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# Clinical Investigation

*Annual Research Progress Report*



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**Madigan Army Medical Center**  
**Tacoma, Washington 98431-5454**

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**ANNUAL PROGRESS REPORT**

30 SEPTEMBER 1991

DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431-5454

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# ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1991

DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431-5454

## 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

During FY 91, the Department of Clinical Investigation, Madigan Army Medical Center, continued its high level of productivity and creativity despite major personnel changes. COL Stephen Plymate ended a distinguished military research career and retired, to be replaced by COL Dan C. Moore as chief of the department. MAJ James MacMillan, research veterinarian, was promoted to LTC and moved on to LAIR, to be replaced by MAJ Douglas Powell. MAJ John van Hamont, research microbiologist, took a laboratory directorship at SHAPE, and was replaced by MAJ Robert Stewart. CPT Rita Hoop, molecular biologist, decided to leave the Army and seek greener pastures with her spouse, leaving her position vacant.

Numbers of protocols supported during FY 91 continued to increase and the number of new protocols submitted was comparable to our five year average, despite temporary losses of staff to Operations Desert Shield and Desert Storm. The Laboratory Animal and Surgery Service provided invaluable training to many reserve hospital staff prior to departure for Southwest Asia. The animal facility also received full accreditation following an inspection this fiscal year. Collaboration with the nearby VAMC and University of Washington continued to be fruitful. New initiatives to increase DCI teaching of research fundamentals in GME programs were put into place, including a 12 hour seminar series and a publication on medical writing for scientific journals.

I would like to acknowledge the entire DCI staff who worked selflessly to support MAMC research in every way possible, as well as the Commanding General, BG John Hutton, and the DCCS, COL Michael Weir, for their strong support of research as an integral part of GME. I am also indebted to my Protocol Coordinator, Nancy Whitten, who spent countless hours writing and compiling this report.

## 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

<u>Description</u>	<u>MANPOWER</u>	
	<u>Rank</u>	<u>MOS</u>
Chief PLYMATE, Stephen R., M.D., COL, MC (Jan 84 - Dec 90)	06	61C9A
Chief MOORE, Dan C., M.D., COL, MC (Jan 91 - Sep 91)	06	60P9A
C, Clinical Studies Service JONES, Robert E., M.D., LTC (P), MC	05	61C9A
Biochemist PRICE, Gary H., Ph.D., LTC, MS (Aug 89 - Jul 91)	05	68C9B
C, Surg & Animal Care Svc MacMILLAN, James G., D.V.M., MAJ (P), VC (Aug 88 - Jul 91)	04	64C9B
C, Surg & Animal Care Svc POWELL, Douglas, D.V.M., MAJ, VC (Aug 91 - )	04	64C9B
C, Microbiology Svc STEWART, Robert S., Ph.D., MAJ, MS (Sep 91 - )	04	68A9B
C, Microbiology Svc van HAMONT, John E., Ph.D., MAJ, MS (Jun 88 - Jul 91)	04	68A9B
C, Biological Research Svc HOOP, Rita C., M.S., CPT, MS	03	68C00
C, Biochemistry Svc MOORE, Katherine Hines, Ph.D., CPT, MS	03	68C00
NCOIC HANDY, Kevin , SSG	E5	92B3M4
Vet Animal Spec HEATH, George, SGT	E5	91T20
Vet Animal Spec SPAHN, Shelley, SGT	E5	91T20
Vet Animal Spec VERZOSA, Neil , SGT	E5	91T20

<u>Description</u>	<u>Rank</u>	<u>MOS</u>
Vet Animal Spec WILLON, Thomas, PV2 (Jul 88 - Jul 91)	E2	91T10
Med Tech MATEJ, Louis A., B.S., M.T.	GS9	0644
Med Tech WRIGHT, James R., B.A., M.T.	GS9	0644
Med Tech STYNER, M. J., B.S., M.T.	GS9	0644
Computer Programmer Analyst (Temp/Permanent Aug 91) PATIENCE, Troy H., B.S.	GS7/ GS9	0334/ 1530
Edit Asst/Steno WHITTEN, Nancy J., B.A.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS5	0318
Maintenance Worker KAEO, Curtis	WG7	4749

Funding FY 91

MEDCASE Equipment	\$177,727.14
Capital Equipment	24,096.65
Civilian Salaries	132,643.32
Military Salaries	497,516.00
Consumable Supplies	112,941.67
Contractual Services	7,295.59
TDY	2,000.00
<u>Total</u>	954,220.37

GRANTS: Amount: 147,112.00 Source: NIH

FOR: Protocol - The Effect of Two Levels of Hyperoxygenation Given via a Manual Resuscitation Bag and Ventilator During Endotracheal Suctioning of Premature Infants

PRINCIPAL INVESTIGATOR: COL Barbara S. Turner, AN

HSC #89222 MAMC #89028



### 3. Progress

During FY 91 there were 346 active protocols that received administrative and/or technical support during the year. Of these, 236 are presently on-going; 3 are in a suspended status, 88 were completed; and 19 were terminated.

There were 71 publications, 2 theses were completed and accepted from approved research studies, and there were 42 presentations at regional, national, or international meetings.

### 4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 21

Number of protocols with a fellow/resident as principal investigator: 67

Number of protocols with a fellow/resident as associate investigator: 118

### 5. Other training programs supported by DCI:

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

Active Duty Graduate Student protocols: 6

### 6. Other protocols supported:

105 protocols held by hospital staff members  
166 group oncology protocols  
1 Fort Wainwright, AK  
1 Environmental Health Agency

## COMMITTEE MEMBERS

Commander

Madigan Army Medical Center  
BG John E. Hutton, Jr., 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  
Statistician, DCI

### Human Use Committee

Chairman

\*Deputy Commander of Clinical Services  
COL Michael R. Weir, 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

\*Deputy Commander of Clinical Services

COL Michael R. Weir, M.D., MC

Chief or delegated representative of:

Department of Clinical Investigation

Department of Nursing

Public Affairs Office

Veterinary Services

Non-institutional member

BRYON L. STEGER RESEARCH AWARD

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 1991:

Arthur Herpolsheimer  
CPT, MC

Maternal and Neonatal Effects of Outlet Forcep  
Delivery Compared to Spontaneous Vaginal Delivery  
in Term Pregnancies

Other nominees were:

Richard A. Beck  
MAJ, MC

Cardiovascular Effects of Pseudoephedrine in  
Medically Controlled Hypertensive Patients

Arthur Herpolsheimer  
CPT, MC

Pulmonary Function of Preeclamptic Women  
Receiving Intravenous Magnesium Sulfate Seizure  
Prophylaxis

Sherri Y. Nottestad  
CPT, MC

Dose Relationship Between I.V. Nitroglycerin and the  
Anticoagulant Effect of I.V. Heparin

Leonard G. Renfer  
CPT, MC

The Effect of 5-Alpha Reductase Inhibitor on Prostate  
Cancer Cell Lines Implanted in Athymic Nude Mice

## PUBLICATIONS

FISCAL YEAR 91

### DEPARTMENT OF CLINICAL INVESTIGATION

- Friedl KE, Dettori JR, Hannan CJ, Patience TH, Plymate SR  
Comparison of the Effects of High Dose Testosterone and 19-Nortestosterone to a Replacement Dose of Testosterone on Strength and Body Composition in Normal Men. *Journal Steroid Biochemistry* 40(4): 607-612, 1991
- Heath G  
On the Streets of Chicago and in the Middle East War Advanced Trauma Life Support Proves Its Worth. *AALAS Bulletin* 30(3): 42, 1991
- Kraemer WJ, Patton JF, Knuttgen HG, Hannan CJ, Kettler T, Gordon SE, Dziados JE, et al  
Effects of High Intensity Cycle Exercise on Sympathoadrenal-Medullary Response Patterns. *Journal of Applied Physiology* 70(1): 8-14, 1991
- Nestler JE, Powers LP, Matt DW, Steingold KA, Plymate SR, Rittmaster RS, Clore JN, Blackard WG  
A Direct Effect of Hyperinsulinemia on Serum Sex Hormone Binding Globulin Levels in Obese Women with the Polycystic Ovary Syndrome. *JCEM* 72(1): 83-89, 1991
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Effects of Sex Hormone Binding Globulin (SHBG) on Human Prostatic Carcinoma. *J Steroid Biochem Molec Biol* 40(4): 833-839, 1991
- Wiren KM, Voderstrasse B, Plymate SR, Matej LA  
Direct Action of Testosterone on Type 1 Collagen Messenger RNA Levels in Osteoblasts. *Clinical Research* 39(1): PA102, 1991

### DEPARTMENT OF DENTISTRY

- Brown MD, Aaron G  
The Effect of Point-of-Use Water Conditioning Systems on Community Fluoridated Water. *Pediatric Dentistry* 13(1): 35-38, 1991
- Brown MD, Aaron GR  
Pseudohypoparathyroidism: Case Report. *Pediatric Dentistry* 13(2): 106-109, 1991
- Goho CD  
Ingestion of Dental Mirror Fragments: Report of a Case. *J Dentistry for Children* 13(4): 337-339, 1991
- Goho CD, Kittle PE  
Override of a N2O/O2 Machine Fail-Safe Mechanism: Case Report. *Pediatric Dentistry* 13(4): 234-235, 1991
- Kittle PE, Aaron GR, Jones HL, Duncan NO  
Incidental Finding of an Intranasal Foreign Body Discovered on Routine Dental Examination: Case Report. *Pediatric Dentistry* 13(1): 49-51, 1991
- Svoboda WE, Aaron GR, Albano EA  
North American Burkitt's Lymphoma Presenting with Intraoral Symptoms. *Pediatric Dentistry* 13(1): 52-58, 1991

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DEPARTMENT OF EMERGENCY MEDICINE

- Gendron BP                    Loxosceles Envenomation - Reply. Amer J Emergency  
Medicine 9(2): 203, 1991
- Gendron BP, Gatrell CB      Spontaneous Rupture of the Spleen in Initial Presentation of  
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DEPARTMENT OF FAMILY PRACTICE

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Kozakowski M                Ambulatory Care. Military Medicine 156: 248-251, 1991
- Lillegard WA                 Strength Training for the Young Athlete. J Back Musculoskel  
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- Lillegard WA,                Introduction to Summer Issue. J Back Musculoskel Rehabil  
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DEPARTMENT OF MEDICINE

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Jaremko W
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Vaughn GE, Matej LA        Immunoactive Luteinizing Hormone (LH) in Men. Clinical  
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Sierra R, Dunning D,  
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DEPARTMENT OF NURSING

Smith PS, Turner BS

The Physiologic Effects of Positioning Premature Infants in  
Car Seats. *Neonatal Network* 9(4): 11-15, 1990

DEPARTMENT OF OB/GYN

Brady K, Duff P,  
Harlass FE, Reid S

Role of Amniotic Fluid Cytogenetic Analysis in the  
Evaluation of Recent Fetal Death. *Amer J Perinatology* 8(1):  
68-70, 1991

Christian SS, Brady K

Cord Blood Acid Base Values in Breech-Presenting Infants  
Born Vaginally. *Obstetrics and Gynecology* 78(5): 778-81, 1991

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Hillier SL, Herd LM,  
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Friedl KE, Wright JR

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Yancy MK, Brady K,  
Read JA

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Death of Monozygotic Twin. *J Clinical Ultrasound* 19(3): 162-  
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DEPARTMENT OF PEDIATRICS

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- Babonis TR, Weir MR, Kelly PC Impedance Tympanometry and Acoustic Reflectometry at Myringotomy. *Pediatrics* 87(4): 475-80, 1991
- Glenn GM, Schofield T, Krober MS Group A Streptococcal Supraglottitis. *Clinical Pediatrics* 29(11): 674-76, 1990
- Hinson RM Diagnostic Approach to Hemolytic Anemia in the Pediatric Patient. *Resident & Staff Physician/Sup*: 3-8, 1991
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- Krober MS, Weir MR Acute Uvulitis Apparently Caused by *Candida Albicans*. *Ped Inf Dis Journal* 10(1): 73, 1991
- Krober MS, Weir MR, Themelis NJ, van Hamont JE Optimal Dosing Interval for Penicillin Treatment of Streptococcal Pharyngitis. *Clinical Pediatrics* 29(11): 646-48, 1990
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DEPARTMENT OF SURGERY

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- Heydorn WH, Velanovich V A 5-Year United States Army Experience with 36,250 Abdominal Hernia Repairs. *American Surgeon* 56(10): 596-600, 1990
- Jones RO, Harkless LB, Baer MS, Wilkinson SV Retrospective Statistical Analysis of Factors Influencing the Formation of Long-Term Complications Following Hallux Abducto Valgus Surgery. *The Journal of Foot Surgery* 30(4): 344-49, 1991
- Kaufmann CR, Maier RV, Kaufmann EJ, Rivara FP, Carrico CJ Validity of Applying Adult Triss Analysis to Injured Children. *Journal of Trauma* 31(5): 691-98, 1991
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- Mooney MJ, O'Reilly MJ Laparoscopic Drain Placement During Laparoscopic Cholecystectomy. *Surg Endos/US Interven Tech* 5(2): 101, 1991
- Morris MR, Namon A, Shaw GY, Panje WR, Mhoon EE The Keratitis, Ichthyosis, and Deafness Syndrome. *Otolaryngology H&N Surgery* 104(4): 526-28, 1991
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- Renfer LG, Kiesling VJ, Kelley J, Vaccaro JA, Belville WD Digitally-Directed Transrectal Biopsy Using Biopsy Gun versus Transrectal Needle Aspiration - Comparison of Diagnostic Yield and Comfort. *Urology* 38(2): 108-112, 1991
- Renfer LG, Vaccaro JA, Kiesling VJ Digital-Directed Transrectal Core Biopsy with Spring-Loaded Biopsy Device (Biopsy). *Urology* 38(2): 161-62, 1991
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- Velanovich V Ponderal Index as a Predictor of Postoperative Complications. *American Surgeon* 56(11): 659-61, 1990
- Velanovich V Operative Decisions. *Theoretical Surgery* 6(1): 38-40, 1991

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- Velanovich V            **A Meta-analysis of Prophylactic Antibiotics in Head and Neck Surgery. Plastic & Reconstructive Surg 87(3): 429-34, 1991**
- Velanovich V            **The Value of Routine Preoperative Laboratory Testing in Multivariate Analysis. Surgery 109(3): 236-43, 1991**
- Velanovich V,  
Andersen CA            **Concomitant Abdominal Aortic Aneurysm and Colorectal Cancer: A Decision Analysis Approach to a Therapeutic Dilemma. Annals of Vascular Surgery 5(5): 449-55, 1991**

**THESES**

**FISCAL YEAR 91**

**DEPARTMENT OF NURSING**

**Keeton DS**

**The Effect of Intraoperative Lumbar Support on the Incidence and Severity of Postoperative Backache. Master of Nursing, Univ of Washington**

**Nye CJ**

**Assessing Parental Stress in the NICU. Univ of Washington**

## PRESENTATIONS

### FISCAL YEAR 91

#### DEPARTMENT OF CLINICAL INVESTIGATION

- |   |  |   |
|---|--|---|
| Moore KH,<br>Plymate SR,<br>Griffin PR,<br>Petra PH         | Enzymatic Deglycosylation of Rabbit<br>SBP and Its Effect on Steroid Binding                                     | The Endocrine Society,<br>Washington, DC, June 91                         |
| Plymate SR,<br>Hoop RC, Loop SM,<br>Hammond GL,<br>Hobbs CJ | Sex Hormone Binding Globulin<br>(SHBG) and SHBG-Related MRNAS<br>and Protein Human Prostate Cancer<br>Cell Lines | The Endocrine Society,<br>Washington, DC, June 91                         |
| Wiren KM,<br>Voderstrasse B,<br>Plymate SR,<br>Matej LA     | Direct Action of Testosterone on Type<br>1 Collagen mRNA Levels in<br>Osteoblasts                                | Western Society for Clinical<br>Investigation, Carmel, CA,<br>February 91 |
| van Hamont JE,<br>Wright J                                  | Analysis of Mixed Lymphocyte<br>Responses to Whole Cell<br>Preparations of Ureaplasma<br>Urealyticum             | American Society for<br>Microbiology, Dallas, TX,<br>May 91               |

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| Foutch R,<br>Magelssen MD,<br>MacMillan JG  | The Esophageal Detector Device: A<br>Rapid and Accurate Method for<br>Assessing Tracheal Versus<br>Esophageal Intubation in a Porcine<br>Model | Society for Academic Emer<br>Medicine/Emer Medicine<br>Research Society Joint<br>Meeting, Edinburgh,<br>Scotland, October 90 |
| Guertler AT,<br>Brewer TG,<br>Lagutchik MS,<br>Januszkiewica AJ,<br>Baskin Si,<br>Martin DG | Effect of Methemoglobinemia on<br>Sheep Exercise Performance.  | US Army Med Res Inst for<br>Chemical Defense<br>Bioscience review,<br>August 91  |

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| Bachinski MS,<br>Cushner HM,<br>Roth BJ, Peller T   | Salicylate Overdose: Quantitation of<br>Renal Excretion with Forced<br>Alkaline Diuresis | Washington State<br>Association of the<br>American College of<br>Physicians, December 90                     |
| Buckner C,<br>Lyons MF,<br>Tsuchida AM              | The Performance of Hemocult II<br>and Hemocult SENSA                                     | 55th Annual Scientific<br>Meeting, American College<br>of Gastroenterology, San<br>Francisco, CA, October 90 |
| Hobbs CJ,<br>Plymate SR,<br>Bell BK,<br>Patience TH | The Effect of Androgens on Glucose<br>Tolerance  | American Federation of<br>Clinical Research, Seattle,<br>WA, May 91  |

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Hobbs CJ, Plymate SR, Jones RE, Patience TH	The Effects of Androgens on Insulin-Like Growth Factor I Levels in Normal Men	Western Society for Clinical Investigation, Carmel, CA, February 91
Jones RE, Bell BK, Plymate SR	Inability of Ejaculated Human Spermatozoa to Incorporate Exogenous Fatty Acids or 1-Hexadecanol Into Ether Lipids	American Society of Andrology, Montreal, Quebec, April 91
Jones RE, Plymate SR, Vaughan GE, Matej LA	Effects of Acute Thermal Injury on Bioactive and Immunoreactive Luteinizing Hormone (LH) in Men	American Federation of Clinical Research, Western Meeting, Seattle, WA, May 91
Lyons MF, Tsuchida AM, Schlepp GE	Is Colonic Neoplasia Associated with Barrett's Esophagus?	55th Annual Scientific Meeting, American College of Gastroenterology, San Francisco, CA, October 90
Nottestad SY	Loculated Pericardial Effusion and Cardiac Tamponade Late After Cardiac Surgery	Washington State Chapter American College of Physicians Meeting, ,December 90
Nottestad SY, Cobos E, Mascette AM	Dose Relationship Between IV Nitroglycerin and the Anticoagulant Effect on IV Heparin	Washington State Chapter of the American College of Physicians, December 90
Pearce WA, Tsuchida AM, Lyons MF, Bowersox J	Diagnosis and Treatment of Complications of Vertical Bonded Gastroplasty	American College of Gastroenterology, 55th Annual Meeting, San Francisco, CA, October 90
Peele ME, Carr FE, Wartofsky L, Burman KD	The Effect of Fasting on the Level of Triiodothyronine Receptor Message in Rat Liver	Society of Uniformed Endocrinologists Washington, DC, June 91
Sowray P, Davidson H, Sierra R, Dunning D, Colman L	High Dose Cisplatin (CDDP), VP-16 with Radiation Therapy for Stage III Non-Small Cell Lung Cancer (NSCLC)	1991 Meeting of the American Society of Clinical Oncology, Houston, TX, May 91

DEPARTMENT OF NURSING

Egan ME, DeVore DJ	A Study of Cultural and Perinatal Factors that Affect Postpartum Outcomes for Asian Women and Their Families	Society for Applied Anthropology, York, England, November 90
Turner BS	Endotracheal Suctioning in Premature Infants	AACN International Conference, Vienna, Austria, August 91

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Turner BS	Endotracheal Suctioning in Critically Ill Patients	American Thoracic Society International Conference, Anaheim, CA, May 91
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DEPARTMENT OF OB/GYN

Herpolsheimer AH, Yancey MK, Jordan GD, Brady WK	Maternal and Neonatal Effects of Outlet Forcep Delivery Compared to Spontaneous Vaginal Delivery in Term Pregnancies	39th Meeting of the American College of Obstetricians and Gynecologists, New Orleans, LA, May 91
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DEPARTMENT OF PEDIATRICS

Beachy JC	The Effect of Asphyxia on Rat Neutrophil Number and Function	American Academy of Pediatrics, Fall Meeting, Boston, MA, October 90
Brown J, Albano E, Krober MS	IVIG Therapy for Viral Associated Hemophagocytic Syndrome	Uniformed Services Pediatrics Seminar, March 91
Fisher R, Kelly PC, Weir MR, Krober MS, Jones R	Necrotic Arachnidism: Don't Blame the Recluse	Uniformed Services Pediatric Seminar, March 91
Glenn G, Krober MS, Kelly PC, Weir MR	Pyridoxine as Therapy in Theophylline-Induced Seizures	Uniformed Services Pediatric Seminar, March 91
Glenn GM, Schofield T, Krober MS	Group A Streptococcal Supraglottitis	Uniformed Services Pediatric Seminar, March 91
Kinney JB, Albano E, Krober MS, Stevenson JG	Atypical Kawasaki Disease	Uniformed Services Pediatric Seminar, March 91
Krober MS	Cryptococcal Meningitis in a Child With Late-Onset Perinatally Acquired AIDS	Uniformed Services Pediatrics Seminar, March 91
Krober MS, Blount W, Kazakowski M	Nutritional Status of Rural Bolivian Children	Uniformed Services Pediatric Seminar, March 91
Krober MS, Weir MR	Acute Uvulitis Apparently Caused by Candida Albicans	Uniformed Services Pediatrics Seminar, March 91
Krober MS, Weir MR, Stracener CE, Bass Jw	Measles Antibody Response After Measles-Mumps-Rubella Vaccine in Children with Concurrent Upper Respiratory Infection	Uniformed Services Pediatric Seminar, March 91

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Krober MS, Weir MR, Themelis NJ, van Hamont JE	Optimal Dosing Interval for Penicillin Treatment of Streptococcal Pharyngitis	Uniformed Services Pediatric Seminar, March 91
Rawlings JS, Polzin W, Brady K, Krober MS	Effect of Intensive Antenatal and Neonatal Screening for Group B Streptococcus on the Incidence of Early Onset Neonatal Sepsis	Uniformed Services Pediatric Seminar, March 91
Stephan MJ, Alvord EC, Pederson RC, Kelly JL, Crothers B	Predominantly Unilateral Moebius Sequence with Co-existent Malformations and Deformations: Neuropathologic Evidence for Vascular Pathogenesis	23rd Annual March of Dimes Clinical Genetics Conference, Vancouver, BC, July 91

DEPARTMENT OF RADIOLOGY

Phillips WT, Rudolph AS, Timmons JH, Klipper R, Blumhardt R	A Simple Method for Producing A Technetium-99M-Labeled Liposome Which is Stable in Vivo	Seventh International Symposium on Radiopharmacology, Boston, MA, June 91
Phillips WT, Rudolph AS, Timmons JH, Klipper R, Blumhardt R	A Stable Technetium-99-M-Labeled Liposome for Biodistribution Studies in Liposome Drug Delivery Systems	International Symposium on Nuclear Imaging, Baltimore, MD, June 91

DEPARTMENT OF SURGERY

Andersen CA, Cavanaugh DG, Thlka B	Central Venous Pyophlebitis Secondary to an Indwelling Catheter	Washington State Chapter American College of Surgeons, Warm Springs, OR, June 91
Andersen CA, O'Reilly MJ, Mooney MJ	Complications of Laparoscopic Cholecystectomy	Seattle Surgical Meeting, Seattle, WA, January 91
Beck RA	Cardiovascular Effects of Pseudoephedrine in Medically Controlled Hypertensive Patients	94th Ann Meet, American Laryngological, Rhinological, and Otolological Society, Waikoloa, HI, May 91
Renfer LG, Plymate SR	The Effect of 5-Alpha Reductase Inhibitor on Prostate Cancer Cell Lines Implanted in Athymic Nude Mice	Kimbrough Urology Meeting, November 90
Thompson IM, Davis R, Vaccaro JA	Radical Retropubic Prostatectomy and Orchiectomy for Stage C Carcinoma of the Prostate	1991 meeting of the American Urological Association, June 91

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# **DETAIL SHEETS FOR PROTOCOLS**

**CLINICAL PSYCHOLOGY SERVICE**

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 90/050                      **Status:** Completed

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**Title:** Sensitivity of the Screening Test for the Luria-Nebraska Neuropsychological Battery-Adult (ST-LNNB-A) to Cognitive Deficits

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**Start Date:** 03/16/90                      **Est. Completion Date:** Mar 91

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**Department:** Clinical Psychology                      **Facility:** MAMC

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**Principal Investigator:** Alberta Klaus-Hagen, Ph.D.

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**Associate Investigators:**                      LTC Kenneth A. Zych, MS  
Timothy S. Clark, Ph.D.

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**Key Words:** cognitive deficits, ST-LNNB-A

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$25.00	04/05/91

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Study Objective: To evaluate the sensitivity of the ST-LNNB-A in the identification of neurobehavioral dysfunction.

Technical Approach: Fifty adult patients referred to the Psychology Service for neuropsychological testing will receive a detailed clinical interview prior to the administration of any tests. They will then be administered the ST-LNNB-A by a psychometrician blinded to the patient's diagnosis and history. Subjects will be administered a full battery of neuropsychological tests, questionnaires, and personality instruments by a psychometrician blinded to the results of the ST-LNNB-A. The subject's total score on the ST-LNNB-A will be compared with the subject's scores on the Trails B, Tonal Memory, and RAVLT subtests of the Halstead-Reitan Battery. In addition, the sensitivity of the ST-LNNB-A will be compared with the sensitivity of the Halstead Impairment Index and the Dodrill Impairment Index. Further, the ST-LNNB-A total score will be compared with the neuropsychologist's impairment rating. Data will be analyzed using nonparametric statistics.

Progress: The study has been completed.

T.S. Clark, Ph.D., original PI.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/056		<b>Status:</b> On-going	
<b>Title:</b> Use of Psychometric Procedures in Assessing ADHD and the Effects of Stimulant Medication					
<b>Start Date:</b> 04/05/91			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Steven C. Parkison, MS					
<b>Associate Investigators:</b> Thomas A. Clinghan, M.D. CPT Robert A. Byrne, MS			LTC Thomas R. Babonis, MC LTC Patrick C. Kelly, MC		
<b>Key Words:</b> ADHD, psychometric procedures, stimulant medication					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To identify psychometric procedures sensitive to Attention-deficit Hyperactivity Disorder (ADHD) and the effects of stimulant medication used in the management of this disorder.

**Technical Approach:** Approximately 30 ADHD children and 30 normal controls will be enrolled. The ADHD children will be randomly assigned to be studied with or without medication. The interviewer will be blinded as to which group the child is in. Both control and ADHD children will be administered the Peabody Picture Vocabulary Test - Revised (a cognitive screening test), the Hand Movements and Mazes subtests, and the Stroop Word-Color Association Test. All of these tests except for the Peabody Test will be readministered approximately four weeks later. The medication status of the ADHD children will then be reversed and these children retested in the same manner as before so that the ADHD children are tested both with and without medication. Student's T test will be used to compare the ADHD (both on and off medication) and control groups. The T test will also be used for comparisons between the on and off medication performances of the ADHD group. Should there be a significant difference, an ANCOVA will be used to statistically control for this difference.

**Progress:** Twenty subjects have been tested. Results to date suggest that the Stroop Color Test is helpful in distinguishing ADHD children from normal children.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/049		<b>Status:</b> On-going	
<b>Title:</b> Establishment of Normative Data for Neuropsychological Instruments with a Military Population					
<b>Start Date:</b> 06/15/90			<b>Est. Completion Date:</b> Mar 91		
<b>Department:</b> Clinical Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Zych, MS					
<b>Associate Investigators:</b> Timothy S. Clark, Ph.D.			Alberta Klaus-Hagen, Ph.D.		
<b>Key Words:</b> neuropsychological instruments, military population					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$200.00		04/05/91	

**Study Objective:** To collect normative data on standardized neuro-psychological instruments using military personnel without significant neurological or psychiatric histories.

**Technical Approach:** One hundred adult subjects will be studied. Each subject will be administered the following tests: Beck Depression Inventory (self-report of depressive symptoms), Benton Temporal Orientation Test (general orientation), Controlled Oral Word Association Test (verbal fluency, semantic memory), D2 (concentration), Grooved Pegboard (fine motor coordination and speed), Halstead-Reitan Neuropsychological Battery --Dodrill's Revision (integrated battery of neuropsychological measures), Item 99 from Luria-Nebraska Neuropsychological Battery (visual-spatial skills), Memory Functioning Questionnaire (self-report checklist of incidence and types of concentration and memory problems), Paced Auditory Serial Addition Task (speed of information processing), Rey Complex Figure (visual-spatial perception), Serial Calculations (concentration, numerical reasoning), Sickness Impact Profile (self-report questionnaire of impact of illness on social, vocational, and emotional functioning), and Symbol Digit Modalities (response speed, attention, visual-motor coordination). Data will be analyzed using appropriate descriptive statistics and the data will be used to assist in interpretation of test findings of neurologic patients.

**Progress:** The study was not implemented in FY 90 due to the departure of Dr. Clark. Dr. Zych was appointed in FY 91 to replace Dr. Clark, but the project has not been started due to a shortage of staff due to Operation Desert Storm.

Dr. Clark original principal investigator

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF CLINICAL INVESTIGATION**

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/019                      **Status:** On-going

**Title:** Mechanisms for Sex-Hormone-Binding-Globulin (SHBG) Regulation of Prostate Carcinoma

**Start Date:** 11/16/90

**Est. Completion Date:**

**Department:** Clinical Investigation

**Facility:** MAMC

**Principal Investigator:** CPT Rita C. Hoop, MS

**Associate Investigators:**

MAJ Curtis J. Hobbs, MC  
CPT Brenda K. Bell, MC  
Geoffrey Hammond, M.D.

LTC John A. Vaccaro, MC  
COL Stephen R. Plymate, MC  
Steve Loop, B.S.

**Key Words:** cancer:prostate,SHBG:regulation

**Accumulative**

**MEDCASE Cost:**

\$0.00

**Est. Accumulative**

**OMA Cost:**

\$0.00

**Periodic Review:**

//

**Study Objective:** To identify and characterize the regulatory factors for SHBG and SHBG-like mRNAs present in human prostate carcinoma cell lines, to determine the genomic alterations in the cell lines of the SHBG gene and how they may relate to or indicate changes in the p53 gene, and to screen a number of primary prostate cancers with probes developed for the mRNA species in order to determine the prevalence with which the genetic rearrangements are present in prostate cancers.

**Technical Approach:** In this project, the investigators will focus on the production and action of SHBG and SHBG-related peptides in human prostate cell lines. First, the factors that regulate the expression of SHBG messenger RNA (mRNA) will be studied. Cell lines derived from prostate cancers will be used, with the HepG2 (a liver cancer cell line) used as a positive control. All cells will be grown to 80% confluence in culture media containing 10% fetal calf serum (FCS). The cells will then be washed and media replaced with FCS free media. The regulatory hormones to be added are thyroxine, estradiol, dihydrotestosterone, testosterone, insulin, and epidermal growth factor. After 72 hours, the cells will be harvested and the RNS extracted. Specific expression of mRNA for SHBG will be determined by Northern blot analysis. The sequence of the SHBG mRNA species will be determined to determine if alternate splicing or genetic rearrangements have occurred. Complementing the sequence analysis, the RNAase protection assay will be used to determine the length of the larger SHBG mRNA species and potential changes in the exon structure. Western blot analysis of conditioned media and cell extracts will be used to determine if these cells are producing authentic SHBG from the mRNA detected in the Northern analysis. Southern blot analysis will be used to study the genomic DNA in these cell lines. Restriction enzymes will be used to obtain fragments averaging 80 kb. The SHBG gene is located close to the p53 oncogene which is often rearranged in cancer cells. Southern analysis will give an indication if the SHBG gene is also abnormal in these cancer cells. In addition to studying the DNA from the cell lines, DNA will be evaluated from primary prostate tumors for potential alterations.

**Progress:** Northern (RNA) blot analysis revealed that all of the prostate carcinoma cell lines tested express a unique set of SHBG-related transcripts. Work is in progress to characterize the nature of these transcripts. Western (protein) blot analysis revealed that all cell lines tested, except for ALVA-41, express some form of the p53 tumor suppressor product, although the p53 gene is transcribed more actively in the DU-145



cells than in the other prostate lines or in HepG2 human hepatoma cells. Finally, genomic Southern (DNA) blot analysis demonstrated that the SHBG gene may be rearranged in the DU-145 cell line relative to HepG2. These data suggest that mutation of the p53 gene contributing to transformation of the prostate may also affect normal expression of SHBG, thus causing autocrine production of a high affinity steroid binding protein which may be associated with cell growth.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/100	<b>Status:</b> On-going
<b>Title:</b> Thyroid Size in Children and Adolescents		
<b>Start Date:</b> 08/21/87	<b>Est. Completion Date:</b> Nov 91	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Dan C. Moore, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> thyroid size, adolescents		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 09/16/88

**Study Objective:** To establish normal dimensions  $\pm$  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:** 219 patients have been entered (41 in FY 91). Patient enrollment is continuing.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/091		<b>Status:</b> On-going	
<b>Title:</b> A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp(6)-Des-Gly(10)-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing Factor (Deslorelin)					
<b>Start Date:</b> 08/17/90			<b>Est. Completion Date:</b> Nov 92		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> precocious puberty, deslorelin, LH					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		08/02/91	

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

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

**Progress:** Three patients have been entered (all in FY 91). One patient dropped out due to the desire not to take shots. Therapy has been effective in blocking progression of puberty in the two patients who have returned for follow-up appointments.

## DETAIL SUMMARY SHEET

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

**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 .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:** The initial phase of the project has involved perfecting the chromatofocusing technique and increasing the sensitivity of the RIA to detect very low concentrations of LH. The actual samples will be run when this process is complete.

## DETAIL SUMMARY SHEET

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

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

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

**Progress:** Thyroid measurement and ultrasound have been accomplished on 37 patients. No data analysis has occurred. Two patients have had minor abnormalities on ultrasound that were not expected by examination.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/024	<b>Status:</b> Completed
<b>Title:</b> Chemical Characterization of Sex Hormone Binding Globulin (SHBG)		
<b>Start Date:</b> 01/16/87	<b>Est. Completion Date:</b> Jun 87	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Katherine H. Moore, MS		
<b>Associate Investigators:</b>		
COL Carl Stones, MC	Philip H. Petra, Ph.D.	
MAJ Charles J. Hannan, MC	LTC (P) Robert F. Jones, MS	
COL Stephen R. Plymate, MC	Louis A. Matej, B.S.	
<b>Key Words:</b> SHBG:Structure		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$814.00	<b>Periodic Review:</b> 10/21/88

**Study Objective:** To determine the factors that regulate SHBG production and its structure and the effects of changes in structure on its steroid binding properties.

**Technical Approach:** Blood from second trimester pregnancy plasma will be purified and amino acid sequencing will be performed. Once sequencing has been completed, the appropriate cDNA probe will be obtained from a cDNA library obtained from Hep G2 cells. The cDNA probe will be tritiated and the studies using insulin, growth hormone, prolactin, estradiol, and testosterone will be performed on the Hep G2 cell cultures with subsequent cDNA hybridization. When these experiments are complete, media will be assayed by RIA or DCC binding assay for SHBG, and RNA will be extracted from the cells. Basically, the cells will be placed in freshly constituted homogenization buffer and disrupted using a polytron homogenizer. The extracts will be left overnight at 4C C and then centrifuged at 2000g for 30 mins. The precipitate pellet will be washed and dissolved in 50 mM tris buffer pH 5 containing 10% SDS and extracted twice with phenylmethylchloride. RNAs will then be precipitated with ethanol dissolved in 10% SDS. Following this, northern blot analysis using 10 mg of RNA will be performed by electrophoresis on 1% agarose formaldehyde gels. Following northern blot analysis, the RNA will be hybridized using either 3H or 32P labelled cDNA probe. After hybridization has occurred, autoradiography will be performed using Kodax XR5 film and quantitation of mRNA synthesis will be determined using scanning densitometer.

**Progress:** This study has been completed.

**PUBLICATION:** Plymate, et al: Effects of Sex Hormone Binding Globulin (SHBG) on Human Prostatic Carcinoma. J Steroid Biochemistry and Molecular Biology 40:833, 1991.

**PRESENTATION:** Endocrine Society Meeting, Seattle, WA, June 1989

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/043	<b>Status:</b> On-going
<b>Title:</b> Sex Hormone Binding Globulin (SHBG): Carbohydrate Function and Characterization		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> May 92	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Katherine H. Moore, MS		
<b>Associate Investigators:</b> MAJ John E. van Hamont, MS Louis A. Matej, B.S.		Philip H. Petra, Ph.D. CPT Robert M. Tuttle, MC
<b>Key Words:</b> SHBG:carbohydrate function,SHBG:characterization,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

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

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

**Progress:** The investigators have been able to show that rabbit SHBG, treated with N-Glycanase (an enzyme which removes asparagine linked sugars) did not change the binding affinity of rabbit SHBG for androgens. Of particular interest in this study was the determination of sialic acid content, as an increased level of this sugar is associated with increased serum half-life. Carbohydrate analysis revealed that the carbohydrate content, including levels of sialic acid of male and pregnant female SHBG was not different. This indicates that yet another mechanism is involved in the increased levels of SHBG seen in pregnancy.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/109	<b>Status:</b> On-going
<b>Title:</b> Characterization of Equine Inhibin: Sequence Analysis and Carbohydrate Composition		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Oct 92	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Katherine H. Moore, MS		
<b>Associate Investigators:</b> Kristine M. Wiren, Ph.D.		
<b>Key Words:</b> equine inhibin, sequence, carbohydrate composition, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$8870.00	<b>Periodic Review:</b> 06/14/91

Study Objective: To purify equine inhibin from follicular fluid, to compare specific activity and carbohydrate chemistry to inhibin from other species, and to determine the sequence of equine inhibin and determine its homology to other known sequences.

