomy with pelvic lymph node dissection. Patients deemed operable will have surgery performed by week 17 or, if the treatment was interrupted, within one week of completing total androgen blockade. Following surgery, all patients, including those that were unresectable or partially resectable, will be followed for subjective/objective evidence of developing toxicities and progression of disease. Following surgery or attempted surgery, no additional therapy is to be given in the absence of progression, at which time patients will go off protocol treatment. Subsequent therapy off protocol treatment is at the discretion of the investigator.

Progress: No patients entered in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 92/104 **Status:** Completed

**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:**
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**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: The study was closed to patient entry 15 Nov. 93. Two patients were enrolled in previous years and both are now decesed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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**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 94 **Protocol No.:** 94/028 **Status:** Completed

**Title:** SWOG 9115: Randomized Study of Standard Chemotherapy versus STAMP V With Autologous Stem Cell Infusion in Stage IV Poor Prognosis Breast Carcinoma

**Start Date:** 11/05/93 **Est. Completion Date:** Nov 96

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

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MAJ Richard C. Tenglin, MC
LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

**Key Words:** Cancer:breast, stem cell infusion, STAMP V

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

Study Objective: To compare the overall survival as well as the time to treatment failure of a high dose program with autologous stem cell infusion as consolidation treatment for patients with poor prognosis, Stage IV breast cancer at the completion of induction chemotherapy to further standard treatment (continuation of outpatient chemotherapy).

Technical Approach: Paients who agree to participate will receive 2-6 cycles of standard chemotherapy (cytoxan, adriamycin, and 5-FU. Those patients achieving a complete response or a partial response to induction chemotherapy will be eligible for randomization to either continuation of induction chemotherapy (CAF) or on. Patients randomized to CAF will continue chemotherapy at MAMC. However, patients randomized to STAMP V with autologous stem cell infusions will be referred to either Wilford Hall Medical center or Brook Army Medical Center for treatment.

Progress: No patients have been enrolled at MAMC.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **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:** Mar 95 |
| **Department:** SWOG | **Facility:** MAMC |

**Principal Investigator:** MAJ Paul C. Sowray, MC

**Associate Investigators:**

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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 94 **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:**
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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 and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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MAJ Kenneth A. Bertram, MC
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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 94 **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:**
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**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 94 **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

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**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 and one patient in FY 94. Both are now deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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**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 and is now deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/097 **Status:** On-going

**Title:** SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III

**Start Date:** 05/06/94 **Est. Completion Date:** Sep 01

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Mark E. Robson, MC

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**Key Words:** Cancer:Hodgkin's, irradiation, vinblastine, doxorubicin

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

Study Objective: The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA,IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

Technical Approach: Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

Progress: Two patients were enrolled in this study, both in FY 94.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:** Mar 95

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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**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 94 **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:** Apr 95

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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**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 94 **Protocol No.:** 94/065 **Status:** Completed

**Title:** SWOG 9143: A Phase II Study of Cisplatin Preceded by a 12-Hour Continuous Infusion of Concurrent Hydroxyurea and Cytosine Arabinoside (ARA-C) for Patients With Untreated Malignant Mesothelioma

**Start Date:** 02/04/94 **Est. Completion Date:** Feb 97

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** CPT Diana S. Willadsen, MC

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**Key Words:** Cancer:mesothelioma, cisplatin, hydroxyurea, ARA-C

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

Study Objective: The objectives of this Phase II study of cisplatin, hydroxyurea and cytosine arabinoside (Ara-C) for patients with advanced unresectable methothelioma involving the pleura, pericardium, peritoneum and/or paratesticular area, and/or metastatic mesothelioma are: 1) To evaluate the response rate of patients with mesothelioma following treatment with this three-drug program. 2) To evaluate the qualitative and quantitative toxicity spectrum of this regimen.

Technical Approach: This study will involve patients with measureable or evaluable disease by CT or MRI. The mesothelioma must be advanced and unresectable and involve the pleura, pericardium, peritoneum, and/or paratesticular area, and/or metastatic mesothelioma. They must also have an adequate marrow reserve. Patients will recieve allopurinol, 600 mg po at least 12 hours before the start of therapy and then 300 mg po qd continuously until off study. Patients will be hydrated with normal saline, to maintain a urine output of at least 100 cc/hr, with intake and output measured every 4 hours. The IV rate should be adjusted every 4 hours to maintain the minimum required output and to match the output if it is greater than the input. Polyantiemetic therapy on a scheduled basis is required. Patients wil receive hydroxyurea, 1260 mg/m$^2$ over 1 hour followed immediately by: Ara-C, 1200 mg/m$^2$ plus Hu 5040 mg/m$^2$ mised in the same bag of 1 liter of normal saline over exactly 12 hours using an infusion pump. At the start of the last hour of Ara-C plus HU, piggy back Mannitol, 25 g in 100 ml D5W, into chermotherapy line over 1 hour. Cisplatin 100 mg/m$^2$ in 250 ml NS will be given upon completion of Mannitol, Ara-C, and HU via infusion pump. Treatment will be given every 28 days until progression of disease or unacceptable toxicity. All patients will be followed until death.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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

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**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 94 **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:**
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**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 94 **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

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**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 patient is still be followed and the other died of the disease.