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

Progress: Messenger RNA has been isolated from horse testis for the purpose of preparing cDNA and determination of the deduced sequence for equine inhibin alpha and beta subunits. Initially, we planned to isolate the mRNA from horse ovaries, but the tissue could not be obtained fresh enough and all the mRNA was degraded. The testes were collected in collaboration with local veterinarians and immediately placed on dry ice. In the laboratory, the tissue was pulverized while still frozen and the mRNA isolated by acid guanidinium thiocyanate-phenol-chloroform extraction. Consensus oligonucleotide probes for inhibin subunits were synthesized based on the known sequences of inhibin alpha and beta subunits. These probes will be used to identify positive clones, which will be sequenced using the Sanger dideoxy method for DNA sequencing.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/020	<b>Status:</b> Completed
<b>Title:</b> Studies on the Production and Glycosylation of SHBG by HepG2 Cells using 35s-Labelled Methionine		
<b>Start Date:</b> 04/15/88	<b>Est. Completion Date:</b> Jun 89	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Stephen R. Plymate, MC		
<b>Associate Investigators:</b>		
MAJ Karl E. Friedl, MC	MAJ Charles J. Hannan, MC	
Benito Que, M.D.	Philip H. Petra, Ph.D.	
Louis A. Matej, B.S.	Thomas Kettler, M.T.	
James R. Wright, M.T.		
<b>Key Words:</b> SHBG:production,Hep G2,Methionine,steroid,peptide		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$602.00	10/21/88

**Study Objective:** To determine the effects of previously identified steroid and peptide hormones which have been shown to affect sex hormone binding globulin (SHBG) levels, *in vivo* and *in vitro* in the Hep G2 cell culture, on production, secretion, and glycosylation of SHBG and to determine the effects of these agents on production of the messenger ribonucleic acid (mRNA) for SHBG in this cell culture system.

**Technical Approach:** Hep G2 cells will be grown to confluence in 25 cm<sup>2</sup> flasks. Confluent cells will then be either continuously labelled with 35S-methionine for 4 hours or pulse labelled for 10 minutes in methionine free media. In the case of the pulse labeling, the label will be chased with a 20,000 fold excess of methionine for three hours following the initial pulse. Flasks will be pretreated with either basal media, T<sub>4</sub>, estradiol, testosterone, or insulin in the concentrations which we have shown in a previous study to have the greatest stimulatory or inhibitory effects on SHBG production by these cells. Following the initial labeling of the cells with 35S methionine, both the supernate and cell lysate will be subjected to specific immunoprecipitation. Following the immunoprecipitation, cells from these same flasks that have not been lysed will be lysed and subjected to dot-blot analysis using a specific cDNA probe from a Hep G2 library for the SHBG mRNA. When all data have been collected, differences in synthesis versus processing will be assessed between the various treatments using the ANOVA method.

**Progress:** This protocol has been completed. No further work was done during FY 91. Two papers have been published and an additional paper has been submitted for consideration for publication. A paper was presented at the 8th International Congress on Hormonal Steroids, The Hague, Netherlands, September 1990.

**PUBLICATION:** Plymate, Hoop, Jones, Matej: Regulation of Sex Hormone-Binding Production by Growth Factors. *Metabolism* 39:967, 1990.

**PUBLICATION:** Plymate, Matej, Jones, Friedl: Inhibition of Sex Hormone-Binding Globulin Production in the Human Hepatoma (Hep G2) Cell Line by Insulin and Prolactin. *JCEM* 67:460, 1988

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/076                      **Status:** Terminated

**Title:** Clinical and Molecular Investigations in Men with Decreased Spermatogenesis and A varicocele

**Start Date:** 05/18/90                      **Est. Completion Date:** Apr 95

**Department:** Clinical Investigation                      **Facility:** MAMC

**Principal Investigator:** COL Stephen R. Plymate, MC

**Associate Investigators:**  
LTC John A. Vaccaro, MC                      LTC (P) Robert E. Jones, MS  
Kristine M. Wiren, Ph.D.                      CPT Rita C. Hoop, MS

**Key Words:** spermatogenesis, varicocele

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	05/03/91

**Study Objective:** To study the structure of the Y chromosome in relation to impaired spermatogenesis and to investigate how a varicocele affects testicle function at a physiological and molecular level in men.

**Technical Approach:** This study will be a collaborative effort with the University of Washington and American Lake VA Medical Center. The investigators propose to determine possible defects in the control of spermatogenesis at the DNA level through the use of a set of DNA probes which detect abnormalities on the Y chromosome that have been associated with decreased sperm production as well as other aspects of the male phenotype. Using a series of DNA probes for the Y chromosome, a subpopulation of infertile males (selected because of azoospermia or severe oligospermia that has been shown to be associated with deletions of the Y chromosome) will be screened. In a homogeneous population of men with decreased sperm production, as determined by the presence of a palpable varicocele, the investigators will determine by clinical and *in vitro* studies if an abnormality in Sertoli cell function is present and how this may relate to abnormal sperm function. The clinical studies are designed to characterize testis responsiveness, and entail the response of the testes to gonadotropin stimulation measured by inhibin and testosterone output. The *in vitro* studies will characterize gene expression. The analysis will be further extended to explore the relationship of temperature as a mechanism of injury of a varicocele by determining the effect of mild heat stress on gene expression. Blood samples will be collected for Y-chromosome-specific DNA analysis from the following groups of men: 150-200 azoospermic and severely oligospermic males, 125-175 infertile men with a varicocele, 240-280 normal men, and 125-175 fertile men with a varicocele.

**Progress:** This study was terminated because funding was delayed and the principal investigator was retiring from the Army. No patients were entered.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/078	<b>Status:</b> Terminated
<b>Title:</b> Immunohistochemical Detection of Phosphotyrosine as a Predictor of Recurrence and Long-Term Survival in Breast Cancer Patients		
<b>Start Date:</b> 10/20/89	<b>Est. Completion Date:</b> Jul 90	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ John E. van Hamont, MS		
<b>Associate Investigators:</b>		
CPT Leonard N. Howard, MC	MAJ Ismail Jatoi, MC	COL James E. Kelley, MC
COL Preston L. Carter, MC		
<b>Key Words:</b> cancer:breast,survival,phosphotyrosine		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1150.00	

**Study Objective:** To determine whether the immunohistochemical detection of phosphotyrosine can serve as a predictor of early recurrence or death in patients with breast cancer.

**Technical Approach:** This will be a retrospective study of approximately 100 patients diagnosed with breast cancer between 1973 and 1978 at Madigan Army Medical Center. Paraffin blocks of breast cancer tissue obtained from the Department of Pathology will be cut and immunohistochemical techniques applied to detect phosphotyrosine and EGF receptor status. One group of patients with phosphotyrosine positive tumors and another group with phosphotyrosine negative tumors will be studied to determine recurrence and survival at 5 years and 10 years. The clinical course of the patients is documented by the Madigan Tumor Registry. Estrogen/ progesterone receptor status, lymph node status, EGF receptor status, and phosphotyrosine status will be compared as predictors of recurrence and long term survival. A pathologist will rate the intensity of the immunohistochemical staining for phosphotyrosine and EGF receptor. To avoid bias in the interpretation of the staining, the patients' names will be excluded and the paraffin blocks will be coded by numbers only.

**Progress:** This protocol was terminated upon the departure of MAJ van Hamont because no further breast samples had been obtained by the investigators. In the previous year, procedures for peroxidase staining of phosphorylated tyrosine and C-Neu in paraffin-mounted tissue sections were established and evaluated using an A431 cell line exposed to recombinant derived epidermal growth factor as a positive control. Paraffin sections from eight breast cancer patients were obtained for immunohistochemical detection of the phosphotyrosine and C-Neu markers.

Original PI: CPT Ismail Jatoi, MC

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF DENTISTRY**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/039	<b>Status:</b> Terminated
<b>Title:</b> Pulpotomy in the Primary Dentition: A Clinical Evaluation of Two Techniques		
<b>Start Date:</b> 03/18/88	<b>Est. Completion Date:</b> Mar 91	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Gerald R. Aaron, DC		
<b>Associate Investigators:</b> John M. Davis, D.D.S, M.S.D.		Peter K. Domoto, D.D.S., M.P.H. MAJ James R. Allinder, DC
<b>Key Words:</b> pulpotomy, technique comparison		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$100.00	04/05/91

**Study Objective:** To compare the clinical success rates of the electrosurgical pulpotomy and formocresol pulpotomy techniques and to describe the various radiographic and clinical findings and advantages and disadvantages associated with each technique.

**Technical Approach:** Subjects 2-12 years who have two or more carious primary teeth which are indicated for a vital pulpotomy will have a routine dental examination to include routine radiographs. Selection of teeth will be based on dental history, clinical appearance, and bite-wing and periapical radiographs. Individual teeth will be randomly assigned to either the electrosurgical or the formocresol technique. Randomization will be determined depending on the number and location of the quadrants involved. Teeth within the same quadrant will be given the same treatment since it would be difficult to rule out crossover effects in the same quadrant. Treatments within the same patient will be compared only when they occur in different quadrants. Dental and post-operative histories will be recorded. A clinical examination, including routine periapical radiographs, will be performed at 6, 12, and 18 months following initial treatment. Clinical success will be determined by absence of abnormal radiographic or clinical findings and the maintenance of the treated teeth in a normal functional relationship in the dental arch. The data from this study will be incorporated with data from two parallel studies being done in the Tacoma area (450 patients total). Since responses to treatment within the same patient can be expected to be more similar than for teeth from different patients, the basic unit of analysis will be the patient, rather than individual teeth. If two teeth are treated in the same patient, McNemar's test for correlated proportion will be used for statistical analysis. If more than two teeth are treated, the Mantel-Haenszel test for stratified analysis will be used.

**Progress:** This was a collaborative study with the University of Washington. The investigators at the University of Washington terminated the study due to slow accrual of subjects and the investigators at Madigan did likewise.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/063	<b>Status:</b> On-going
<b>Title:</b> Survey of Drugs Utilized by Pediatric Medical Patients and Their Potential Dental Implications		
<b>Start Date:</b> 05/03/91	<b>Est. Completion Date:</b> Jan 92	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Charles R. Brown, DE		
<b>Associate Investigators:</b> LTC Herschel L. Jones, DE		
<b>Key Words:</b> drug survey, pediatric patients, dental implications		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To evaluate the potential dental effects of the active and inactive ingredients in medications requiring multiple, long term dosages taken for chronic medical conditions by children ages 6 months through 12 years and to determine the potential hard and soft tissue dental effects that should be considered during the dispensing of these drugs.

**Technical Approach:** The proposed research project is primarily a descriptive study based on a review of medications taken by patients treated in the Pediatric Clinic. Information will be derived from medical and dental records. Type of disorder and type, dosage, form (tablet, liquid, etc), physical characteristics (acidic, basic, etc), active/inactive ingredients, and length of time medications have been used will be recorded. Possible dental implications of the active and inactive ingredients will be listed. If after viewing the medications being used possible dental implications are found, further investigations will be conducted by reviewing the comprehensive dental examinations portion of the clinical record of the patients in the Pediatric Dentistry Department. Findings will be assessed to determine if these implications bear out.

**Progress:** Approximately 500 dental records have been reviewed and condition or disease has been documented and medications listed.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/059	<b>Status:</b> On-going
<b>Title:</b> The Influence of Prophylactic Administration of Intravenous Ondansetron on Post Operative Nausea and Vomiting and Length of Stay in the Post Anesthesia Care Unit		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> May 92	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Cecil R. Dorsett, DC		
<b>Associate Investigators:</b>		
COL Jerre M. Griffin, DE	MAJ Frederick W. Burgess, MC	MAJ Charles R. Weber, DC
Mark J. Bergin-Sperry, RN		
<b>Key Words:</b> nausea,vomiting,prophylaxis,ondansetron,length of stay		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

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

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

**Progress:** Twenty patients have been evaluated. Of the patients evaluated thus far, it appears that the administration of ondansetron does decrease the incidence of post-operative nausea and vomiting. There has been no increase in the time spent in the recovery room and there have been no adverse reactions.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/057	<b>Status:</b> Completed
<b>Title:</b> The Reliability of Cephalometric Evaluation in Genioplasty: A Retrospective Study		
<b>Start Date:</b> 05/19/89	<b>Est. Completion Date:</b> Apr 90	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Carlton J. Floyd, DC		
<b>Associate Investigators:</b> COL Douglas B. Boyd, DC		
<b>Key Words:</b> genioplasty, cephalometric evaluation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 05/03/91

**Study Objective:** To retrospectively determine the frequency of the genioplasty procedure associated with mandibular and maxillary procedures performed at MAMC, to determine the reliability of diagnostic and prediction cephalometric evaluation currently in use in the Oral and Maxillofacial Training Program, and to assess the extent and long term stability of the skeletal and soft tissue changes of the procedures performed.

**Technical Approach:** The records of 30 subjects, ages 16-50, will be reviewed for chief complaint, physical exam, admission diagnosis, primary operation performed, type of genioplasty performed, and complications. Preoperative, prediction, and postoperative cephalograms will be reviewed and the following cephalometric analyses performed: anterior-posterior position of hard tissue chin or pogonion preoperatively, anterior-posterior position of hard tissue chin immediately postoperatively, anterior-posterior position of hard tissue chin 6 and 12 months postoperatively, anterior-posterior position of soft tissue chin or pogonion preoperatively, and anterior-posterior position of soft tissue pogonion at 6 and 12 months postoperatively. Immediate postoperative soft tissue analysis will not be performed due to edema. The presurgical and postsurgical tracing of the body of the symphysis of the mandible will be superimposed and the net hard tissue and soft tissue changes calculated. Measurements will be based on a coordinate grid system. The surgical advancement and postoperative changes will be related to soft tissue changes by calculation of mean ratio equations. Regression equations will be used to evaluate the relationship between the dependent (changes in the soft tissue skin) and independent variables (surgical advancement of hard tissue pogonion, the percent of osseous relapse, the time span since surgery, and the net advancement of hard tissue). Patients will be reported by diagnostic group and not individually.

**Progress:** Twenty subjects were entered in the study. The protocol has been completed and the final copy of the paper is being rewritten.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/044		<b>Status:</b> Completed	
<b>Title:</b> Clinical Evaluation of Primary Dentition Wear and Temporomandibular Joint Dysfunction Signs					
<b>Start Date:</b> 03/16/90			<b>Est. Completion Date:</b> Feb 91		
<b>Department:</b> Dentistry			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Curtis D. Goho, DC					
<b>Associate Investigators:</b>			LTC Herschel L. Jones, DE		
<b>Key Words:</b> dentition wear, temporomandibular joint dysfunction					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 04/05/91

**Study Objective:** To evaluate the correlation between dental wear in the primary dentition and clinically observable signs of temporomandibular joint dysfunction.

**Technical Approach:** Study and control groups will be randomly selected from the population examined as a routine part of the dental health month screenings provided by the Dental Activity and from the population examined as a routine part of dental care in the Pediatric Dentistry Residency Program. The control group will show no sign of dental wear into the dentin. The study group will show dental wear into the dentin. Clinical examinations will be done by multiple observers, trained in examination procedures, and evaluated for inter-rater reliability. Examination will consist of gentle palpation of the temporalis, masseter, and sternocleidomastoid muscles with measurement of maximum opening of the mouth and any deviation of the mandible during opening, gentle palpation of the area overlying the temporomandibular joint during opening and closing to detect pain, auscultation for noises (clicks, pops, grinding) without the aid of a stethoscope, and examination of the teeth for wear facets in accordance with an established grading system. The findings will then be compiled and a statistical evaluation for correlation, utilizing the chi-square test, will be done to determine significant associations between variables.

**Progress:** The protocol has been completed, 97 subjects were studied. Analysis of the data showed no correlation between dental wear and temporomandibular joint dysfunction. A paper has been accepted by Pediatric Dentistry.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/045	<b>Status:</b> Completed
<b>Title:</b> Prevalence of Abnormal Oral Findings and the Dental Needs in a Selected Patient Population with Cerebral Palsy		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Nov 90	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Cynthia M. Guzman, MC		
<b>Associate Investigators:</b> COL Gerald R. Aaron, DC		
<b>Key Words:</b> cerebral palsy, dental needs		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$200.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine the prevalence of enamel hypoplasia attrition, caries, and malocclusion in patients with cerebral palsy and to survey their dental needs.

**Technical Approach:** Thirty subjects, ages 4-18 years of age, with a confirmed diagnosis of cerebral palsy will be studied. Parents will complete a prestudy questionnaire to assess their knowledge of the existence of dental care for the cerebral palsy patients. The dental officer will complete a dental screening exam to determine the dental needs of these patients. No control group will be utilized, but the results will be reported based on race, age, and gender of the subjects. Descriptive statistical methods will be used to analyze the data.

**Progress:** The study has been completed. 23 subjects were studied. Results indicated that attrition was most prevalent amongst spastics and dyskinetics. Hypoplasia was found in the central incisors and cusps of first permanent molars. Caries incidence was low and a positive correlation between spastic cerebral palsy and Class II malocclusion was demonstrated.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/037	<b>Status:</b> On-going
<b>Title:</b> The Presence of Human Immunodeficiency Virus (HIV) in the Saliva of Pediatric Acquired Immunodeficiency Syndrome (AIDS) Patients		
<b>Start Date:</b> //	<b>Est. Completion Date:</b> Feb 92	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Jerald K. House, DE		
<b>Associate Investigators:</b> Dr. Sandra Burchett, M.D. James R. Wright, M.T.		LTC Paul E. Kittle Jr., DE MAJ John E. van Hamont, MS
<b>Key Words:</b> HIV, AIDS, pediatric patients		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To evaluate the presence or absence of HIV in the saliva of pediatric AIDS patients and to evaluate possible etiologic factors that affect its concentration in the oral cavity.

**Technical Approach:** Approximately 20 children, birth to 13 years of age, who have been diagnosed as having AIDS, will be entered in the study. An oral examination will be conducted to establish a rating for each patient's oral hygiene and gingival health, using the gingival index established by Loe and Silness (1967). Whole saliva samples will be collected from each patient by having the patient either chew a small piece of paraffin and expectorate into a sterile collection tube or by sterile suction in infants or preoperative children. Parotid saliva will then be collected with a parotid collection cup. Salivary samples will be analyzed by ELISA to determine the presence of HIV antigen, by reverse transcriptase assay to establish viability, and by polymerase chain reaction to quantify the virus. The results of the laboratory tests for each of the samples and sample sites will be correlated with the patient's age, sex, disease stage, oral hygiene, gingival health, and oral conditions.

**Progress:** Twenty subjects have been entered and samples collected. The polymerase chain reaction assay has been tested and confirmed.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/032	<b>Status:</b> On-going
<b>Title:</b> An Assessment of Parental Desire to Accompany Their Child in the Dental Operatory		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Feb 91	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Herschel L. Jones, DE		
<b>Associate Investigators:</b> LTC Paul E. Kittle Jr., DE		
<b>Associate Investigators:</b> COL Gerald R. Aaron, DC		
<b>Key Words:</b> dental, parental desire		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To evaluate whether or not parents prefer to be present in the dental operatory with their child, to determine which procedures they prefer to be present for, to determine if the age of the child has an impact on parental preference, to determine if there is a change in parental preference over the course of multiple appointments, and to evaluate if a reported history of negative parental dental visits is associated with a desire to accompany the child.

**Technical Approach:** The parents of approximately 75 children who have had no prior dental treatment and require at least one operative appointment will be studied. Parents of a child over the age of six or with a medically compromised child will be excluded. Parents will fill out an intake questionnaire to determine: if they desire to accompany the child into the operatory and the reasons for their decision, the age and educational level of the parent(s), the child's age, sex, and family member number, if the parent(s) were given a choice to accompany other children into the operatory and, if so, did the parent(s) accompany the child, the dental experiences with other children (positive or negative), and the parents opinions as to the effect of their presence on the child in the operatory. At the completion of the final appointment, the parent(s) will complete an out-take questionnaire to determine on which procedures/appointments they accompanied the child and the reasons why they accompanied the child on all, some, or none of the appointments.

**Progress:** Six patients were entered in the study in FY 91 for a total of eight entries. Finding patients to meet the inclusion criteria of "no prior dental treatment prior to referral" has been much more difficult than the investigators anticipated.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/068		<b>Status:</b> On-going	
<b>Title:</b> Parental Recall of Informed Consent for General Anesthesia Dental Procedures					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Feb 91		
<b>Department:</b> Dentistry			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Paul E. Kittle Jr., DE					
<b>Associate Investigators:</b> LTC Herschel L. Jones, DE			COL Gerald R. Aaron, DC		
<b>Key Words:</b> informed consent,dental					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		05/03/91	

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

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

**Progress:** Thirty-five patients were enrolled in the study in FY 91.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/038	<b>Status:</b> On-going
<b>Title:</b> The Effect of Dentists' Attire on Initial Anxiety Levels in Children		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Feb 92	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Lawrence W. Meadors, DE		
<b>Associate Investigators:</b> COL Gerald R. Aaron, DC		
<b>Key Words:</b> dentistry, anxiety levels, dentist attire		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

Study Objective: To determine if a dentist's attire has any effect on the initial level of a child's anxiety when presenting for dental examination or dental treatment.

Technical Approach: Subjects: 80 children aged 2-4 years, 80 children aged 5-6 years, and 80 children aged 7-9 years.

Two population groups will be studied: Group I will be children presenting to the Pediatric Dental Program for initial evaluation who have not had any previous dental treatment other than examination. Group II will be patients currently being treated in the program who have had at least 4 previous restorative appointments and are returning for recall evaluation. The two groups will be represented equally in the age groupings. Color photographs will be made of a single male dentist wearing: (a) Army Class B uniform and long white clinic coat, (b) surgical scrubs, (c) Army battle dress uniform, (d) open collar shirt and casual pants, (e) clown costume without facial makeup. The dentist will be wearing gloves, mask, and safety glasses. There will be three diagrammatic faces at the bottom of each photo: a smiling face, a straight face, and a frowning face. The subjects will be asked to look at each photo and point to the face that tells how the photo makes them feel. A score of +2 will be recorded for each smiling face, a 0 for each straight face, and a -2 for each frowning face. Association between variables will be tested using ANOVA, association between the two groups will be tested using the t-test at a level of significance ( $p < 0.05$ ).

Progress: Forty children have been entered in the study.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/046	<b>Status:</b> Completed
<b>Title:</b> The Fearful Pediatric Dental Patient's Response to Desensitization Techniques		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Jan 91	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Adoldina M. Polk, DS		
<b>Associate Investigators:</b> MAJ Steven C. Parkison, MS		LTC Paul E. Kittle Jr., DE
<b>Key Words:</b> dental techniques, desensitization		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To evaluate whether there is a reduction in a child's fear at the dental restorative appointment when desensitization techniques are performed before treatment.

**Technical Approach:** The study population will consist of 30, six to ten year old children who have had at least one unsuccessful dental appointment due to apprehensiveness/fear. Group 1 will undergo a desensitization session consisting of filmed modeling (child visit to the dentist for a restorative procedure) and coping skills (breathing relaxation skills, pleasant imagery, calming self-talk). Group 2 will undergo a desensitization technique involving filmed modeling, coping skills, and procedural and sensory information. These children will view the dental instruments used for a restorative procedure and a mock dental procedure using a doll/dentiform will be conducted. Each session will be composed of a group of five children and will be conducted 1-2 days before the treatment appointment. The treating dentist will be unaware of the desensitization method that was used. The children will be videotaped at the restorative treatment appointment and multiple trained pediatric dental raters will view the videotape and submit a behavioral analysis grade for each child. A standardized, accepted clinical behavioral scale will be used to evaluate behavior categories and interrater reliability will be performed. Data will be analyzed by a non-parametric test of differences between groups, based on the behavioral scale.

**Progress:** This protocol has been completed. Approximately 30 subjects had been anticipated, but the investigators were able to obtain only nine. The following inferences were made from the data available: anxiety and behavior are directly related. Some patients were afraid of things other than the dental procedure, such as choking. Social issues also affected anxiety. Dentists should not assume that disruptive behavior is because of fear of the dental procedures, exclusively. Eight patients were treated successfully with no sedation.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/081	<b>Status:</b> On-going
<b>Title:</b> Determination of Optimum Dose and Schedule of Intravenous Dexamethasone for Prevention of Postsurgical Edema After Orthognathic Surgery		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Jul 91	
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Charles R. Weber, DC		
<b>Associate Investigators:</b> COL Douglas B. Boyd, DC		
CPT Michael C. Daines, MC		
<b>Key Words:</b> orthognathic surgery, edema: prevention, dexamethasone: optimum dose		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$780.00	05/03/91

Study Objective: To determine the most effective dose and schedule for using intravenous dexamethasone for the prevention of postsurgical edema following orthognathic surgery.

Technical Approach: Thirty patients will undergo the usual preoperative workup for orthognathic surgery to include panoramic and cephalometric radiographs, mounted diagnostic dental casts, history, and physical examination. Standardized photographs will be obtained on the day prior to surgery, the evening of the day of surgery, and on postop days 1, 2, and 3 for measurement of edema, using a modification of the system of Hooley and Francis. Erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) specimens will be obtained the day prior to surgery, at 1800 hours on the day of surgery, and at 0600 hours on postop days 1, 2, and 3. The patients will be randomly assigned in a double-blind manner to no dexamethasone (control), dexamethasone, 16 mg IVPB immediately preoperatively with no additional doses, or dexamethasone, 16 mg IVPB immediately preoperatively with additional doses of 8 mg IVPB every six hours for three doses. Edema measurements will be matched and correlated with ESR and CRP results. Results from the three experimental groups will then be compared to determine the optimum dose and schedule for administering dexamethasone to minimize postsurgical edema.

Progress: Sixteen patients were entered in the study in FY 91 for a total of 20 subjects.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/061		<b>Status:</b> On-going	
<b>Title:</b> Comparison of Induction and Recovery From Propofol-Nitrous Oxide versus Methohexital-Isflurane-Nitrous Oxide Anesthesia in Ambulatory Oral Surgery Patients					
<b>Start Date:</b> 07/12/91			<b>Est. Completion Date:</b> Apr 92		
<b>Department:</b> Dentistry			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Robert J. Wygonski, DC					
<b>Associate Investigators:</b> COL Douglas B. Boyd, DC		MAJ Frederick W. Burgess, MC COL Jerre M. Griffin, DE			
<b>Key Words:</b> anesthesia, induction, propofol-nitrous oxide, methohexital-isoflurane-nitrous oxide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

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

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

**Progress:** Eight subjects have been entered.

**DETAIL SHEETS FOR PROTOCOLS**

**ENVIRONMENTAL HEALTH AGENCY**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/071		<b>Status:</b> Completed	
<b>Title:</b> Pest Management Study No. 16-66-0531-91 (US Army Environmental Health Activity-West)					
<b>Start Date:</b> 06/14/91			<b>Est. Completion Date:</b> Aug 91		
<b>Department:</b> EHA			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Lester D. Hale, Ph.D.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Lyme disease,ticks,small mammals,flora,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To determine the potential for Lyme disease to become endemic at Fort Lewis and Yakima Firing Center.

**Technical Approach:** The Project Officer (Dr. Hale) will obtain as much information as possible concerning the status of Lyme disease at and around the Ft Lewis from the Preventive Medicine Officer, the Occupational Health Nurse, the Post Veterinarian, the Wildlife Biologist, the Environmental Science Officer, and Washington State and local health officials. Tick bite information will be obtained from Madigan Army Medical Center and health clinic records. Along with selected personnel from Ft Lewis and Madigan Army Medical Center, the Project Officer will collect information on the topography, flora, and fauna of the training areas at Fort Lewis. Then small mammals will be trapped and ear tissue biopsies will be taken. Any ticks on the animals will be collected. Also, tick drags will be conducted to collect ticks from vegetation, etc. The ticks will be identified to determine if any of the collected species have been reported to be vectors of Lyme disease. The ticks will be examined for *Borrelia burgdorferi*, the causative agent of Lyme disease, and the ear tissue biopsies will be cultured for *Borrelia burgdorferi*. A final report will be provided to the Commander concerning the potential for Lyme disease in the Ft Lewis area.

**Progress:** The protocol has been completed and a report is being printed. There was no evidence of *Borrelia burgdorferi* found in the 58 animals trapped.

# **DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF EMERGENCY MEDICINE**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/040	<b>Status:</b> Completed
<b>Title:</b> Evaluation of Cognitive Capacity After Administration of Intravenous Morphine		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> Aug 91	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Daniel M. Andress, MC		
<b>Associate Investigators:</b>		Steven A. Pace, MD
<b>Key Words:</b> cognitive capacity, morphine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if the cognitive capacity of healthy volunteer subjects is impaired after administration of a typical therapeutic dose of IV morphine sulfate.

**Technical Approach:** Thirty healthy adult volunteers will be randomly divided into three groups of 10. After initial evaluation including screening history and physical examination, the study drug will be administered. Group I will receive a placebo of IV normal saline prior to taking a cognitive capacity screening test and the Bender Gestalt Visual Motor Test. The tests will be repeated in four weeks to evaluate for potential test result improvement due to repetitive administration of the tests. Group II will receive the normal saline placebo prior to taking the tests and four weeks later, this group will receive 0.1 mg/kg of IV morphine sulfate prior to taking the tests again. Group III will receive 0.1 mg/kg of IV morphine prior to the first tests and normal saline prior to the tests repeated at four weeks. Paired T test analysis will be used to evaluate the results of the cognitive test evaluation for each patient who is acting as his own control between placebo and morphine infusion. Analysis of variance will be used to compare the three groups to study the potential improvement of results due to repetitive testing.

**Progress:** Thirty patients were studied. No cognitive differences were seen with or without morphine administration.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/062	<b>Status:</b> On-going
<b>Title:</b> The Physiologic Toll of Internship		
<b>Start Date:</b> 05/17/91	<b>Est. Completion Date:</b> Jun 92	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Janus D. Butcher, MC		
<b>Associate Investigators:</b>		
Mark S. Grajcar, MC	MAJ Wade A. Lillegard, MC	
Marilyn P. Johnson, MC	CPT Thomas W. Irvine, MC	
<b>Key Words:</b> internship, stress, physiologic toll		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To measure any change(s) in physical fitness parameters in a group of residents over the course of their first year Graduate Medical Education training, to follow changes in diet and exercise habits during the GME training period. These results will be compared with any observed change in physical fitness and scores on a depression screening tool will be followed and compared with other measurements.

**Technical Approach:** A sample of 50 subjects will be sought, not including any individuals with risk factors who will be screened out using the PAR-Q. Informed consent will be obtained, and the subjects will begin the study.

At the onset, demographic data will be collected, to include: marital status, number of children, state of origin, religion, and income level of the subject's parents. Four questionnaires will also be given: Harvard Alumni Study Questionnaire (HASQ) to quantify exercise behavior in the preceding months, Beck's depression scale, Hamilton's anxiety questionnaire, and a nutrition questionnaire. A lipid profile will be drawn.

Overall fitness level will be assessed using these measurements: VO<sub>2</sub>max, push-ups, sit-ups, grip strength, sit and reach technique (flexibility), skin fold (for body fat determination), FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub>, weight, resting heart rate, and blood pressure.

Data will be collected and normality assessed. Physiologic measurements will be evaluated by t-test or ANOVA where appropriate. The ordinal data, specifically the attitudinal surveys will be evaluated using the Wilcoxon rank sum test.

**Progress:** Forty eight subjects have been entered with initial exercise testing completed and two survey periods completed.

## DETAIL SUMMARY SHEET

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<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/025	<b>Status:</b> On-going
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**Title:** Evaluation of a Urine Pregnancy Test Kit in the Emergency Department

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<b>Start Date:</b> 01/18/91	<b>Est. Completion Date:</b> Jun 91
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<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC
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**Principal Investigator:** LCDR Laurence D. Conley

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<b>Associate Investigators:</b>	CPT William T. Hurley, MC
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**Key Words:** pregnancy test,urine,emergency room

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<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

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**Study Objective:** To accurately describe and evaluate the use of a urine beta human chorionic gonadotropin (BHCG) test kit in the Emergency Department and to determine if the test correlates with the clinical laboratory's qualitative serum BHCG assay.

**Technical Approach:** Approximately 300 female subjects who clinically require pregnancy testing in the Emergency Department to identify gestational problems such as ectopic pregnancy or various types of abortion will be entered in the study. Several simple urine test kits are advertised as useful in the Emergency Department. Studies evaluating these kits in previous studies have used trained laboratory personnel, not the nursing personnel who would utilize the kits in the Emergency Department. The Wampole Test Kit will be used in this study. A serum sample will be sent to the clinical laboratory for BHCG qualitative testing, a urine sample will be tested using the Wampole One-Step kit, and a urine sample will be tested using the urine dipstick with leukocyte esterase method. Exclusion criteria for samples will include leukocytes, bacteria, or bilirubin in the urine sample, hemolysis or bilirubin in the serum samples, dilute urine, patient use of medication such as pyridium, equivocal results in colorometric determination, and tests requiring a dilutional procedure. Results of the three tests will be compared for reliability using KAPPA statistics.

**Progress:** Patients are still being entered in the study. To date, 235 patients have been entered.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/020                      **Status:** Terminated

**Title:** Treatment of Obstructive Pulmonary Disease with Intravenous Magnesium Sulfate in the Emergency Department

**Start Date:** 02/16/90                      **Est. Completion Date:** May 90

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

**Principal Investigator:** CPT Jeffrey M. Cortazzo, MC

**Associate Investigators:** CPT Lee E. Payne, MC, USAF  
MAJ Bruce S. Grover, MC

**Key Words:** obstructive pulmonary disease, magnesium sulfate

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

**Study Objective:** To determine the therapeutic efficacy of intravenous magnesium sulfate infusion in emergency room treatment of acute exacerbation of chronic obstructive pulmonary disease.

**Technical Approach:** Subjects: 100 patients > 45 years, with a >10 pack-year history of cigarette smoking, history of chronic outflow obstruction with FEV<sub>1</sub> <70% of predicted or <60% of FVC, and acute exacerbation of COPD with several days of worsening dyspnea associated with increased cough and sputum. A spirometry will be performed to document the FEV<sub>1</sub> and FVC. Patients with a definitive history of asthma, hypotension, renal failure, lobar or segmental consolidation, or treated with methylxanthines in the emergency room will be excluded. Patients will have an IV heparin lock and complete blood count, serum theophylline and magnesium levels, and a chest x-ray will be done. They will then receive albuterol, 2.5 mg in 2 cc of normal saline, by nebulizer. The nebulizer will be repeated at 20 and 40 minutes. At the second nebulizer period, patients will be randomized to IV magnesium sulfate (0.5 mmol/min to equal 2 g total magnesium sulfate) or an IV placebo, given over 20 minutes. They will also receive methylprednisolone, 125 mg IVP, while receiving the second nebulizer treatment. Patients will be placed on cardiac and automatic blood pressure monitors, and deep tendon reflexes, respiratory rate, and spirometry will be assessed just prior to the second and third nebulizer treatments and at 60 minutes. Disposition and further treatment of the patients will be at the discretion of the treating physician. Patients who clear after one nebulized albuterol treatment will be excluded from data analysis. FEV<sub>1</sub>, PEF, respiratory rate, ED disposition (admission vs discharge), and subjective scores from a patient survey will be analyzed using ANOVA.

**Progress:** Approximately 60 patients were enrolled in the study. The study was terminated due to the small number of eligible patients and the very slow accrual rate.



DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/023                      **Status:** Completed

**Title:** A Comparison of the Efficacy of Intravenous Prochlorperazine and Metoclopramide as Pretreatment to Dihydroergotamine in the Treatment of Headaches

**Start Date:** 12/21/90                      **Est. Completion Date:** Apr 91

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

**Principal Investigator:** MAJ Robby M. Eaves, MC

**Associate Investigators:** Steven A. Pace, MD

**Key Words:** headache, prochlorperazine, metoclopramide, dihydroergotamine

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

**Study Objective:** To determine the relative efficacy of prochlorperazine and metoclopramide as initial treatment for headache and to determine which medication better potentiates dihydroergotamine (DHE) in a randomized double blind study.

**Technical Approach:** One hundred (100) patients, 18-61 years, presenting to the Emergency Room for headache who meet study criteria will be studied. Patients will be placed in a monitored bed for continuous cardiac and blood pressure monitoring and will complete a headache questionnaire and a linear pain scale. Patients will be randomized to either Group A (10 mg IV prochlorperazine) or Group B (10 mg IV metoclopramide). A linear pain scale will be obtained at 30 minutes prior to administration of DHE 0.75 mg and a third pain scale will be obtained 30 minutes after the administration of the DHE. If the headache is not relieved, a second dose, .50 mg, of DHE will be given. A pain scale would be completed 30 minutes after the second DHE treatment. Headaches relieved by prochlorperazine or metoclopramide will end protocol treatment at this point. Patients with unrelieved headache will be appropriately treated. The data will be analyzed using Student's t test and chi-square methods to determine the differences between study groups.

**Progress:** The protocol has been completed and a paper is being written.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/012	<b>Status:</b> On-going
<b>Title:</b> Diagnostic Value and Clinical Significance of the Electrocardiogram During Chest Pain		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT William J. Frohna, MC		
<b>Associate Investigators:</b> MAJ Alice M. Mascette, MC		Steven A. Pace, MD
<b>Key Words:</b> chest pain, ECG		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine the negative predictive value of the electrocardiogram obtained during chest pain in predicting the presence or absence of ischemic heart disease.

**Technical Approach:** Patients, ages 25 to 80, who present to the Emergency Room with a complaint of chest pain and who have an ECG performed with no changes to suggest ischemia or infarction will be studied. Patients will be divided into either outpatient or inpatient groups for data collection. The outpatient group will be those who, primarily due to the atypical nature of their chest pain history, are discharged by the physician for routine outpatient followup. These patients will be studied prospectively by undergoing an exercise stress test (EST). The inpatient group will be those patients, who by virtue of the typical nature of their chest pain are admitted to the CCU for more urgent or invasive diagnostic testing in spite of the lack of ECG changes on presentation. Inpatients will be studied retrospectively since their care ethically will need to be dictated by the clinical course and primary cardiologist. The records of these patients will be reviewed to determine if there was objective evidence of ischemia either by EST or by cardiac catheterization. In this way, two sets of data will be derived for two populations of patients who do not have ECG changes consistent with ischemia or infarction on the ECG obtained during chest pain. By comparing this negative finding with the presence or absence of ischemic heart disease as judged by EST or cardiac catheterization, the negative predictive value of this test can be determined for patients likely to have a low prevalence or high prevalence of ischemic heart disease, i.e., outpatient follow-up or inpatient evaluation.

**Progress:** Thirty patients have been enrolled.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/089	<b>Status:</b> Completed
<b>Title:</b> Prehospital Intubation Assessment Methods		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Marc D. Magelssen, MC		
<b>Associate Investigators:</b> MAJ Richard G. Foutch, MC		CPT Jeffrey E. Short, MC
<b>Key Words:</b> intubation, esophageal detector device		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$830.00	<b>Periodic Review:</b> 05/03/91

**Study Objective:** To evaluate the prehospital methods for assessing the correct placement of an intubation tube and to compare the various methods for accuracy, ease of use, estimated time to use, and preference of the paramedics.