# Detail Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/167 **Status:** Completed

**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:**
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**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 94 **Protocol No.:** 94/063 **Status:** On-going

**Title:** SWOG 9158: A Phase II Evaluation of Trans-Retinoic Acid and Alpha Interferon in Patients with Squamous Cell Carcinoma of the Lung (Stage (IV)

**Start Date:** 02/04/94 **Est. Completion Date:** Feb 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

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**Key Words:** Cancer:lung, trans-retinoic acid, alpha interferon

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

Study Objective: 1) To assess the response rate to trans-Retinoic Acid and Alpha Interferon used in a daily schedule for patients with advanced (TNM Stage IV), well differentiated squamous cell carcinoma of the lung. 2) To further define the qualitative and quantitative toxicities of this regiment administered to this patient population in a Phase II study.

Technical Approach: Patients with a histologically confirmed diagnosis of advanced, well differentiated squamous cell carcinoma of the lung will be invited to participate in this evaluation of trans-Retinoic Acid and Alpha Interferon for the treatment of Stage IV Squamous Cell Carcinoma of the lung. After baseline evaluation, patients will be started on a fixed dose of trans-Retinoic Acid, 150 mg/m$^2$/d P.O. in divided doses (b.i.d.) with meals and 3 X 10(6) I.U./m$^2$ of Roferon-A subcutaneously once daily for 5 day/week. Measurable disease will be assessed for response or progression by chest x-ray at least every four weeks and CT scan (if needed) every 8 weeks. Patients will continue to receive therapy until they have stable disease after 16 weeks of therapy, one year after documentation of complete response, two years after documentation of a partial response, disease progression, relapse, or toxicity. All patients will be followed until death. Data will be interpreted by sponsors.

Progress: No patients have been enrolled in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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

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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 serum repository study in FY93.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/115 **Status:** On-going

**Title:** SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133

**Start Date:** 06/03/94 **Est. Completion Date:** Jun 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** Undefined investigator

**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:Hodgkin's, quality of life

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

Study Objective: 1) To evaluate prospectively the health status and quality of life (QOL) of early stage Hodgkin's Disease patients receiving either subtotal nodal irradiation or short course chemotherapy plus subtotal nodal irradiation. 2) To describe the short-term, acute effects of two treatments for early stage Hodgkin's Disease patients on patient report of symptoms and on patient QOL. 3) To evaluate the intermediate and long-term effects of two treatments for early stage Hodgkin's Disease patients on patient QOL over five years.

Technical Approach: Patients enrolled in the companion protocol, SWOG-9133, will be asked to complete questionnaires before registration into this study, at 6 months; and annually for seven years. These questionnaires seek to identify and quantitate those differences pertaining to quality of life issues that the added chemotherapy may have in early stage Hodgkin's disease patients.

Progress: No patients have been enrolled in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/107 **Status:** On-going

**Title:** SWOG 9210: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD-P to VAD-P/Quinine for Induction; (2) Randomization of Prednisone Dose Intensity for ....

**Start Date:** 05/07/93 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

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

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

**Key Words:** Cancer:myeloma, VAD-P, VAD-P,Quinine

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

Study Objective: (1) To compare the effectiveness of the VAD-P chemotherapy regimen when administered alone or in combination with the chemosensitizer quinine intended to block the emergence of multidrug resistance during remission induction in previously untreated patients with multiple myeloma; (2) To evaluate the chemosensitizing potential of quinine to reverse drug resistance in myeloma patients randomized to VAD-P induction who fail to achieve at least 25% regression with chemotherapy alone. 3. To compare the value of alternate day prednisone 10 mg versus 50 mg for remission maintenance for patients proven to achieve at least 25% regression.

Technical Approach: Patients with proven multiple myeloma (all stages) who have not received prior chemotherapy are eligible for participation in this trial. A dynamic allocation scheme will be used to randomize patients to one of the two induction treatment arms.

INDUCTION: ARM I patients will receive Vincristine 0.4 mg IV q.d. on days 1-4, Doxorubicin 9 mg/m$^2$ q.d. IV on days 1-4, Dexamethasone 40 mg q.d. PO on days 1-4, and Prednisone 50 mg Q.O.D. on days 9, 11, 13, 15, 17, and 19. This cycle will be repeated Q 21 days for a minimum of 6 to 8 cycles (6 months) or a maximum of 17 cycles (12 months). Patients who fail to achieve ≥ 25% tumor regression after 12 months of treatment on Arm I (VAD-P) or relapse or progress on Arm I, will be eligible for crossover to VAD-P/Q.

ARM II and Crossover schedule patients will receive VAD-P as outlined above on days 2-5 and will also receive Quinine 400 mg t.i.d. on days 1-6 (VAD-P/Q).

Patients with ≥ 25% tumor regression after 9 to 12 months of induction therapy or patients who achieve ≥ 50% tumor regression after 6 months of induction therapy will be randomized to either of two maintenance regimens. If, in the judgement of the physician the patient will continue to benefit from induction therapy, they may continue up to 12 months.

MAINTENANCE: ARM III patients will receive Prednisone, 10 mg Q.O.D., until relapse and ARM IV patients will receive Prednisone 50 mg Q.O.D. until relapse.

Progress: One patient has been enrolled (FY(94) in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/026 **Status:** Completed

**Title:** SWOG 9213: A Phase II Evaluation of Fazarabine for Patients With Poor-Prognosis Extensive Stage Small Cell Lung Cancer

**Start Date:** 11/05/93 **Est. Completion Date:** Oct 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
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
MAJ Richard F. Williams, MC

**Key Words:** Cancer:small cell lung, Fazarabine

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

Study Objective: 1) To evaluate the efficacy, as measured by the response rate, of fazarabine given by a 72 hour continuous infusion in the treatment of previously untreated, extensive stage small cell lung cancer patients whose performance status and serum albumin levels indicate poor prognosis. 2) To assess the safety, in terms of toxicity and overall survival, of fazarabine.

Technical Approach: Eligible patients will be treated with fazarabine 2.0 mg/m$^2$/hour by 72 hour continuous infusion via a peripheral or central intravenous catheter after evaluation of blood chemistry, urinalysis, and hematology. Patients with a complete or partial response or stable disease after course 1 will receive an additional course of therapy at 21 days. Patients with less than a complete or partial response after 2 courses of therapy will be removed from protocol treatment. In the absence of progression, therapy will continue at 21 day intervals. If a complete response or a stable partial ressponse is achieved after six cycles of therapy, then two additional cycles of therapy will be given and the patient will be removed from the protocol treatment. Approximately one month after completion of chemotherapy, patients who appear to be in complete remission or stable partial remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent disease with all previously positive tests being repeated. If a complete or partial remission is confirmed, the patient will continue on study and will be followed without further therapy until disease progression occurs.

Progress: No patients have been entered in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/090 **Status:** On-going

**Title:** SWOG 9216: A Randomized Phase III Study of CODE Plus Thoracic Irradiation Versus Alternating CAV and EP for Extensive Stage Small Cell Lung Cancer

**Start Date:** 04/02/93 **Est. Completion Date:** Mar 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
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CPT Jennifer L. Cadiz, MC
CPT James S. D. Hu, MC
CPT Diana S. Willadsen, MC

**Key Words:** Cancer:lung, cisplatin, adriamycin, vincristine, etoposide, cyclophosphamide, irradiation

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

Study Objective: To determine if chemotherapy dose intensification and thoracic irradiation will improve the response rate and overall survival rate in patients with extensive small cell lung cancer.

Technical Approach: Patients with extensive, measurable or evaluable disease will be randomized to 1 of 2 arms. Those randomized to Arm 1 will receive CODE (cisplatin, vincristin, doxorubicin, and etoposide) administered as follows: Cisplatin 25 mg/m$^2$ IV over 15 minutes weekly; Vincristine 1 mg/m$^2$ IV over 15 minutes weeks 1, 2, 6, 8; Doxorubicin 40 mg/m$^2$ IV over at least 10 minutes weeks 1, 3, 5, 7, 9; Etoposide 80 mg/m$^2$ IV over 20 - 30 minutes day 1 of weeks 1, 3, 5, 7, 9 and Etoposide 80 mg/m$^2$ PO days 2 & 3 of weeks 1, 3, 5, 7, 9. Those randomized to Arm 2 will receive alternating CAV/EP scheduled as follows: Cyclophosphamide 100 mg/m$^2$ IV 100 mg every 1 - 2 minutes of weeks 1, 7, 13; Doxorubicin 50 mg/m$^2$ IV over at least 10 minutes on day 1 of weeks 1, 7, 13; and Vincristine 1.2 mg/m$^2$ IV over 2 - 3 minutes day 1 of weeks 1, 7, 13 and Etoposide 100 mg/m$^2$ IV over 20 - 30 minutes days 1, 2 & 3 of weeks 4, 10, 16; Cisplatin 25 mg/m$^2$ VI over 15 minutes days 1, 2, & 3 of weeks 4, 10, 16. Supportive drugs (corticosteroid, gastroprotective agent, antifungal agent, prophylactic antibiotic Colony-stimulating factor, will be given according to set criteria.

After complete protocol cytotoxic chemotherapy, all patients will be re-staged, with repeat of any investigation that was abnormal prior to entry. If a patients should refuse re-staging, but appears on the available evidence to be in complete response, prophylactic cranial irradiation may be offered at the discretion of the investigator.

Patients on ARM 1 who achieve a complete response or partial response at the primary site with a complete response at all known metastatic sites will receive both thoracic irradiation to the mediastinum and site of the primary and prophylactic cranial irradiation beginning 3 to 4 weeks after completion of systemic therapy. These may be given concurrently and are obligatory.

Patients on Arm II who achieve a complete response will receive at least prophylactic cranial irradiation and this is obligatory. Other radiation therapy for patients in this arm is non-obligatory but may be given at the discretion of the investigator and should begin 3 to 4 weeks after completion of systemic therapy.

Progression-free survival will be compared between treatment arms. Generalized Wilcoxon and log-rank statistics will be used to compare survival experience between the two arms. A Cox proportional hazards model will be used to assess prognostic factors, and treatment effect will be tested after controlling for important prognostic variables. Response rates and toxicities between the two treatment arms will be compared by Fisher's exact test. Logistic regression will be used to assess and adjust for prognostic factors with respect to complete response.

Some patients responding to the CODE regimen will not be able to continue the weekly chemotherapy because of unacceptable constitutional toxicity or patient refusal. These patients should be offered the standard regimen (alternating CAV and EP) as they may be able to tolerate a chemotherapy program allowing sufficient time between treatments to convalesce from side effects.