**Technical Approach:** Patients, 18 years or older, who are nasally or endotracheally intubated in the prehospital or emergency department setting will be entered into the study, except for those with cricothyroidotomy or tracheostomy. Physicians and paramedics will be briefed on the various methods of insuring recognition of esophageal intubation. These methods at MAMC include the Esophageal Detector Device (EDD), visualizing the tube passing through the vocal cords, listening over the lungs and epigastrium, moisture in the tube with exhalation, and continued evidence of adequate oxygenation of the patient. The physician or paramedic will assess the intubation tube placement, using all of the methods listed above. After Emergency Department personnel have taken over the care of the patient, the paramedic will complete a questionnaire that obtains data on the accuracy, ease of use, estimated time to use, and preference of methods as well as route (nasotracheal or orotracheal) and type of patient (medical or trauma). Final determination of tube placement will be verified by the emergency medicine physician upon arrival to the Emergency Department. Data will be entered into a spreadsheet with an ID number assigned to each data sheet. Differences will be isolated between the various methods. This will include: descriptive statistics on the data from the questionnaire, ANOVA for confidence in accuracy, and chi-square to isolate the best correlation in device placement.

**Progress:** This protocol has been completed. Approximately 100 patients were entered in the study. A manuscript should be completed by January 1992.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/027	<b>Status:</b> On-going
<b>Title:</b> Determination of Effectiveness of the Esophageal Detector Device in Young Porcine Animal Models		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Apr 92	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LCDR Timothy C. May		
<b>Associate Investigators:</b> LTC Blake P. Gendron, MC		
CPT Marc D. Magelssen, MC		
<b>Key Words:</b> endotracheal tube placement, EDD, porcine, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	\$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00
		<b>Periodic Review:</b> //

Study Objective: To determine if there is a difference in accuracy between a 10 cc and the standard 50 cc syringe when used as an esophageal detector device (EDD) in an immature porcine model.

Technical Approach: Four pigs from the same litter will be used. One will be used as soon as possible after weaning and then subsequently one every two weeks totaling four evaluations approximating maturation of the airways. An attempt will be made to use the same 10 evaluators for each study period. For each pig there will be a total of 40 evaluations by the 10 evaluators: 10 of the tracheal tube and 10 of the esophageal tube using the 50 cc EDD and 10 of each tube using the 10 cc EDD. At each session, the researcher will intubate the animal's esophagus and the trachea using two appropriate and equally sized endotracheal tubes and an appropriate laryngoscope blade. Placement of each tube will be confirmed by visualization, auscultation, and fiberoptic bronchoscopy. Each evaluator will use the 50 cc EDD on one of the tubes and then use the 10 cc EDD on one of the tubes to determine where each tube is placed. The evaluator will leave the room and the pigs will be ventilated. The evaluator will then reenter the room and repeat the evaluations. The evaluator will be blinded as to the location of the ED tubes and the two tubes will be evaluated in random order. The pig will be sacrificed and slides of the trachea distal to the ET tube will be made to evaluate maturation of the cartilage by H&E staining. The lungs will be weighed and determination of lung volumes will be measured by syringe aspiration and inflation to attempt to draw a correlation between lung size and volume such that effectiveness of the EDD can be evaluated.

Progress: Due to renovation of facilities and TDY of the principal investigator, this study has not been implemented.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/014		<b>Status:</b> Completed	
<b>Title:</b> Measurement of Radiation Exposure to All Personnel in an Emergency Department					
<b>Start Date:</b> 12/07/90			<b>Est. Completion Date:</b> Mar 91		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Annette R. Nathan, MC					
<b>Associate Investigators:</b>			MAJ John E. Reed, MC		
<b>Key Words:</b> radiation exposure, emergency room					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0.00</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
					<b>Periodic Review:</b> //

**Study Objective:** To determine the actual radiation exposure to all emergency health care workers in a three month period and compare this with national and international standards to determine if international standards are being exceeded.

**Technical Approach:** All emergency health care personnel assigned to the Emergency Department MSCA area for at least one month during the three month period of the study will be asked to participate. Participants will wear a dosimeter badge on the right lapel and one on the dominant ring finger during duty hours for the three month study period. The number of hours worked each day, the number of major trauma or medical resuscitations participated in each day, and the number of fluoroscopic procedures involved in each day will be recorded. Personnel will be asked not to vary from usual routine for purposes of the study. Five controls will be set up with administrative personnel who do not normally go into the Emergency Department MSCA area. The controls will be asked to remove the dosimeter if they do go into the MSCA area. These controls will also record the number of hours worked. Five control dosimeters will be placed in the area where the nurses dosimeters are stored while not at work and five dosimeters will be placed in the area where the physicians control dosimeters are stored when not at work. The outpatient radiology department will keep track of the number of portable x-rays done each day and these numbers will be examined in the final analysis. At the end of the three month study period, the dosimeters will be collected and each individual's exposure measured. The individual exposures will be examined and compared with the standards as put forth by the National Council of Radiation Protection and Measurements.

**Progress:** Eighty subjects were studied. Data analysis is complete and an abstract is being written.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/016	<b>Status:</b> Completed
<b>Title:</b> Occult Sinusitis in the Symptomatic Asthma Patient		
<b>Start Date:</b> 04/21/89	<b>Est. Completion Date:</b> Jul 89	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Lee E. Payne, MC, USAF		
<b>Associate Investigators:</b> Rush A. Youngberg, M.D. MAJ James I. Stubblefield, MC		
<b>Key Words:</b> asthma:symptomatic,occult sinusitis		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$100.00	<b>Periodic Review:</b> 05/03/91

**Study Objective:** To define the incidence of occult sinus abnormalities in asthma patients and correlate with activity of reactive airway disease by looking at the incidence of abnormalities on presentation to the Emergency Service with acute exacerbation of asthma and at follow up during the asymptomatic period and to examine the relationship between the incidence of asthma and sinusitis.

**Technical Approach:** Approximately 100 adult patients will be studied. Patients >55, febrile, or pregnant will be excluded. A prospective analysis of asthma patients will be made as they present acutely to the emergency room. Patients will be treated in the usual manner. A peak flow study and a routine physical exam with special attention to nose, pharynx, and face for evidence of clinical sinusitis will be performed. A complete sinus series will be taken, and the subjects will be asked to fill out a questionnaire regarding sinusitis symptoms, current medications, latest exacerbation of reactive airway disease requiring more than routine medications, history of sinusitis, and smoking history. At 12 weeks the sinus series will be repeated and an assessment will be made concerning interim status and therapeutic interventions. Data will be analyzed using descriptive statistics, contingency tables, graphs, and logistic regression.

**Progress:** Data collection has been completed on 54 subjects and a paper is being written for submission for publication.

MAJ Stubblefield original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/078	<b>Status:</b> Suspended
<b>Title:</b> Oral Versus Intravenous Steroid: A Prospective Study in Acute Asthma		
<b>Start Date:</b> 11/01/91	<b>Est. Completion Date:</b>	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LCDR Richard S. Perren		
<b>Associate Investigators:</b> MAJ Kirin M. Russell, MC		
<b>Key Words:</b> asthma:acute,steroids:oral,steroids:IV		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 11/01/91

**Study Objective:** To compare the efficacy of oral prednisone and intravenous methylprednisolone in the treatment of adults with acute asthma exacerbation by comparing FEV<sub>1</sub>, patient's subjective index, and physician evaluation of clinical course.

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

**Progress:** This study has not been implemented because the principal investigator was reassigned and it has not been revised according to the stipulations of the Human Use Committee. The protocol was suspended in May 91. A new investigator has been assigned and is in the process of revising the protocol to meet the requirements of the Human Use Committee.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 82/025                      **Status:** On-going

**Title:** Emergency Room Procedure Training

**Start Date:** 02/19/82

**Est. Completion Date:** Feb 87

**Department:** Emergency Medicine

**Facility:** MAMC

**Principal Investigator:** LTC Matthew M. Rice, MC

**Associate Investigators:**

MAJ Steven C. Dronen, MC

MAJ Mel D. Robinson, MC

MAJ Stanley P. Liebenberg, VC

LTC Cloyd B. Gatrell, MC

COL Frederick Burkle, MC

LTC Samuel T. Coleridge, MC

**Key Words:** emergency room, training protocol, Animal Study

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:**    \$0.00

**OMA Cost:**

\$1360.00

03/01/91

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 sessions 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:**

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:**

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 tub placement
8. Auto transfusion from hemothorax
9. Twist drill decompression
  
10. Skull trephination

Progress: One training session, which 50 physicians attended, was held FY 91.

MAJ Dronen original PI



DETAIL SUMMARY SHEET.

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/016	<b>Status:</b> On-going
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret Model		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Matthew M. Rice, MC		
<b>Associate Investigators:</b> LTC Patrick C. Kelly, MC		LTC Cloyd B. Gatrell, MC
<b>Key Words:</b> training protocol,pediatrics,intubation,ferret,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$400.00	03/01/91

**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 utilizing this protocol in FY 91.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/079	<b>Status:</b> On-going
<b>Title:</b> Effects of Trendelenburg's Position on Oxygen Consumption and Cerebral Perfusion Pressure in the Adult Pig		
<b>Start Date:</b> 03/01/92	<b>Est. Completion Date:</b> Jan 92	
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Joseph B. Rusinko, MC		
<b>Associate Investigators:</b> MAJ John E. Reed, MC		
<b>Key Words:</b> oxygen consumption, cerebral perfusion, position, pig, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** This study will evaluate the effect of the head-down or Trendelenburg position on cerebral perfusion pressure and cerebral oxygen consumption in a hemorrhagic pig model.

**Technical Approach:** This study will use 12 pigs divided into two groups. The first group will consist of 2 pigs as a pilot study to determine optimal study conditions. These two animals will undergo splenic ligation on the day of the study. Following splenic ligation the animals will be studied before and after varying degrees of hemorrhage to include 5, 10, 15, and 20 percent total body weight. These animals will also be evaluated to determine the optimal head-down position by studying the animals at 10 degrees and 20 degrees head-down position. Results of this pilot study will determine the degree of hemorrhage and the degree of head-down positioning for the remaining animals in the study.

The second group of ten animals will serve as their own controls and will be subjected to 15 minutes of baseline data collection of MAP, CO, and ICP followed by hemorrhage as determined in the pilot study. There will be a 15 minute post hemorrhage stabilization period followed by head-down positioning for 15 minutes after which the animals will be returned to the baseline position for 15 minutes post intervention. During these time intervals, data will be collected on the parameters described above.

Tabulated data will be analyzed for statistical differences by a paired T-test and the repeated data measurements will be analyzed using repeated measured analysis of variance.

**Progress:** This study is awaiting final approval by the Laboratory Animal Use and Care Committee and has not been implemented.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF FAMILY PRACTICE**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/057	<b>Status:</b> Completed
<b>Title:</b> Use of Civilian Care and Satisfaction With Care by Family Practice Enrollees At Madigan Army Medical Center		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Bruce M. LeClair, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> civilian care,satisfaction,family practice enrollee		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine the differences in CHAMPUS utilization, preventive services, and satisfaction between Family Practice enrollees and other military medical beneficiaries.

**Technical Approach:** Random samples from DEERS enrollees and Family Practice enrollees (n=300) will be sent a questionnaire which asks them about their use, preferences and satisfaction with military and civilian care and their use of CHAMPUS. Four groups will be defined (75 subjects/group): Family Practice spouses, non-Family Practice spouses, Family Practice retirees (or spouses) and non-Family Practice retirees (or spouses). Prior to mailing the questionnaires, telephone contact will be made to insure that potential recipients are indeed in the area. Follow-up cards will be sent to remind non-responders and, if total numbers do not reach necessary levels, telephone surveys will be attempted. It should be noted that there will be no change in usual source or standard of care.

Statistical inferences will be made based on multivariate analysis, chi-square analysis, t-tests, ANOVA, or Kendall's tau were appropriate.

**Progress:** The project has been completed. One hundred seventy two surveys were returned. The principal investigator is in the process of writing a thesis as a requirement for a Masters Degree in Public Health.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/058	<b>Status:</b> On-going
<b>Title:</b> An Analysis of Selected Elements of Family Function and Related Variable in Adolescent Pregnancy		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LCDR Evelyn L. Lewis		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> pregnancy:adolescent,family function,adolescent:female,parent participation		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

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

**Technical Approach:** Subjects will be contacted as they are indentified through the organizations and schools who are participating, a total of 400 subjects is the target sample. In the instance where there are groups of subjects, a presentation will be made about the protocol. Prior to receiving the questionnaires, subjects will be given a consent form for themselves and a parent or guardian. Once parents/guardians who wish to participate are identified, they may be accessed in one of three ways: 1) personally contacted by PI, 2) brought home by the subject, 3) mailed to parent/guardian. The latter two are followed up by a phone call to reinforce and encourage participation and packet completion.

Data will be analyzed using the chi-square method looking at the frequency distribution in the balanced mid-range and extreme family types of pregnant and nonpregnant teens. The data will also be used to compare balanced families vs those non-balanced families in the remaing four quadrants. The third method of analysis will employ a score called Distance from Center of Circumplex (DFC). This is a linear score used for correlational analysis and is an indication of the distance of an individual's cohesion and adaptablility score from the center of the model. And finally, discriminant function analysis will be used to predict group membership or status on a categorical or nominal level variable on the basis of two or more independent variables.

**Progress:** Approximately 200 subjects have been entered with the majority of the data entered in the computer.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/048		<b>Status:</b> On-going	
<b>Title:</b> Evaluation of Pre- and Postpartum Depression Among Pregnant Wives of Alerted and Deployed Soldiers					
<b>Start Date:</b> 02/01/91			<b>Est. Completion Date:</b> Jul 91		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Dawn E. Light, MC					
<b>Associate Investigators:</b>			MAJ Philip M. Bayliss, MC		
<b>Key Words:</b> depression, pregnancy, deployed soldiers					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

Study Objective: To determine the impact of depression, in the pregnant military wife, induced by being put on alert or deployment of the spouse.

Technical Approach: The initial phase will be descriptive to validate a clinical impression that a problem exists and to assist physicians in identifying patients who are at risk for complications. The self-rating Zung depression scale will be used to collect data. Repetitive screening of a portion of the population at various stages of pregnancy will serve to answer the question about the rates of depression at different times in pregnancy. The labor and delivery chart review will be used to look for increased rates of complications and will attempt to correlate the expected higher rates with the depression risk factor. Multivariate analysis will be necessary to limit the effect of extraneous variables such as age, race, gravidity, parity, sponsor's rank, substance abuse, and maternal baseline health and obstetrical history. Finally, the follow-up depression screen will again be descriptive, but an attempt will be made to predict the individuals with elevated depression scores based on their antepartum scores.

Progress: Approximately 300 patients have been enrolled.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/001	<b>Status:</b> Completed
<b>Title:</b> The Association Between Smoking Cessation and Family Functioning		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Frederick U. Vorwald, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> smoking cessation, family functioning		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$80.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the association between outcomes of smoking cessation attempts and family functioning.

**Technical Approach:** The population will consist of 60 subjects, 18 years or older, who are participating in a smoking cessation program, with an equal distribution between males and females. Subjects will complete an initial questionnaire to obtain demographic data, smoking history, and characteristics of the immediate family members living in the household. The Dyadic Adjustment Scale and the FACES II instruments will also be administered to the subject at this time as a measure of the subject's baseline family functioning. Follow-up will be conducted upon completion of the smoking cessation program and at 1, 2, and 3 months post-treatment. Only successful graduates will be followed post-treatment. At each follow-up, the subject will complete a smoking status questionnaire, the Dyadic Adjustment Scale, and the FACES II instrument. Data will be analyzed to determine the association among initial cessation of smoking, maintenance of abstinence, and family functioning, using the Statistical Package for the Social Services.

**Progress:** Protocol has been completed. 48 subjects were followed to three months post treatment. The data suggest that there is an association between smoking cessation and short-term maintenance and perceived family functioning in participants of smoking treatment programs. A thesis has been submitted in partial fulfillment of the requirements for the Degree of Master of Arts in Social Sciences at Pacific Lutheran University.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE**



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/055		<b>Status:</b> On-going	
<b>Title:</b> Multicenter Clinical Evaluation of Penicillin Skin Testing					
<b>Start Date:</b> 03/16/90			<b>Est. Completion Date:</b> Jun 90		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL W. Pierre Andrade					
<b>Associate Investigators:</b>					
COL Bernard Branch, MC		COL James S. Brown, MC			
MAJ Marcia L. Muggelberg, MC		COL Richard W. Weber, MC			
COL William F. Tuer, MC		MAJ Allen F. Kossoy, MC			
COL Michael Martin, MC		Robert A. Ledoux			
CAPT David Moyer, MC		CAPT William L. Ebbeling, MC			
				CAPT Fang L. Lin, MC	
<b>Key Words:</b> penicillin skin testing					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

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

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

**Progress:** Approximately 100 subjects have been entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/044                      **Status:** On-going

**Title:** Fludarabine Phosphate in Patients with Refractory Chronic Lymphocytic Leukemia and non-Hodgkin's Lymphoma

**Start Date:** 05/03/91                      **Est. Completion Date:** Feb 94

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

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC H. Irving Pierce, MC
LTC Howard Davidson, MC	MAJ William A. Phillips
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	MAJ Robert L. Sheffler, MC
MAJ Robert B. Ellis, MC	CPT Jennifer L. Cadiz, MC
LTC Mahammed Nagy, MC	

**Key Words:** leukemia:chronic lymphocytic,fludarabine phosphate

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To assess the response rate of a new investigational agent, Fludarabine Phosphate, against chronic lymphocytic leukemia (CLL) and non-Hodgkin's lymphoma, and to assess the frequency of toxicity of this drug.

**Technical Approach:** This study has been made available to a large variety of medical centers in this country so that a wide variety of patients with these disease processes may be fully assessed for response to disease. Responses will be defined as: complete remission (resolution of all measurable tumor on two consecutive assessments one month apart); partial response (50% reduction in the sum of the cross products of each measurable lesion).

Patients with CLL or non-Hodgkin's lymphoma which has proved refractory to standard therapy will be eligible. Patients will have a history, physical exam, CBC, 908, chest x-ray, and urinalysis before entry. Further studies such as CT scans will be done as indicated for individual patients. All patients will receive Fludarabine 20-30 mg/m<sup>2</sup> IV bolus for five consecutive days once every four weeks until maximal response or disease progression occurs. The patients will undergo weekly CBC's and chemistry panels during the first cycles of therapy. The patients will undergo physical examination, including neurologic assessment, prior to the initiation of each cycle of therapy.

Follow-up will be monthly on an indefinite basis.

**Progress:** Two patients have been entered at MAMC with no adverse reactions.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/079	<b>Status:</b> Completed
<b>Title:</b> Salicylate Overdose: Quantitation of Renal Excretion With Forced Alkaline Diuresis		
<b>Start Date:</b> 10/21/88	<b>Est. Completion Date:</b> Jan 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Matthew S. Bachinski, MC		
<b>Associate Investigators:</b>		
CPT Donna L. Mercado, MC	MAJ Howard M. Cushner, MC	CPT Bernard J. Roth, MC
CPT Thomas P. Peller, MC	CPT LeRoy Southmayd, MC	
<b>Key Words:</b> salicylate,renal excretion,forced alkaline diuresis		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1900.00	//

**Study Objective:** To assess the effectiveness of a forced alkaline diuresis in reducing plasma salicylate concentrations in patients who present with acetylsalicylic acid blood levels of >50 mg/dl and have adequate renal function.

**Technical Approach:** Patients as stated above will be admitted to the ICU and followed, receiving the standard of care plus: baseline labs for SGOT, SGPT, LDH, bilirubin, calcium, magnesium and phosphorus, history taken to quantify as closely as possible the amount of aspirin ingested and the time of ingestion, IV D5W with 150 mEq NaHCO<sub>3</sub>/L at 50-150 cc per hour, weight every 12 hours, chest x-ray each day, calcium and magnesium every 12 hours, labs to include arterial blood gas, electrolytes, BUN, creatinine, and serum salicylate level, every 6 hours, urine collection every 6 hours for dipstick pH, volume measurement, urine salicylate level and sodium determination. IV infusion rate will be adjusted to patient size and age. Pulmonary edema will be monitored by chest x-ray and physical examination, arterial blood gases, electrolytes, calcium, and magnesium will be monitored and adjustments made to maintain chemical homeostasis. Patients will be treated until serum salicylate is <30 mg/dl. Patients' normal outpatient medications not containing aspirin will be allowed.

**Progress:** The protocol has been completed. Four subjects were entered in the study. A paper was presented at the December 1990 meeting of the Washington State Chapter of the American College of Physicians.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 88/047		<b>Status:</b> Terminated	
<b>Title:</b> Investigation Into Thyroid Function Abnormality Associated with Hexabrix, a New Intravenous Iodine-Containing Contrast Agent					
<b>Start Date:</b> 04/15/88			<b>Est. Completion Date:</b> Jun 88		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Brenda K. Bell, MC					
<b>Associate Investigators:</b> CPT Jennifer A. Nuovo, MC			CPT Patrick D. Gorman, MC		
<b>Key Words:</b> Hexabrix, thyroid function					
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$1800.00		<b>Periodic Review:</b> 06/14/91	

**Study Objective:** To look for evidence of thyroid function abnormality following the use of Hexabrix, a new iodine containing intravenous contrast agent, and to compare clinical evidence of thyroid dysfunction, i.e., goiter, nodular thyroid, Hashimoto's thyroiditis, with the evidence of iodine-induced hyper-or hypothyroidism.

**Technical Approach:** Subjects with no evidence of thyroid function abnormality and patients with goiter undergoing cardiac catheterization, with the administration of Hexabrix or Hypaque contrast material, will be studied. Patients will be examined for the presence of goiter or nodular thyroid disease and a baseline thyroid function test, including TSH and T3 by RIA, will be done. The thyroid function tests will be repeated at three days and at one month after administration of the contrast agent. The amount of contrast agent administered will be used to calculate the milligrams of iodine that the patient was administered.

**Progress:** Originally, 21 subjects were entered in the study, but complete data is available on only four subjects. There was a major problem with patients forgetting the one month thyroid function tests. Since the data were incomplete and several months passed when no work was done on the project, CPT Bell and the other investigators scrapped the previous data and started over using the same plan. Fifteen new subjects were entered in the study, with data completion on only four subjects since many of the patients were sent to other medical centers for further treatment. Dr. Bell was reassigned and the decision was made to terminate the protocol since data collection had been so difficult.

MAJ Nuovo original PI  
Dr. Bell new PI, Aug 88.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/034		<b>Status:</b> Completed	
<b>Title:</b> Performance of Hemocult II and Hemocult SENSEA					
<b>Start Date:</b> 03/17/89			<b>Est. Completion Date:</b> Oct 89		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Carole A. Buckner, MC					
<b>Associate Investigators:</b> MAJ Amy M. Tsuchida, MC			MAJ Michael F. Lyons II, MC		
<b>Key Words:</b> occult blood					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		04/05/91	

**Study Objective:** To compare the performance of Hemocult II and Hemocult SENSEA stool cards in the detection of fecal occult blood in patients undergoing diagnostic colonoscopy.

**Technical Approach:** Approximately 150 subjects, either sex, >40 years of age for whom colonoscopy has been ordered by a gastroenterologist as part of the required diagnostic testing will follow a special diagnostic diet for at least two days prior to fecal sample collection and through the sample collection period. Participants will collect samples and prepare test slides from three consecutive bowel movements. Detailed instructions will be provided regarding the sampling and test procedures. Patients will return samples and then undergo planned diagnostic workup, regardless of the guaiac results. The workup will include colonoscopy and any other clinically indicated endoscopic and/or radiologic studies. Data Form 1 containing history and current diagnostic workup results and Data Form 2 containing fecal occult blood results will be used for data collection. For Hemocult II and Hemocult SENSEA, the percentage of the positive subjects and the percentage of the negative subjects will be calculated. These findings will then be related to actual GI pathology based on colonoscopy findings. Chi-square analysis will be used to determine sensitivity and specificity of Hemocult II and Hemocult SENSEA.

**Progress:** 114 patients were studied. Sensitivity of Hemocult II and Hemocult SENSEA was not statistically different in detection of fecal occult blood in patients with colonic neoplasms.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/059                      **Status:** On-going

**Title:** Acute Coronary Angiographic and Hemodynamic Response to Cigarette Smoking in Chronic Smokers With Coronary Artery Disease

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

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

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

**Associate Investigators:**                      MAJ Alice M. Mascette, MC  
MAJ Doreen Saltiel, MC

**Key Words:** coronary disease, cigarette smoking

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost:     \$0.00	OMA Cost:             \$3525.00	05/03/91

**Study Objective:** To examine changes in the caliber of stenotic coronary lesions by computer assisted quantitative coronary cineangiography and variation in measurements of coronary sinus flow and resistance induced by cigarette smoking.

**Technical Approach:** The subjects will be 25 chronic cigarette smokers who are referred for diagnostic cardiac catheterization for the evaluation of chest pain. Smoking, long-acting nitrates, beta blockers, and calcium blockers will be discontinued 12 hours prior to the study, and the patient will be NPO 6-12 prior to the study. Patients will be premedicated with 10 mg Diazepam, orally, and diagnostic coronary and left ventricular cineangiography will be performed. The left coronary injection that best identifies the coronary lesion(s) will be acquired on digital subtraction for computer measurement of the percent narrowing at the baseline state. The ambulation of the image intensifier will be annotated so an identical projection can be repeated later. While the vasodilatory effects of the contrast medium dissipate, a coronary sinus flow catheter will be inserted through a right basilic vein and advanced under pressure monitoring and fluoroscopic guidance into the right atrium. The catheter will then be positioned in the midportion of the coronary sinus and confirmed by contrast medium injection. A left Judkins or Sones catheter will be positioned at the level of the aortic root for arterial pressure recording and blood sampling during coronary sinus flow measurements and subsequent re-engagement into the left coronary artery for repeat coronary cineangiography. Baseline arterial pressure, heart rate, rate-pressure product, and simultaneous blood sampling from the arterial and coronary sinus catheter for calculation of the arterial-coronary resistance will be recorded. The patient will then smoke two filtered cigarettes containing 1.1 mg of nicotine and 17 mg of tar over an 8 minute period. All measurements will be repeated over a 30-60 second period, immediately following the cessation of smoking, and a repeat left coronary injection of contrast medium will be acquired on digital subtraction in the same projection as the baseline injection for stenosis measurement, within 5 minutes of cessation of smoking.

**Progress:** Due to the strict exclusion criteria, it has been more difficult than expected to enroll patients. Three patients have been entered, all of whom were found to have normal epicardial coronary arteries and therefore were entered as control patients. As expected, all three patients showed a rise in coronary sinus flow after smoking two cigarettes containing 1.1 mg nicotine over eight minutes. Heart rate increased in all three subjects and blood pressure in two out of three after smoking, which is the expected outcome in patients who have normal coronary arteries.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/071	<b>Status:</b> Completed
<b>Title:</b> Hepatitis B Vaccine (Recombivax) Abbreviated Schedule Vaccination		
<b>Start Date:</b> 08/19/88	<b>Est. Completion Date:</b> Mar 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Ronald H. Cooper, MC		
<b>Associate Investigators:</b> LTC Maria Sjogren, MC		CPT Robert J. Kazaragis, MC
<b>Key Words:</b> hepatitis, Recombivax, vaccine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3785.00	<b>Periodic Review:</b> //

**Study Objective:** To test and compare the efficacy of conventional and reduced dosages of intradermally and intramuscularly administered Recombivax, given in an abbreviated schedule.

**Technical Approach:** Subjects: 75, male/female, ages 18-45 Exclusion criteria: history of hepatitis or positive hepatitis B serology, chronic disease or immunosuppressive condition or malignancy, pregnancy, prior vaccination with hepatitis B virus vaccine or receipt of hepatitis B immune globulin within 12 months. Evaluations before entry: medical history form and interview, hepatitis B surface antigen and antibody, hepatitis B core antibody, serum alanine and aspartate aminotransaminase levels, and a completed blood count. The subjects will be randomized to one of three arms: 10 mg dose Recombivax IM at 0, 4, and 7 weeks 2 mg dose Recombivax ID at 0, 4, and 7 weeks 1 mg dose Recombivax ID at 0, 4, and 7 weeks HBsAg, anti-HBs, and anti-HNc will be followed at days 0, 30, 60, 90, 180, and 360. Individuals who fail to achieve a protective level of anti-HBs will be revaccinated at one year with 10 mg IM, Recombivax. Data analysis: Chi-square analysis of geometric mean titers of anti-HBs and comparison of antibody titers and response rates to previously published studies.

**Progress:** The study has been completed. More than 90% of the vaccine recipients had a clinically significant (>10 I.U.) antibody response to the Recombivax abbreviated schedule. An abstract was presented at the Washington State/American College of Physicians Annual meeting in December 1989.

CPT Kazragis original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/080	<b>Status:</b> Terminated
<b>Title:</b> Evaluation of Two Doses of SQ 32,756 (BV-araU) and Matching Placebo Capsules in the Treatment of Primary Varicella-Zoster Virus Infection (Chickenpox) in Immunocompetent Patients		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Ronald H Cooper, MC		
<b>Associate Investigators:</b> LTC Rodney A. Michael, MC		
<b>Key Words:</b> Varicella-zoster virus, chickenpox, BV-araU		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$100.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the safety, efficacy, and dose response of SQ 32,756 administered orally once daily in doses of 10 mg and 40 mg for five days for the treatment of primary varicellazoster virus infection in immunocompetent patients.

**Technical Approach:** This will be a multicenter study of approximately 360 patients, designed as a randomized, double-blind, placebo-controlled clinical trial, with parallel and approximately equal patient enrollment into the three treatment groups. Patient enrollment will consist of immunocompetent patients with onset of primary varicella-zoster virus rash of <72 hours duration. Patients must be at least 13 years old and have no previous history of varicella-zoster. All females of childbearing potential must have a negative serum pregnancy test prior to drug administration. On the day of enrollment, prior to the initiation of therapy, a baseline patient evaluation will be performed which will include: complete history and physical examination, history of exposure to varicella-zoster virus, evaluation and documentation of varicella lesions, hematologic, chemistry and urinalysis laboratory tests, lesion vesicle aspirate for varicella-zoster viral culture, lesion basal cell scraping for DFA, and acute phase serology for serology reference lab. Hematology, chemistry and urinalysis tests will be repeated on days 2 and 5 and at one week post-treatment (day 11-13). Patients will be evaluated by the physician for the 5day treatment period and thereafter until all body lesions have either crusted or resolved without progressing to later stages normally associated with crusting. All patients, regardless of crusting status, will be evaluated on day 7 and at 1 and 2 weeks post-treatment. Differences in the time until achievement of selected clinical endpoints for the three treatment groups, as well as the frequencies of adverse experiences, will be compared using appropriate statistical procedures. Data pertaining to demographic characteristics will be displayed and summarized with descriptive statistics. Chi-square or ANOVA will be used to test the monogeneity of the treatment groups. If a difference is found, its effect on the efficacy comparison will be investigated.

**Progress:** This protocol was terminated by Bristol Myers Squibb due to a finding of increased incidence of tumors in rats at 20 months of an ongoing 24 month carcinogenity study. All investigations of the drug in immunocompetent patients have been cancelled, but investigations of the drug in immunosuppressed patients will continue.



### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/099	<b>Status:</b> On-going
<b>Title:</b> Azithromycin in the Treatment of Nongonococcal Urethritis: A Multicenter Double-Blind, Double-Dummy Study Employing Doxycycline as A Comparative Agent		
<b>Start Date:</b> 09/27/91	<b>Est. Completion Date:</b> Aug 93	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Ronald H. Cooper, MC		
<b>Associate Investigators:</b> LTC Rodney A. Michael, MC		
<b>Key Words:</b> nongonococcal urethritis, azithromycin, doxycycline		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

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

**Technical Approach:** This will be a randomized, double-blind, double-dummy, comparative study of azithromycin versus doxycycline. Participants in this study will be patients with acute NGU. All patients must have a Gram-stained urethral smear with five or more PMNL per field (at least three non-adjacent oil immersion fields [X 1000]). All patients will be cultured at baseline. Those with positive cultures for gonorrhea will be discontinued from the study. All others, with or without positive cultures, will be followed. Patients will be randomly assigned in a 2:1 fashion to therapy with a single 1 gm oral dose of azithromycin or oral doxycycline, 100 mg b.i.d. x seven days, respectively, each with placebos for the alternate drug. Evaluations will be performed at baseline and at one and four weeks following completion of treatment. Laboratory safety profiles will also be obtained at these times.

The primary measures of treatment efficacy will be the clinical and bacterial outcomes. The distribution of bacterial response will be compared between treatments using the chi-square statistic. If this test leads to a statistically significant result, the percentage of bacterial eradications will be compared using the Fisher Exact test. The percentage of clinical cures will be compared between treatments using the Fisher Exact test.

**Progress:** New study, awaiting approval from HSC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/070                      **Status:** On-going

**Title:** High Dose Cisplatin, VP-16 With or Without Radiation Therapy in Advanced Nonsmall Cell Lung Cancer

**Start Date:** 05/15/87                      **Est. Completion Date:** Dec 90

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

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	COL Donald H. Kull, MC
MAJ Thomas M. Baker, MC	MAJ Ruben D. Sierra, MC
CPT David R. Bryson, MC	CPT Margaret M. Barnes, MC
LTC Lauren K. Colman, MC	MAJ David M. Dunning, MC
COL Irwin B. Dabe, MC	

**Key Words:** nonsmall cell,cancer:lung

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	06/14/91

Study Objective: To evaluate proposed treatment schedules with respect to response rates, toxicities, and overall survival.

Technical Approach: Approximately 20 patients will be treated in three groups. Treatment will be determined by extent and location of cancer and by previous therapy. Group I: Limited non-small cell lung cancer (NSCLC) with prior radiotherapy will be treated with cis-platinum, 100 mg/m<sup>2</sup>, days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/m<sup>2</sup>, on days 1-3, 29-31, and 57-59. There will be no radiotherapy. Group II: Limited NSCLC, no prior radiotherapy, will be treated with cis-platinum, 100 mg/m<sup>2</sup>, days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/m<sup>2</sup>, days 1-3. They will also receive radiotherapy to the chest for 5-6 weeks starting day 29. Prophylactic whole brain radiotherapy will be given for three weeks starting 3-4 weeks after chest radiotherapy is completed for patients achieving clinical partial or complete remission. Group III: Extensive NSCLC will receive the same regimen as Group 1. Response rate will be defined as number of patients who achieve a complete or partial response divided by the total number of patients evaluable for response (completed at least four weeks of the treatment program). Patients will be evaluable for toxicity if they received at least one dose of chemotherapy.

Progress: No new patients were entered in FY 91 due to the principal investigator's deployment to Operation Desert Storm. Twenty-six patients were entered in previous years. All toxicities were predictable. Early data indicate that this combined modality regimen appears to be effective in Stage III NSCLC and that ototoxicity is the limiting side effect. A paper was presented at the 1991 meeting of the American Society of Clinical Oncology. The investigators plan to enter at least six more patients.

Replaced COL Irwin B. Dabe, MC, Sep 89

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/050	<b>Status:</b> On-going
<b>Title:</b> Sucralfate and Aluminum Absorption		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> Jul 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Amy E. Ellingson, MC		
<b>Associate Investigators:</b> MAJ Amy M. Tsuchida, MC		MAJ Michael F. Lyons II, MC
<b>Key Words:</b> aluminum, bone absorption, sucralfate		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine if standard treatment with Sucralfate demonstrates a significant amount of aluminum absorption through measurement of serum and urine aluminum concentrations, to determine if increased serum aluminum content as a result of standard Sucralfate therapy is adequately cleared by kidneys in normal subjects, and to determine if increases in aluminum levels as a result of standard therapy lead to effect on bone metabolism/mineralization (as seen in aluminum toxicity causing osteomalacia).

**Technical Approach:** Baseline labs as stated below and a 24 hour urine will be obtained on day 1 of the study and patients will receive a 1 gram IM injection of deferoxamine. On day 7, the patients will begin sucralfate with a dosage of 1 gram, PO, 30 minutes before each meal and at bedtime. This regimen will continue for 42 days. Serum sodium, potassium, chloride, BUN, creatinine, magnesium, albumin, phosphate, calcium, and aluminum levels as well as 24 hour urine for aluminum, calcium, phosphorus, and creatinine will be obtained on days 1, 2, 7, 28, 49, 53, 54, and 58. Serum osteocalcin and PTH levels will be drawn on days 1, 7, 49, and 53. A second IM injection of deferoxamine will be given after collection of labs at day 53. Data will be analyzed as paried results assessing a difference between paried data with Student's t-test.

**Progress:** Eight volunteers have completed the 8 week protocol, including 8 blood draws and 24 hour urines, 6 weeks of carafate therapy, and 2 IM injections of deferoxamine, without any ill effects.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/067	<b>Status:</b> Completed
<b>Title:</b> The Effect of Androgens on Glucose Tolerance		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Curtis J. Hobbs, MC		
<b>Associate Investigators:</b> LTC (P) Robert E. Jones, MS		COL Stephen R. Plymate, MC CPT Brenda K. Bell, MC
<b>Key Words:</b> glucose tolerance, androgens, steroids, testosterone		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine whether the administration of supraphysiological doses of androgens impair glucose tolerance as measured by the tolbutamide modified intravenous glucose tolerance test.

**Technical Approach:** Twenty healthy male volunteers, ages 18-30, will participate in a double-blind, randomized, double crossover design. Individuals who use tobacco or have used anabolic steroids within the prior six months will be excluded. Each of the 20 subjects will be randomly assigned to receive either testosterone enanthate, 300 mg IM q week, or nandrolone decanoate, 300 mg IM q week. Each participant will receive a placebo for the initial two weeks of the study, followed by a six-week treatment period with either testosterone enanthate or nandrolone decanoate. A four-week wash-out period will follow. Participants will then be crossed over to the agent they did not receive the first half of the protocol. Once again, a two-week placebo treatment period will be followed by a six-week treatment period. At baseline, all subjects will have health records reviewed and a physical exam. All subjects will undergo anthropometric measurements, weight determination, semen analysis (two samples at least one day apart), testicular volume determination, and CBC, SMA-20, SHBG, total testosterone, free testosterone, LH, FSH, and serum lipid determinations. Total and free testosterone, CBC, SMA-20, SHBG, and serum lipids will be repeated at the end of each two week placebo period and at the end of each treatment period. A tolbutamide modified intravenous glucose tolerance test will be performed at the end of each two week placebo period and at the end of each six week treatment period. Each individual will serve as both control and subject. Data will be analyzed using the Statview II program for the Macintosh computer system.

**Progress:** The study has been completed, 25 subjects were enrolled. The data indicate that pharmacological doses of either testosterone or 19-nortestosterone for 6 weeks do not impair glucose tolerance in normal men. To the contrary, these androgens may improve glucose tolerance by facilitating insulin-independent mechanisms of glucose disposal.