Progress: No patients have entered the study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/010 **Status:** On-going

**Title:** SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup

**Start Date:** 10/01/93 **Est. Completion Date:**

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:** None

**Key Words:** Cancer: prostate, Finasteride

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

Study Objective: The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

Technical Approach: Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

Progress: Approximately 40 patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/136 **Status:** On-going

**Title:** SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer

**Start Date:** 07/02/93 **Est. Completion Date:** Jul 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**
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**Key Words:** cancer:non-small cell lung, 13-cis retinoic acid

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

Study Objective: To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

Technical Approach: Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

Progress: Two patients were enrolled in this study at MAMC in FY 94 and are being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/064 **Status:** On-going

**Title:** SWOG 9223: Evaluation of Trans-Retinoic Acid Plus Alpha Interferon in Stage IV Melanoma

**Start Date:** 02/04/94 **Est. Completion Date:** Feb 97

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Richard C. Tenglin, MC

**Associate Investigators:**
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
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MAJ Richard F. Williams, MC

**Key Words:** Cancer:melanoma, trans-retinoic acid, alpha interferon

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

Study Objective: 1) To evaluate the response rate in patients with melanoma treated with a combination of all trans-Retinoid Acid and Alpha Interferon. 2) To evaluatge the qualitative and quantitative toxicities of the combination of all trans-Retinoic Acid and Alpha Interferon.

Technical Approach: Patients enrolled in this study must have a histologically proven diagnosis of malignant melanoma with metastatic disease. All patients will receive trans-retinoic acid 37.5 mg/m$^2$ b.i.d. orally with meals for three weeks followed by one week of rest. Alpha interferon will be given as a subcutaneous injection every Monday, Wednesday, and Friday continuously while the patient is on protocol treatment. There is no rest period for interferon administration. If the trans-retinoic acid is well tolerated after the first course, it will be dose escalated to 75 mg/m$^2$. One course of therapy consists of 4 weeks. Patients will remain on therapy until evidence of progression occurs or other criteria for removal are met. All patients will be followed until death.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/027 **Status:** Completed

**Title:** SWOG 9229: A Phase II Study of Concurrent Cisplatin, Prolonged Oral Etoposide and Vincristine Plus Chest and Brain Irradiation for Limited Small Cell Lung Cancer

**Start Date:** 11/05/93 **Est. Completion Date:** Oct 96

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
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MAJ Luke M. Stapleton, MC
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**Key Words:** Cancer:small cell lung, cisplatin, etoposide, vincristine, irradiation

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

Study Objective: 1) To evaluate the efficacy, as measured by the complete response rate and overall survival, of prolonged, oral etoposide combined with cisplatin and vincristine plus concurrent chest/brain irradiation, followed by cyclophosphamide, Adriamycin and vincristine (CAV), in the treatment of patients with limited small cell lung cancer. 2) To assess the feasibility and safety of this induction/consolidation program.

Technical Approach: Eligible patients will receive 3 cycles of Cisplatin 50 mg/$m^2$, Etoposide 50 mg/$m^2$, and Vincristine 2 mg. Each cycle will be given at 4 week intervals. Chest radiotherapy will begin on day 1 of the protocol with the first dose of chemotherapy, 5 days a week for 5 weeks (4500 cGy). Prophylactic crtanial irridiation will begin on day 15 of the study. The brain dose will be 3000 cGy/15 fraction at 200 cGy per fraction given five days per week over three weeks. After the completion of induction chemotherapy/radiation therapy, the patient will receive consolidation chemotherapy with vincristin, Adriamycin and cyclophosphamice (VAC) beginning on week 16 after adequate hematologic recovery.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/096 **Status:** Completed

**Title:** SWOG 9235: Phase II Trial of Casodex in Advanced Prostate Cancer Patients Who Failed Conventional Hormonal Manipulation

**Start Date:** 04/01/94 **Est. Completion Date:** Apr 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ James B. Thrasher, MC

**Associate Investigators:**
COL John C. Norbeck, MC
T.O. Taylor
CPT Bradley F. Schwartz, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
COL J. N. Wettlaufer, MC
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CPT Michael D. Bagg, MC
MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
MAJ Timothy P. Rearden, MC

**Key Words:** Cancer:prostate, Casodex

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

Study Objective: To assess the overall response rate to Casodex in patients with advanced prostate cancer who relapsed or progressed after conventional hormonal manipulation and to assesss the tolerance and toxicity of Casodex through a combination of physician and patient reporting.

Technical Approach: Paients with a histologic diagnosis of adenocarcinoma of the prostate who have had a prior bilateral orchiectomy and or LHRH analogues of DES therapy and demonstrated objective evidence of progression or relapse will be given Casodex 150 mg po daily until progression or serious adverse reactions occur. The disease must be assessed at least every 12 weeks. Patients will be monitored for hematological, hepatic and renal effects from the treatment.

Progress: This study was closed to patient entry, 15 May 94. No patients were enrolled at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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:**
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CPT Diana S. Willadsen, MC

**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 and is still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 93/109 **Status:** Completed

**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
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MAJ Luke M. Stapleton, MC
MAJ Kenneth A. Bertram, MC
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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 94 **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:**
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
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**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 94 **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:**
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MAJ Richard C. Tenglin, MC
CPT Diana S. Willadsen, MC

**Key Words:** Cancer:Hodgkin's, Cancer:non-Hodgkin's, taxol

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

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 94 **Protocol No.:** 93/137 **Status:** Completed

**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

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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: This study was closed to patient entry, 1 Feb 94. One patient was enrolled in this study at MAMC and is now deceased.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/161 **Status:** On-going

**Title:** SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:**
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CPT Diana S. Willadsen, MC
CPT John R. Caton, MC

**Key Words:** Cancer:colon, resection, chemotherapy:perioperative, 5FU, levamisole

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

Study Objective: To determine if (1) adjuvant therapy with one week of continuous 5-FU given within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging the disease free interval and increasing survival in patients who are treated with 5-FU/Levamisole only. Endpoints include: treatment failure - as described by recurrence of local/regional or distant metastases - and survival. (2) To establish within ECOG a Central Tissue Repository for paraffin blocks and a frozen tissue bank.