A paper was presented at the American Federation for Clinical Research (Western Section) Feb 91, and at the American Federation for Clinical Research, National Section, in May 91.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/013	<b>Status:</b> On-going
<b>Title:</b> Is Continuous Enteral Feeding Alone Adequate Prophylaxis Against Gastroduodenal Bleeding of Stress Induced Mucosal Lesions		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> Nov 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Thomas W. Irvine, MC		
<b>Associate Investigators:</b> MAJ Michael F. Lyons II, MC MAJ Amy M. Tsuchida, MC		LTC Anthony S. Sado, MC MAJ Gregory E. Schlepp, MC
<b>Key Words:</b> mucosal lesions, continuous feeding		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if continuous enteral feedings are protective against the development of symptomatic stress-induced mucosal lesions of the gastroduodenal tract in ventilator-dependent intensive care patients.

**Technical Approach:** A total of 90 subjects, male or female, requiring ventilator support for >48 hours will be studied in a randomized double blind manner. Patients will undergo a complete medical history and physical examination prior to study entry. All patients will be given gastroduodenal prophylaxis with H2 blockers until they are eligible for entry into the study (>48 hours on ventilator). At the point when these patients are capable of enteral feeding, they will be randomly assigned to one of three groups: enteral feeding and H2 blocker, enteral feeding and Carafate, or enteral feeding alone. Their daily course will be monitored for evidence of a gastroduodenal bleed manifested by coffee ground nasogastric (NG) aspirate on three consecutive readings, frankly bloody NG aspirate, menatemesis, or melena. With evidence of a bleed, the patient will be taken off study and treated appropriately. Baseline CBC, serum electrolytes, Ca, Mg, Phos, LFT's, prealbumin, UUN, CXR, and EKG will obtained. NG aspirate and pH assessment will be done every four hours with CBC, serum electrolytes, Ca, Mg, Phos, and CXR repeated daily. UUN and albumin will be repeated every third day, and LFT's and prealbumin will be repeated every week. Patients will remain on study as long as they are patients in the ICU and their condition allows them to remain in their randomly assigned study arm. Data analysis will involve the aforementioned laboratory studies as well as age, sex, underlying illness, complications, total hospital days, total ICU days, total ventilator days, enteral feed, protein balance, calories/day, and GI bleed. Data will be analyzed by the chi square method.

**Progress:** Thirteen patients have been enrolled in the enteral feeding/H2 blocker group and 12 patients in the enteral feeding alone group. Preliminary data suggest that the enteral feeding alone is adequate GI prophylaxis. There has been no evidence of GI bleeds in the EF/H2B Group. One patient in the EF alone group developed stress ulceration after he had been NPO for 24 hours without any GI prophylaxis and after emergent cholecystectomy which was felt to be his source of sepsis.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/062	<b>Status:</b> On-going
<b>Title:</b> Determination of the Sensitivity and Specificity of Light Reflection Rheography for the Diagnosis of Deep Venous Thrombosis in the Lower Extremity		
<b>Start Date:</b> 07/28/89	<b>Est. Completion Date:</b> Jun 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Duane J. Jeffers, MC		
<b>Associate Investigators:</b>		
Nancy N. Greenfield, M.S.	MAJ Dipankar Mukharjee, MC	Michael Bertoglio, B.S.
SGT Charles Adams	COL Charles A. Andersen, MC	
<b>Key Words:</b> Light reflection rheography, venous thrombosis		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$6000.00	<b>OMA Cost:</b> \$760.00	//

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

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

Progress: No new patients were enrolled on this study in FY 91 due to the deployment of the principal investigator to Operation Desert Storm. Seventeen patients have been entered in previous years with no adverse effects.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/084	<b>Status:</b> Terminated
<b>Title:</b> <i>In Vivo</i> and <i>In Vitro</i> Comparisons for Sex Hormone Binding Globulin (SHBG) Production in Morbid Obesity		
<b>Start Date:</b> 10/21/88	<b>Est. Completion Date:</b> Sep 89	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> CPT Rita C. Hoop, MS MAJ John P. Kushner, MC	COL Preston L. Carter, MC COL Stephen R. Plymate, MC	
<b>Key Words:</b> SHBG:production,obesity		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$4750.00	//

**Study Objective:** To determine the molecular basis for the reduction of serum SHBG levels in morbid obesity.

**Technical Approach:** Subjects: 5 morbidly obese subjects undergoing a vertical banded gastroplasty (VBG) and 5 lean, age and sex matched controls undergoing and elective cholecystectomy. Three liver biopsies will be obtained intraoperatively. Subcutaneous fat will be obtained along the incision site. One core, which represents the *in vivo* portion of the study, will be immediately frozen and the remaining samples will be dispersed with collagenase/DNase and placed in a short term culture with 10% fetal calf serum and 3 mM L-glutamine supplemented Dulbecco's modified Eagle's media (DMEM). After three days, the media will be removed and replaced with unsupplemented DMEM. L-thyroxine (1 mM) and insulin (10 nM) will be added to each of the test flasks while the control flask will be treated with vehicle alone. After two days, the spent culture media will be removed and frozen for later SHBG analysis. The cells will be harvested with trypsin, washed, and frozen. Detection of SHBG mRNA will be performed according to the method of White and Bancroft (J Biol Chem 257: 8569, 1982), employing a custom oligonucleotide probe coupled to an enzymatic detection system. Specificity of the probe will be ensured by simultaneously hybridizing matched subcutaneous fat samples and by probing at the hepatocyte lysate with a <sup>32</sup>P labeled completed cDNA probe for human SHBG. The tissue culture media will be assayed for SHBG as previously described (Plymate, et al, J Clin Endocrinol Metab 67:460, 1988). Differences in relative levels of SHBG mRNA (estimated as number of molecules per hepatocyte) between controls and test subjects will be determined using an unpaired t test. The comparisons between media levels of SHBG and cellular levels of SHBG mRNA (L-thyroxine/ insulin supplemented versus controls) will be handled with a paired t test. If multiple comparisons are required, an ANOVA will be used.

**Progress:** The protocol has been terminated because the patients cancelled out of surgery too often making patient accrual very difficult. One patient was entered in FY 90.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/023	<b>Status:</b> On-going
<b>Title:</b> Investigations into the Mechanisms of Phospholipid Synthesis in Human Spermatozoa		
<b>Start Date:</b> 11/21/86	<b>Est. Completion Date:</b> Dec 87	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b>		
CPT Kevin J. Carlin, MC	MAJ Charles J. Hannan, MC	COL Stephen R. Plymate, MC
<b>Key Words:</b> spermatozoa, phospholipid synthesis		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1600.00	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 labelled fatty acids, CoASH, ATP, Mg<sup>2+</sup>, and Tris. The reaction will be terminated by delipidating the sperm with CHCl<sub>3</sub>: 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 labelled 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 <sup>3</sup>H-palmitoyl carnitine to look for labelled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabeled 22:6 with <sup>3</sup>H-16:0 and following the appearance of 16:0 in phosphatidyl choline. Conversely, the effect of 16:0 on <sup>14</sup>C-22:6 will be studied.

**Progress:** No further work was done on this study in FY 91 due to deployment of the PI to Operation Desert Storm. Previous work has demonstrated that fresh human spermatozoa can incorporate palmitic and docosahexaenoic acid into exogenous and endogenous lysophosphatides. Presented at the 1988 Meeting, Amer Soc Andrology (Jones, Plymate: J Androl 9:41, 1988). Publication: Journal of Andrology 10:346-50, 1989.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/083	<b>Status:</b> On-going
<b>Title:</b> Influence of Calcium on Phosphatidylcholine Synthesis in Human Spermatozoa		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Sep 89	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> COL Stephen R. Plymate, MC		MAJ Charles J. Hannan, MC
<b>Key Words:</b> spermatozoa, phosphatidylcholine, calcium, spermatozoa		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$2444.00	//

**Study Objective:** To determine the effects of calcium on the synthesis of phosphatidylcholine from free fatty acids and lysophosphatidylcholine (LPC) in freshly ejaculated human spermatozoa.

**Technical Approach:** Semen samples will be centrifuged at 650g for 15 minutes and washed twice in an isotonic buffer. The sperm pellet will be resuspended at a concentration of  $2 \times 10^8$  in the isolation buffer. Approximately  $1 \times 10^7$  sperm will be used per assay. The incubation buffer conditions will be identical to those previously established in the DCI lab. In brief, the incubation mixture contains 20 mM ATP, 20 mM MgCl<sub>2</sub>, 50 mM LPC, 10 mM fatty acid, 5mM dithiothreitol, 0.1 mM coenzyme A, and 280 mM Tris. The reaction is initiated with the addition of washed spermatozoa. After one hour, the phospholipids are extracted and separated by thin layer chromatography. Enzymatic rates are calculated as nmoles fatty acids incorporated into phosphatidylcholine/ $10^7$  sperm/hour. The investigators have shown that there are two types of substrate blanks in this system. The first, a coenzyme A blank, assess ligase and acyl transferase activity and consequently provides data on the activities of these two enzymes while the second, the LPC blank, yields information on the generation of acyl acceptors presumably through the activity of phospholipases. By using either 16:0 or 22:6 as acyl substrates and utilizing the LPC blank, the phospholipase A1 can be differentiated from A2, Because LPC is added to the incubations, the LPC blanks become all the more critical in determining the possibility of calcium control of this pathway. The concentration of calcium in the incubations will be 1.7 mM, and the concentration of A23187, a calcium ionophore, will range from 10-30 mM. If an effect is seen which suggests ligase modulation, ligase activity will be specifically addressed using both whole sperm or a Triton x 100 extract of sperm. The rates of acyl substrate utilization will be compared by an ANOVA, rates obtained with and without LPC will be compared with a Student's t test. Ligase activity will be assessed using kinetic techniques previously described (Biol Reprod 39:76, 1988).

**Progress:** The investigators conclude that short term incubation of human sperm with A23187 appears to suppress 22:6 incorporation into phosphatidylethanolamine and does not influence phosphatidylcholine synthesis. Presentation: American Society of Andrology 1990 (J Androl 11: P49, 1990).

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 85/084                      **Status:** On-going

**Title:** Purification of Long Chain Fatty Acid: CoASH Ligase from Human Spermatozoa

**Start Date:** 08/23/85                      **Est. Completion Date:** Sep 86

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

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

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

**Key Words:** spermatozoa, fatty acid: long chain, CoASH ligase

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$708.00	04/05/91

**Study Objective:** To isolate and purify long chain fatty acid: CoASH ligase (AMP) (E.C. 6.2.1.3).

**Technical Approach:** Human sperm will be collected and prepared. Ligase will be protected with 5 mM p-aminobenzamidine and extracted with 1.0% Triton X-100. The crude preparation will be delipidated by serial washings with n-butanol, acetone, and ether. The final pellet will be dried under nitrogen and reconstituted in 10 mM phosphate buffer. Affinity chromatography with Blue Sepharose CL-6B will be the principle purification step. Ligase will be eluted from the column with palmitoyl CoA dissolved in phosphate buffer. Fractions will be collected, read at 280 nm to determine the presence of protein, and assayed for ligase activity. It is possible that several proteins which require nucleotides will be retained on the column, the eluate obtained by adding a palmitoyl CoA solution should contain those enzymes which possess a relatively high affinity for acyl CoA. Ligase acyl CoA:L-glycerol -3-phosphate transferase, palmitoyl carnitine O-acyl transferase and palmitoyl CoA deacylase would fall into the latter category. Ligase differs from the other acyl CoA dependent enzymes by virtue of an approximate 50-100 fold lesser affinity for palmitoyl CoA and an absolute requirement for ATP. By using a concentration gradient of palmitoyl CoA and/or an ATP elution step, these properties should facilitate purification of ligase. Classical purification procedures for ligase are extremely complicated and involve multiple intermediate steps. On the other hand, affinity chromatography of a related enzyme using a related matrix yielded a 14-fold increase in specific activity with a single pass over the column. Purity and sizing of ligase will be accomplished by isoelectric focusing, polyacrylamide gel electrophoresis, and size exclusion chromatography (either HPLC or Sephadex G200). Protein will be determined with a BioRad kit and ligase specific activity will be calculated after each purification step.

**Progress:** No further work was done on this study in FY 91 due to the deployment of the PI to Operation Desert Storm. The investigators are trying to isolate sperm plasma membranes.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/057		<b>Status:</b> Completed	
<b>Title:</b> Synthesis of Phospholipids in Spermatozoa From the Laboratory Rat ( <i>Rattus norvegicus</i> ): A Pilot Study					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> May 90		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS					
<b>Associate Investigators:</b> COL Stephen R. Plymate, MC			MAJ John P. Kushner, MC		
<b>Key Words:</b> spermatozoa, phospholipids, rat, Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$320.00		04/05/91	

**Study Objective:** To determine the suitability of the laboratory rat as an animal model to study modifications of sperm membrane phospholipids during maturation.

**Technical Approach:** Mature, sexually rested male rats will be euthanized and both testes and epididymes will be removed. Testicular sperm will be harvested and epididymal sperm will be flushed from the lumen with normal saline. Sperm will be washed in an isotonic buffer and resuspended at a concentration of 200 million/ml. Long chain fatty acid: CoA ligase will be measured with  $^3\text{H}$ -16:0 and  $^{14}\text{C}$ -22:6 as substrates. Phospholipid synthesis from labeled free fatty acids and either lyso-phosphatidylcholine or lyso-phosphatidylethanolamine will be determined using thin layer chromatography to separate phospholipid classes. Ligase activity will be calculated as nmoles fatty acyl CoA formed/min/mg protein. Phospholipid synthesis will be expressed as nmoles fatty acid incorporated/hr/10 million sperm. Descriptive statistics will be used in the analysis.

**Progress:** Incorporation of  $^{14}\text{C}$ -22:6 into phosphatidylcholine did not occur in sperm isolated from the epididimis. Therefore, the laboratory rat is not a good model to study.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/038	<b>Status:</b> On-going
<b>Title:</b> Detailed Studies Into Membrane Lipid Synthesis in Human Sperm		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Feb 99	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> CPT Brenda K. Bell, MC		
COL Stephen R. Plymate, MC		
<b>Key Words:</b> lipid synthesis, human sperm		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$3494.00	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  $2 \times 10^8$  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 mM fatty acid, either  $^3H$ -9,10-16:0,  $^{14}C$ -1-16:0, or  $^{14}C$ -1-22:6. The reaction will be initiated by the addition of  $10^7$  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  $^{14}C$ -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  $^{14}C$ -22:6, 1-palmitoyl32-lyso PI (phosphatidylinositol) or -PC (phosphatidylcholine) and  $^3H$ -1-hexadecanol in the aforementioned buffer. Alternatively,  $^3H$ -hexadecanol,  $^{14}C$ -22:6, unlabeled 16:0 will be coincubated with dihydroxyacetone phosphate (DHAP). The reaction will be terminated after 1 hour and lipids will be extracted and dried. Incorporation of labeled fatty acids into sphingomyelin (SM) will be determined by detection of the fatty acyl radiolabel in the SM region of the thin layer chromatography (TLC) plates. After resolubilization in chloroform and methanol, lipids will be separated on LK5 TLC plates. Standards will be run on each plate and spots corresponding to standards will be scraped and counted. Plasmalogen formation will be assessed by performing mild acid hydrolysis on the extracted phospholipids prior to TLC or before rechromatography and determining DPM's in the fatty aldehyde and lysophospholipid regions. The presence of ether lipids will be determined by their resistance to alkaline and enzymatic hydrolysis prior to TLC. Mono and diacyl phospholipid synthesis will be assessed by free fatty acid release from SM and by using phospholipases A2 (PLA2) and B (PLB).

**Progress:** Preliminary data indicated that, under the conditions employed in these assays, ether lipids cannot be synthesized by ejaculated human sperm. An abstract was presented at the 1991 meeting of the American Society of Andrology.

No further work was done on the study in FY 91 due to the deployment of the PI to Operation Desert Storm.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 83/081	<b>Status:</b> On-going
<b>Title:</b> Studies on Fatty Acid Activation in Spermatozoa: Kinetics and Localization		
<b>Start Date:</b> 09/16/83	<b>Est. Completion Date:</b> Sep 84	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> COL Bruce L. Fariss, MC		COL Stephen R. Plymate, MC
<b>Key Words:</b> spermatozoa, fatty acid		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$785.00	<b>Periodic Review:</b> 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 (<sup>3</sup>H)-coenzyme A as the radioactive trace. Approximately 0.2 m C of (<sup>3</sup>H) 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<sup>8</sup>/ml. The assay mixture will contain palmitic acid, ATP, Mg<sup>++</sup> 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 LineweaverBurk 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 further work was done on this protocol in FY 91 due to the deployment of the PI to Operation Desert Storm. Results of preliminary studies can be found in the following articles. Jones, Plymate: Biol Reprod 39:76, 1988 . Jones, Plymate: Ann NY Acad Sci 513:571, 1987. Jones, Plymate: J Andrology 7:323, 1986

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/026	<b>Status:</b> On-going
<b>Title:</b> Neutral and Polar Lipid Synthesis in Human Spermatozoa: A Correlation with Morphology and Function		
<b>Start Date:</b> 01/15/88	<b>Est. Completion Date:</b> Jun 89	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> MAJ Karl E. Friedl, MC		COL Stephen R. Plymate, MC MAJ Charles J. Hannan, MC
<b>Key Words:</b> spermatozoa, lipids, morphology		
<b>Accumulative MEDCASE Cost:</b> \$40000.00	<b>Est. Accumulative OMA Cost:</b> \$2000.00	<b>Periodic Review:</b> 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 <sup>3</sup>H-16:0 and <sup>14</sup>C-22:6. Total lipids will be extracted using the method of Bligh and Dyer. The chloroform phase will be taken to dryness under N<sub>2</sub> at 42°C and subsequently reconstituted in a minimal volume of chloroform. The chloroform mixture will be applied to a silicic acid column and subsequently 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 eluates 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/10<sup>6</sup> sperm or nmoles phospholipid P/hour. After extracting the sperm with 0.1% Triton X100, ligase activity will be measured. Both 16:0 and 22:6 will be used as substrates in the incubations. Ligase activity will be expressed as nmoles acyl CoA formed/min/mg protein. The seminal plasma concentrations of these compounds will be measured using an enzymatic spectrophotometric technique. These parameters will be considered separately in relationship to ligase activity and lipid synthesis. Semen samples will be handled and analyzed according to the current WHO guidelines. Morphology will be assessed on fixed smears, and motility will be objectively quantified with an automated semen analyzer. With the exception of the sperm density, the semen quality will be blinded to the person performing the biochemical analyses. Incorporation rates and the distribution of the fatty acid labels and ligase activity will be correlated with sperm morphology and motility of the semen sample using either linear regression or chi-square analyses.

**Progress:** No further work was done on this study in FY 91 due to the deployment of the PI to Operation Desert Storm. The investigators are attempting to isolate sperm plasma membranes.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/070	<b>Status:</b> On-going
<b>Title:</b> Characterization of Serovar-Specific Ureaplasma Antigens by Analysis with Monoclonal Antibodies		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Oct 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC (P) Robert E. Jones, MS		
<b>Associate Investigators:</b> MAJ John E. van Hamont, MS		
<b>Key Words:</b> antigens, ureaplasma, monoclonal antibodies		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3700.00	<b>Periodic Review:</b> //

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

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

**Progress:** Serovar VIII was shown to induce the production of antibodies which failed to react with the serovar VIII immunizing antigen but were specific for any one of a number of non-serovar VIII antigens. These data suggest that *Ureaplasma* could potentially exert a mitogenic effect on its host's immune system. Additionally, ELISA and Western blot Analysis of serovars III, V, and VIII indicated that ureaplasma-specified antigens can induce antibodies which specifically cross-react with either heterologous medium components, spermatozoa, human hepatocytes, mouse hepatocytes, or spleen tissue. Ureaplasma antigens identified in this study could potentially induce an autoimmune response in a colonized host. Finally, a semiautomated fifty percent color change unit (CCU/50) titration employing fractional logarithmic dilutions was developed and evaluated for the quantitation of *Ureaplasma* in clinical samples. Results indicate that the CCU/50 assay could serve as a useful tool in further defining the association of *Ureaplasma urealyticum* with nongonococcal urethritis. A paper reporting the findings of this study was presented at the American Society for Microbiology Meeting in May 1991 as well as at four different national scientific meetings in 1990, and a paper has been submitted for consideration for publication.

Dr. van Hamont, original PI.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/077	<b>Status:</b> Completed
<b>Title:</b> Accuracy of Four Hour and Six Hour Urine Urea Nitrogen Measurements in Patients Receiving Nutritional Support		
<b>Start Date:</b> 05/18/90	<b>Est. Completion Date:</b> Dec 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Lynn M. Keenan, MC		
<b>Associate Investigators:</b> MAJ Richard H. Snyder, MC		
<b>Key Words:</b> nitrogen, four, six hr urine, measurement accuracy, nutrition		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$118.00	//

**Study Objective:** To determine the efficacy of 4 hour and 6 hour urine urea nitrogen measurements in the evaluation of nutritional balance.

**Technical Approach:** Thirty medical or surgical patients with or without Foley catheters, receiving total parenteral or enteral nutrition will be studied. The following information will be obtained from the patient's chart: diagnosis, baseline albumin, pre-albumin, total lymphocyte count, electrolytes, magnesium, phosphorus, and calcium. On day one of the study, a four hour urine specimen will be obtained between 0800 and 1200 hours. Patients will then have a six hour urine specimen obtained from 1200 to 1800 hours. On day two of the study, a 24 hour urine collection will be begun for urine urea nitrogen and creatinine. Specimens will then be processed for determination of urea nitrogen, and the 24-hour specimens will be processed for creatinine. Values for urine urea nitrogen will then be placed into the following formulas to determine positive or negative nitrogen balance: Nitrogen balance = intake nitrogen - output nitrogen. Output nitrogen =  $UUN \text{ mg}/100 \text{ cc} \times \text{urine vol} + 100 + 20\% \text{ of } UUN + 2 \text{ gm/day}$ . The values for 4 and 6 hour urine samples will be extrapolated to fit into the formula. Urine and serum creatinine will be obtained to calculate creatinine clearance. The Student's t-test will be utilized to review the data obtained.

**Progress:** The study has been completed, 31 patients were studied. The data indicate that the 4 hour and 6 hour urine urea nitrogen measurements can not reliably predict the 24 hour values in the critically ill patient.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/098	<b>Status:</b> On-going
<b>Title:</b> Does Laparoscopy Add to the Diagnosis of Nonfocal Liver Disease?		
<b>Start Date:</b> 01/04/91	<b>Est. Completion Date:</b> Apr 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Michael F. Lyons II, MC		
<b>Associate Investigators:</b> MAJ Amy M. Tsuchida, MC		CPT Robert J. Lodato, MC MAJ Gregory E. Schlepp, MC
<b>Key Words:</b> liver disease, laparoscopy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

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

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

**Progress:** Forty-six laparoscopies were evaluated, with a 62% correlation between pre and post laparoscopy diagnosis and pathological diagnosis.

## DETAIL SUMMARY SHEET

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<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/051	<b>Status:</b> On-going
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**Title:** A Long-Term Screening Project for the Prevention of Adenocarcinoma of the Esophagus in Patients with Barrett's Esophagus, Intestinal Metaplasia of the Stomach and Partial Gastrectomy for Peptic .....

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<b>Start Date:</b> 03/15/91	<b>Est. Completion Date:</b> Mar 97
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<b>Department:</b> Medicine	<b>Facility:</b> MAMC
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**Principal Investigator:** MAJ Michael F. Lyons II, MC

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<b>Associate Investigators:</b> MAJ Gregory E. Schlepp, MC MAJ Mark D. Brissette, MC	MAJ Amy M. Tsuchida, MC COL Michael J. Carlon, MC
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**Key Words:** cancer:esophagus,Barrett's,stomach

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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Study Objective: To prospectively follow patients with Barrett's Esophagus, intestinal metaplasia of the stomach, and postpartial gastrectomy in an attempt to identify precancerous or early cancerous changes in tissues utilizing histology, flow cytometry, immunochemistry, and cytogenetics.

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

Progress: This study is awaiting revision and final approval by the IRB. No patients have been entered.

DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/073	<b>Status:</b> On-going
<b>Title:</b> Vagal Nerve Stimulation via Neurocybernetic Prosthesis for the Control of Chronic Epilepsy		
<b>Start Date:</b> 06/21/91	<b>Est. Completion Date:</b> Jan 96	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ John W. McBurney, MC		
<b>Associate Investigators:</b> CPT Renee M. Bernier, MC		
<b>LTC Joseph P. McCarty, MC</b>		
<b>Key Words:</b> epilepsy, vagal nerve stimulation, neurocybernetic		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine whether stimulation of the vagus nerve via an implanted electrical stimulating device is effective in reducing frequency of simple partial, complex partial, and secondarily generalized seizures in patients with frequent seizures uncontrolled by standard antiepileptic drugs.

**Technical Approach:** In this blinded, randomized, parallel, controlled study, we anticipate entering 2 to 8 subjects. After an initial screening period in which a baseline frequency for seizures is established, the Neurocybernetic Prosthesis will be implanted. This prosthesis is an implantable multi-programmable generator that delivers constant current electrical signals to the vagus nerve for the purposes of reducing the frequency and/or severity of epileptic seizures. The device is implanted into the subcutaneous chest pocket just below the clavicle similar to a cardiac pacemaker. The stimulation signal is transmitted from the prosthesis to the vagus nerve via stimulation with programming software and a programming wand. After a two week recovery phase, patients will be randomized to either a high or low stimulation parameter group. Over the next five days the patients will undergo a gradual "ramp up" with stimulator settings to the maximum tolerated level in the high group and to a level sufficient to produce a physiological response such as a sensation in the throat or a change in voice in the low group. Efficacy and side effects data will then be collected for 14 weeks. Patients in both groups may use a magnet to induce a stimulus in order to abort seizures. The magnet current setting in the low stimulation group will be set and maintained at 0 milliamps. After the initial 14 weeks, the investigators may adjust the settings on the prosthesis in an uncontrolled phase of the study.

**Progress:** This study is awaiting approval from HSC. No patient have been entered.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91      **Protocol No.:** 91/072      **Status:** Terminated

**Title:** Valproate Prophylaxis of Post-traumatic Seizures

**Start Date:** 06/21/91      **Est. Completion Date:** Feb 96

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

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

**Associate Investigators:**  
Sureyya S. Dikmen, Ph.D.      H. Richard Winn, M.D.  
Alan J. Wilensky, M.D., Ph.D.      Nancy R. Temkin, Ph.D.  
Gail Anderson, Ph.D.      Sharon Chabal, R.N.  
Robert Hendryx, Pharm.D.      Kelly Kobayashi, Pharm.D.

**Key Words:** seizures, valproate

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

**Study Objective:** To test the hypothesis that prophylactic treatment of severely head-injured patients with therapeutic doses of a single anticonvulsant, valproate, will decrease the incidence of post-traumatic seizures. The second aim is to determine if such treatment has any significant side effects, including medical complications and impact upon the neuropsychological, emotional, and psychosocial functioning of head injured patients.

**Technical Approach:** The study is a two-group randomized, double-blind trial. The experimental group receives a loading dose of valproate within 24 hr of injury and thereafter a dose of valproate sufficient to keep plasma levels within the therapeutic range (50-150 mg/l). This group is split into two subgroups. One subgroup discontinues valproate after a month, the other discontinues valproate at 6 months. The control group treatment follows from the results of our Dilantin study. It consists of a loading dose of phenytoin, one week of maintenance phenytoin, then placebo for the rest of the six months. We considered using only placebo from time zero as the control regimen, but the results of our phenytoin study made this approach ethically difficult to justify. Untreated observation until 2 years post injury follows for both groups. Information pertaining to seizure occurrence and drug effects is gathered at visits scheduled 1 month post-injury and, beginning 3 months after the injury, at 3 month intervals up to 24 months after injury. Comprehensive neuropsychological and psychosocial examinations are done at 3, 9, and 18 months after surgery (when physically possible). An effective sample size of 164 experimental and 82 control patients in each group will be needed as determined by power analysis.

**Progress:** Although the study design and feasibility of this protocol were approved by the Clinical Investigation Committee, the Human Use committee disapproved this study due to the inability to obtain consent in a considerable number of these patients who would be entering the study through a trauma center.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/016	<b>Status:</b> Completed
<b>Title:</b> Higher Cortical Functioning in School Aged Children with Headache		
<b>Start Date:</b> 01/16/87	<b>Est. Completion Date:</b> Jan 89	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Joseph P. McCarty, MC		
<b>Associate Investigators:</b> MAJ William M. McClintock, MC		CPT Barry S. Anton, USAR
<b>Key Words:</b> headache,cortical functioning,children:school aged		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/21/88

**Study Objective:** To determine if subtle deficits in higher cortical functioning may contribute to migraine headache.

**Technical Approach:** Three groups of school aged children between the ages of six and twelve years will be studied. Group 1: Ten children with muscle contraction headaches (intermittent at least one headache every two months for one year). Group 2: Ten children with migraine headaches (intermittent at least one headache every two months for one year). Group 3: Ten siblings of children from group 1 or group 2 with no history of headache or other medical condition (controls). Subjects in the two experimental groups will have no history of progressive neurologic disease or other serious medical condition. A complete history (including onset of headache, frequency, cause, intensity, location and character of pain, associated symptoms, and relief factors), family history of headache, physical exam, neurological examination and neurophysiological assessment will be conducted on each patient. The neuropsychological examination will include the following standardized test instruments: Wechsler Intelligence Scale for Children (Revised), Wide Range Achievement Test Revised, Trail Making Test, Bilateral Name Writing, Word Fluency Test, Bilateral Finger Agnosia, Token Test for Children, Grooved Pegboard, Digit Symbol Test (oral and written), and Child Behavior Checklist. Tests will be given to all children in the same sequence. In order to assess current medical status and screen for medical disorders that might affect neuropsychological test results, medical records of all subjects will be thoroughly reviewed. A parent of each child will be asked to complete a problem check list and a detailed medical history questionnaire.

**Progress:** The protocol has been completed, 55 subjects were studied. A poster presentation, utilizing data from this study, was presented at the 1990 meeting of the Association for Applied Psychophysiology and Biofeedback. The investigators had originally planned to study more subjects, but made the decision in FY 91 to close the protocol due to staffing shortages.

Replaced Dr. McClintock, Oct 88.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/065                      **Status:** Completed

**Title:** A Comparison of 7 vs 14 days Therapy with Trimethoprim/Sulfamethoxazole  
in the Treatment of Acute Pyelonephritis

**Start Date:** 03/18/88                      **Est. Completion Date:** May 89

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

**Principal Investigator:** LTC Rodney A. Michael, MC

**Associate Investigators:**  
CPT Patrick D. Gorman, MC                      CPT William A. Pearce, MC  
CPT Paula S. Vogel, MC

**Key Words:** pyelonephritis, trimethoprim, sulfamethoxazole

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	07/28/89

Study Objective: To compare 7 vs 14 days of TMP/SMX treatment in acute pyelonephritis and also to compare the results to those of a previous study of 14 days of TMP/SMX plus gentamicin.

Technical Approach: All patients will initially receive intravenous TMP/SMX every 12 hours for at least six doses and until afebrile. Thereafter, patients will receive oral TMP/SMX twice daily and continue oral therapy as outpatients. Group A will receive 14 days of therapy and Group B will receive 7 days of therapy. All subjects will have a physical exam and a symptom assessment before the institution of therapy and daily while in the hospital. Urine samples will be obtained before therapy and daily thereafter during the hospital stay. Quantitative aerobic bacterial cultures will be performed on all specimens. Antibody coated bacteria testing will be performed on all initial specimens which grow > 10<sup>3</sup> cfu/ml of a recognized uropathogen. A dipstick urinalysis will be done on all urine specimens. Vaginal cultures and blood specimens will be obtained upon admission and again on the third day. Patients will return to clinic at one and four weeks following completion of therapy. At each follow-up visit, patients will undergo symptom assessment and a physical exam and urine specimens, cultures of the vagina, and blood samples will be collected. At the one week visit patients will be questioned regarding self-administration of medications and will return the dosing calendar which they were given at discharge. At two weeks following the end of therapy, patients will return to provide a clean-catch midstream urine specimen for culture and urinalysis. Appropriate statistical techniques will be used to compare the baseline characteristics of the patient population and to analyze the adverse effects and clinical laboratory data. Categorical data analysis of the efficacy data will be performed as warranted.

Progress: No patients have been entered in the last three years due to the departure of all investigators. Dr. Michael was unable to find time to do more work on this protocol after he took over as the PI in July 1991. Although 25 patients were entered, many data sheets are incomplete, therefore no paper is being written.

Dr. Michael replaced Dr. Vogel as the PI, Jul 89.  
Dr. Vogel replaced Dr. Gorman as PI, Aug 88.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/060	<b>Status:</b> Terminated
<b>Title:</b> Clinical Evaluation of PS Medical Lumbar Access Catheter		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Apr 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC William J. Morris, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> catheter,lumbar:catheter		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1000.00	05/03/91

**Study Objective:** To clinically evaluate the safety and effectiveness of the Lumbar Access Catheter (LAC) for temporary, repeated lumbar CSF access and morphine delivery to either the epidural or subarachnoid space.

**Technical Approach:** Approximately 100 patients will be studied in this multi-institution protocol. Patient eligibility will be based on pain of cancerous origin or therapies associated with cancer, conventional pain management methods have been unsatisfactory, previous opioid experience, infection free, and life expectancy at least 1 month. Pregnant patients will be excluded. The LAC is designed to provide short term access to either the lumbar epidural space or the lumbar subarachnoid space for morphine sulfate delivery and will also provide a means for sampling cerebrospinal fluid. The use of this device also allows the investigator to evaluate a patient's ability to withstand infusion therapy. The specific lumbar access location will be determined by the investigator based on the individual patient's condition and pain management requirements. The surgical technique for placement of the LAC is similar to that used for other lumbar catheters and is not investigational in nature. The catheter will be left in place for a period of 7 days for the delivery of a preservativefree morphine sulfate. To avoid the introduction of unnecessary variables, only Duramorph will be used. The initial dosage and delivery route will be determined for each patient by the investigator, based on the patient's daily narcotic experience prior to device placement. The decision to increase or decrease the dosage throughout the investigation will be the responsibility of the investigator. A morphine administration log will be maintained on a daily basis to monitor morphine in-take. A satisfactory device performance assessment will be determined by the absence of the following characteristics: kinked catheter, broken catheter, catheter occlusion, catheter migration, leakage of fluid into surrounding tissues, leakage of fluid from connector, filter or injection site, or filter occlusion.

**Progress:** This study was terminated by the manufacturer of the devices because another similar device has been approved by the FDA. No patients were entered at MAMC because the protocol was terminated before approval was received from HSC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/061		<b>Status:</b> Terminated	
<b>Title:</b> Clinical Evaluation of PS Medical Lumbar Access Device					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b> Apr 91		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC William J. Morris, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> lumbar:access device					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$1000.00		05/03/91	

**Study Objective:** To clinically evaluate the safety and effectiveness of the Lumbar Access Device (LAD) for repeated lumbar CSF access and morphine delivery to either the epidural or subarachnoid space.

**Technical Approach:** Approximately 100 patients will be studied in this multi-institution protocol. Patient eligibility will be based on pain of cancerous origin or therapies associated with cancer, conventional pain management methods have been unsatisfactory, previous opioid experience, tolerance to bolus injection of morphine sulfate in lumbar subarachnoid or lumbar epidural space, infection free, life expectancy at least 1 month, and tissue surrounding port implantation site sufficient to accommodate port size. Pregnant patients will be excluded. The LAD is designed to provide percutaneous access to either the lumbar epidural space or the lumbar subarachnoid space for morphine sulfate delivery to manage a patient's cancer pain and will also provide a means for sampling cerebrospinal fluid. The specific lumbar access location will be determined by the investigator based on the individual patient's condition and pain management requirements. The surgical technique for placement of the LAD is similar to that used for other lumbar catheters and is not investigational in nature. To avoid the introduction of unnecessary variables, only Duramorph will be used. The initial dosage and delivery route will be determined for each patient by the investigator, based on the patient's daily narcotic experience prior to device placement and preoperative epidural or subarachnoid morphine bolus assessment. The decision to increase or decrease the dosage throughout the investigation will be the responsibility of the investigator. A morphine administration log will be maintained on a daily basis to monitor morphine in-take. A follow-up report will be completed at 1 week, 2 weeks, and 1 month following device implantation. Subsequent follow-ups will be performed on a monthly basis up to 12 months. A satisfactory device performance assessment will be determined by the absence of the following characteristics: kinked catheter, broken catheter, catheter/port occlusion, device-caused necrosis/tissue erosion, component migration, catheter/port junction disconnect, and leakage of fluid into surrounding tissues.

**Progress:** This study was terminated by the manufacturer of the device because another similar device was approved by the FDA. No patients were entered at MAMC because the protocol was terminated before approval was received from HSC.



DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/062                      **Status:** Completed

**Title:** A Prospective Evaluation of Cholesterol Embolism After Left Heart Catheterization

**Start Date:** 06/15/90                      **Est. Completion Date:** Oct 91

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

**Principal Investigator:** CPT Timothy R. Murray, MC

<b>Associate Investigators:</b>	CPT William T. Browne, MC
MAJ Howard H. Cushner, MC	COL Roger F. Chamusco, MC
MAJ Duane J. Jeffers, MC	COL Klaus B. Jade, MC
MAJ Alice M. Mascette, MC	CPT Donna L. Mercado, MC
CPT James W. Norys, MC	MAJ Doreen Saltiel, MC
MAJ Anthony R. Truxal, MC	

**Key Words:** embolism,cholesterol,catherization,left heart

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To study prospectively the clinical manifestations and complications of cholesterol embolism in patients undergoing left heart catheterization and to measure the incidence of cholesterol emboli, the sensitivity and specificity of tests used to diagnose cholesterol emboli, and to define short term prognosis.

**Technical Approach:** Approximately 400 patients <50 years old will be studied. Standard precatheterization evaluation will be performed to include a complete history, physical examination, and standard lab studies, as well as hand differential and erythrocyte sedimentation rate (ESR). Post-catheterization Day 1, the patient will be examined for post-catheterization assessments, with close attention to the skin and retinal exam. Samples will be obtained for amylase, CBC with hand differential, and ESR. Any abnormalities will be documented and confirmed by Dermatology, Nephrology, or Ophthalmology. At 45 days post-catheterization, the patient will return for a follow-up visit and complete a questionnaire regarding a review of post-discharge symptoms. At this followup, a repeat history and physical exam will be completed as well standard laboratory studies, plus amylase, CBC with hand differential, and ESR. Data will be analyzed to define the incidence of cholesterol embolism and likelihood ratios for specific findings (likelihood ratio = sensitivity/1 specificity).