Technical Approach: Patients with primary colon cancer will be randomized to either receive 7 days of continuous intravenous 5-fluorouracil (5-FU) within 24 hours completion of colon surgery or not to receive any perioperative chemotherapy.

The only investigational part of this protocol is the administration of chemotherapy during the period right after subjects colon operation. The operation and the use of 5-FU/levamisole are all standard treatment.

Progress: New study has not been started.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/105 **Status:** On-going

**Title:** SWOG 9252: Prospective Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II and Stage IIIa Non-small Cell Lung Cancer, Intergroup

**Start Date:** 05/06/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

**Associate Investigators:**
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LTC Robert D. Vallion, MC
MAJ Richard F. Williams, MC

**Key Words:** Cancer:lung, non-small cell, cisplatin, etoposide

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

Study Objective: 1) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in prolonging survival in patients with completely resected Stage II and IIIa non-small cell lung cancer. 2) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in preventing local recurrence in patients with resected Stage II or IIIa non-small cell lung cancer.

Technical Approach: Patients who have undergone a surgery for Stage II or IIIa disease are eligible to participate in this trial. Patients will be stratified for nodal status (N1, N2), histology (squamous, other), weight loss in previous 6 months (< 5%, >= 5%), and lymph node dissection (sampling, complete node resection). After stratification they will be randomized to receive radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) alone or radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) concurrent with Cisplatin (DDP) 60 mg/m$^2$ IV days 1, 29, 57, 85 and Etoposide (VP-16) 120 mg/m$^2$ IV days 1, 2, 3; 29, 20, 31; 57, 58, 59; 85, 86, 87. Patients will be followed for 5 years. The statistical analysis will be based mainly on the stratified logrank test for comparison of two treatments. The second endpoint of local recurrence rate will be also analyzed as will the time to recurrence.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/073 **Status:** On-going

**Title:** SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea.... Diagnosed Chornic Myelogenous Leukemia in Chronic Phase

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

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Mark E. Robson, MC

**Associate Investigators:**
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MAJ Richard F. Williams, MC

**Key Words:** Cancer:leukemia, chronic myelogenous, trans-retinoic acid, alpha interferon, hydroxyurea

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $9686.00 | **Periodic Review:** | // |
|---|---|---|---|---|---|

Study Objective: 1). To estimate whether treatment of Chronic Myelogeneous Leukemia (CML), with all-trans retinoic acid in combination with either hydroxyurea or interferon alfa-2a is sufficiently effective based on either hematologic or cytogenetic response, to justify its investigation in phase III trials. 2). To assess the toxicities associated with all-trans retinoic acid plus hydroxyurea or itnerferon alfa-2a in chronic phase CML.

Technical Approach: Patients qualifying for this study will be stratified by age (< 45 vs >=45), splenomegaly (present vs absent), prior hydroxyurea (yes or no), and ANC at diagnosis (<50,000 ul). Patients will then be randomized to one of two treatment arms as follows: Arm I: ATRA and HU or Arm II: ATRA and IFN. This randomization will be dynamically balanced to assure roughly equal numbers of patients within levels of the stratifying factors.

All patients in both arms will begin treatment with HU to control or keep the WBC ≤ 20,000/ul and platelets ≤ 800,000/ul. All therapy will include allopurinol. Patients will receive this HUS treatment for a minimum of 21 days and a maximum of 42 days. Patients with WVA ≤ 20,000/ul, platelets ≤ 800,00/ul, and no evidence of progressive splenomegaly after 21 - 42 days of HU will then bergin treatment on their assigned regimens. Patients who do not achieve a WBC ≤ 20,000/ul, platelets ≤ 800,000/ul, and absence of progressive splenonegaly after 42 days will be removed from protocol treatment. Arm I patients will receive ATRA 150/mg/$m^2$/d x 7 days followed by 7 days rest and HU 500 mg qd adjusted to maintain WBC and platelets to predefined levels. Arm II patients will receive acetaminophen 650 mg 1/2 hr before administration of IFN initiated a 3 MIU/$m^2$/d 5 days/week escalated by 1 MIU/$m^2$ each week to a maximum of 5 MIU/$m^2$/day and ATRA 150 mg/$m^2$/d x 7 days followed by 7 days rest. Treatment regimens will continue until the onset of accelerated or blast phase or relapse from CR or PR. Bone marrow aspiration and biopsy to monitor disease status are required at 3 and 6 months and every 6 months thereafter. Serial blood and urine specimens will be obtained for laboratory analysis.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **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

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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 Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/111 **Status:** On-going

**Title:** SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + ...

**Start Date:** 05/06/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

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**Key Words:** Cancer:rectal, 5-FU, Leucovorin, Levamisole, radiotherapy

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

Study Objective: 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protacted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatrment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival.;2) To obtain descriptive information regarding relapse patterns and tolerance.

Technical Approach: Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 $mg/m^2/d$) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to and following chemo-radiotherapy as follows: ;a. Arm A: bolus IV injection of 5-FU alone;b. Arm B: protracted venous infusion of 5-FU alone;c. Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvid radiotherapy. After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years.