**Progress:** The protocol has been completed, 70 patients were entered in the study. A manuscript is in preparation.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/097	<b>Status:</b> On-going
<b>Title:</b> The Use of Thyroid Tissue Obtained by Fine Needle Aspiration (FNA) as Substrate for Polymerase Chain Reaction (PCR) Amplification of Thyroglobulin and the Papillary Thyroid Cancer (PTC) Oncogene		
<b>Start Date:</b> 09/27/91	<b>Est. Completion Date:</b> Apr 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Peele, MC		
<b>Associate Investigators:</b> CPT Robert M. Tuttle, MC		
<b>Key Words:</b> cancer:thyroid,PCR,thyroglobulin,FNA,PTC oncogene		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$1250.00	<b>Periodic Review:</b> //

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

**Technical Approach:** Twenty patients undergoing fine needle aspiration of the thyroid for clinically indicated evaluation of thyroid nodules or masses will be offered participation in this study. Four to six aspirations will be performed as per the clinic routine. The aspiration needle will be rinsed into a centrifuge tube containing RPMI cell culture media. The adequacy of aspirated material present on slides prepared in the clinic for cytologic interpretation will be determined according to accepted guidelines. The purpose of the FNA is to provide adequate material for the cytologic evaluation. Clinical material present in excess of this standard will be considered for use in this protocol. Excess aspiration material will be collected by needle rinses into 1000 µl of either RPMI cell culture media or phosphate buffered saline (PBS). Cells will be rapidly pelleted by centrifugation after the rinse to remove excess plasma proteins. The cell pellet will be resuspended in 25 µl DEPC treated water and rapidly chilled to -70 deg C. This material will then be stored until laboratory study begins.

PCR will be used to amplify thyroidal genomic and mRNA. The material collected from the FNA will be heated to 65 deg C in the presence of RNasin and hypotonic DEPC treated water to linearize the nucleic acids. The mRNA and DNA will serve as the templates for the PCR amplification. Three sets of PCR primers and oligomers will be synthesized. All the primer sets have an engineered span containing a restriction enzyme site (HINDIII) on the 5' portion to allow insertion of the amplified material into a sequencing vector. Thyroglobulin will be amplified as the positive control, the oncogenes PTC and RET will be amplified from aliquots of the same material. The first step in the amplification of the mRNA will be the synthesis of first strand complementary DNA. The cDNA and linearized DNA will be amplified as per standard

PCR protocols for 35 cycles. The amplified products are separated on an agarose gel and blotted onto a nylon membrane, the blot will be probed with the specifically engineered oligonucleotide probes to determine the molecular identity of the amplified PCR products. Amplified fragments of interest will be cloned into an expression vector and sequenced using Taq polymerase and conventional dideoxynucleotide chain elongation termination.

Progress: New study, no patients entered.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/082	<b>Status:</b> On-going
<b>Title:</b> Iontophoresis Therapy for Rheumatoid Arthritis		
<b>Start Date:</b> 07/19/91	<b>Est. Completion Date:</b> Aug 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Kathryn K. Riordan, MC		
<b>Associate Investigators:</b> MAJ Thomas L. Irvin, MC		
<b>Key Words:</b> arthritis:rheumatoid,iontophoresis		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of synovitis of the hand and wrist joints in patients with rheumatoid arthritis (RA), specifically to determine if iontophoresis will be effective in reducing synovitis in RA and as effective as a local injection of corticosteroid.

**Technical Approach:** In patients with active RA from two to five joints will be selected for study, with at least 1+ swelling, clinically judged as candidates for local injection of corticosteroid. One additional joint will be identified to monitor for systemic effect (control joint) using the same criteria as for the study joints. No therapeutic interventions will be made on the control joint, the control joint is determined as the initial joint randomized on the randomization protocol. The joints will be randomized as follows: (A) Iontophoresis "treatment" with corticosteroid for 6 treatments, two per week for 3 weeks and one sham needle "injection" at the third week. (B) One injection of 20 mg of 40 mg/ml triamcinolone acetonide using a 22 gauge needle per standard injection therapy at the third week following sham iontophoresis twice weekly for three weeks. (C) Sham iontophoresis without corticosteroid for twice weekly for three weeks and one sham needle "injection" at the third week (Placebo joints).

The treatment of the patient's systemic disease activity will continue throughout the study. Changes in systemic therapy will continue to be made as it is deemed appropriate by the patient's primary physician. The patient's local medical therapy of the joints under investigation, including splinting and exercises, will remain constant for one week preceding and during the first 2 months of the study. Injection of other joints other than those included in the study will not be allowed for the first two months of the study or within one week preceding the study.

The sham needle injection will be an injection of 0.1 cc sterile normal saline using a 27 gauge needle. The patient and a physician evaluator will be blinded as to the specific treatment. The same physician evaluator will see the patient on each visit. Thus 2 medical care personnel will monitor the patient at the initial and weekly visits - one (unblinded) will administer the medication and the other (blinded) will evaluate the effectiveness of the treatment. The patient will be unblinded 4 weeks after completion of the treatments. The blinded physician will reexamine the patient after completion of the treatments at 1, 2, 3, 4, 8, and 12 weeks. At the time that the patient is unblinded, if a specific joint continues to be markedly symptomatic, alternative therapeutic interventions will be discussed. If additional treatment is started at this time that joint will not be included in the longterm data. Reasons for withdrawal from treatment groups will be analyzed and discussed in final data analysis.

Progress: This study has not been implemented. The PI is awaiting final approval from HSC to accept the use of loaned equipment.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/083	<b>Status:</b> On-going
<b>Title:</b> Iontophoresis Therapy for Bursitis and Tendinitis		
<b>Start Date:</b> 07/19/91	<b>Est. Completion Date:</b> Aug 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Kathryn K. Riordan, MC		
<b>Associate Investigators:</b> MAJ Thomas L. Irvin, MC		
<b>Key Words:</b> bursitis,tendinitis,iontophoresis		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of lateral epicondylitis, bicipital tendinitis, subdeltoid bursitis, olecranon bursitis, and achilles tendinitis. The research questions to be answered are: Will iontophoresis be effective in treating bursitis and tendinitis and is iontophoresis more, less, or equally as effective as a local injection of corticosteroid.

**Technical Approach:** Subjects with acute, subacute, and chronic bicipital tendinitis, lateral epicondylitis, subdeltoid bursitis, olecranon bursitis, and achilles tendinitis will be asked to enter the study. All subjects will receive standard therapeutic exercises, including ice or local heat applications but no ultrasound or "deep heat" therapy. All subjects will receive naproxen 500 mg bid for one month. If not tolerated, the subject will use ibuprofen 800 mg tid. All subjects with lateral epicondylitis will wear an elastic "tennis elbow splint" during the study. The subjects will be randomized as follows: (A) Iontophoresis "treatment" with corticosteroid twice weekly for 3 weeks, and one sham needle "injection" (normal saline) at the third week. (B) One injection of 20 mg of 40 mg/ml triamcinolone acetonide using a 22 gauge needle per standard injection therapy, at the third week following sham iontophoresis, twice weekly for three weeks. (C) Sham iontophoresis without corticosteroid twice weekly for 3 weeks and one sham needle "injection" at the third week.

Subjects with achilles tendinitis will be randomized to groups A and C only without a sham injection. The same evaluator will see the patient on each visit and will be blinded as to treatment received. The patient will be unblinded 4 weeks after completion of the treatments. The blinded physician will reexamine the subject after completion of the treatments at 1, 2, 3, 4, 8, and 12 weeks.

The following data will be collected on the treated joints: Tenderness and swelling assessment, ROM, subject's evaluation of pain and swelling, subject's evaluation of improvement, and physician's evaluation of improvement.

The Phoresor II iontophoretic drug delivery system will be used for all iontophoresis. Dexamethasone sodium phosphate 0.5cc will be used in the iontophoresis treatments. Lidocaine hydrochloride 4% will be used in all treatments (including shams).

**Progress:** The protocol has not been implemented. The PI is awaiting approval from HSC to accept the use of loaned equipment.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/099		<b>Status:</b> On-going	
<b>Title:</b> Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b> Sep 91		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Bernard J. Roth, MC					
<b>Associate Investigators:</b>			LTC William H. Cragun, MC		
<b>Key Words:</b> pleural effusion,albumin,congestive heart failure					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**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 thoracenteses. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria.

**Progress:** One patient has been entered in the study. The investigators are in the process of trying to get other medical centers to take part in the study in order to accrue sufficient patients.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/015	<b>Status:</b> On-going
<b>Title:</b> Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure		
<b>Start Date:</b> 11/16/90	<b>Est. Completion Date:</b> Oct 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Bernard J. Roth, MC		
<b>Associate Investigators:</b> MAJ Bruce S. Grover, MC		LTC William H. Cragun, MC
<b>Key Words:</b> positive pressure ventilation, air flow obstruction, nasal mask		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$260.00	<b>Periodic Review:</b> //

**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 minute walking distance. Spirometry, pulse oximetry, and end-tidal capnography will be repeated once weekly for four weeks. After four weeks, baseline studies will be repeated and an overnight polysomnography will be performed which includes electroencephalogram, electromyogram, electro-oculogra, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous capnography. At this time the patient will be tested to determine if he tolerates intermittent positive pressure ventilation through a nose mask (nIPPV). Patients who tolerate nIVPP will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAPA and nIPPV patients using Student's T test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or PaCO<sub>2</sub> will be considered a positive result of nIPPV.

**Progress:** Six patients have been entered in the study.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/043	<b>Status:</b> On-going
<b>Title:</b> The Effects of Testosterone Replacement in Hypogonadal, Malnourished Patients with Chronic Obstructive Pulmonary Disease (COPD)		
<b>Start Date:</b> 09/15/89	<b>Est. Completion Date:</b> Oct 89	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Bernard J. Roth, MC		
<b>Associate Investigators:</b> MAJ John P. Kushner, MC		COL Stephen R. Plymate, MC MAJ Bruce S. Grover, MC
<b>Key Words:</b> CPOD, testosterone, hypogonadal, malnourished		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$65.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine if testosterone replacement in malnourished, hypogonadal male patients with COPD will result in improved nutritional status, and, if so, does this lead to improved respiratory muscle strength and increased exercise endurance.

**Technical Approach:** Twenty male patients >40 years will have baseline spirometry, maximum inspiratory and expiratory pressures, maximum voluntary ventilation, 6 minute walking distance, triceps skin fold, midarm muscle circumference, testosterone and lipoprotein profiles, electrolytes, liver function test, ABG, total lymphocyte count, hematocrit, transferrin, albumin, nitrogen balance, creatinine height index, anergy panel, % ideal body weight, and % usual body weight. A clinical assessment (history and physical exam) will be done and a diet history taken. Patients will be allowed to continue usual medications and activities and exercise will be unrestricted. If either total or free testosterone is low, the patient will be admitted to the hospital for five days. A dietary regimen will be initiated with a regular diet, supplemented on Day 3 with Pulmocare, one can three times a day. Calorie counting will be performed to assess nitrogen balance on Days 2 and 5. An interview and patient log will be used to count calories. Patients will be randomized to either testosterone enanthate, 100 mg/ml, or placebo injections. Injections will be given on Day 3 and then once a week for four doses. On Day 5 repeat studies will include: ABG, 24 hr urine urea nitrogen, calorie count, weight, change in weight, and testosterone profile. At the end of weeks 2 and 4 all baseline tests will be repeated except for ABG. This protocol was amended in Sep 89 in order to determine the relationship of testosterone to pulmonary function, as measured by FEV<sub>1</sub>, 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<sub>1</sub> 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:** Thirty-six subjects were studied on Part I of this study. There appears to be a high rate (53%) of hypogonadism in patients with COPD. Four patients have been entered on Part 2 of the study.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/036                      **Status:** On-going

**Title:** Infarct Artery Patency & Reocclusion: A Randomized Multicenter Trial  
Comparing a "Front-Loaded" 90 Min Infusion of Recombinant Human Tissue-  
Type Plasminogen Activator with the Standard 3 Hour Infusion

**Start Date:** 05/18/90                      **Est. Completion Date:** Dec 91

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

**Principal Investigator:** MAJ Doreen Saltiel, MC

<b>Associate Investigators:</b>	COL Roger F. Chamusco, MC
MAJ Alice M. Mascette, MC	CPT Sheri E. Nottestad, MC
LTC Cloyd B. Gatrell, MC	MAJ Rodney C. Davis, MC
COL Joseph A. Paris, MC	LTC (P) Dale Wortham, MC
LTC George Rebecca, MC	MAJ Thomas Martyak, MC

**Key Words:** plasminogen activator, infarct artery patency

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$15000.00	04/05/91

Study Objective: To determine whether a "front loaded" 90 minute infusion of recombinant human tissue-type plasminogen activator (rt-PA) is superior to the standard 3-hour infusion in terms of infarct artery patency and reocclusion.

Technical Approach: This will be a multicenter study of 160 patients <75 years of age. Patients with symptoms of chest pain typical of an acute myocardial infarction with onset within six hours of presentation, accompanied by electrocardiographic ST elevation of 1 mm or more in two or more contiguous leads or tall peaked hyperacute T-waves in two or more contiguous leads will be studied. Patients will be randomized over a period of 12-18 months to receive either a standard FDA approved 3-hour intravenous infusion of 100 mg of rt-PA or a "front-loaded" 90 minute intravenous infusion of 100 mg of rt-PA. One hour after completion of the infusion of rt-PA, all patients will undergo diagnostic coronary and left ventricular cineangiography. Infarct vessel patency will be determined in accordance with the thrombolysis in myocardial infarction (TIMI) grading system. Patients will undergo a second coronary arteriogram 7-10 days later and infarct vessel patency will be reassessed.

Progress: Thirty four (34) subjects have been studied. Thus far, the data indicate no difference in the two groups.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/035	<b>Status:</b> Suspended
<b>Title:</b> Home Intravenous Antibiotic and Heparin Therapy in a Military Setting		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Feb 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Phillip S. Schwartz, MC		
<b>Associate Investigators:</b> CPT Anne E. Vockroth, MC		MAJ Richard H. Snyder, MC
<b>Key Words:</b> IV therapy, antibiotic therapy, heparin therapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To demonstrate the safety and cost effectiveness of home intravenous antibiotic and heparin therapy in a military hospital setting.

**Technical Approach:** Approximately 30, medically stable patients > 18 years will be enrolled. Eligible patients will be those requiring >10 days total antibiotic therapy (minimum 5 days of home care) and patients requiring 7-14 days of heparin therapy secondary to deep venous thrombosis. Before patients are released from the hospital, the patient and a family member will be given instruction in maintaining the access device, drug mixture and storage, infusion technique, therapy monitoring, and trouble shooting of potential side effects of the therapy. If proficiency and compliance can not be documented after an appropriate period of instruction, the patient will be taken off study. A home health nurse will be present for the first dose of medication. Thereafter, the medication will be given by the patient or the trained family member. The home health nurse will make periodic home visits to check on the patient's progress (at least every three days). Samples for laboratory analysis will be drawn by the home health nurse as recommended for the drug each individual patient is receiving. The paired t-test will be used to compare actual cost to hospital cost and safety will be described using frequencies.

**Progress:** Approximately 10 subjects were entered in the study.

The protocol has been suspended because there was some question for the need of more subjects and also an appropriate consent form upon continuing review.

Dr. Vockroth, original PI.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/082	<b>Status:</b> On-going
<b>Title:</b> A Pilot Study of Carboplatin and Daily Oral Etoposide in the Treatment of Advanced Non-Small Cell Lung Cancer		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Jun 93	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Everardo E. Cobos Jr., MC	LTC Howard Davidson, MC	MAJ Patrick L. Gomez, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:lung:non-small cell,carboplatin,etoposide		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3000.00	<b>Periodic Review:</b> //

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

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

**Progress:** Seven patients were entered in FY 91 for a total of nine subjects. A small number of responses has been seen. The significance will be determined when 14 patients have been accrued.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/007	<b>Status:</b> On-going
<b>Title:</b> Treatment of Thrombocytopenia, Hemolytic Anemia, or Neutropenia with Ascorbic Acid		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Oct 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	LTC Howard Davidson, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> ascorbic acid, thrombocytopenia, hemolytic anemia, neutropenia		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$585.00	<b>Periodic Review:</b> //

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

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

**Progress:** Two additional patients were entered in the study in FY 91 for a total of four subjects. Accrual has been slow but is continuing.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 84/040		<b>Status:</b> On-going	
<b>Title:</b> Treatment of Graves' Ophthalmopathy with Cyclosporin					
<b>Start Date:</b> 04/20/84			<b>Est. Completion Date:</b> Sep 86		
<b>Department:</b> Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary L. Treece, MC					
<b>Associate Investigators:</b>		COL Stanley C. Allison, MC			
COL Francis G. LaPianan, MC		COL Leonard Wartofsky, MC			
LTC (P) Robert E. Jones, MS		CPT Andrew Ahmann, MC			
<b>Key Words:</b> ophthalmopathy:Graves',cyclosporin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$200.00		04/17/87	

**Study Objective:** To assess the efficacy of Cyclosporin treatment on the ophthalmopathy of Graves' disease.

**Technical Approach:** This will be a collaborative study with the Endocrine Services at the other MEDCEN's. The study will be composed of a random cross-over design comparing cyclosporin treatment to the most commonly employed current therapy, high dose oral prednisone. Since responses tend to be seen rapidly the drugs will each be administered for three weeks. Each patient's response to one drug will be compared to his own response to the other drug. A total of 20 patients will be evaluated initially with random alternating allocation to either Group A or Group B: Group A: (1) prednisone, 40 mg, T.I.D. x three weeks (2) full evaluation of response (3) cyclosporin 5-10 mg/kg/day x three weeks Group B: Reverse order of Group A. Clinical assessment will be weekly with ophthalmopathy index and T<sub>4</sub>, T<sub>3</sub>, etc, at 0, 4, 6, 9, and 12 weeks. TRH will be done at 0, 4, and 9 weeks, and cyclosporin or prednisone levels will be done at 2, 3, 4, 7, 8, and 9 weeks.

**Progress:** No patients were entered in this study in FY 91. Two patients were entered at MAMC in previous years. Recruitment of suitable patients has been unexpectedly slow, apparently due to a decline in severe Graves' ophthalmopathy nation wide.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 81/056	<b>Status:</b> On-going
<b>Title:</b> The Effect of Nephrosis on Treated Hypothyroidism		
<b>Start Date:</b> 03/17/81	<b>Est. Completion Date:</b> Sep 86	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Gary L. Treece, MC		
<b>Associate Investigators:</b>		
COL Stephen R. Plymate, MC	COL Stanton R. Brown, MC	CPT Jeffrey Addison, MC
MAJ Howard M. Cushner, MC	MAJ Charles J. Hannan, MC	
<b>Key Words:</b> hypothyroidism, nephrosis		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$2425.00	//

**Study Objective:** To document an anticipated increased dosage requirement for patients with treated hypothyroidism who develop the nephrotic syndrome. Related objectives include answers to the questions: (1) does nephrosis unmask hypothyroidism and (2) does nephrosis mask hyperthyroidism?

**Technical Approach:** SUBJECTS: normals, normals treated with L-Thyroxine for one month, patients with hyperthyroidism, patients with hypothyroidism, primary untreated or treated for one month with L-thyroxine, and patients with the nephrotic syndrome untreated or treated for one month with L-thyroxine. All subjects will have a 24-hr urine for volume, creatinine, total protein, urine protein, electrophoresis, T<sub>4</sub>, and T<sub>3</sub>. Fasting samples will be drawn for SMAC-20, T<sub>4</sub>, T<sub>3</sub> resin, T<sub>3</sub> by RIA, TSH, THAT (an extra tube will be drawn for free T<sub>4</sub>, reverse T<sub>3</sub>, and TBG). A fasting TRH test will be done and blood for TSH will be drawn at 0, 30, and 60 mins post injection. The above procedures will be repeated after at least 30 days on one or more doses of T<sub>4</sub> for the treated groups. Urine protein electrophoresis will not be performed on urine with a total protein of <150 mg for 24 hrs, patients with known cardiovascular disease or >50 years will be excluded from the treated groups, and 24-hr urines will be obtained prior to or at least 72 hours after the TRH test.

**Progress:** No additional patients were entered in FY 91. Three of the eight subjects entered in previous years had evidence of primary hypothyroidism on the basis of the TRH testing. One subject had an elevated baseline TSH but normal response to TRH. Those found to be hypothyroid have been treated with thyroid hormones. Follow-up TRH testing has been incomplete. Urinary T<sub>4</sub>, T<sub>3</sub> assay development has not been accomplished. Preliminary results indicate a higher incidence of hypothyroidism associated with the nephrotic syndrome than previously reported.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 82/005                      **Status:** On-going

**Title:** The Utility of Urinary Free Cortisol to Monitor Replacement Therapy for Adrenal Insufficiency

**Start Date:** 11/20/81                      **Est. Completion Date:** Sep 86

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

**Principal Investigator:** COL Gary L. Treece, MC

<b>Associate Investigators:</b>	COL Bruce L. Fariss, MC
MAJ Robert E. Jackson III, MC	LTC (P) Robert E. Jones, MS
LTC Daniel H. Knodel, MC	MAJ William R. Sheldon Jr., MC

**Key Words:** adrenal insufficiency, urinary free cortisol

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$700.00	11/27/87

**Study Objective:** To evaluate the possible usefulness of monitoring urinary free cortisol as an objective parameter of therapy that may avoid both underand over-medicating patients with chronic adrenal insufficiency.

**Technical Approach:** Ten euthyroid patients with spontaneous or surgically induced adrenal insufficiency will be evaluated. Patients taking Aldactone will not be included unless it can be withdrawn. Patient involvement will be divided into 3 parts. During all 3 parts, the dose of any mineralocorticoid will not be altered. Patients having been on previous maintenance dose of glucocorticoid for at least 3 days and free of acute illness will be asked to collect 2 consecutive 24 hr urines for free cortisol, 17 LH corticosteroids, and creatinine. A fasting plasma cortisol, an ACTH level, and a 2-hr post-dose cortisol will be drawn on one of the days that the urine is being collected. Patients will then be asked to take an amount of glucocorticoid, orally, equivalent to 50% of their maintenance dosage for 7 days, after which blood and urine will be obtained. If a difference should be found in any of the parameters between patients taking hydrocortisone vs cortisone, several patients will be asked to switch to an equivalent amount of the other drug in the maintenance dosage for 7 days after which blood and urine will be obtained. If a difference should be found in any of the parameters between patients taking mineralocorticoid and those not taking such a drug, several patients on mineralocorticoid will be asked to discontinue the drug for 7 days and be restudied. Several patients not taking mineralocorticoid will be asked to take Florinef 0.1 mg/day orally for 7 days and be restudied as above. At the conclusion of the study, the patients will be given their maintenance dose and type of drug(s) unless otherwise clinically indicated.

**Progress:** No additional patients were entered in FY 91. In previous years, four patients have been entered. Patient recruitment has been slow due to the rarity of patients with primary adrenal insufficiency.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/019	<b>Status:</b> Completed
<b>Title:</b> A Comparison of Ranitidine 300 mg HS, Ranitidine 300 mg BID, Ranitidine 300 mg TID, and Ranitidine 300 mg QID in the Treatment of Duodenal Ulcer Disease		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Jan 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Amy M. Tsuchida, MC		
<b>Associate Investigators:</b> MAJ Gregory E. Schlepp, MC		MAJ Michael F. Lyons II, MC
<b>Key Words:</b> duodenal ulcer, Ranitidine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine the dose-response relationship between ranitidine and duodenal ulcer healing by 4 weeks using ranitidine 300 mg HS, ranitidine 300 mg BID, ranitidine 300 mg TID, and ranitidine 300 mg QID, to compare ranitidine 300 mg HS and ranitidine 300 mg QID in terms of the rate of duodenal ulcer healing at 4 weeks, to compare the treatment groups in terms of pain relief, antacid consumption, and changes in fasting serum gastrin levels, and to evaluate the safety of ranitidine when administered for up to 4 weeks at total daily doses of 1200 mg, 900 mg, 600 mg, and 300 mg.

**Technical Approach:** This is a multicenter, manufacturer-sponsored, randomized, double-blind, active-controlled, 4-week study. Six hundred patients from approximately 60 sites throughout the U.S. will be enrolled. Patients at least 18 years old are eligible provided they exhibit endoscopic evidence of at least one duodenal ulcer that is >5 mm at its longest dimension. Patients who have unhealed duodenal ulcer(s) following 8 weeks of anti-ulcer therapy within 90 days prior to entry will be excluded as will patients who require concurrent treatment with nonsteroidal anti-inflammatory drugs. Patients will be randomized to receive either ranitidine 300 mg HS, ranitidine 300 mg BID, ranitidine 300 mg TID, or ranitidine 300 mg QID for 4 weeks. All patients will receive Maalox antacid tablets for pain relief, as needed, throughout the study. An endoscopy will be performed after 4 weeks of treatment. Patients who heal at 4 weeks will be considered treatment successes. Endoscopic healing is defined as complete re-epithelialization of the ulcer(s) with or without erythema. All ulcers must heal for a patient to be considered healed. The study will be discontinued at 4 weeks regardless of ulcer status. Patients will be evaluated as to whether their ulcer(s) healed, ulcer pain was relieved, and antacid consumption decreased.

**Progress:** This study has been closed due to sufficient patient accrual. Twelve patients were entered at MAMC. The majority of patients had resolution of ulcers with no adverse effects.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/039                      **Status:** On-going

**Title:** Investigation Into the Acute Decline in Serum Testosterone Levels in Healthy Men Exposed to Acute Stress

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

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

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

**Associate Investigators:**                      CPT Brenda K. Bell, MC  
COL Stephen R. Plymate, MC                      CPT Katherine H. Moore, MS

**Key Words:** testosterone, stress

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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**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 actually. Again, the B/I ratio of LH 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:** Eight subjects have been entered. To date, the data indicate that hypoglycemia appears to be associated with an increase in serum LH bioactivity despite a steady decline in LH immuno- activity. This increase in LH bioactivity is not accompanied by a rise in serum testosterone. These data indicate that the earliest response of the hypothalamic-pituitary-testicular axis to an acute stress is a transient increase in LH bioactivity. Testosterone does not rise with increasing LH bioactivity indicating that acute stress may have a direct effect on the testis.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/081	<b>Status:</b> On-going
<b>Title:</b> The Effect of Thyroid Hormone Suppression on Thyroid Nodules Found to be Indeterminate by Fine Needle Aspiration		
<b>Start Date:</b> 07/19/91	<b>Est. Completion Date:</b> Dec 92	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Robert M. Tuttle, MC		
<b>Associate Investigators:</b>		
MAJ John P. Kushner, MC	LTC (P) Robert E. Jones, MS	COL Ernest L. Mazzaferri, MC
MAJ Arnold A. Asp, MC	MAJ James H. Timmons, MC	
<b>Key Words:</b> thyroid nodules, thyroid hormone suppression, needle aspiration		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

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

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

Progress: No patients entered to date.

## DETAIL SUMMARY SHEET

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

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

**Start Date:** 07/19/91                      **Est. Completion Date:** Jul 93

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

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

<b>Associate Investigators:</b>	COL Ernest L. Mazzaferri, MC
COL Stephen R. Plymate, MC	David Gardner, MD
LTC (P) Robert E. Jones, MS	Christina Wang, MD
MAJ Arnold A. Asp, MC	MAJ Charles J. Hannan, MC
William Bremner, MD. Ph.D.	

**Key Words:** cancer:thyroid,gonads,radioactive iodine

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

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

**Technical Approach:** All euthyroid men undergoing thyroid surgery at the six participating institutions will be screened for entry into this protocol. This group will include at least 20 men with known thyroid cancer in whom RAI therapy may or may not be planned as was men undergoing non-cancer related thyroid surgeries. Those patients determined to be candidates for RAI ablation post-operatively by their primary physicians will constitute the study group. Those men who do not receive RAI post-operatively will constitute the control group.

Both the control group and the study group will follow identical protocols. Initial entry labs will be drawn before surgery. Subsequent labs (testosterone, TSH, LH, semen samples, etc.) will be obtained just before RAI is administered and at 2, 4, 6, and 8 months after RAI administration. The control group will have identical samples obtained at 1, 3, 5, 7, and 9 months after surgery. Since 4-6 weeks is required post-operatively for the TSH to rise high enough to allow administration of RAI, this sample schedule will allow both groups to be sampled at the same time. In addition, GnRH and clomiphene stimulation will be done at months 5 and 9 after surgery in both groups. Semen analysis will be started with an estimation of motility using the World Health Organization graded scale of 1 - 4+. A portion of the sample will be frozen and a slide prepared for final interpretation at MAMC-DCI. This final interpretation will evaluate the specimen for sperm count and morphology. In this way all sperm counts can be done by a single investigator, minimizing or eliminating inter-observer variation.

Repeated-measures ANOVA will be performed on the lab values taken over time to determine differences in control vs study groups.

**Progress:** Five subjects have been enrolled.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/094	<b>Status:</b> Completed
<b>Title:</b> The Effect of 5-alpha Reductase Inhibitor on Dihydrotestosterone Levels Within Prostate Tumors Implanted in Athymic Nude Mice		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b> Dec 90	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Robert M. Tuttle, MC		
<b>Associate Investigators:</b> CPT Leonard G. Renfer, MC		COL Stephen R. Plymate, MC
<b>Key Words:</b> tumor:prostate,5-alpha reductase inhibitor,dihydrotestosterone,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1100.00	06/14/91

**Study Objective:** To determine if 5 $\alpha$  -reductase inhibitors lower dihydrotestosterone levels in prostate tumor cells, to determine if treatment with 5 $\alpha$ -reductase inhibitor results in growth inhibition of prostate cancer cell lines, and to determine if these effects compare to those achieved with castration plus/minus adrenal suppression.

**Technical Approach:** A total of 60 athymic nude mice will be used in the study. All mice will be implanted with human prostate tumor PC-3. Ten days will be allowed for the cells to implant. At the end of 10 days, one group of 10 mice will undergo castration and a second group of 10 mice will undergo castration and daily injections of dexamethasone. Daily injections of a 5 $\alpha$  -reductase, 4 MA, will be given to three additional groups of 10 mice (without castration) at doses of 1.0, 0.5, and 0.25 milligrams. A control group of 10 mice will be included. At 21 days, the animals will be euthanized and the tumors harvested. Serum levels of testosterone will then be recorded as well as tumor levels of dihydrotestosterone. Tumor size and weight will be recorded in all animals. Data analysis will include comparison of tumor size and weight of each of the six groups as well as serum testosterone, tumor testosterone (T), and dihydrotestosterone (DHT) levels, and tumor DHT/T ratios using analysis of variance methods.

**Progress:** This protocol has been completed. Eighty mice were studied. The correlation between the final estimated tumor size and actual weight was significant at p=0.001. There was no difference in tumor growth rates between treatment groups during period one or two. With the exception of low dose 4-MA, all treatment groups showed a statistically significant decrease in serum testosterone compared to controls. Final tumor weights did not differ among the various treatment groups. We conclude that 4-MA, while known to cause significant changes in intratumor DHT/T ratio, did not affect the tumor growth characteristics or final tumor size in the PC-3 cell line implanted into athymic nude mice. This may suggest that DHT is not the primary growth mediator in the PC-3 cell line.

CPT Renfer original PI.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/105	<b>Status:</b> Terminated
<b>Title:</b> Efficacy of Oral Versus Intravenous Estrogens for the Control of Uremic Bleeding		
<b>Start Date:</b> 01/04/91	<b>Est. Completion Date:</b> Jan 91	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC		
<b>Associate Investigators:</b>		
CPT Jennifer L. Cadiz, MC	CPT Donna L. Mercado, MC	
MAJ Howard M. Cushner, MC	MAJ Everardo E. Cobos Jr., MC	
<b>Key Words:</b> uremic bleeding,estrogens:Oral vs IV		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$2500.00	//

**Study Objective:** To determine if oral estrogens are as effective as IV estrogens in correcting abnormal bleeding times in uremic patients.

**Technical Approach:** The effectiveness of oral estrogens for the control of uremic bleeding will be compared to intravenous estrogens by measuring the bleeding time in affected patients. The sample will include 20 nephrology patients with a bleeding time greater than 8 minutes and severe chronic renal failure or endstage renal disease on dialysis, with uremia (creatinine clearance of <25 cc/min and platelet transfusion <2 weeks prior to enrollment). Collected data will include history of bleeding, age, sex, and type of renal disease. Bleeding times will be compared via an unpaired T test.

**Progress:** This protocol was terminated because almost all of the nephrology patients were unwilling to participate because of the blood draws/bleeding times or were unable logistically to come to the hospital during the study periods. One patient was entered.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/047	<b>Status:</b> On-going
<b>Title:</b> The Relationship of the Sense of Coherence and Hardiness to the Nutritional Status of Anorectic Head and Neck Cancer Patients Currently Undergoing Radiation Therapy		
<b>Start Date:</b> 02/01/91	<b>Est. Completion Date:</b> Feb 93	
<b>Department:</b> Medicine	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Stacey B. Young, AN		
<b>Associate Investigators:</b> LTC Loretta Forlaw, AN		
<b>Key Words:</b> cancer:head & neck,radiation,nutritional status		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To investigate the relationship of the sense of coherence and hardiness to the nutritional status of anorectic head and neck cancer patients.

**Technical Approach:** Five Army Medical Centers will participate in this study. A sample of 90 adult male and female patients, 18 years and older will be studied. Patients must have head and neck cancer with pharyngeal, laryngeal, or mouth cancer, anorexia for at least one week, have a functional gastrointestinal tract, and have been receiving radiation therapy for 3-4 weeks. Demographic data will be collected on each patient. Sense of coherence will be measured using the 29 item Sense of Coherence Questionnaire (Antonvosky, 1987). Hardiness will be measured using the 40 item Health Related Hardiness Scale. Anorexia will be measured using the 25 item Anorexia Tool. The principal investigator will do a physical examination to include the patients height, weight, and skinfold measurements. Nutritional status will be determined by the patient's anthropometric data, energy expenditure, and serum albumin. A three day dietary diary will be use to gather information on the patient's actual intake for comparison to estimated nutritional requirements. Descriptive statistics will be used to summarize demographic information. Stepwise multiple regression analysis will be used to describe any statistical relationship among variables.

**Progress:** Nineteen subjects have been entered in this study, only one from MAMC. No significant findings have been identified to date.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF NURSING**



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/002		<b>Status:</b> Completed	
<b>Title:</b> The Relationship Between Paternal Childbirth Involvement Behaviors and Adjustment to Parenthood Variables for Unprepared, Primiparous Couples Who Share Labor and Birth					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b> Oct 92		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Susan L. Burroughs, AN					
<b>Associate Investigators:</b>			Mary R. Nichols, RN		
<b>Key Words:</b> childbirth behaviors, couples					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> //

**Study Objective:** To examine the relationships between demographic factors, parental-fetal attachment, paternal childbirth involvement, maternal satisfaction with childbirth, parenting self-esteem, and ease of transition to parenthood in primiparous, military couples previously unprepared by prenatal classes who subsequently share the childbirth experience.

**Technical Approach:** The population will consist of 90 married couples, living with their spouse, 28 weeks or more gestation, expecting their first child, without anticipated prenatal complications, who have not attended childbirth education classes. Husbands and wives will be asked to complete separate questionnaires to obtain demographic information and feelings toward the unborn child. Four weeks after delivery, the husbands and wives will complete separate questionnaires to obtain information about the labor and delivery experience and information regarding adjustment to being a new parent. The study will specifically examine the relationship between paternal childbirth involvement behaviors and selected adjustment to parenthood variables. The adjustment to parenthood variables include: maternal satisfaction with childbirth, competence in the parental role, and ease of transition to parenthood. In addition, the relationship between prenatal attachment, demographic factors, paternal childbirth involvement and the selected adjustment to parenthood variables will be examined. The data will be analyzed using a Stepwise Multiple Regression to determine the relationship among variables, and other multivariate techniques will be used as necessary (Tabachnick & Fidell, 1983). The qualitative data provided by fathers in the postnatal questionnaire will be reported in the appendix of the final report when not included in the analysis section. The qualitative data will be reduced and organized by generating categories, themes, and patterns which emerge from the answers with subsequent interpretation by the investigators (Marshall & Rossman, 1990).

**Progress:** Approximately 500 subjects were entered in the study. A thesis has been written as a requirement for the completion of a doctorate in Nursing at the University of Texas by associate investigator Mary R. Nichols.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/012                      **Status:** Completed

**Title:** Staff Nurses' Attitudes About and Preception of Effectiveness of Health Promotion

**Start Date:** 01/19/90                      **Est. Completion Date:** Dec 89

**Department:** Nursing                      **Facility:** MAMC

**Principal Investigator:** MAJ Patricia J. Chessher, AN

**Associate Investigators:**                      LTC Vicky M. Sheldon, AN

**Key Words:** health promotion,nurses

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 02/01/91
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**Study Objective:** To describe the predisposing, enabling, and reinforcing factors perceived by staff nurses as affecting their use of health promotion, to determine under what conditions staff nurses consider health promotion activities for a patient can be effective, and to determine the extent to which staff nurses consider it is their responsibility to promote their patients' health.

**Technical Approach:** Approximately 60 staff nurses from the Acute Care Nursing Section will be enrolled. A study packet containing a cover letter and a questionnaire will be distributed to each subject. A follow-up postcard will be sent to each subject at three weeks to urge individuals to return the questionnaire, if they have not done so. The questionnaire will consist of two parts. Section one addresses knowledge, attitudes, and perceptions of the effectiveness of health promotion as well as the amount of time available to teach health promotion to patients and the time spent in teaching health promotion. Section two is a demographic data form. Descriptive statistics, central tendency, distribution and range will be used for data analysis. Correlations and associations between measures and self-reported behavior will be done. Demographic data will be used to describe the characteristics of the sample.

**Progress:** The project has been completed. This protocol was done as a partial fulfilment for a Master of Nursing degree at the University of Washington by an active duty student. MAJ Chessher was reassigned after completion of the program without leaving any information on the study. We have been unable to locate her. We learned from the University of Washington that the project was completed.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/026	<b>Status:</b> On-going
<b>Title:</b> The Primary Needs of Relatives of Critically Ill Patients		
<b>Start Date:</b> 02/01/91	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Brenda C. Conway, AN		
<b>Associate Investigators:</b> CPT Anna I. James, AN		CPT Kathy K. Prue-Owens, AN
<b>Key Words:</b> critically ill patients:needs of relatives		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To identify the primary needs of relatives of patients in the ICU and how important those needs are and to identify the primary needs of family members of pediatric patients in an adult ICU.