Progress: One patient was enrolled in this study at MAMC and is in the follow-up stage.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/162 **Status:** On-going

**Title:** SWOG 9307: Extended Administration of Oral Cyclophosphamide for the Treatment of Poor Prognosis Extensive Disease Small Cell Lung Cancer

**Start Date:** 09/21/94 **Est. Completion Date:** Aug 93

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Robert D. Vallion, MC

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**Key Words:** Cancer:small cell lung, chemotherapy, etoposide, cyclophosphamide

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

Study Objective: (1) To estimate the response rate of extended oral administration of Etoposide and cyclophosphamide in poor prognosis extensive disease small cell lung cancer; (2) To evaluate the qualitative and quantitative toxicities of this regimen administered in a Phase II study; (3) To investigate possible correlations between peak and trough plasma etoposide levels versus complete response, toxicity, and survival.

Technical Approach: Untreated patients with extensive disease small cell lung cancer have a median survival of approximately 9 weeks. All patients will receive oral Etoposide and cyclophosphamide therapy once a day for 14 days. The dose for both chemotherapy agents will be 50 mg PO QD for the first cycle, with escalation allowed on later cycles. Ease of self administration and good subjective patient tolerance should make this combination of active agents particularly suitable for this patient population

This treatment will continue for at least 6 months unless the patient experiences unacceptable side effects or if the disease becomes worse, at which time the physician will remove their from the study. Cranial Radiation will be given at the beginning of chemotherapy is cancer has already entered the brain.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/106 **Status:** On-going

**Title:** SWOG 9308: Randomized Trial Comparing Cisplatin With Cisplatin Plus Intravenous Navelbine in the Treatment of Previously Untreated, Stage IV Non-small Cell Lung Cancer Patients

**Start Date:** 05/06/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:**
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**Key Words:** Cancer:lung, non-small cell, cisplatin, Navelbine

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

Study Objective: 1) Compare the effect of cisplatin alone with that of intravenous Navelbine plus cisplatin on tumor response rate, survival, and time to treatment failure in patients with Stage IV non-small cell lung carcinoma. 2) Compare the toxicity of the two treatment regimens in patients with Stage IV non-small cell lung carcinoma.

Technical Approach: At the time of registration, patients will be stratified by LDH (normal vs abnormal) and classified by the following: a. disease status (measurable vs. evaluable), b. prior surgical resection or RT (yes vs. no), c. histology (squamous cell vs. large cell vs. adenocarcinoma vs. unspecified). They will then be randomized to either of two arms. Arm I patients will receive Cisplatin 100 mg/m$^2$ over 30 - 60 minuetes every 28 days X 4. Arm II patients will receive Navelbine 25 mg/m$^2$ repeated weekly X 16 plus Cisplatin 100 mg/m$^2$ over 30 - 60 minutes every 28 days X 4. Patients will be evaluated every 3 months for the first year, every 6 months the second year, then yearly thereafter.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/170 **Status:** On-going

**Title:** SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast.... 0-3 Positive Nodes

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:**
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CPT John R. Caton, MC

**Key Words:** cancer:breast, chemotherapy, cyclophosphamide, doxorubicin, positive nodes

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

Study Objective: (1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide; (2) To obtain tumor tissue for biologic studies.

Technical Approach: Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/107 **Status:** On-going

**Title:** SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phse III

**Start Date:** 05/06/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

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

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**Key Words:** Cancer:myeloma, BCNU, Cyclophosphamide, Cyclosporine, Dexamethasone, Doxorubicin, G-CSF, Interferon-alpha 2b, Melphalan, Mesna, Methotrexate, Prednisone, Vincristine

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

Study Objective: 1. To perform a randomzied trial, in newly diagnosed patients with symptomatic multiple myeloma (MM), of standard therapy versus myeloablative therapy, in order to examine whether the greater tumor cytoreduction effected by intensive therapy and manifested by higher incidence of complete remission translates into extended overall survival and progression-free survival.;2. To randomize responding patients with >= 75% tumor cytoreduction to interferon-alpha 2b (IFN) versus no maintenance in order to evaluate the role of IFN in MM.

Technical Approach: Symptomatic patients of all stages of multiple myeloma with reasonable performance status will be randomized to high dose chemotherapy with autologous bone marrow transplant or standard VBMCP combination chemotherapy after induction VAD therapy. A required peripheral stem cell harvest will be done for those randomized to the ABMT arm for future high dose therapy if failure occurs. This will be an option for those randomized to the standard arm. Those patients that have an HLA compatible sibling donor will be eligible for allogeneic BMT. A second randomization will be done for those with continued gfreater than 75 percent regression of disease in the ABMT or standared chemotherapy arm while those receiving allo-BMT will be continued on GVHD prophylaxis.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/114 **Status:** On-going

**Title:** SWOG 9323: Laboratory/Clinical Correlative Studies in Non-Small Cell Lung Cancer: Ancillary Study to SWOG 9252 (INT-0115, E3590, RTOG 91-05, NCCTG 91-24-51)

**Start Date:** 06/03/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

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**Key Words:** Cancer:lung, K-ras, p53, antigen, EHF receptor levels, p105, Factor 8

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

Study Objective: 1) To determine the incidence of K-ras and p53 mutations; assess Group A blood antigen and EHF receptor levels; and assess p105 and Factor 8 levels in patients with completely resected Stage II or IIIa SCLC. 2) Correlate these results with patient histology, TNM stage, time to relapse, and survival.

Technical Approach: SWOG 9323 requires that tissue samples of lung cancer resected from each patient enrolled on SWOG 9252 be sent to three central research laboratories. Investigators will study the tissue samples for the tumor markers, K-ras, p-53, and others. Investigators are evaluating these tumor markers to determine if they can predict how patients might respond to treatment for non-small cell lung cancer.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/058 **Status:** On-going

**Title:** SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary

**Start Date:** 02/04/94 **Est. Completion Date:** Nov 03

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

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MAJ Richard F. Williams, MC

**Key Words:** cancer:breast, histologic grading

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

Study Objective: 1) To evaluate the reproducibility of a combined histopathologic grading system of breast cancer. 2) To evaluate the ability of the grading system to predict time to treatment relapse (TTR) and survival. 3) To use multivariate analyses to evaluate the prognostic importance of the grading data relative to the other clinical and biological factors determined as part of SWOG 8294.

Technical Approach: This is a pathology study utilizing the patient set from SWOG 8294. Patients reviewed as part of that study (where cases with adequate specimens for flow cytometry were evaluated and provisionally graded) will be registered to this study. Slides will be reviewed by three investigators and cases will be grouped into 3 prognostic categories. The power calculation for testing the association of this gradfing system with survival will be based on the "2 degree of freedom" logrank test. The Cox proportional hazards model will also be used in the analysis to adjust the comparisons for effects of other factors.

Progress: Seven patients were enrolled in this study in FY94 and all are still being followed.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/120 **Status:** On-going

**Title:** SWOG 9332: Phase III Trial of Adriamycin Versus Taxol Versus Taxol Plus Adriamycin Plus G-CSF in Metatastatic Breast Cancer, Intergroup

**Start Date:** 06/03/94 **Est. Completion Date:** May 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

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**Key Words:** Cancer:breast, adriamycin, Taxol, G-CSF

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

Study Objective: 1) To compare the objective response rate and time to progression of single-agent Adriamycin, single-agent Taxol, and the combination of Adriamycin and Taxol in patients with previously untreated metastatic breast cancer.;2) To compare the toxicity of Adriamycin, Taxol, and Adriamycin and Taxol given in combination.;3) To determine whether Taxol and Adriamycin exhibit crossover resistance to each other.;4) To compare the quality of life of patients who have received Taxol, Adriamycin, or the combination of Tacol and Adriamycin as first-line therapy for metastatic breast cancer.;5) To compare the quality of life of patients who have received Taxol or Adriamycin as second-line therapy.;6) To evaluate the relation of steady state Taxol levels to therapeutic response and toxicity.

Technical Approach: This is a randomized trial to compare the efficacy of single agent Taxol vs Adriamycin vs a Taxol and Adriamycin combination. Women with histologically confirmed breast carcinoma with progressive regional or metastatic cancer will be randomized between three Arms with single agent Adriamycin 60 $mg/m^2$ for 1 day, repeated every 21 days with crossover to Taxol with progression of disease; single agent Taxol 175 $mg/m^2$ every 3 weeks X 8 with crosswover to single agent Adriamycin upon progression; or combination of Taxol 150 $mg/m^2$ and Adriamycin 50 $mg/m^2$ every 3 weeks X 8, plus G-CSF days 3 and 12. End points will be response, toxicity severity and quality of life characteristics.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/121 **Status:** On-going

**Title:** SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell...

**Start Date:** 06/03/94 **Est. Completion Date:** Jun 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** LTC Robert D. Vallion, MC

**Associate Investigators:**

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**Key Words:** Cancer:non-small cell lung, chemotherapy, radiotherapy, surgical resection

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

Study Objective: 1) Access whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year)s survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer.;2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases.;3) To obtsain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

Technical Approach: Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/m$^2$ IVPB days 1, 8, 29, 36 and VP-16 50 mg/m$^2$ IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II. Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5-year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

Progress: No patients have been enrolled in this study at MAMC.

# Detail Summary Sheet

| | | |
|---|---|---|
| **Date:** 30 Sep 94 | **Protocol No.:** 94/122 | **Status:** On-going |
| **Title:** SWOG 9339: Evaluation of Topotecan in Esophageal Carcinoma, Phase II | | |
| **Start Date:** 06/03/94 | **Est. Completion Date:** May 98 | |
| **Department:** SWOG | **Facility:** MAMC | |
| **Principal Investigator:** MAJ Timothy P. Rearden, MC | | |
| **Associate Investigators:**<br>LTC Howard Davidson, MC<br>MAJ Patrick L. Gomez, MC<br>MAJ Robert B. Ellis, MC<br>CPT James S. D. Hu, MC<br>CPT Diana S. Willadsen, MC | MAJ Luke M. Stapleton, MC<br>MAJ Kenneth A. Bertram, MC<br>MAJ Mark E. Robson, MC<br>MAJ Richard C. Tenglin, MC<br>LTC Robert D. Vallion, MC<br>MAJ Richard F. Williams, MC | |
| **Key Words:** Cancer:esophageal, topotecan | | |
| **Accumulative MEDCASE Cost:** $0.00 | **Est. Accumulative OMA Cost:** $0.00 | **Periodic Review:** // |

Study Objective: To evaluate the response rate of esophageal carcinoma treated with topotecan; and to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study.