**Technical Approach:** One hundred (100) family members (one per patient) of patients who have been in the ICU for least 48 hours will be entered in the study. At least 50 will be family members of pediatric patients. Information concerning the sex, relationship to the patient, education, occupation, age, and the age of the patient will be collected. The investigator will administer the Critical Care Family Needs Inventory (Molter and Leske, 1983) to the family members by reading the questions and having the participant reply as (1) not important, (2) slightly important, (3) important, or (4) very important. Descriptive statistics will be used for data analysis.

**Progress:** A total of 48 family members has been interviewed. To date, the most important needs identified by family members consistently were to feel there was hope, to know the patient's prognosis, to have questions answered honestly, to feel the hospital cared about the patient, and to be called at home about change in the condition. Subject entry will continue until family members of 50 adult patients and 50 pediatric patients have been enrolled.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/049	<b>Status:</b> Completed
<b>Title:</b> The Effect of Intraoperative Lumbar Support on the Incidence and Severity of Postoperative Backache		
<b>Start Date:</b> 02/01/91	<b>Est. Completion Date:</b> Apr 91	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Dennis S. Keeton, AN		
<b>Associate Investigators:</b> MAJ Lance C. Campbell, AN		
<b>Key Words:</b> postoperative backache, lumbar support		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if placing a cylindrical pillow in the lumbar area of adult surgical patients undergoing general anesthesia in the flat supine position will decrease the incidence and severity of postoperative backache.

**Technical Approach:** A convenience sample of 160 patients undergoing non-emergent surgery will be enrolled in the study. Patients will be randomly assigned to intervention and control groups. Prior to induction of general anesthesia the pillow will be placed by the principal investigator. The principal investigator will then leave the room and the assigned staff anesthetist will open a sealed envelope to determine if the subject is in the control or intervention group. The pillow will be removed for those in the control group by the staff anesthetist after induction of general anesthesia. At the end of the operation, the pillow will be removed from under those in the intervention group before transfer to the Recovery Room. The principal investigator will examine the subject's record to calculate the total intervention time, the time that the subject first ambulated, the type of analgesia, its dose, frequency, and time of most recent administration. A postoperative questionnaire, which compiles data evaluating the presence or absence of backache and includes a Likert-type scale for the subject's description of the severity of backache will be administered on the first postoperative day. Descriptive statistics will be used to describe the sample and to verify successful randomization and group comparability. Comparison of the intervention group to the control group will be made on the basis of the presence or absence of postoperative backache using the Chi-square test. The relationship of other variables to the incidence of backache will be tabulated and examined for the strength of correlation, if appropriate. Those variables include the subject's age, gender, weight, type of surgery, duration of surgery, history of backache, severity of backache, time to first ambulation, and postoperative analgesia.

**Progress:** Thirty subjects received lumbar support (intervention group) and 32 patients did not (control group). Two subjects in the control group and five subjects in the intervention group reported postoperative backache. No significant differences existed at a 95% confidence interval. A chi-square test with continuity correction showed no significant difference between the two groups in the incidence of postoperative backache. An unpaired t-test showed no significant difference in the severity of backache between groups.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/031	<b>Status:</b> On-going
<b>Title:</b> Tracheal Epithelial Injury and Body Core Temperature Changes Related to Ventilator Inspired Gas Temperatures in Piglets		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Lori A. Loan, R.N.		
<b>Associate Investigators:</b>		LTC Barbara S. Turner, AN
<b>Key Words:</b> body core temperature, tracheal epithelial injury, piglets, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To determine the effect on the tracheal epithelium and the body core temperature of six different ventilator inspired gas temperatures (32, 33, 34, 35, 36, and 37 degrees centigrade) as compared to a non-ventilated control in newborn piglets.

**Technical Approach:** This will be a seven group experimental design study with random assignment to groups. The independent variables are the six controlled ventilator inspired gas temperatures. The dependent variable is tracheal trauma as measured by light microscopy and scanning electron microscope for the number and percentage of cell types remaining after acute injury. Piglets, aged 7-10 days and weighing 5-10 kg will be randomly divided into seven groups of 5 piglets each. After sedation, an endotracheal tube will be placed through the cords and secured in position to prevent tube movement. The piglet will be placed on a pressure ventilator and gases will be heated to a controlled temperature depending on the group and humidified to 100%. An arterial line will be placed and kept open with IV fluids. The piglets will be connected to a cardiorespiratory monitor and an oxygen saturation monitor and kept on a heating pad with rectal temperatures recorded hourly. At the completion of 6 hours of ventilation the piglets will be euthanized. The control animals will be sedated and then euthanized. The trachea and mainstream bronchi will be dissected free and sectioned into 13 cross sections. The percentage of cell loss and the number of each cell type will be compared for each section between the piglets in the experimental groups using Student's t test. Total injury scores will be compiled for all piglets by averaging the 12 sections and results compared between groups. Number of inflammatory cells, basal cells with altered shapes, and the area of fibrin deposits will be determined for each tracheal section using video image analysis. Student's t test will be used to test for differences between groups. The ratio of ciliated cells to goblet cells and goblet cells to submucosal glands will be calculated. Analysis of variance will be used to determine differences among the groups. Data will be analyzed using descriptive and inferential statistics. Data on piglet age, weight, and sex will be compiled for each group. The groups will be compared using an analysis of variance with post hoc analysis to determine if group differences exist.

**Progress:** This study has not been implemented. The investigator is awaiting approval to accept grants from the National Association of Neonatal Nurses and the American Nurses Foundation.

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/090                      **Status:** Completed

**Title:** An Exploration of the Effects of Aging and Exercise on Maximal Oxygen Intake in Women Between the Ages of 22 to 41 Years

**Start Date:** 07/20/90                      **Est. Completion Date:** Aug 90

**Department:** Nursing                      **Facility:** MAMC

**Principal Investigator:** MAJ Laurie A. McNabb, AN

**Associate Investigators:**                      LTC Barbara S. Turner, AN

**Key Words:** aging, oxygen intake

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost:    \$0.00	OMA Cost:            \$45.00	06/14/91

**Study Objective:** To determine whether estimates of maximal oxygen consumption obtained from a field test of a two-mile run can, in fact, accurately discriminate between cardiovascular fitness levels in two different age groups of women.

**Technical Approach:** Active duty Army Nurse Corps female officers will be studied, 25 between the ages of 22 and 31, and 25 between the ages of 32 and 50. The subjects will complete a two-mile run and will be timed. Estimates of maximal oxygen consumption will be calculated from the two-mile run times. The subjects will also be asked to complete a questionnaire which will elicit information on the type and the amount of exercise the subjects regularly perform. Predicted values of maximal oxygen intake as determined by the two-mile run time and the age will be compared between the two age groups by using the Student's t test. Relationships of age and physical activity status will be examined and plotted by using simple linear regression analysis.

**Progress:** The study has been completed, 43 women were entered in the study. The study found that the field test of a two-mile run is sensitive enough to detect predicted age-related declines in fitness. It could, therefore, be used as a relatively inexpensive method for mass screening for basic cardiovascular fitness in selected presumably healthy groups of people. Statistical analysis revealed that there was a significant relationship between run time and age. Exercise practices that markedly influenced run performance were the number of exercise sessions per week and habitual exercise pattern throughout the year.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/006		<b>Status:</b> Completed	
<b>Title:</b> Assessing Parental Stress in the NICU					
<b>Start Date:</b> 11/17/89			<b>Est. Completion Date:</b> Dec 89		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Carla Nye, RN					
<b>Associate Investigators:</b>			LTC Lorna R. Imbruglio, MC		
<b>Key Words:</b> stress, parental, NICU					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		04/05/91	

**Study Objective:** To examine the aspects of the Neonatal Intensive Care Unit (NICU) environment that parents find stressful.

**Technical Approach:** Fifty mother-father dyads will be studied. The charge nurse will determine if the parents are emotionally stable enough to be asked to take part in the study. Parents will be asked to fill out the Parental Stressor Scale: Neonatal Intensive Care Unit and a parent background information form. Parents will complete the forms separately. Demographic data will be obtained from the infant's chart. The investigator will attempt to determine the sources of parental stress in the NICU, if the mothers' overall perceptions of stress differ from the fathers', if single mothers' perceptions of overall stress differ from those of married mothers, if the experience of previously having an infant in an NICU is related to overall perception of stress, if there is a relationship between gestational age of the infant and the parent's overall perceptions of stress, if there is a relationship between the severity of the infant's medical complications and the parent's perception of stress, and if there is a relationship between the years of schooling the parent has completed and the perceptions of stress in the Staff Behaviors and Communication dimension. The Statistical Package for the Social Sciences will be used to analyze the data. T-tests will be used to assess the differences between mothers and fathers, single mothers and married mothers, and previous experience with the NICU versus no previous experience. Relationships between parent and infant characteristics and overall stress scores will be answered using correlative statistics.

**Progress:** The study has been completed. Thirty-two mothers and 26 fathers of 32 infants were studied. The data suggest that mothers experience the NICU environment and the transition to parenthood more acutely than do fathers, as suggested by higher maternal stress means for most items. A thesis has been written as a partial fulfillment of a Master's of Nursing Degree at the University of Washington for the principal investigator.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/046	<b>Status:</b> On-going
<b>Title:</b> Pregnancy Attitudes, Ambivalence, and Symptom Distress		
<b>Start Date:</b> 02/01/91	<b>Est. Completion Date:</b> May 91	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Irene M. Rich, AN		
<b>Associate Investigators:</b> LTC Susan L. Burroughs, AN		
<b>Key Words:</b> pregnancy:attitudes,ambivalence,symptom distress		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the changes that occur in the measures of general pregnancy attitudes, ambivalence, and psychological symptom distress during the three trimesters of pregnancy and to determine the relationships (correlational and predictive) among measures of general pregnancy attitudes, ambivalence, psychological symptom distress, and selected demographic variables during the three trimesters of pregnancy.

**Technical Approach:** A total of 420 research subjects from three military treatment facilities will be entered in the study. The proposed research employs a combination of quantitative and qualitative research methodologies. The Pregnancy Questionnaire is an investigator developed, 86 item, modified visual analogue tool which contains two scales. The first scale, the Rich Pregnancy Attitude (RPA) scale, is used to assess general pregnancy attitudes quantitatively. The second scale, the Rich Ambivalence Scale, is used to assess ambivalence in pregnant women quantitatively. The Pregnancy Questionnaire: Focused Interview Guide will be used to conduct interviews for the qualitative portion of the research. The Rich Visual Analogue (RVA) is an investigator-developed tool designed to quantify levels of ambivalence and general pregnancy attitudes. A panel of experts will score the RVA on review of transcripts from focused interviews. Psychological symptom distress will be measured using scores obtained on Derogatis (1977) Symptom Checklist -90-Revised (SCL-90-R). The women will be systematically assigned to one of three study groups. Group 1 will provide the quantitative data by completing the demographic data form, the RPA/RA Scales, and the SCL-90-R. Women in Group 2 (a subsample of 45 women - 15 per pregnancy trimester) will provide both quantitative and qualitative data. These women will complete the demographic data form, the RPA/RA scales, and the SCL-90-R and will be interviewed using the Focused Interview Guide. Women in Group 3, a subsample of 120 women (40 per pregnancy trimester) will provide information on the test-retest reliability of the RPA/RA scales by completing the same questionnaires as in Group 1, and then repeating the procedure one week later.

**Progress:** 602 surveys mailed out, 433 respondents. The principal investigator has completed quantitative analysis and is performing the qualitative analysis at present. A thesis will be written within the next three to four months.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/097	<b>Status:</b> Completed
<b>Title:</b> Descriptive Study of the Sleep Patterns of the Mechanically Ventilated Premature Infant Before, During, and After Endotracheal Suctioning		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> Sep 90	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Arlene E. Roots, AN		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> endotracheal suctioning, sleep patterns, infant:mechanically ventilated		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To identify and describe the sleep patterns, sleep behaviors, and selected physiological responses of the mechanically ventilated premature infant before, during, and after endotracheal suctioning.

**Technical Approach:** Ten infants, 26-37 weeks gestation, will be studied. A polysomnography using 11 electrodes will be used. Two electrodes will be attached to the frontoparietal area of the head to measure brain wave activity (electroencephalogram), two near the outer canthi of the eyes to measure eye movement (electro-oculogram), two to the chest to measure heart rate and respiration, two to the chin to record the presence or absence of muscle activity (electromyogram), and two to the forehead, and one to the occipital area which are attached to ground and biocalibrate the EEG machine to the infant. Measurements of oxygen saturation levels will be obtained from a noninvasive saturation monitor. Heart rate and respiration rate will also be measured from the continuous hard copy readout of the polysomnographic recording. Demographic, physiological, and behavioral variables will also be recorded. Recording of the EEG pattern will begin 5 minutes prior to the suctioning sequence, continue throughout the event, and will continue for a minimum of 15 minutes after the event is completed. Data will be collected on one to three endotracheal suctioning events during the 24 hours following entry into the protocol. Sleep scoring will be done on the basis of 30 second epochs and continuous output of heart rate, respiration rate, and oxygen saturation will also be scored in 30 second epochs. Descriptive statistics will be used to describe the sample characteristics. Measures of central tendency and dispersion will be used to describe the population and all sleep parameters. Data will be aggregated across all subjects and differences between the 3 periods of presuctioning, suctioning, and postsuctioning will be analyzed using appropriate analysis of variance techniques. Effects of extraneous variables on the major study variables will be determined by appropriate correlational techniques based on the level of measurement.

**Progress:** This study has been completed. A delay in TDY and travel caused the principal investigator to have only two days at Madigan and only patient was studied.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/084	<b>Status:</b> On-going
<b>Title:</b> A Study to Evaluate the Effects of Heparinized and Non-heparinized Flush Solutions on the Patency of Arterial Pressure Monitoring Lines		
<b>Start Date:</b> 10/04/91	<b>Est. Completion Date:</b> Dec 91	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Connie K. Schultz, AN		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> arterial pressure lines, patency, heparin, non-heparin solutions		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** The purpose of this study is to evaluate the effect of heparinized and non-heparinized flush solutions on the patency of arterial pressure monitoring lines. Specifically, the research will:

- 1) Determine if there is a significant difference in duration of patency of arterial pressure monitoring lines maintained with heparinized versus non-heparinized flush solutions. Patency will be measured by acceptable square waveform test and free backflow of blood every four hours for seventy-two hours after insertion of the line or until the line is removed, whichever comes first.
- 2) Determine the relationship of potentially confounding variables such as site of insertion, length of catheter, and gauge of catheter to duration of patency of arterial pressure monitoring lines maintained with heparinized and non-heparinized flush solutions.

**Technical Approach:** A minimum of 30 subjects will be entered (male and female). Subjects will be randomized into a heparin or non-heparin flush group. Descriptive data will be collected for each subject (i.e. time of catheter insertion, location of insertion, length of catheter, gauge of catheter, etc). Data is then collected every four hours for 72 hours. Other data collections include patency check and any deviations from protocol. Time of line patency for the heparinized flush solution group will be compared with time of line patency for the non-heparinized flush solution group using log rank tests on product limit survival estimates. Stratified analyses or proportional hazard regression models will be used to control for the effects of covariates such as length of catheter, size of catheter, or site of insertion if there are significant differences in survival rates based on these covariates.

**Progress:** The study has not been implemented because training materials have not yet arrived.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/028                      **Status:** On-going

**Title:** The Effect of Two Levels of Hyperoxygenation Given via a Manual Resuscitation Bag and Ventilator During Endotracheal Suctioning of Premature Infants

**Start Date:** 05/19/89                      **Est. Completion Date:** May 94

**Department:** Nursing                      **Facility:** MAMC

**Principal Investigator:** LTC Barbara S. Turner, AN

**Associate Investigators:** None

**Key Words:** endotracheal suctioning, infant, resuscitation bag

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 06/14/91
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**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<sub>2</sub> 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<sub>2</sub>/FIO<sub>2</sub> 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<sub>2</sub> by MRB, 20% increase over baseline FIO<sub>2</sub> by MRB, 10% increase over baseline FIO<sub>2</sub> by ventilator, and 20% increase over baseline FIO<sub>2</sub> by MRB.

**Progress:** Twenty-three subjects were entered. A review of the data to date shows no differences in O<sub>2</sub> saturation, CIP, TcCO<sub>2</sub>, MAP, or MAW based on levels of hyperoxygenation or method of administering breaths during endotracheal suctioning. A total of 40 subjects will be required to complete the protocol.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/072	<b>Status:</b> On-going
<b>Title:</b> Piglet Tracheal Epithelial Injury and Regeneration Following Endotracheal Suctioning		
<b>Start Date:</b> 05/18/90	<b>Est. Completion Date:</b> May 93	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Barbara S. Turner, AN		
<b>Associate Investigators:</b> LTC Tom E. Wiswell, MC		MAJ James G. MacMillan, VC
<b>Key Words:</b> epithelium,regeneration,endotracheal suctioning,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	04/05/91

**Study Objective:** To determine the difference in: acute cell loss from the tracheal epithelium following six controlled endotracheal suctioning procedures using positive end-expiratory pressure (PEEP) and zero end-expiratory pressure (ZEEP), the process of tracheal epithelial regeneration following PEEP and ZEEP, in the length of time for complete tracheal epithelial regeneration between the PEEP and ZEEP groups, and the growth of the tracheas of piglets undergoing endotracheal suctioning and those in the sham and control groups.

**Technical Approach:** Control animals (14) will be sedated and then euthanized (two at a time) acutely on days 3, 7, 10, 14, 17, and 21, and the trachea harvested. Sham piglets (14) will be sedated, intubated, and ventilated for 6 hours, without suctioning taking place. They will be euthanized at time periods as above and the trachea harvested. Group 1 (35) and Group II (35) piglets will be intubated and ventilated. After the piglets have been stabilized on the ventilator each will receive either PEEP (Group 1) or ZEEP (Group II) once every 60 minutes for the six hours of mechanical ventilation. The piglets in Groups 1 and 2 will be euthanized in groups of 5, acutely and at 3, 7, 10, 14 and 21 days post-suctioning and the trachea harvested. At the time of necropsy, the location of the tip of the endotracheal tube will be marked by placing a ligature in the tracheal wall. The heart and lungs will be removed en bloc and grossly examined. The trachea and mainstem bronchi will be dissected free and sectioned into 13 cross sections for examination, including scanning electron microscopy and light microscopy. Descriptive and inferential statistics will be used to determine the total epithelial cell count, goblet cell count, and ciliated cell count from each section. The ratio of ciliated cell to goblet cells will be calculated for all cross sections to determine the tracheal epithelial response to injury. Changes in the cell counts over time will be analyzed. Corrected predicted total epithelial cell counts will be determined, using the control piglets as a standard, correcting for tracheal diameter.

**Progress:** This study has not be implemented because the investigators are awaiting a decision on grant approval from the NCI.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/034	<b>Status:</b> On-going
<b>Title:</b> Tracheal Trauma and Regeneration Following Suctioning		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> Feb 95	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Barbara S. Turner, AN		
<b>Associate Investigators:</b> LTC Tom E. Wiswell, MC		
<b>Associate Investigators:</b> MAJ James G. MacMillan, VC		
<b>Key Words:</b> tracheal trauma,suctioning,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To examine the trauma and healing of the tracheal epithelium following the two types of negative pressure used during endotracheal suctioning (ETS) by neonatal nurses, continuous negative pressure (CNP) and intermittent negative pressure (INP).

The research questions to be answered are (1) what is the immediate (acute) effect on the tracheal epithelium of ETS using INP versus CNP, (2) what is the response of the tracheal epithelium (chronic effect) of ETS using INP versus CNP over the 21 days immediately following ETS, and (3) are there differences acutely and chronically in the percentage of tracheal epithelial circumferences that are covered by basal cells, ciliated epithelium, and goblet cells based on exposure to suctioning using INP versus CNP.

**Technical Approach:** The sample will consist of 98 Chester White swine that will be randomly divided into 4 groups: Control (n=14), sham (n=14), Group I - intermittent negative pressure (n=35), and Group II - continuous negative pressure (n=35). Groups I and II will be intubated, mechanically ventilated, and receive 6 controlled ETS procedures (1 /hour) during 6 hours of ventilation. The swine will either be euthanized immediately after the sixth ETS procedure or recovered and euthanized at 3, 7, 10, 14, and 21 days post ETS. Swine in the control and sham groups will be euthanized at the same time points. All tracheas will be harvested and sectioned into 13 sections beginning at the second tracheal ring and extending to the 9th tracheal ring. Each section will be graded using video image analysis for determination of the percentage of circumference denuded, the numbers of cells, types of cells, and ratio of cell types remaining. Injury scores for each swine in each group at each time period will be determined.

**Progress:** The study has not been started. The investigators are awaiting funding.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 91/016                      **Status:** Completed

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**Title:** The Effects of Total IV Anesthesia Using Propofol, Ketamine, and Vecuronium on Cardiovascular Parameters and Wake Up Time

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**Start Date:** 01/04/91                      **Est. Completion Date:** Oct 91

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**Department:** Nursing                      **Facility:** MAMC

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**Principal Investigator:** CPT Annette L. Wuest, AN

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**Associate Investigators:**                      CPT Michael J. Bayhi, AN  
CPT Madeline B. Dunnihoo, AN                      CPT Michael J. Meyer, AN  
1LT Michael L. Robinson, AN                      MAJ Henry J. Walker, AN

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**Key Words:** cardiovascular parameters, propofol, ketamin, vecuronium

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

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**Study Objective:** To determine if a continuous intravenous infusion utilizing propofol, ketamine, and vecuronium will provide adequate anesthesia in ASA I and II class patients safely, with regards to preservation of hemodynamics, wake up time, adequate intraoperative analgesia and amnesia, and PACU behavior.

**Technical Approach:** Fifty adult patients who present for elective surgery will receive a standard preoperative interview and lab tests. Patients will then receive standard preoperative medications and be monitored in accordance with standard Anesthesia Service procedures. After routine venous access has been established, an induction sequence of ketamine (2 mg/kg), propofol (1-2 mg/kg), and vecuronium (0.1 mg/kg) will be administered. Maintenance of anesthesia will be accomplished with an infusion of propofol, ketamine, and vecuronium. Infusions will be terminated 10-15 minutes prior to the end of surgery and residual neuromuscular blockade will be reversed in normal fashion. The times of relaxant reversal and tracheal extubation will be recorded. Patients will be assessed in PACU as satisfactory or unsatisfactory based upon judgements of the anesthetist and supervising faculty. A follow-up visit by the investigators will be conducted 24 hours postoperatively. Patients will be asked questions in regard to perioperative events. Mean and standard deviations will be determined on cardiovascular parameters, duration of anesthesia, total dosage utilized, time of relaxant reversal to extubation, and time to regaining of consciousness.

**Progress:** The protocol has been completed with 41 subjects studied. The investigators found the use of total IV anesthesia with propofol, ketamine, and vecuronium for induction and maintenance of general anesthesia to be a safe, acceptable alternative to volatile agents and narcotics in ASA I and ASA II type patients.

# **DETAIL SHEETS FOR PROTOCOLS**

## **NUTRITION CARE DIVISION**

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/041                      **Status:** On-going

**Title:** Dental Liquid Ration Evaluation

**Start Date:** 04/05/91

**Est. Completion Date:** Apr 92

**Department:** NutC

**Facility:** MAMC

**Principal Investigator:** CPT Pamela Charney, SP

**Associate Investigators:** None

**Key Words:** liquid rations,evaluation,dental

**Accumulative  
MEDCASE Cost:**

\$0.00

**Est. Accumulative  
OMA Cost:**

\$0.00

**Periodic Review:**

//

**Study Objective:** To compare acceptance and consumption of a new 5-day liquid diet to the dental liquid diets currently being served in military hospitals and service institutions.

**Technical Approach:** Twenty military hospitals and service institutions will participate in the study. Subjects will consist of approximately 150 patients with maxillofacial and oral injuries, 25 cancer, and 25 geriatric patients who require dental liquid or pureed diet. The Dental Liquid Ration is a newly developed ration to be used both in garrison and field environments for the nutritional management of patients requiring a dental liquid diet. The ration provides a five day menu and consists of powders that mix easily with water and taste like normal meal components. Subjects will be asked to rate the appearance, flavor, texture, consistency, ease of sipping, temperature, portion size, and overall acceptability of each liquid product served. Estimates of fluid consumption will be collected and subjects' nutrient intakes will be evaluated. A questionnaire will be filled out by dietitians and dietetic technicians to obtain opinions about the two diets.

**Progress:** Two subjects have completed the study. Several others were enrolled who were unable to complete the study due to discharge.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF OB/GYN**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/022	<b>Status:</b> On-going
<b>Title:</b> Preterm Delivery Prevention		
<b>Start Date:</b> 07/28/89	<b>Est. Completion Date:</b> Jun 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Philip M. Bayliss, MC		
<b>Associate Investigators:</b>		
MAJ Glenn D. Jordan, MC	COL Patrick Duff, MC	MAJ W. Kim Brady, MC
MAJ Douglas A. Milligan, MC	MAJ Jerome N. Kopelman, MC	
<b>Key Words:</b> preterm delivery prevention		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$5960.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To evaluate the efficacy of an empiric course of intravenous antibiotics, given in conjunction with tocolytics, in the treatment of premature labor, and to evaluate the efficacy of a short seven day course of oral tocolytic therapy compared to the standard long term therapy in preventing recurrent premature labor.

**Technical Approach:** Approximately 200 reproductive age patients will be cultured for cervical, vaginal, and urinary pathogens. An IV catheter will be placed and IV tocolytic therapy will be begun. Agents used for IV tocolysis will be ritodrine or magnesium sulfate. All patients will receive standard therapy. Patients enrolled in the investigation will then be randomized to receive in a double-blind fashion either IV ampicillin/sulbactam (Unasyn, 1.5 mg IV every six hours for 48 hours) followed by oral amoxicillin/clavulanic acid (Augmentin, 250 mg PO t.i.d. for five days) or a placebo administered in a similar form. Patients randomized to placebo will receive 48 hours of an IV placebo followed by five days of oral placebo. The second part of the study will begin when patients would routinely be switched to long term oral tocolytic therapy. Patients will be randomly assigned to receive terbutaline sulfate, 5 mg every three hours for either seven days total oral therapy or until term (37 weeks). This portion of the study will not be blinded. Outcomes to be measured will be gestational age at delivery, duration of pregnancy from entry into the study until delivery, readmissions for premature labor, incidence of chorioamnionitis, and endometritis. Neonatal parameters to be measured include birth weights, Apgar scores, duration of NICU stay, incidence of neonatal infection, RDS, duration of ventilatory support, necrotizing enterocolitis, and intraventricular hemorrhage. Differences between treatment groups will be analyzed by the chi-square test and t test as appropriate. Revision (Aug 90): The IV antibiotics arm of this study was dropped due to an inability to obtain a suitable placebo.

**Progress:** Twenty subjects were entered in FY 91.

Dr. Douglas Milligan, original PI.  
Dr. Jerome Kopelman, intermim PI (Aug 90)  
Dr. Bayliss, new pi (Apr 90)

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/023		<b>Status:</b> Terminated	
<b>Title:</b> Prophylactic Antibiotics in the Management of Preterm Rupture of the Membranes					
<b>Start Date:</b> 07/28/89			<b>Est. Completion Date:</b> Jun 90		
<b>Department:</b> OB/GYN			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Philip M. Bayliss, MC					
<b>Associate Investigators:</b>			<b>Associate Investigators:</b>		
MAJ Glenn D. Jordan, MC			COL Patrick Duff, MC		
MAJ Douglas A. Milligan, MC			MAJ W. Kim Brady, MC		
			MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> preterm membrane rupture					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$3574.00		04/05/91	

**Study Objective:** To evaluate the benefit of prophylactic antibiotics in obstetric patients with preterm premature rupture of the membranes in a randomized, prospective, blinded manner.

**Technical Approach:** Upon entry into this investigation, patients (n=100) will be randomly assigned to receive 48 hours of intravenous ampicillin/sulbactam (Unasyn) or placebo. The dose of Unasyn will be 1.5 g every six hours. After 48 hours, patients receiving Unasyn will be switched to oral amoxicillin/clavulanic acid (Augmentin), 250 mg every eight hours until delivery. Patients receiving intravenous placebo will be switched after 48 hours to an oral placebo. The assignment of patients to treatment and placebo arms will be blinded to both the patient and physician. Obstetric management will not otherwise differ from current standards of practice to include use of tocolytics in patients with no evidence of infection and use of antenatal corticosteroids when indicated. Diagnosis of intra-amniotic infection will dictate delivery and treatment with appropriate antibiotics regardless of treatment group. Measured maternal outcomes are to include latent interval (period from rupture of membranes to delivery), gestational age at delivery, and rates of chorioamnionitis and endometritis. Fetal outcomes to be measured will be birth weight, Apgar scores, duration of NICU stay, rates of neonatal infection as defined by the treating pediatrician. RDS and duration of ventilator support, necrotizing enterocolitis, intraventricular hemorrhage, and neonatal death. Differences between treatment groups will be analyzed by the chisquare test and the t test, as appropriate.

**Progress:** No patients were entered in this study. The protocol was terminated in September 1990 because a suitable placebo could not be located.

Dr. Douglas Millitan, original PI.  
Dr. Jerone Kopelman, interim PI (Aug 90)  
Dr. Bayliss, new PI, Apr 90

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 87/049                      **Status:** Completed

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**Title:** A Comparison of Cefazolin versus Cefotetan as Single Dose Prophylaxis in Vaginal Hysterectomy

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**Start Date:** 02/27/87                      **Est. Completion Date:** Apr 88

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**Department:** OB/GYN                      **Facility:** MAMC

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**Principal Investigator:** CPT Timothy J. Boley, MC

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**Associate Investigators:**                      LTC I. Keith Stone, MC  
COL Patrick Duff, MC                      CPT Arthur H. Herpolsheimer, MC  
CPT Katherine S. Foley, MC                      LTC David J. Magelssen, MC

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**Key Words:** cefazolin, cefotetan, hysterectomy

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<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$600.00	04/05/91

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**Study Objective:** To evaluate the efficacy of a single dose of two cephalosporins as prophylaxis for vaginal hysterectomy.

**Technical Approach:** This will be a randomized double blind study with 100 patients included in each arm. Study patients will be given either cefotetan or cefazolin intravenously immediately prior to the vaginal incision. Preoperative evaluation will include CBC and urine culture. Each patient will undergo the standard vaginal preparation with povidone-iodine prior to surgery. Postoperatively, patients will be evaluated for evidence of febrile morbidity, pelvic cellulitis, urinary tract infection, bacteremia, septic shock, and pelvic abscess. Other parameters to be considered include duration of hospitalization and fever index. Patients will also be evaluated two to four weeks postoperatively. Differences in treatment effect will be evaluated by means of the chi-square test (discrete data) and independent sample t-test (continuous data).

**Progress:** One hundred ninety-seven patients were entered in this study. No adverse reactions to the medications have been reported. All data collection has been completed and data analysis has begun.

Dr. Boley, original PI, Feb 87.  
Dr. Patrick Duff, PI, Jul 88.  
Dr. Katherin Foley, PI, Apr 89.  
Dr. David Magelssen, PI, Jun 89.  
Dr. Boley returned, Aug 91.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/003	<b>Status:</b> Completed
<b>Title:</b> Prophylactic Tocolysis of Twins		
<b>Start Date:</b> 11/21/86	<b>Est. Completion Date:</b> Dec 88	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ W. Kim Brady, MC		
<b>Associate Investigators:</b>		COL John A. Read II, MC
<b>Key Words:</b> tocolysis,twins		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$952.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if an orally administered tocolytic agent and modified bed rest regimen in patients with twin gestation is superior to bed rest alone as a method for the prevention of preterm labor/delivery, and to determine if an orally administered prophylactic tocolytic agent significantly reduces the incidence of intrauterine growth retardation (IUGR)/discordant growth in twin gestation.

**Technical Approach:** One hundred patients with known twin gestation at 20-26 weeks gestation confirmed by ultrasound will be entered in a randomized double blind study. All patients will be advised to stop working, abstain from intercourse, and institute maximum bed rest at home (a minimum of 8 hours of bed rest during the day in addition to the normal hours of sleep). All patients will undergo the following baseline laboratory studies: EKG, glycosylated hemoglobin, one hour glucose challenge test, endocervical/vaginal cultures for Group B streptococci, Chlamydia trachomatis and N. gonorrhoea organisms. The one hour glucose and hemoglobin values will be repeated at 32 weeks gestation. All patients will be seen weekly after 20 weeks and a pelvic examination for cervical changes and Bishop's score will be performed. All endocervical cultures will be repeated if weekly external tocometer tracing demonstrates evidence of increased uterine activity compared to the previous week's uterine activity. At delivery, placentas will be weighed and maternal and umbilical artery glycosylated hemoglobin values will be obtained. Study patients will receive terbutaline, 5.0 mg orally every 4 hours while awake (0600-2200 hrs), from the time of entry into the study until 37 weeks gestation. The control group of patients will receive a placebo and will undergo the same laboratory and clinical testing. Chi-square/ Fisher Test and T-test will be used to analyze the data.

**Progress:** The protocol has been completed, 65 patients were entered. The principal investigator is in the process of writing a paper.

**DETAIL SUMMARY SHEET.**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/074	<b>Status:</b> Terminated
<b>Title:</b> Documentation of Ureteral Function via Intraoperative Ultrasound		
<b>Start Date:</b> 06/15/90	<b>Est. Completion Date:</b> Jul 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT John B. Browning, MC		
<b>Associate Investigators:</b> CPT Kevin C. Turner, MC		
<b>LTC Gordon O. Downey, MC</b>		
<b>Key Words:</b> ureteral function,ultrasound		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	08/02/91

**Study Objective:** To evaluate the ability of standard ultrasound equipment to demonstrate the presence or absence of ureteral function in the operating room.

**Technical Approach:** Subjects 10, age range 18-75 years Routine and indicated preoperative evaluations will be performed depending on the medical history and specific planned surgery for the patient. After obtaining informed consent, a preoperative ultrasound will be performed. At completion of the intra-abdominal procedure, but prior to closure to the abdominal layers, the ultrasound transducer will be covered by a sterile drape and applied to the bladder. Normal ureteral function will be identified by "jets" of urine emanating from the ureteral orifices, bilaterally. Lack of function will require follow-up to include possible cystotomy and/or postoperative intravenous pyelogram, as part of necessary procedures for these patients. The preoperative and intraoperative ultrasound will be compared using descriptive statistics.

**Progress:** No patients have been entered in this study. The study was terminated in August 1991 due to the inability to assign a principal investigator.

CPT Turner, original principal investigator

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/083	<b>Status:</b> Terminated
<b>Title:</b> Ultrasound Compared to Intravenous Pyelography in Demonstrating Ureteral Function Into the Bladder		
<b>Start Date:</b> 06/15/90	<b>Est. Completion Date:</b> Sep 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT John B. Browning, MC		
<b>Associate Investigators:</b> CPT Kevin C. Turner, MC CPT Richard W. Knight, MC	LTC Gordon O. Downey, MC LTC John A. Vaccaro, MC	
<b>Key Words:</b> ureteral function,ultrasound,bladder		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 08/20/91

**Study Objective:** To evaluate the ability of standard ultrasound equipment to demonstrate the presence or absence of ureteral function, followed by immediate confirmation with intravenous pyelograph.

**Technical Approach:** Number of subjects = 100. Age range 18-75. Patients scheduled for routine or emergent evaluation of the urinary tract via IV pyelography will be asked to participate. Immediately prior to IV pyelography, an ultrasound evaluation of the bladder will be performed transcutaneously, looking for ureteral function. Normal function will be noted as "jets" of urine emanating from the ureteral orifices. Descriptions of depth of subcutaneous tissue as well as presence or absence of ureteral function will be made by an investigator blinded to the patient's history. Following this, the scheduled IV pyelogram will be performed and evaluated by the Urology Department. Statistical correlations between studies will be made with the ultimate intent to demonstrate an estimate for sensitivity and specificity of this technique.

**Progress:** No patients were entered on the protocol. The protocol was suspended when the principal investigator was unexpectedly reassigned. The protocol was terminated in August 1991 due to the lack of a principal investigator.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 87/061                      **Status:** Completed

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**Title:** A Phase III Trial of Intraperitoneal Interferon vs Intraperitoneal Cisplatinum for Minimal Residual Ovarian Carcinoma Following Systemic Chemotherapy (Schering C86504)

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**Start Date:** 04/17/87                      **Est. Completion Date:** Indef.

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**Department:** OB/GYN                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** COL William L. Benson, MC  
COL Roger B. Lee, MC

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**Key Words:** cancer:ovarian,interferon,intraperitoneal cisplatinum,chemo

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<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	04/05/91

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**Study Objective:** To confirm the response rate seen with i.p. Intron in minimal residual ovarian carcinoma, to compare the efficacy of i.p. platinum versus i.p. Intron in inducing responses in this group of patients, and to compare toxicities of the different treatment arms.

**Technical Approach:** This is a randomized, multi-institutional, phase III clinical trial for patients with ovarian carcinoma with approximately 40 patients entered in each arm. Prior to randomization, patients shall have had maximal surgical debulking followed by 4-12 cycles of conventional chemotherapy utilizing cisplatinum, and second-look operation. Patients with minimal residual disease and positive cytology will be eligible. Patients will be entered in the study no later than two weeks following secondlook operation, and a Tenckhoff or Port-A Cath or similar catheter will be placed surgically as soon as possible following randomization. Treatment with intraperitoneal therapy will begin no later than one month following second-look surgery. Patients will be randomized to receive Intron or platinum and all patients will be treated with 12 weeks of therapy. The patients will undergo an exploratory laparotomy at the conclusion of the final therapy unless there is gross measurable disease by physical examination, CT scan, or ultrasound exam which obviates the need for laparotomy. An assessment of disease status will be done at selected points of patient follow-up. Patients will be evaluable for efficacy after receiving one month of therapy. All patients entered will be evaluable for toxicity.

**Progress:** No patients have been entered in this study at MAMC. The protocol was closed by Schering due to sufficient patient accrual.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/017	<b>Status:</b> On-going
<b>Title:</b> Surgical Management of the Bowel and Urinary Tract in Gynecologic Surgery (Swine Model)		
<b>Start Date:</b> 01/20/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL Richard P. Belts, MC		LTC David J. Magelssen, MC MAJ John W. Cassels JR, MC
<b>Key Words:</b> gynecologic surgery, training protocol, swine, bowel, urinary tract, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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 anastomoses will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

**Progress:** One training session utilizing this protocol was held in FY 91. The small number of sessions was due to the large number of personnel from MAMC who were deployed to Operation Desert Storm.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 88/024                      **Status:** Completed

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**Title:** Randomized Trial of Spontaneous Vaginal Versus Outlet Forceps Delivery in Term Pregnancies

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**Start Date:** 05/20/88                      **Est. Completion Date:** Jun 88

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**Department:** OB/GYN                      **Facility:** MAMC

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**Principal Investigator:** CPT Arthur H. Herpolsheimer, MC

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**Associate Investigators:**  
MAJ Frederick E. Harlass, MC                      COL William L. Benson, MC  
CPT Michael K. Yancey, MC                      MAJ Jose Garcia, MC

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**Key Words:** delivery:vaginal,delivery:outlet forceps

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Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$480.00	04/05/91

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**Study Objective:** To compare two methods of vaginal delivery in a prospective randomized fashion in order to determine if there is any increase in maternal or neonatal morbidity with either method relative to the other.

**Technical Approach:** Patients with a term gestation (37-42 weeks), who have had an uncomplicated course of labor and no evidence of fetal distress, will be studied. Data collection will include duration of second stage of labor, infant birth weight, Apgar scores, cord gases, the presence of maternal or fetal birth trauma, estimates of blood loss, and pre and postdelivery hematocrits. Evaluation of neonates will include a detailed examination of the infants plus a cranial ultrasound. Approximately 600 patients will be randomly assigned to either spontaneous or low forceps delivery. Cord blood samples will be obtained shortly after cord clamping. Cord gases will be recorded and the nursery staff will be notified of any abnormal findings. The cranial ultrasound will be performed within 24-72 hours following birth. The maternal hematocrit will be evaluated by routine methods on admission to the hospital and on the third postpartum day. The remainder of the information will be obtained from a review of the maternal in-patient record. Data will be compared utilizing the Student's t test or chi-square analysis, as appropriate.

**Progress:** The protocol has been completed, 165 patients were entered in the outlet forcep delivery arm and 168 were entered in the spontaneous vaginal delivery arm. The data showed that the use of outlet forceps in patients with uncomplicated labor has no significant immediate effect on the neonate. Furthermore, outlet forcep delivery does not significantly shorten the second stage of labor, but is associated with an increased incidence of maternal perineal trauma. A paper has been accepted for publication in Obstetrics and Gyencology. An abstract was presented at the May 1991 meeting of the American College of Obstetricians and Gynecologists.

Replaced Dr. Yancey as principal investigator, Sep 89.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 87/069		<b>Status:</b> Completed	
<b>Title:</b> Low-Dose Aspirin in the Prevention of Pregnancy-Induced Hypertension and Pre-eclampsia in Primigravida Women					
<b>Start Date:</b> 05/15/87			<b>Est. Completion Date:</b> Apr 89		
<b>Department:</b> OB/GYN			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jerome N. Kopelman, MC					
<b>Associate Investigators:</b>					
COL John A. Read II, MC		COL Patrick Duff, MC			
COL William L. Benson, MC		MAJ Frederick E. Harlass, MC			
MAJ Charles J. Hannan, MC		MAJ Jose Garcia, MC			
		MAJ W. Kim Brady, MC			
<b>Key Words:</b> pre-eclampsia, aspirin, pregnancy, hypertension, primigravida					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$5952.00		05/03/91	

**Study Objective:** To investigate the effect of low-dose aspirin taken daily from 22 weeks gestation until delivery, on the development of pregnancy-induced hypertension and pre-eclampsia in normotensive primigravida women.

**Technical Approach:** Healthy primigravida women will be enrolled in the study at 22 weeks gestation. Pre-entry evaluations will include CBC, platelet count, PT/PTT, and ultrasound to confirm dates. Patients will be randomized to either 81 mg of aspirin per day or a placebo in a double blind fashion to be taken until delivery. There will be approximately 300 women in each group. Patients will receive standard antenatal care with visits every 2 weeks until 36 weeks and weekly visits thereafter. Index of aspirin ingestion will be determined by measuring malondialdehyde levels at 28 weeks and again when the patient presents for delivery. Levels of thromboxane B2 and 6-keto-prostaglandin F1 alpha will be measured via 24 hr urine collections performed at 28 and 36 weeks gestation. The thromboxane B2 and 6-keto-prostaglandin F1 alpha urine specimens will be collected and 50 samples from each group of patients will be randomly selected and respective radioimmunoassays will be performed. The thromboxane A2/prostacyclin balance between the two groups will be compared. Malondialdehyde assays will be run on all samples. Mode of delivery, neonate apgar scores, and routine neonatal laboratory tests will also be compared. Serial ultrasounds with biometric measurements will be performed at 28 and 34-36 weeks to assess fetal growth. Serial umbilical artery doppler FVW studies will be done at entry into the study, at 2 weeks, and again when scheduled ultrasounds are done. This information will be compared to the respective patient's thromboxane/prostacyclin data and clinical outcome.

**Progress:** The study has been completed, 110 patients were enrolled. A paper is being written for submission for publication.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/034	<b>Status:</b> On-going
<b>Title:</b> Cordocentesis in an Animal Model		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Dec 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Jerome N. Kopelman, MC		
<b>Associate Investigators:</b> COL John A. Read II, MC MAJ Douglas A. Milligan, MC		
<b>Key Words:</b> cordocentesis, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	04/05/91

**Study Objective:** To determine if an animal model can be developed to allow physicians inexperienced in the technique of cordocentesis to develop the requisite skills.

**Technical Approach:** Approximate gestational date will be obtained on six pregnant goats, using either ultrasound or radiologic evaluation. When each individual goat nears term, a laboratory session will be held. The goat will be placed under general anesthesia and sterilely prepped. Under direct ultrasound guidance, a 20 gauge spinal needle will be placed through the abdomen and into the uterus. The umbilical cord will be visualized with the ultrasound and the needle guided into the umbilical vein. After the procedure, the animals will be kept separate from the rest of herd for four days in order to facilitate the identification of complications of the procedure. Data collection will include number and type of complications to the animals, as well as a description of any technical problems encountered during the procedure.

**Progress:** No further work was done on this study during FY 91 due to the reassignment of the principal investigator and a decrease in staffing due to Operation Desert Storm. One animal was scanned in FY 90. The investigators have been unable to visualize cords well. They plan to attempt new scans with a different machine.

Dr. Milligan original PI

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/106	<b>Status:</b> On-going
<b>Title:</b> Evaluation of Efficacy of Twelve Hour Urine Collections in the Diagnosis of Pre-eclampsia		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> Dec 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Wilma I. Larsen, MC		
<b>Associate Investigators:</b> MAJ Jerome N. Kopelman, MC		CPT Montgomery E. Thorne, Jr., MC
<b>Key Words:</b> pre-eclampsia, 12 hour urines		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$230.00	//

**Study Objective:** To determine the efficacy of 12-hour urine collection as compared to 24-hour urine collection in evaluating proteinuria of pre-eclampsia, specifically addressing timing of 12-hour collection in a 24-hour period and fraction of protein in 12-hour collection as compare to 24-hour collection.

**Technical Approach:** Twenty patients who present with any of the criteria for pre-eclampsia will be included in the study. All samples will be obtained while the patient is at bed rest. Two separate aliquots (between 1800-0600 and 0600-1800) will be collected and analyzed for protein and total volume. The two aliquots will then be combined and analyzed again. Statistical analysis will involve testing each aliquot versus the combined sample (24 hour urine).

**Progress:** Twenty-five (25) subjects (all in FY 91) have been entered in the study. Thus far the data seem to indicate that 12 hour urine samples will be useful in the evaluation of pre-eclampsia. They are not, however, equal to one half of the 24 hour specimen.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/028	<b>Status:</b> Terminated
<b>Title:</b> The Urethral Cytology of Patients with Urethral Syndrome		
<b>Start Date:</b> 05/20/88	<b>Est. Completion Date:</b> May 88	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC David J. Magelssen, MC		
<b>Associate Investigators:</b> CPT Kevin P. Sargeant, MC		
<b>Key Words:</b> uret. ral syndrome, urethral cytology		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$30.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine if demonstrable differences in urethral cytology exist between gynecologic patients with the urethral syndrome and those without it.

**Technical Approach:** The study population will consist of 25 to 30 women being followed in the urogynecologic clinic. Patients having symptoms referable to the urinary tract (frequency, urgency, dysuria, dyspareunia, low back pain, chronic pelvic pain) and sterile urine cultures will be eligible. They will be divided into two groups: patients with urinary tract symptoms and sterile urine cultures and patients seen in the clinic but not having symptoms referable to the urinary tract. A wool-tipped Calgi swab will be dipped in normal saline and then introduced into the urethra and used to swab the urethral tract. The swab will then be placed in Saccomanno's fixative and transported to Cytology for examination. The results will be collected from the lab, divided into normal cytology versus any unusual or abnormal features and evaluated for statistical significance using the chi-square test.

**Progress:** This protocol was terminated because it was felt to be infeasible for completion due to the reorganization of the patient clinic and the principal investigator was then deployed to Operation Desert Storm.

Replaced Dr. Sargeant as PI, Jul 88

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/024	<b>Status:</b> On-going
<b>Title:</b> The Evaluation of an Endocervical Brush Device in a Population of Pregnant Patients		
<b>Start Date:</b> 03/01/91	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Karen M. Nelson, MC		
<b>Associate Investigators:</b> MAJ W. Kim Brady, MC		MAJ Jerome N. Kopelman, MC CPT Stefanie S. Christian, MC
<b>Key Words:</b> endocervical brush, pregnancy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

Study Objective: To determine the difference in endocervical cell yield between endocervical cytology brush techniques and standard cotton swab techniques in a population of pregnant patients and to determine the safety of the endocervical cytology brush technique.

Technical Approach: Patients, 18-45 years, undergoing new OB evaluation will be randomized to either Group A or Group B. Patients in Group A will have Papanicolaou smears performed using the Ayer spatula and the cytobrush. Patients in Group B will have Papanicolaou smears performed using the Ayer spatula and a moistened cotton swab. The cytologic specimens will be evaluated in the routine manner. The safety, endocervical cell yield (smear adequacy), and the yield of dysplastic and microinvasive lesions will be determined and the results of the two groups compared using the unpaired t test and the chi square test.

Progress: Patient entry is continuing. Approximately 1000 patients have been entered in the study.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/037                      **Status:** Completed

**Title:** Incidence of Antiphospholipid Antibodies in the Presence of Intrauterine Growth Restriction (IUGR)

**Start Date:** 03/16/90                      **Est. Completion Date:** Jan 91

**Department:** OB/GYN                      **Facility:** MAMC

**Principal Investigator:** MAJ William J. Polzin, MC

**Associate Investigators:**                      MAJ Jerome N. Kopelman, MC  
MAJ W. Kim Brady, MC                      COL John A. Read II, MC

**Key Words:** IUGR, antiphospholipid antibodies

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$399.00	04/05/91

**Study Objective:** To determine the incidence of antiphospholipid antibodies in pregnancies complicated by intrauterine growth restriction (IUGR), to rule out other etiologies such as congenital infection, chromosomal abnormalities, and maternal disease, and to determine if there is an association between the antibody titer and the severity of disease expression.

**Technical Approach:** Patients with estimated fetal weight (EFW) >10th percentile for the correct estimated gestational age, determined by ultrasound, will be excluded. Blood samples will be evaluated for maternal hemoglobin, hematocrit, and presence of antibodies to rubella, cytomegalovirus (CMV), and Toxoplasma gondii and tested for the presence of lupus anticoagulant, anticardiolipin antibody, and antinuclear antibody. Thromboxane, antithrombin III, and prostacyclin levels will be measured. Cervical cultures for Neisseria gonorrhoea, Group B Streptococcus, and Listeria monocytogenes will be performed. If the EFW is <7th percentile, amniocentesis will be done assessing fluid for antibodies to rubella, toxoplasma organisms, and CMV. The amniotic fluid will be cultured aerobically and anaerobically for Listeria. Fetal karyotype and a L/S ratio will be done if >32 weeks gestation. If cultures or antibody screens are positive, cord blood at the time of delivery will be obtained to compare with the maternal results in order to determine incidence of vertical transmission. Continuous wave doppler flow studies of the umbilical artery will be done monthly. Ultrasounds and amniotic fluid volume assessment will be done weekly to assess growth. Further antepartum testing will be done as indicated. Predictive value of antepartum surveillance will be assessed by comparison to actual birth weight and perinatal outcome. Association of antiphospholipid antibodies with the presence of IUGR will be reported as a percentage. The validity of the test will be assessed with a 2x2 table determining sensitivity, specificity, positive predictive value, and negative predictive value.

**Progress:** This study has been completed, 55 subjects were studied. The findings show that there is a significant association between the presence of circulating maternal anticardiolipin antibodies and the occurrence of IUGR in pregnancy.

A paper has been accepted for publication in Obstetrics and Gynecology.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/073	<b>Status:</b> Completed
<b>Title:</b> The Prevalence of Positive Urine Toxicology Screens in a Military Obstetric Population		
<b>Start Date:</b> 05/18/90	<b>Est. Completion Date:</b> Jul 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ William J. Polzin, MC		
<b>Associate Investigators:</b>		
MAJ W. Kim Brady, MC	MAJ Jerome N. Kopelman, MC	
LTC Michael L. Smith, MS	COL John A. Read II, MC	
<b>Key Words:</b> toxicology,urine,OB		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$2200.00	05/03/91

**Study Objective:** To determine the prevalence of positive drug screens in the obstetric population served by Madigan Army Medical Center.

**Technical Approach:** An extra aliquot of urine will be decanted from the routine urine specimen obtained at the new obstetric patient visit for toxicology evaluation at AFIP. Immunoassay techniques will be used to identify metabolites of cocaine, marijuana, amphetamines, opiates, and alcohol, with confirmation by mass spectrophotometry. Specimens will contain no information whereby the donor could be identified. A number code will be used to connect the urine to the status, rank, age, race, gravidity, and parity of the donor. The results will be reported as a percentage of positive tests per total number of patients tested. Further demographic breakdown will be done for study comparisons. A sample size of 500 is selected to give a 95% confidence factor that population comparisons are valid, even if the incidence is as high as 3% positive.

**Progress:** This study has been completed, 470 samples were evaluated. Analysis of the data demonstrates that the MAMC obstetric population has a significantly lower prevalence of illicit drug use than other populations previously reported.

A paper has been accepted for publication by Obstetrics and Gynecology.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/063                      **Status:** Completed

**Title:** The Incidence of the Lupus Anticoagulant in the Pregnant Population

**Start Date:** 10/20/89

**Est. Completion Date:** Oct 90

**Department:** OB/GYN

**Facility:** MAMC

**Principal Investigator:** CPT Randal D. Robinson, MC

**Associate Investigators:**

CPT Sheri E. Nottestad, MC

CPT Donna S. Whittaker, MS

MAJ Everardo E. Cobos Jr., MC

COL John A. Read II, MC

MAJ Mark H. Kozakowski, MC

MAJ W. Kim Brady, MC

MAJ William J. Polzin, MC

COL Michael J. Carlon, MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

**Key Words:** lupus anticoagulant, pregnancy

**Accumulative**

**MEDCASE Cost:**

\$0.00

**Est. Accumulative**

**OMA Cost:**

\$1087.00

**Periodic Review:**

05/03/91

**Study Objective:** To determine the frequency of the lupus anticoagulant in the pregnant population, the frequency of fetal wastage in the pregnant patient with the lupus anticoagulant, and the percentage of spontaneous abortions due to the presence of the lupus anticoagulant.

**Technical Approach:** Approximately 1500 pregnant females between 18 and 35 years of age without known coagulopathy will be studied. Before entry a physical exam, including detailed obstetric history and thromboembolic disease history, prothrombin (PT) and partial thromboplastin time (PTT), and anticardiolipin antibody (ACA) will be done. Subjects with a prolonged PTT will undergo evaluation to include 1:1 mixing study and platelet neutralization procedure, Russell viper venom test if 1:1 mixing study is consistent with the lupus anticoagulant. Subjects who have a normal PTT will be followed for the remainder of the pregnancy and have a PTT and ACA drawn at the time of delivery. If the PTT is prolonged, the 1:1 mixing study and platelet neutralization procedure will be repeated and then performed again at the time of delivery. If a fetal death or spontaneous abortion occurs, anticardiolipin antibody will be done. A prolonged PTT and a correctable platelet neutralization procedure at any stage will constitute the presence of the lupus anticoagulant. The frequency of the lupus anticoagulant in pregnancy will be calculated as well as the frequency of spontaneous abortion when the lupus anticoagulant is present. Revision May 90: This revisions changed the population to include all pregnant women and added an objective to determine the number of patients who convert during the gestation period. The written consent form was waived by the IRB since the blood would be drawn for patient care and this protocol would fit the category of a health care delivery study.

**Progress:** This protocol has been completed, 1495 patients were studied. The incidence of lupus anticoagulant was determined to be .2% (3/1495) and the incidence of anticardiolipin antibody was 4% (60/1495). An abstract has been submitted to the American College of Obstetricians and Gynecologists for presentation at the annual meeting.

MAJ Kozakowski original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/050	<b>Status:</b> Completed
<b>Title:</b> Objective Measurement of Thyroid Volume During Pregnancy		
<b>Start Date:</b> 04/21/89	<b>Est. Completion Date:</b> Nov 90	
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Montgomery E. Thorne, Jr., MC		
<b>Associate Investigators:</b> COL Gary L. Treece, MC		MAJ W. Kim Brady, MC
<b>Key Words:</b> thyroid volume, pregnancy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$465.00	05/03/91

**Study Objective:** To objectively measure thyroid gland size and volume using ultrasonography of the thyroid, antepartum and postpartum, in healthy pregnant women to determine if the thyroid enlarges during pregnancy.

**Technical Approach:** Ten nonpregnant controls and 10-20 pregnant women will be studied. Baseline thyroid function tests, history and physical exam will be performed as early as possible during the pregnancy. Ultrasonic examinations of the thyroid will be done once each trimester (at least six weeks apart) and again at six weeks post partum. Thyroid function tests will be obtained again at six weeks postpartum to detect postpartum thyroid dysfunction. Thyroid gland size and volume will be determined by two different investigators, ultrasonically measuring the length of each lobe of the thyroid and the cross-sectional areas of multiple sections of each lobe at 0.5 cm intervals and calculating the volume by means of integration formulas. The volumes of the lobes will be added to determine the total thyroid volume.

Controls will be age and weight matched using the subject's first trimester weight. Baseline thyroid function tests and one thyroid ultrasound will be performed on the control subjects.

Each patient will serve as her own control with the data for thyroid gland volume summed and averaged for each trimester and postpartum and then compared using multiple t-tests. The measured thyroid gland volumes in the pregnant and postpartum subjects will also be compared to the thyroid gland volumes measured in the ten normal control women. Both the subjects and the control thyroid volume measurements will be compared to those recorded in the literature ( $17.5 \pm 4.2$  ml).

**Progress:** The study has been completed, ten subjects were studied. A 3% increase was seen in the size of the thyroid gland during pregnancy, which is not statistically significant.

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/014                      **Status:** Completed

**Title:** Antepartum GBS Screening

**Start Date:** 01/20/89

**Est. Completion Date:** Aug 89

**Department:** OB/GYN

**Facility:** MAMC

**Principal Investigator:** CPT Montgomery E. Thorne, Jr., MC

**Associate Investigators:**

MAJ John C. Schilhab, MS  
CPT Michael J. Murray, MC

LTC Charles E. Henley JR, MC  
MAJ W. Kim Brady, MC

**Key Words:** group B streptococci

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$2000.00	04/05/91

**Study Objective:** To define more clearly the natural history of group B streptococcal (GBS) carriage in the last trimester of pregnancy so as to be able to quantify the positive and negative predictive values of a culture result at four week intervals beginning at 26 weeks until the time of delivery.

**Technical Approach:** The first 500 women, ages 14-45, who are followed from 26 weeks to delivery and who give informed consent will be studied. Women presenting with ROM prior to presentation to labor and delivery and in whom amniotic fluid bacteriostatic quality might interfere in the detection of GBS will be excluded. The vaginal introitus and rectum will be cultured at 26, 30, 34, and 38 weeks and prior to delivery. Blood agar with gentamicin will be used as the culture media. Any gram positive cocci will be definitively identified using the catalase test (GBS beta hemolytic) bacitracin disc (GBS resistant), and CAMP test (GBS positive). No treatment will be given until the time of delivery. Each of the interval cultures will be compared to the colonization status of the patient at the time of presentation in labor. The negative and positive predictive values will be calculated. The time of presentation will be recorded in order to assess the percentage of patients who would deliver prior to six hours and thus not benefit from rapid latex fixation testing.

**Progress:** This protocol has been completed, 112 subjects were studied. A paper is being written.

Dr. Murray original PI

# **DETAIL SHEETS FOR PROTOCOLS**

## **PREVENTIVE MEDICINE SERVICE**

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/014                      **Status:** Suspended

**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:** 02/16/90                      **Est. Completion Date:** Jun 91

**Department:** PM                      **Facility:** MAMC

**Principal Investigator:** MAJ Margot R. Krauss, MC

**Associate Investigators:** MAJ John G. McNeil, MC  
COL Kevin M. McNeill, MC

**Key Words:** HIV, risk factors, antibody seroconversion

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	03/01/91

**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:** The multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion to 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 installations where cases seroconvert and will be matched for age (+ 2 yrs), gender, ethnicity, rank (junior enlisted, senior enlisted, officer), 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 an HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographic information, medical history, risk factors for drug use, risk factors for sexual history, and risk factors for 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 associations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be employed. 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 (e.g., proportional hazards, conditional logistic regression) analyses.

**Progress:** Four patients and seven controls were entered in the study. The protocol was suspended as of 30 Sep 90 due to a lack of funding. Funding has not been reinstated to date. The investigators expect funding to resume within the next couple of months.

MAJ McNeil original PI

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF PEDIATRICS**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/004	<b>Status:</b> On-going
<b>Title:</b> Tympanometry Guidance for Treatment of Otitis Media		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b> Nov 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Thomas R. Babonis, MC		
<b>Associate Investigators:</b>		
COL Marvin S. Krober, MC	LTC Patrick C. Kelly, MC	COL Michael R. Weir, MC
<b>Key Words:</b> otitis media, tympanometry		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if a change in antibiotics on the fourth day of treatment for acute otitis media in patients at high risk for treatment failure will improve the ultimate outcome.

**Technical Approach:** The subject population will be 450 children, 2 months to 21 years, with acute otitis media, diagnosed by acute onset symptoms with abnormal ear drum appearance and abnormal flat (type B) tympanograms at four days treatment with amoxicillin. Participants will be randomly assigned to amoxicillin, Augmentin, Septra, Pediazole, or Suprax. Children will return 10-12 days later and then at 30 days after starting medication for repeat clinical evaluation and tympanography. Demographic data will be collected at the first visit and clinical data at each subsequent visit. If clinical status requires change of antibiotics, the patient will be withdrawn from further participation. There will be no restriction on the use of other non-antibiotic medications. Chi-square or 2X5 contingency table analysis will be used as appropriate to demonstrate significance of changes observed in the typanograms. Power analysis has shown that 90 patients will be needed for each antibiotic arm in order to demonstrate a 50% improvement in outcome.

**Progress:** No patients have been entered during the summer months because of the highly seasonal nature of otitis.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/093	<b>Status:</b> On-going
<b>Title:</b> Health Habits and Lifestyles in Families of Children Less Than Two Years of Age		
<b>Start Date:</b> 09/06/91	<b>Est. Completion Date:</b> Oct 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Thomas R. Babonis, MC		
<b>Associate Investigators:</b>		Kathi Kemper, M.D.
<b>Key Words:</b> health,lifestyle,children:<2 YO		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To assess the feasibility of screening women for tobacco, alcohol, and illicit drug use in the setting of a pediatric clinic using self-administered questionnaires, to assess the prevalence of positive screening tests for tobacco, alcohol, and drug use among women of young children attending pediatric clinics, and to test the association between positive screening tests for substance abuse in mothers of young children and risk factors for substance abuse described in other populations.

**Technical Approach:** The questionnaire will be given to mother while she is in waiting room awaiting care for her child. To preserve anonymity, no identifying information will appear on the questionnaire, and none of the information on the questionnaire will be shared with anyone else without the expressed written consent of the mother after filling out the questionnaire. Potential subjects who refuse will be asked their reasons for refusal and their age, child's age and race will be noted in order to assess the potential for non-response bias.

One hundred subjects will be sought and randomly given one of two questionnaires (therefore 50 in each group). One emphasizes questions on drug use and the other questions on alcohol use.

Analysis will include simple descriptive statistics, comparison of participants to non-participants by maternal and child age and race. Chi-square tests will be used to test the association between positive screening tests and marital status, family history of substance abuse, household substance abuse, and positive screening tests for depression. Multivariate analyses will be used to control for potential confounding factors and effect modification between variables to arrive at adjusted odds ratios for risk of substance abuse.

**Progress:** Fifteen subjects have been entered.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 91/055                      **Status:** On-going

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**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 Behaviors in Childhood

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**Start Date:** 04/05/91                      **Est. Completion Date:** Jun 92

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**Department:** Pediatrics                      **Facility:** MAMC

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

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**Associate Investigators:**                      LTC Patrick C. Kelly, MC  
Jennifer S. Achilles

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**Key Words:** OCD, screening, Yale Brown Compulsive Scale, symptom checklist, children: 7 - 18 YO

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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**Study Objective:** To determine if the short interview is a clinically useful format for identifying Obsessive Compulsive Disorder (OCD) in childhood and to further evaluate the diagnostic screening properties of the CY-BOCS as a semi-structured interview looking for OCD in childhood.

**Technical Approach:** Approximately 1000 subjects will be selected for interviewing. This will consist of 500 subjects 7 to 12 years old and 500 subjects 13 to 18 years old. Subjects will be randomly selected from appointment rosters. While the parent(s) and child are waiting in the waiting room, they will be asked about participating in this protocol. We will explain that this will involve a 10 minute interview of parent(s) and child in a private exam room.

Using the chi-square test, comparisons will be made between the positive and negative short interview groups, between the positive and negative CY-BOCS interview groups, between the positive and negative physical exam finding groups, between the positive trichotillomania/eating behavior and negative groups. Concordance of all positive groups will be assessed. Demographic data in positive and negative groups will be compared. From analysis of the above groups, information on the selectivity of the short interview versus the CY-BOCS for OCD diagnosis at followup will be formulated. Minimal prevalence rates of OCD will be assessed for this clinic sample. All positive interview groups and physical exam findings will be compared with diagnoses and medical problems at followup evaluation. All diagnoses and medical problems will be determined at followup interview, as the gold standard for establishing any diagnosis or medical problem in this study.

Data in all the negative groups will be assessed for frequency of "1" level symptoms, trichotillomania symptoms, and eating disorder symptoms on the CY-BOCS according to age, sex and sponser rank. This will also be correlated with any later DSM diagnoses, which may come about on followup clinical interviews.

**Progress:** One hundred and ten subjects have been entered in the study.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/048		<b>Status:</b> Completed	
<b>Title:</b> The Token Test for Children in Identifying and Following Treatment Efficacy in Attention Deficit Hyperactivity Disorder					
<b>Start Date:</b> 03/16/90			<b>Est. Completion Date:</b> Mar 91		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Edward J. Coll, MC					
<b>Associate Investigators:</b>			LTC Patrick C. Kelly, MC		
<b>Key Words:</b> ADHD, token test, hyperactivity, children					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		04/05/91	

**Study Objective:** To determine if the Token Test for Children (TTC) is a possible diagnostic indicator for attention deficit hyperactivity disorder (ADHD) or can be used in following standard treatment response in ADHD.

**Technical Approach:** ADHD subjects will be obtained through a routine Developmental Pediatrics referral. Subjects will fulfill DMS III-R criteria for ADHD, routine clinical indications for trial of methylphenidate therapy, and have no prior stimulant or antidepressant use. Control subjects will have no ADHD or learning disability. The TTC will be administered to all subjects and repeated at two weeks after the initial testing. The TTC is divided into five subtests of increasingly complex measures of receptive language and yields age-dependent standard scores for the overall test and each of the five subsets. The ADHD group will have a methylphenidate therapy trial commencing after initial TTC. TTC testing will be performed 1-3 hours after dosage. TTC scores between the study groups will be analyzed with the unpaired T test and analysis of variance with repeated measures will also be used. Additional data will be obtained from the ADHD group by parent and teacher questionnaires. These behavior rating scales will be used before and two weeks after methylphenidate therapy: Conners (parent and teacher) and ACTeRS (teacher only).

**Progress:** Sixteen ADHD subjects and sixteen age-matched control subjects were entered. The results did not support the hypothesis that the TTC would assist in identifying ADHD children or in determining adequate response to standard methylphenidate therapy in those children. However, there may be mitigating circumstances such as the size of the population and a bias in selection of subjects such that individuals with both ADHD and language difficulties were either referred less to the clinic or that they were less likely determined to be candidates for a trial of medication. A prospective study examining characteristics of a consecutively diagnosed ADHD population would be helpful, rather than a subpopulation at the initiation of medical therapy.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/079	<b>Status:</b> On-going
<b>Title:</b> Use of Metoclopramide With Chloral Hydrate for Sedation		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Jan 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Vincent A. Dubravec, MC		
<b>Associate Investigators:</b> CPT George D. Patrin, MC		
LTC Joseph P. McCarty, MC		
<b>Key Words:</b> sedation, metoclopramide, chloral hydrate		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$42.06	<b>Periodic Review:</b> 05/03/91

**Study Objective:** To demonstrate a more complete and reliable sedative effect with chloral hydrate, utilizing less drug, by adding metoclopramide to the preprocedure regimen.

**Technical Approach:** Approximately 100 children, age range 6 months to 12 years, requiring sedation for CT, MRI, or EEG, will be studied. One hour prior to the exam time, the subjects will be given 50 mg/kg of chloral hydrate po along with either 0.4 mg/kg (maximum 5 mg) Reglan or placebo, in a randomized fashion. If not asleep within 45 minutes, they will get an additional 25 mg/kg of chloral hydrate.

Questionnaires will be completed immediately after the procedure by the parent and by the technician detailing the time of onset of sedation, its completeness, and any failed events or untoward effects. Placebo will be compared to Reglan regarding dose of chloral hydrate needed, effect on onset of action, duration, and completeness in terms of allowing the test procedure to be done.

**Progress:** Twenty-three patients were entered in the study in FY 91.

Dr. Patrin original PI.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/071	<b>Status:</b> On-going
<b>Title:</b> Pyridoxine as Specific Therapy and Prophylaxis in the Treatment of Theophylline-Induced Seizures in Mouse and Rabbit Models		
<b>Start Date:</b> 05/18/90	<b>Est. Completion Date:</b> May 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b>		
COL Michael R. Weir, MC	CPT Gregory M. Glenn, MC	
LTC Patrick C. Kelly, MC	LTC Joseph P. McCarty, MC	
<b>Key Words:</b> seizures, prophylaxis, pyridoxine, mouse, rabbit, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$420.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To investigate the therapeutic efficacy of pyridoxine in seizures secondary to theophylline overdose in rodent models.

**Technical Approach:** Part I Inbred male mice will be divided into a control group of 10 mice (250 mg/kg aminophylline, 75% expected to seize) and a pretreatment group. The pretreatment group will be subdivided into four groups of 10 mice and given 25, 50, 100, and 250 mg/kg of IP pyridoxine, respectively. A third group will be given 250 mg/kg of IP aminophylline and then pyridoxine at the onset of seizure, and subdivided into four groups of 10 mice, given 25, 50 100, and 250 mg/kg, respectively. Time to seizure and mortality rate will be observed. In this fashion, it is anticipated that a dose-response range can be established based on human models. Part II: After a successful dose-response range has been established in Part I, initial EEG trials with external electrodes will be attempted on conscious untreated rabbits. If reliable EEG results can not be obtained in this manner, then the rabbits will be anesthetized and stainless steel screw electrodes will be placed overlying the dura in both centroparietal areas with a reference electrode placed in the frontal sinus. Bipolar recording of EEG activity will be recorded on a Grass recorder and EKG and respirations will also be monitored using the Grass recorder. Six New Zealand white rabbits will be anesthetized and given 115 mg/kg of IV aminophylline over 50 minutes with an expected seizure rate of 80% with a mean time to seizure of 108 minutes. The first group of 3 animals will be pretreated with the same mg/kg dose of pyridoxine as found to be effective in Part I. The second group of 3 animals will be given a mg/kg dose of pyridoxine as found to be effective in Part I at the onset of seizures. If apnea occurs, assisted ventilation will be given for a maximum of 10 minutes to minimize the mortality secondary to apnea alone. Time to seizure, duration of seizure and mortality rates will be noted. Pre and post aminophylline PLP levels will be determined as well as PLP, theophylline, and standard chemistries at the onset of seizure. Once seizures are controlled with the pyridoxine, PLP and theophylline levels will again be determined. These findings will be correlated with EEG findings. Revision I (20 Jul 90): Initial findings (using mice) indicated that pyridoxine may have an effect in preventing theophylline seizures. The investigators then did a pilot study in an attempt to maximize the therapeutic effect by providing 500 mg/kg pyridoxine, after 250 mg/kg theophylline and noted a significant delay in time to seizure. The protocol was revised to allow the investigators to serially inject 250 mg/kg of pyridoxine at 5, 15, and 50 minutes after the theophylline dose in order to provide pyridoxine levels over the time frame of seizures in the control group and to achieve an experimental number, balanced

by sex. In previous experimental groups, female mice appeared to predominate in the seizure group. Therefore, 20 additional control females will be studied in order to alleviate any effect due to sex. If results are promising, the investigator will then commence with Part II of the protocol, using larger animals. Revision II (17 Aug 90): A revision was approved to add a study of the use of propranolol in place of pyridoxine in the acute model with the 30 mice given theophylline as before. Instead of a large single dose of pyridoxine, a large single dose of propranolol will be given. Several doses will be given in order to find a dose-range. Also a chronic model using 30 mice will be studied. Animals will be given half the acute dose of theophylline daily for five days. Half of the animals will be given the mg equivalent dose of pyridoxine while the remainder will be given isovolemic saline. Revision III (21 Sep 90): The studies showed that EEG changes caused by aminophylline could be reversed with acute pyridoxine, followed by a 230 mg/kg/50 min pyridoxine infusion. The animals developed theophylline levels of 192 mg/ml immediately and fell to 99 mg/ml at 3-4 hours and were asymptomatic when returned to their cages. Six of 6 animals died shortly thereafter, raising the question of whether prolonged infusion of pyridoxine until blood levels fell to therapeutic ranges in 3 half-lives would result in saving the subject. Therefore, the protocol was amended to study 6 rabbits with prolonged pyridoxine infusion (approximately 12 hours).

Progress: Theophylline administered to mice produced seizures and death in about 70% of the animals. Pyridoxine reduced the number of deaths and doubled the average time to death in those animals that did die. Some rabbits had abnormal EEG's after theophylline, which returned to baseline after pyridoxine. Additional work is needed to produce a higher quality EEG recording and better document baseline normal EEG.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/108	<b>Status:</b> On-going
<b>Title:</b> Role of Anticonvulsants in Theophylline Toxicity		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> LTC Joseph P. McCarty, MC		LTC Patrick C. Kelly, MC COL Michael R. Weir, MC
<b>Key Words:</b> theophylline toxicity, anticonvulsants, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$916.00	<b>Periodic Review:</b> 06/14/91

**Study Objective:** To test whether conventional anticonvulsants have any effect on the EEG in theophylline toxicity.

**Technical Approach:** Each rabbit will receive 115 mg/kg aminophylline intravenously, followed within 30 minutes by either valium (0.2 mg/kg), phenobarbital (20 mg/kg), or phenytoin (12 mg/kg), with six animals receiving each anticonvulsant. The remaining six animals will receive aminophylline as above, followed by pyridoxine 45 mg/kg IV push and then 230 mg/kg/hour for a one hour infusion. EEG tracings will be obtained at 15 minute intervals for three hours. The rabbits will then be observed for a period of three days. Results will be of a descriptive nature with mean  $\pm$  standard deviation being the primary statistic.

**Progress:** This protocol will be implemented after a solution is found to the technical problems with obtaining adequate EEG recordings as noted per protocol #90/71 in conjunction with protocol #91/52.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/053                      **Status:** On-going

**Title:** Role of Glutamine and 4-aminobutyraldehyde in Pyridoxine-Treated Theophylline Toxicity

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

**Department:** Pediatrics                      **Facility:** MAMC

**Principal Investigator:** COL Marvin S. Krober, MC

<b>Associate Investigators:</b>	LTC Patrick C. Kelly, MC
COL Michael R. Weir, MC	John Enriquez
CPT Katherine H. Moore, MS	MAJ John W. McBurney, MC

**Key Words:** seizures, glutamine, 4-aminobutyraldehyde, theophylline toxicity, Animal Study

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

Study Objective: To test whether seizure activity can be altered with glutamine or 4-aminobutyraldehyde in theophylline toxicity that has been altered with pyridoxine.

Technical Approach: Female mice will be given aminophylline for toxicity, followed by equivalent doses of pyridoxine. They will then be given varying doses of glutamine and 4-aminobutyraldehyde in order to determine the maximal effective doses. For the next phase, the study animals will receive theophylline and pyridoxine and the dose chosen above of either glutamine (6 animals) or 4-aminobutyraldehyde (6 animals). Groups of six will also receive half and twice the chosen amount of theophylline and pyridoxine. Control groups will consist of three animals and will use test drugs in: each drug alone (mid range dose), with pyridoxine and with theophylline, theophylline alone and with pyridoxine, and pyridoxine alone. The animals will be observed for time to seizure and time to death. Eighteen rabbits will have baseline EEG recordings done and then will be returned to the cage and observed to explore the limits of EEG changes and variation in rabbits. Six animals will receive 115 mg/kg aminophylline followed by pyridoxine 115 mg/kg plus glutamine as derived from the mouse studies. The most effective mouse dose will be reduced by a fraction that corresponds to the reduction in aminophylline dose, i.e., 115/250. With that as a base dose, double and half doses will again be used. Six animals will be similarly treated with 4-aminobutyraldehyde. Two animals will receive theophylline only, two theophylline and pyridoxine, and two will receive the best dose of both study medications with theophylline and pyridoxine. EEG recordings will be obtained at 15 minute intervals. Baseline blood samples will be drawn for pyridoxal-5'-phosphate and again after aminophylline, pyridoxine, and glutamin/aminobutyrate. Spinal taps will be attempted on some animals for determinations of GABA and glutamine. The animals will be observed for a period of three hours with EEG monitoring, followed by three days in cages. Consistent presence or absence of effect on the EEG is expected. Analysis of blood levels of PLP and CSF levels of GABA and glutamine will be by repeated measures ANOVA with post-hoc testing by paired t-tests. The resulting paper will be descriptive.

Progress: A small number of mice have been treated with various combinations of theophylline, glutamine, and 4-aminobutyraldehyde. 4-aminobutyraldehyde appeared to reverse the toxicity caused by theophylline.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/052	<b>Status:</b> On-going
<b>Title:</b> Role of Anticonvulsants with Pyridoxine in Theophyllin Toxicity in Rabbits		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> COL Michael R. Weir, MC		LTC Patrick C. Kelly, MC MAJ John W. McBurney, MC
<b>Key Words:</b> anticonvulsants,theophylline toxicity,rabbit,pyridoxine,Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To test whether conventional anticonvulsants have an adjunctive effect on the EEG in theophylline toxicity treated with pyridoxine.