Technical Approach: Patients enrolled in this study will receive Topotecan 1.5 mg/m$^2$ via continuous infusion IV over 24 hours on days 1, 8, 15, and 22. The retreat interval will be every 42 days (weekly X 4 weeks; 2 week rest period). Patients will continue this treatment schedule as long as they show complete remission, partial remission, or stable disease. Response assessments are to be performed every cycle along with laboratory analysis.

Progress: No patients have been enrolled in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/123 **Status:** On-going

**Title:** SWOG 9348: Evaluation of the Standard DCNU/DTIC/Cisplatin/Tamoxifen Regiment in Disseminated Malignant Melanoma, Phase II

**Start Date:** 06/03/94 **Est. Completion Date:** Jun 98

**Department:** SWOG **Facility:** MAMC

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

**Associate Investigators:**
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**Key Words:** Cancer:melanoma, BCNU, DTIC, Cisplatin, Tamoxifen

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

Study Objective: To esstimate the response rate of the combination of BCNU/DTIC/cisplatin/tamoxifen in patients with disseminated malignant melanoma in order to select the appropriate regimen for combination with alpha-interferon in a future Phase III trial; and to accurately determine the toxicities of this drug combination in order to assess its feasibility in a future Phase III trial.

Technical Approach: Participants in this study must not be receiving or planning to receive concomitant biologic therapy, surgery, radiation therapy, hormonal therapy, or other chemotherapy or other treatment while on this protocol. DTIC, 220 mg/m$^2$ IV on days 1-3 & 22-24; cisplatin, 25 mg/m$^2$ IV on days 1-3 & 22-24; BCNU, 150 mg/m$^2$ IV on day 1; and tamoxifen, 110 mg/m$^2$ B.I.D. daily will be given throughout treatment. Retreatment interval is 6 weeks. Patients will continue on this regimen until they fulfill one of the defined criteria for removal from treatment. Patients will undergo frequent laboratory evaluations for toxicities. After completion of therapy, patients will be followed every three months for one year, every six months for the next two years, and annually thereafter.

Progress: No patients have been enrolled in this study.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 94/163 **Status:** On-going

**Title:** SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study

**Start Date:** 09/21/94 **Est. Completion Date:** Sep 98

**Department:** SWOG **Facility:** MAMC

**Principal Investigator:** MAJ Robert B. Ellis, MC

**Associate Investigators:**
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**Key Words:** cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes

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

Study Objective: To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

Technical Approach: Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

Progress: No patients have been enrolled in this study.

# DETAIL SHEETS FOR PROTOCOLS

# UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 88/017 **Status:** Completed

**Title:** UWNG 87-01: Phase II Study of TPDCFH for Recurrent Malignant Brain Tumor

**Start Date:** 12/11/87 **Est. Completion Date:** Sep 90

**Department:** UWNG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**
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**Key Words:** tumor:brain,chemotherapy,TPDCFH

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $100.00 | **Periodic Review:** 12/04/92 |
|---|---|---|---|---|

Study Objective: To determine whether TPDCFH chemotherapy for recurrent malignant glioma will increase time to progression and survival rate and to document the toxicity attendant on combined treatment.

Technical Approach: Patients will be eligible for this study if: they have received primary surgical treatment, radiotherapy, or adjuvant chemotherapy, but no radiotherapy or chemotherapy for 8 weeks prior to entry; the tumor is a histopathologically confimred recurrence of a malignant supratentorial glioma; liver and renal functin are not seriously imparied; Karnofsky peroformance status is >60%. Recurrence will be signaled by worsening neurologic symptoms and signs measured by a neurologic examination. Enlargement of tumor volume as measured in contrast and noncontrast CT scan will serve as an additional criteron of recurrence. All patients will receive the following schedule: 0-66 hrs: 6 thioguanine, 30 $mg/m^2$, q. 6 hr p.o. x 12 doses; 60-78 hrs: procarbazine, 50 $mg/m^2$, q. 6 hr p.o. x 4 doses; 60 hrs: dibromodulcitol, 400 $mg/m^2$, p.o.; 72 hrs: CCNU, 100 $mg/m^2$, p.o. and days 14 & 15: 5-FU, 1 $g/m^2$, continuous infusion over 48 hrs: Day 15: hydroxyurea, 1 $g/m^2$ , p.o., 4 hours before the 5-FU infusion ends and at 4 hour intervals for a total of 3 doses. The cycle will be repeated on days 37-48, depending 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: This study has been closed to patient entry. No patients were entered at MAMC.

# Detail Summary Sheet

**Date:** 30 Sep 94 **Protocol No.:** 89/013 **Status:** On-going

**Title:** UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System

**Start Date:** 01/20/89 **Est. Completion Date:** Nov 92

**Department:** UWNG **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

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MAJ Kenneth A. Bertram, MC

**Key Words:** lymphoma:central nervous system,chemoradiotherapy,methotrexate

| **Accumulative MEDCASE Cost:** | $0.00 | **Est. Accumulative OMA Cost:** | $328.00 | **Periodic Review:** 12/04/92 |
|---|---|---|---|---|

Study Objective: To evaluate this regimen, the end-points of analysis will be: time to progression of disease from beginning of therapy, response rates and disease stabilization rates, survival time measured from the beginning of therapy, quality of life, and activity level measured by Karnofsky performance status.

Technical Approach: Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver function, and a performance status of >70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m$^2$, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses, parenterally, on an every 6 hour basis, following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time, the patient will be removed from the protocol and cen be treated with other therapy as indicated. Patients will be followed until death.

Progress: The protocol has been closed to patient entry. One patient was enrolled and is still being followed.

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