**Technical Approach:** The rabbit model, which will be used, allows for a 30 minute IV infusion of aminophylline, which reflects the clinical circumstances of theophylline overdose. Each rabbit will receive 115 mg/kg aminophylline IV over 30 minutes, followed by pyridoxine (115 mg/kg) over 20 minutes, followed by either valium (0.2 mg/kg), phenobarbital (20 mg/kg), or phenytoin (12 mg/kg) IV over 3-15 minutes. Eighteen animals will be studied in groups of six for each medication. An additional six animals will be used for two theophylline controls, for two theophylline-pyridoxine controls, and two for the combination study of the two most promising anticonvulsants. EEG tracings will be obtained at 15 minute intervals and blood will be drawn for pyridoxal-5'-phosphate at baseline, after aminophylline, after pyridoxine, and after anticonvulsants. For some animals, CSF will be obtained by spinal needle puncture, cisternal tap, or cisternal catheter at baseline, after aminophylline, after pyridoxine, and after anticonvulsants for determinations of GABA and glutamine. The animals will then be observed for a period of three hours with EEG monitoring followed by three days in cages and then sacrificed. We expect the results to show consistent presence or absence of effect on the EEG. The resulting paper will be descriptive.

**Progress:** No animals have been studied. The implementation of this protocol is dependent upon further development of EEG recordings in rabbits as per protocol MAMC 90/071.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/076	<b>Status:</b> On-going
<b>Title:</b> Protective Role of Pyridoxine in Gentamicin Nephrotoxicity		
<b>Start Date:</b> 10/20/89	<b>Est. Completion Date:</b> Sep 90	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> COL Michael R. Weir, MC		
<b>LTC Jose D. Masi, MC</b>		
<b>Key Words:</b> nephrotoxicity, gentamicin, pyridoxine, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3135.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To test whether pyridoxine has a protective effect on gentamicin nephrotoxicity.

**Technical Approach:** Following a period of quarantine and observation, rabbits will be premedicated with xylazine and ketamine and then taken to the operating suite in groups of seven. One animal will receive 100 mg of pyridoxine as a control. The remaining animals will receive either 20 mg/kg or 60 mg/kg of gentamicin intramuscularly. One animal at each gentamicin dose will then receive either saline or 10 mg pyridoxine or 100 mg pyridoxine. These medications will be repeated daily for five days. Blood will be drawn for pyridoxal 5'-phosphate (PLP), gentamicin, and creatinine on days 1 (before injection), 3, and 5. Following the last injection in the morning, the animals will be sacrificed in the late morning or early afternoon using pentobarbital or suitable substitute, and one kidney from each animal will be recovered for fixation for blinded and pathologic interpretation. In each of two subsequent weeks, seven more animals per week will be studied similarly. This is a descriptive study in which the investigators hope to show that there is a general relationship between renal pathology and the average fall in PLP or, potentially, a relationship between pathology and gentamicin blood levels. BMDP and SPSS will be used to analyze data. If there are striking differences between the renal pathology of the various animals, the pathology will be scored for rank testing versus PLP, creatinine, gentamicin levels, and B6 dose.

**Progress:** Satisfactory tissue toxicity in kidney was not achieved with the dose of gentamicin that was used. The protocol will have to be revised to use a higher dose of aminoglycoside.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/092	<b>Status:</b> On-going
<b>Title:</b> Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses		
<b>Start Date:</b> 07/20/90	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> MAJ Thomas A. Perkins, MC		COL James S. Rawlings, MC MAJ Joanna C. Beachy, MC
<b>Key Words:</b> HIV, diagnostic assays, children		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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:** Six patients were entered in this study in FY 91. Patients were followed clinically and with serial lab data to include PCR, P24 antigen, and HIV blood cultures.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/093	<b>Status:</b> On-going
<b>Title:</b> Epidemiology of HIV in Pediatric and Perinatal Patients: A Natural History Study		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Jul 93	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> MAJ Thomas A. Perkins, MC                      COL James S. Rawlings, MC MAJ Joanna C. Beachy, MC		
<b>Key Words:</b> HIV, epidemiology, pediatric		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To establish a Pediatric AIDS Center (PAC) to identify at-risk dependents of HIV positive individuals, compile a high-risk HIV pediatric registry, collect basic epidemiologic data, and conduct longitudinal follow-up studies to assess the transmission and progression of HIV infection following heterosexual and/or perinatal exposure.

**Technical Approach:** This is a multicenter study, which originated at Walter Reed Army Medical Center and is being funded by an NIH grant. The Armed Forces are required, by Department of Defense directive, to screen all active duty personnel for antibody to HIV. Army personnel who are positive for HIV antibody are reported to the US Army HIV Data System (USAHDS). The PAC will identify and follow all eligible pediatric beneficiaries of HIV positive soldiers by comparing USAHDS reports with computer linked family records in the Defense Enrollment Eligibility Reporting System data files. Dependents who are identified from matching records will be entered into an HIV high-risk patient registry. To validate the matching process and to facilitate evaluation of high-risk families, a physician network with coordinators at each Army regional medical center will be established. The regional coordinators will work with the PAC to provide an accurate clinical evaluation, obtain appropriate laboratory studies, and organize regular followup for high-risk patients. Each patient will be evaluated for HIV infection with antibody screening, HIV culture, and antigen assay. Infection will be staged according to current Center for Disease Control (CDC) recommendations. Clinical information from the initial evaluation and subsequent follow-up visits will be entered into computer-managed patient files at the PAC. CDC classifications will be updated with results from the most current evaluation. Once the PAC has been established, the investigators anticipate that the HIV registry and PAC could be expanded to follow patients from all three branches of the Department of Defense.

**Progress:** Two patients were entered in this study in FY 91. Full history, physical examination, and lab data were recorded at visits every three months and forwarded to the central processing facility at WRAIR.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/107	<b>Status:</b> On-going
<b>Title:</b> Perinatal HIV Infection: Epidemiology and Natural History		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Apr 95	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b>		
MAJ Thomas A. Perkins, MC	COL James S. Rawlings, MC	MAJ Joanna C. Beachy, MC
MAJ W. Kim Brady, MC		
<b>Key Words:</b> HIV, epidemiology, natural history		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To develop a clinical perinatal center for the diagnosis and management of pregnant women with human immunodeficiency virus (HIV) infection and their newborn infants and to systematically collect clinical, laboratory, and epidemiologic data describing the course and natural history of perinatal HIV infection.

**Technical Approach:** Preliminary screening will be performed with the ELISA test and positives will be confirmed by Western blot assay, and the women will be staged according to the Walter Reed Staging System. The initial evaluation will include a physical examination, assessment of fetal growth and well being, HIV culture, quantitative T-cell subset analysis, CBC, serology for CMV, toxoplasmosis and herpesvirus, and blood samples for p24 antigen assay, *in situ* hybridization, and polymerase chain reaction (PCR). Reassessment will be done during each trimester of pregnancy and at the time of birth using the same test measures as in the initial evaluation. At the time of birth, the placenta and a segment of the umbilical cord will be sent for electron-microscopic, histochemical, and immunofluorescent analysis. Postpartum cervical cultures will be obtained for CMV and Herpes virus cultures. A sample of breast milk will be obtained for HIV culture in women who forego suppression of lactation. Infants will be evaluated at birth and then every three months for two years. Laboratory tests will be the same as for the mother with the addition of urine, rectal, and nasopharyngeal cultures for CMV. Physical exam in infants will also include assessment for fetal embryopathy. Subjects will be divided into two subsets: (1) HIV+ mother and HIV+ infant and (2) HIV+ mother and HIVinfant. Descriptive statistics will be used to describe the entire sample and prevalence comparisons will be made for the two major subsets. Analytic methods may involve both univariate and multivariate techniques.

**Progress:** Three patients (all in FY 91) have been entered in this study. Full history, physical examination, and laboratory data were recorded periodically for each patient. Patient data sheets were transmitted to the central processing point at WRAIR.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/018	<b>Status:</b> On-going
<b>Title:</b> Role of Pyridoxine in Gentamicin-Lasix Nephrotoxicity in Rabbits		
<b>Start Date:</b> 02/01/91	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Marvin S. Krober, MC		
<b>Associate Investigators:</b> COL Michael R. Weir, MC		
<b>Key Words:</b> nephrotoxicity, gentamicin-Lasix, pyridoxine, rabbit, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To test whether or not the nephrotoxicity and altered blood-brain barrier associated with a gentamicin-lasix combination can be altered by pyridoxine.

**Technical Approach:** Twenty-two New Zealand white rabbits will be divided into the following groups:

- gentamicin + lasix + saline (7 rabbits)
- gentamicin + lasix + pyridoxine (7 rabbits)
- pyridoxine only (2 rabbits)
- gentamicin only (2 rabbits)
- lasix only (2 rabbits)
- saline only (2 rabbits).

On day one of the study, baseline blood samples will be obtained for measurement of creatinine, gentamicin, and PLP (the active form of pyridoxine) levels. The animals will receive IM injections by group for five days. On days 5, 8, and 12 blood samples will again be obtained to measure creatinine, gentamicin, and PLP levels. The IM injections will be repeated on days 8 - 12. The animals will be sacrificed on day 12 and the kidneys and the brains will be sent to the pathologist who will grade the pathology on the following 5 point scale:

- (1) no significant pathology
- (2) focal ATN involving <10% of the tubules
- (3) mild ATN involving 10-25% of the tubules
- (4) moderate ATN involving 26-50% of the tubules, widespread ballooning necrosis of tubular epithelium, definite nuclear degeneration (at least focally), proteinaceous material in tubules, +/- interstitial inflammation and tubular regenerative changes, and
- (5) severe changes involving over 50% of the tubules with changes as in #4 but more wide spread. Changes in blood levels of creatinine, gentamicin, and PLP will be compared between the two study groups by ANOVA.

**Progress:** This protocol has been delayed in implementation pending satisfactory adjustment of dose of gentamicin alone in producing nephrotoxicity.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/058		<b>Status:</b> On-going	
<b>Title:</b> Neonatal Emergency Procedure Training in the Rabbit Model					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Thomas A. Perkins, MC					
<b>Associate Investigators:</b>			LTC Matthew M. Rice, MC		
<b>Key Words:</b> training protocol, neonatal, rabbit, neonatal emergency procedure, Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$864.00		04/05/91	

**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 housestaff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands on attempts by the interns and residents. The animal lab will allow the student to observe and practice to proficiency those lifesaving skills necessary in the management and stabilization of the neonatal patient. Telazol, 15 mg/kg, and xylazine, 5 mg/kg IM, will be administered to induce and maintain anesthesia. Additional anesthesia will be administered in increments as needed. The rabbits will be intubated with a 2-3 mm i.d. endotracheal tube and ventilation will be maintained as necessary with 100% oxygen. Tracheal intubation, venous cutdown, needle thoracentesis, and chest tube insertion will be performed by each intern or resident in attendance.

**Progress:** One session was held in FY 91 and 40 residents were trained.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/075	<b>Status:</b> On-going
<b>Title:</b> The Effects of Prolonged Parental-Child Separation on School-Aged Children Due to Military Deployment		
<b>Start Date:</b> 07/12/91	<b>Est. Completion Date:</b> Apr 92	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> 1LT Pamela S. Smith, AN		
<b>Associate Investigators:</b> MAJ Mary Sue Reagan, AN		
MAJ Steven C. Parkison, MS		
<b>Key Words:</b> parental,child separation,military deployment,children:school aged		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To determine the psychosocial effects of parental separation on school-aged children due to military deployment of a parent.

**Technical Approach:** A questionnaire, Child Behavioral Checklist (CBCL), will be distributed to 60 families. The control group will consist of 20 families with the active duty parent remaining in the home. An additional 40 families will be surveyed, 20 with children whose mother was stationed in Southwest Asia and 20 children whose father was stationed in Southwest Asia. Children with developmental disabilities or psychiatric disorders will be excluded.

The CBCL will be scored using the computer disc standard scoring tool. The CBCL scoring tool rates children in three different areas: social, activities, and school. Children will be matched as closely as possible across all three groups for age, sex and parent rank. An ANOVA will be performed for statistical analysis to compare children in the three groups and in the three different areas of performance.

**Progress:** Questionnaires were distributed and 57 were returned completed. Data analysis is in progress. Preliminary review of the data suggests a noticeable increase in behavioral problems of those children with their mother absent when compared to the other two groups.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/071	<b>Status:</b> On-going
<b>Title:</b> Comparison of Effectiveness of Lidocaine HCL vs Hyaluronidase in the Early Treatment of Soft Tissue Extravasation Injuries in New Zealand White Rabbits		
<b>Start Date:</b> 09/15/89	<b>Est. Completion Date:</b> Oct 89	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Michael R. Weir, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> extravasation injuries, lidocaine HCL, hyaluronidase, rabbit, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$614.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine if lidocaine HCl is a superior therapeutic agent in the treatment of soft tissue extravasation when compared to more traditional therapy.

**Technical Approach:** The agents which produce cell death by direct cellular toxicity when extravasated include such drugs as Adriamycin, methotrexate, and Renografin. This study will focus on the efficacy of lidocaine HCl versus hyaluronidase as a primary therapeutic agent in the treatment of soft tissue extravasation injury produced by the subcutaneous infusion of Renografin. One pig will be used to attempt to create an extravasation injury. If this attempt is successful, then an extravasation injury will be created in three additional pigs. Each animal will have its flank closely shaven. Renografin will be injected subcutaneously into two areas of the flank in order to create the extravasation injury. X-rays will be used to determine the distribution of the Renografin. After the injury has been created, one injection site on each pig will be infused with normal saline and the other site injected with either hyaluronidase alone, lidocaine HCl alone, or a combination of lidocaine HCl and hyaluronidase. In this manner, each pig will serve as its own control. Lesions will be monitored daily for the presence or absence of blister formation and these results photographed and recorded. Measurements will include necrosis and induration. The data will be analyzed by comparing the daily induration and blister or ulcer size to healing or to scar.

**Progress:** The original protocol was to be performed using rabbits with three groups of three rabbits each. However, the investigators were unable to produce an extravasation injury in the rabbit after attempting this in three different sites. The skin of the rabbit is not nearly as adherent to the subcuticular tissues as human skin. Since the skin of the pig is more closely analogous to human skin in this regard, the investigators revised the protocol (Sep 90) to use pigs with one in each group in a pilot study. Implementation of the revised protocol has been delayed due to animal facility renovation.

# **DETAIL SHEETS FOR PROTOCOLS**

## **DEPARTMENT OF SURGERY**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/007	<b>Status:</b> On-going
<b>Title:</b> General Surgery Stapling Familiarization Lab (Swine Model)		
<b>Start Date:</b> 11/21/86	<b>Est. Completion Date:</b> Oct 87	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Charles A. Andersen, MC		
<b>Associate Investigators:</b>		
COL Stanley C. Harris, MC	COL Preston L. Carter, MC	LTC Richard A. Hall, MC
MAJ Stephen B. Smith, MC	MAJ Michael J. O'Reilly, MC	COL Daniel G. Cavanaugh, MC
COL Michael J. Barry, MC	LTC James A. Knight, MC	LTC Richard M. Dearman, MC
<b>Key Words:</b> training protocol, stapling, swine, Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$500.00	<b>Periodic Review:</b> 04/05/91

**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 .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:** All current surgery staff performing laparoscopic cholecystectomy were trained with this protocol prior to credentialing. New techniques including appendectomy with stapler are ongoing. Twelve training sessions were held in FY 91.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/035                      **Status:** On-going

**Title:** The Effects of Combined General and Epidural Anesthesia on the Physiologic Response to Hemorrhagic Shock in Swine: II

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

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** LTC Douglas M. Anderson, MC

**Associate Investigators:**                      MAJ Frederick W. Burgess, MC  
LTC Michael J. Sborov, MC                      LTC Joseph J. Mancuso Jr., MC

**Key Words:** hemorrhagic shock, anesthesia, physiologic response, swine, Animal Study

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0.00	\$0.00	//	

**Study Objective:** To compare the hemodynamic aberration induced by a 20% estimated blood volume hemorrhage in swine under general anesthesia and combined general/epidural anesthesia, to compare the influence of colloid versus crystalloid on the occurrence of hypotension following the induction of epidural anesthesia and subsequent hemorrhage, and to study the effect of an intravenous dopamine infusion on the hemodynamic response to a moderate hemorrhage in swine under the influence of combined general/epidural anesthesia.

**Technical Approach:** Yorkshire-Duroc immature female pigs will be randomized into four treatment groups of 6 pigs each. The groups will include an epidural saline control, one group receiving bupivacaine plus crystalloid hydration, one group receiving bupivacaine plus hespan hydration, and a fourth group receiving epidural bupivacaine with crystalloid hydration plus a background infusion of dopamine at 5 mcg/kg/minute. Following an overnight fast, all animals will receive an IM injection of midazolam and general anesthesia will be induced by mask assisted inhalation of halothane. The experiment will begin with the blinded administration of an epidural injection of saline (control) or 0.5 % bupivacaine HCl. Warmed saline (controls) or warmed Hespan (all other animals) will be administered to maintain the MAP and HR within 20% of baseline values. Hemodynamic measurements and blood studies will be repeated every 30 minutes and Evans blue dye will be administered and serial blood samples taken at 0, 2, 4, and 8 minutes. With completion of the last timed sample, the animals will be hemorrhaged 5 mg/kg every 10 min for 30 mins (total hemorrhage 15 mg/kg). Hemodynamic measurements will be made at 30 min intervals beginning 30 minutes after the onset of blood removal. Hematocrit and total protein will be determined at 30 mins post hemorrhage and every hour thereafter up to the 218 min time point. Evans blue plasma volume determinations will be repeated at 30 minutes post hemorrhage and at the 218 minute time point. Arterial blood gas measurements will be made at periodic intervals. The principal parameters of statistical interest include heart rate, mean arterial pressure, and systolic and diastolic blood pressure. Statistical analysis will employ a two way analysis of variance model to include the factors of treatment (+/- local anesthetic) taken as a fixed effect and time taken as a repeated measure. If a significant F occurs, the Student-Neuman-Keuls test will be used to determine statistical significance.

**Progress:** The study has not been started due to a change in the attending veterinarian and the renovation of facilities.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/028	<b>Status:</b> On-going
<b>Title:</b> The Influence of Prophylactic Administration of Intravenous Crystalloid and Colloid Solutions on the Incidence of Hypotension Following Subarachnoid Anesthesia		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Frederick W. Burgess, MC		
<b>Associate Investigators:</b> MAJ David M. Colonna, MC		LTC Douglas M. Anderson, MC LTC Michael J. Sborov, MC
<b>Key Words:</b> anesthesia, hypotension, prophylactic agents		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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 euvoletic 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:** Twenty patients have been entered into the protocol. Preliminary review of the data suggests there is no benefit to the administration of a crystalloid or colloid preload prior to initiating spinal anesthesia. There have been no anesthetic related complications. Thus far, urinary retention has not occurred in any patient.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/029                      **Status:** On-going

**Title:** A Comparative Study of the Influence of 0.0625% Bupivacaine on the Analgesic Efficacy of a Continuous Fentanyl Infusion Administered via a Lumbar or Thoracic Epidural Catheter in Patients Undergoing Abdominal Aortic Surgery

**Start Date:** 04/05/91                      **Est. Completion Date:** Jun 92

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** MAJ Frederick W. Burgess, MC

**Associate Investigators:**                      LTC Douglas M. Anderson, MC  
LTC Michael J. Sborov, MC                      COL Charles A. Andersen, MC

**Key Words:** surgery:abdominal aortic,bupivacaine,fentanyl

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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**Study Objective:** To determine if the epidural catheter location influences postoperative epidural narcotic requirements.

**Technical Approach:** Male patients presenting for abdominal aortic surgery who agree to participate will be randomized in a double blind fashion to one of four groups with eight patients per group. The groups will receive lumbar fentanyl, lumbar fentanyl/bupivacaine, thoracic fentanyl, or thoracic fentanyl/bupivacaine. General anesthesia will be induced with etomidate and anesthesia will be maintained with a constant infusion of the unknown epidural solution at 10 ml/hour and inhaled isoflurane. Postoperative assessment of pain control will be made using a visual analog scale (VAS). The epidural infusion will be titrated to maintain patient comfort (VAS equal to or <3). For complaint of severe pain (VAS >5), a 50 mcg bolus dose of fentanyl will be provided. VAS scores will be recorded at 6 hour intervals. The total amount of mixture infused 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 samples will be drawn at 8 and 24 hours from the initiation of the infusion. Arterial blood gases will be evaluated at one hour postoperative and at 8 and 24 hours from the start of the epidural infusion. Comparisons between groups will focus on the total 24 hour fentanyl requirement, plasma fentanyl levels at 8 and 24 hours, and arterial blood pH, paO<sub>2</sub> and paCO<sub>2</sub>. VAS pain scores will also be quantitated at 6 hour intervals to ascertain that comparable levels of analgesia were provided.

**Progress:** Five patients have been enrolled in the protocol. There have been no protocol-related complications.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/030	<b>Status:</b> On-going
<b>Title:</b> Determination of the Ideal Bupivacaine/Fentanyl Concentration for Continuous Thoracic Epidural Infusion for Postoperative Analgesia in Thoracotomy Patients		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Jun 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Frederick W. Burgess, MC		
<b>Associate Investigators:</b> LTC Michael J. Sborov, MC		LTC Douglas M. Anderson, MC COL Daniel G. Cavanaugh, MC
<b>Key Words:</b> thoracotomy, postoperative analgesia, bupivacain, fentanyl		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine the optimal concentration of local anesthetic (bupivacaine) for continuous thoracic epidural infusion to reduce the total amount of narcotic required for postoperative analgesia following thoracic surgery.

**Technical Approach:** Patients undergoing thoracic surgery will be randomized to one of four groups, with 8 patients per group: plain fentanyl 4 mcg/ml, fentanyl/bupivacaine 0.125%, fentanyl/bupivacaine 0.0625%, and fentanyl/bupivacaine 0.031 %. General anesthesia will be induced with etomidate or sodium pentothal. Anesthesia will be maintained with a constant infusion of the unknown epidural solution at 8 ml/hours and inhaled isoflurane. Postoperative assessment of pain control will be made with the use of a visual analog scale (VAS). The epidural infusion will be titrated to maintain patient comfort (VAS of 3 or less). For complaint of severe pain (VAS >5), a 50 mcg bolus dose of fentanyl will be provided. VAS scores will be recorded at 6 hour intervals. The total amount of mixture infused 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 samples will be drawn at 8 and 24 hours from initiation of the infusion. Arterial blood gases will be evaluated at 1 hour postoperative and at 8 and 24 hours from the start of the epidural infusion. Comparisons between groups will focus on the total 24 hour fentanyl requirement, plasma fentanyl levels at 8 and 24 hours, and arterial blood pH, paO<sub>2</sub>, and paCO<sub>2</sub>. VAS pain scores will be quantitated at 6 hour intervals to ascertain that comparable levels of analgesia were provided.

**Progress:** Eighteen patients have been enrolled in this protocol. Three subjects were dropped from the protocol secondary to epidural catheter dislodgement or malfunction. There have been no protocol-related complications. Review of the data suggests that the addition of dilute bupivacaine to epidural fentanyl infusions does not reduce the amount of fentanyl required for analgesia.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/090	<b>Status:</b> On-going
<b>Title:</b> Selective Blockade of the Vagus Nerve to Relieve Referred Shoulder Pain Associated with Pulmonary Surgery in Human Subjects		
<b>Start Date:</b> 08/16/91	<b>Est. Completion Date:</b> Dec 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Frederick W. Burgess, MC		
<b>Associate Investigators:</b>		
LTC Richard M. Dearman, MC	COL Daniel G. Cavanaugh, MC	LTC Douglas M. Anderson, MC
MAJ James D. Helman, MC		
<b>Key Words:</b> shoulder pain, pulmonary surgery, vagus nerve		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$50.45	//

**Study Objective:** To determine if the referred shoulder pain associated with thoracotomy for lobectomy and pneumonectomy can be blocked by the infiltration of local anesthetic around afferent vagal fibers of the involved lung.

**Technical Approach:** This study is designed as a double blind, random assignment clinical trial with a control and a treatment group. The target sample size is 8-10 subjects per group. Subjects will be assigned in a random fashion to receive either 0.9% NaCl or 0.5% bupivacaine for infiltration into the pulmonary ligament prior to closure of the thoracic cavity. Postoperative pain management will be provided with a thoracic epidural infusion of narcotic/local anesthetic. Each subject will be evaluated at 1 and 24 hours postoperatively for the presence of referred shoulder pain.

Demographic data on each patient to include height, weight, age, sex and surgical procedure will be collected and analyzed where appropriate by Chi-square analysis or an unpaired t-test. Pain scores at 1 and 24 hours will be analyzed by the Mann-Whitney rank sum test. The presence or absence of referred pain will be analyzed by Chi-square analysis.

**Progress:** This protocol has only recently been approved by the Human Use Committee and no patients have been entered.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/018	<b>Status:</b> Completed
<b>Title:</b> A Prospective Comparison of Arthroscopic vs Open Anterior Cruciate Ligament Reconstructions Utilizing the Central One Third of the Patellar Tendon		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Jan 91	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Scott E. Cameron, MC		
<b>Associate Investigators:</b> MAJ William J. Wilson, MC		
<b>Key Words:</b> cruciate ligament, cruciate ligament reconstructions		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To compare arthroscopic and open anterior cruciate ligament reconstructions utilizing the central one third of the patellar tendon.

**Technical Approach:** Fifty (50) patients will be entered in this prospective, double-blind study. Patients will be randomized to ACL reconstruction utilizing either the open or the arthroscopic method. Open reconstructions will be performed as described by Lambert (Clin Ortho 172:85, 1983), with the exception that the central one third of the patellar tendon will be used as a free graft as opposed to a vascularized graft. The arthroscopic procedure varies from the open procedure in that the graft is passed without formal arthrotomy and generally a notchplasty is a more limited procedure. The notch is not widened unless the graft is physically impinged by the femur. Although open excision of the fat pad is not performed, often a portion of the fat pad is removed with the shaver. Central one third patellar tendon ACL reconstructions will be studied, acute vs chronic, with or without meniscal pathology. Patients scheduled for arthroscopic reconstructions that have to be converted to open procedures will be excluded as well as those who are restricted in weight bearing secondary to osteochondral defects that have been drilled or secondary to meniscal repairs. The methods will be compared as to operating time, tourniquet time, pain medicine required during the first three post-operative days, incidence of infrapatellar contracture syndrome, range of motion at 1, 3, and 6 months post-surgery, isokinetic (Cybex) muscle (quadriceps and hamstring) testing at six months, Lachmans, pivot shift, anterior drawer test, KT 1000 measurements at six months, and possibly a subjective patient evaluation at the six month mark. Standard descriptive statistics will be used for all collected variables. In addition, comparisons between the two procedures will be performed on range of motion, Cybex measurements, and atrophy using the Student's t test, and the Mann Whitney nonparametric test will be used to compare pain.

**Progress:** The study has been completed. Data collection was completed on 45 subjects. Although trends generally favored the arthroscopic group, statistical significance was achieved in only three parameters. The one month post operative range of motion, the six month post operative thigh atrophy, and the Cybex test were statistically different favoring the arthroscopic method. A paper has been accepted for presentation at the 1992 meeting of the American Academy of Orthopaedic Surgeons.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 87/089		<b>Status:</b> Completed	
<b>Title:</b> The Effect of a Veterans Administration Geriatric Assessment and Rehabilitation Unit on Elderly Surgery Patients from an Army Medical Center					
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Dec 90		
<b>Department:</b> Surgery			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Preston L. Carter, MC					
<b>Associate Investigators:</b> Kenneth L. Mostow, J.D.			David A. Silverman, M.D. MAJ Stephen B. Smith, MC		
<b>Key Words:</b> geriatric rehab unit,geriatric assessment					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		//	

**Study Objective:** To determine if frail, elderly surgery patients treated in the Geriatric Assessment and Rehabilitation Unit (GARU) at American Lake VA Medical Center (ALVAMC) will have better outcomes with improved cost-benefit and cost-effectiveness than those receiving the standard care at Madigan Army Medical Center (MAMC).

**Technical Approach:** The study population will consist of 160 elderly (>65) patients who have had surgery at MAMC with one or more medical or functional problems that will interfere with discharge. Persons with severe dementia or terminal phase disease will be excluded. The patients will be enrolled five days after surgery and randomly assigned to either remain at MAMC and receive the usual care or be transferred to ALVAMC and treated at the newly created GARU. The GARU utilizes an interdisciplinary team trained in geriatrics to provide specialty care to frail elderly patients at risk of institutionalization. Before randomization, study patients will be interviewed to obtain baseline data regarding demographic background, medical and social history, and physical and mental function. A relative or close friend will be interviewed to confirm this information. The patients will be reassessed to include patient and proxy interview at discharge and at 3 and 12 months after discharge. Standardized and validated instruments will be used to measure changes in the physical and mental functioning of both groups to include the Personal Self-Maintenance Scale, the Instrumental Activities of Daily Living Scale, the Kahn-Goldfarb Mental Status Questionnaire, and the Yesavage Depression Scale. Data will also be collected to determine the cost of the health care provided to both groups from their admission for surgery until one year after discharge. Data analysis will be performed primarily with descriptive statistics. Means and standard deviations will be calculated for preand post-test variables, such as placement location at discharge and changes in functional and mental status. Death rates and cost will also be analyzed.

**Progress:** This protocol has been completed. However, all of the investigators relocated to other areas before a report was written so no information is available on the results of the study. Fifty patients were entered and there were no reported adverse effects of the research.

MAJ Smith original PI. Funded by a joint VA/DoD grant.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 79/064	<b>Status:</b> On-going
<b>Title:</b> Implantation of Intraocular Lenses		
<b>Start Date:</b> 03/16/79	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Kevin J. Chismire, MC		
<b>Associate Investigators:</b>		
LTC David P. George, MC	MAJ Anthony R. Truxal, MC	Ronald K. Sugiyama, M.D.
COL Thomas H. Mader, MC	MAJ Lawrence J. White, MC	COL Floyd L. Wergeland Jr., MC
MAJ Leslie P. Fox, MC	COL Floyd L. Wergeland Jr., MC	MAJ Mark S. Dwyer, MC
COL Stanley C. Allison, MC	MAJ Mark S. Dwyer, MC	
<b>Key Words:</b> intraocular lenses		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$200.00	09/21/90

**Study Objective:** To become proficient in intraocular lens implantation and to gain investigator status with FDA requirements, in order to provide a new technique in ophthalmic surgical care for our patients.

**Technical Approach:** Technical Approach: 1. Obtain appropriate instruments to accomplish the procedure. 2. Obtain research investigator status with companies that have FDA approval to supply the lenses. 3. Implant lenses in 10 rabbits as a training experience for surgical nurses and assistants in this procedure. 4. Implant lenses in appropriately selected patients in order to provide visual rehabilitation. 5. To eventually establish this as a routine procedure in the military medical armamentarium of ophthalmic care.

**Progress:** Approximately 80 IOL's were implanted in FY 91. IOL's have withstood the test of time, are considered safe for most patients, and are no longer considered investigational. However, the protocol will remain open in order to use updated lenses that are awaiting FDA approval.

Replaced LTC Mader as the PI, July 1989.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 86/016                      **Status:** On-going

**Title:** Teaching Program for Practical Microsurgery

**Start Date:** 01/17/86                      **Est. Completion Date:** Indef.

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** MAJ Michael Q. Cosio, MC

<b>Associate Investigators:</b>	COL Richard A. Camp, MC
COL Jackie L. Finney, MC	COL Thomas G. Griffith, MC
LTC Donald B. Blakeslee, MC	LTC Robert J. Kenevan, MC
MAJ Stephen D. Clift, MC	MAJ Viswanatham Piratla, MC
LTC Bruce R. Wheeler, MC	MAJ Michael R. Morris, MC

**Key Words:** training protocol, microsurgery, Animal Study

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$690.00	03/01/91

**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:** No training sessions were held utilizing this protocol in FY 91 due to the large number of staff who were deployed to Saudi Arabia. Four rats have been ordered and three to four residents will attend a training session when the animals arrive.

MAJ Cosio replaced LTC Wheeler as the principal investigator in Sep 89.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/104	<b>Status:</b> Completed
<b>Title:</b> Evaluation of the Effectiveness of the U.S. Army's Hearing Conservation Program: An Epidemiologic (Prevalence) Study		
<b>Start Date:</b> 09/21/90	<b>Est. Completion Date:</b> Nov 90	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard W. Danielson, MC		
<b>Associate Investigators:</b> Thomas W. Kremenski		
<b>Key Words:</b> hearing conservation effectiveness		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$335.00	<b>Periodic Review:</b> //

**Study Objective:** To determine and accurately describe the distribution and magnitude of hearing loss that pervades the population of combat arms branch soldiers stationed at Ft Lewis, Washington.

**Technical Approach:** The effectiveness of the U.S. Army Hearing Conservation Program will be assessed by comparing data collected prior to 1990 to data collected before the introduction of this program. Data includes age, rank, branch of service (determined via an individual's MOS), audiometric data (i.e., hearing threshold levels), and hearing profile. Data will be stratified by age and rank within each branch. The prevalence of each hearing profile category within each branch will be determined. The mean hearing threshold levels for each test frequency and within each branch will be calculated. The prevalence of hearing profiles and the means of the hearing threshold levels will be compared across each branch and these measures will also be compared with the findings reported in the study by Walden, et al, (1975), Tech Rep IAO 4745, WRAMC, US Army Audiology and Speech Center, Washington, DC.

**Progress:** This protocol has been completed and a thesis is being written by the associate investigator for a Master's degree in Nursing.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/008                      **Status:** Completed

**Title:** Radical Retropubic Prostatectomy and Orchiectomy for Stage C Carcinoma of the Prostate

**Start Date:** 02/16/90

**Est. Completion Date:** Nov 94

**Department:** Surgery

**Facility:** MAMC

**Principal Investigator:** MAJ Rodney C. Davis, MC

**Associate Investigators:**  
MAJ Ian M. Thompson, MC

LTC John A. Vaccaro, MC

**Key Words:** cancer:prostate,retropubic prostatectomy,orchiectomy

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$1800.00	//

**Study Objective:** To determine the efficacy of combined hormonal and surgical therapy for carcinoma of the prostate.

**Technical Approach:** This study will be done in collaboration with Brooke Army Medical Center, using approximately 30 patients. Patients with histologically proven adenocarcinoma of the prostate and evidence of Stage C disease will be eligible. Staging will be done by prostatic acid phosphatase, bone scan, IVP, and cystoscopy (normal and no evidence of extraprostatic spread). Initial evaluation of eligible patients will include CT scan of the pelvis, transrectal ultrasound, BUN/creatinine/SGOT/LDG/alkaline phosphatase, urinalysis, urine culture, CBC with platelet count, physical exam, rectal exam, serum testosterone, and PSA. Histologic evaluation of the prostate biopsy will include Gleason's grade. Patients will be placed on either Lupron therapy, one injection/day for two months, or they will undergo bilateral simple orchiectomy. The initial evaluations will be repeated at the end of the two month treatment period. Patients will then undergo staging pelvic lymphadenectomy. If palpably enlarged lymph nodes are noted, frozen section diagnosis will be obtained. If frozen section confirms nodal positive disease, no further therapy will be provided and patients will be removed from the study. If frozen sections at the time of staging lymphadenectomy are negative of if nodes are palpably normal, patients will undergo radical retropubic prostatectomy. The following data will be recorded during hospitalization: duration of hospitalization, intraoperative and postoperative complications, number of blood units transfused, duration of catheterization, nodal status, seminal vesicle status, and capsular status. Patients will be followed at 3, 6, 9, and 12 months with rectal exam, prostatic acid phosphatase, creatinine, BUN, and bone scan. Follow-ups will then continue once yearly, indefinitely. As survival statistics for Stage C carcinoma of the prostate are readily available and reproducible, the study will not be controlled. Available survival statistics for untreated Stage C carcinoma of the prostate will be compared with study patients using the methodology of Kaplan and Meier (J Amer Stat Ass 53:1958).

**Progress:** One patient was entered in this study study from MAMC. The study has been completed. A paper was presented by Dr. Thompson, the principal investigator at BAMC, in June 1991 at the American Urological Association.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 85/021	<b>Status:</b> On-going
<b>Title:</b> Advanced Trauma Life Support Course		
<b>Start Date:</b> 01/18/85	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC William E. Eggebrotten, MC		
<b>Associate Investigators:</b> COL Stanley C. Harris, MC		MAJ Leslie W. Yarbrough, VC
<b>Key Words:</b> training protocol, ATLS, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1600.00	03/01/91

**Study Objective:** To provide training to general surgery, emergency medicine, and family practice residents and, specifically, to teach proper management of the initial one hour following major trauma.

**Technical Approach:** During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

**Progress:** Three training sessions were held during FY 91.

COL Harris original PI

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 91/098                      **Status:** On-going

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**Title:** Randomized Prospective Study Comparing Intermittent Pneumatic Compression of the Calf to Intermittent Sequential Pneumatic Compression of the Whole Leg

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**Start Date:** 09/27/91                      **Est. Completion Date:** Oct 93

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**Department:** Surgery                      **Facility:** MAMC

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**Principal Investigator:** MAJ Kurt L. Hansberry, MC

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**Associate Investigators:**                      MAJ Ian M. Thompson, MC  
COL Charles A. Andersen, MC                      MAJ James H. Timmons, MC

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**Key Words:** pneumatic compression,intermittent,sequential,calf,leg

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$3055.00	//

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Study Objective: To determine the best mechanical device to prevent deep venous thrombosis (DVT) and subsequent pulmonary uembolism, 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 or the other 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 days 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: New study, no patients entered.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/096	<b>Status:</b> Completed
<b>Title:</b> Craniofacial Onlay Bone Augmentation with a Xenogeneic Osteoinductive Implant in a Rabbit Model		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Apr 91	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Hugh E. Hetherington, MC		
<b>Associate Investigators:</b> MAJ Michael R. Morris, MC		COL Jeffrey O. Hollinger, MC
<b>Key Words:</b> bone augmentation,rabbit,Animal Study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 06/14/91

**Study Objective:** To assess the potential use of a biodegradable xenogeneic osteoinductive implant as a craniofacial onlay and compare this with allogeneic demineralized membranous bone implants and autogenous membranous bone onlay grafts. Survival, maintenance of implanted volume and shape, and the extent of bony replacement will be assessed.

**Technical Approach:** The study will consist of three parts, the production of the demineralized bone and osteoinductive implants, the placement of both implant types and autogenous membranous bone onlay grafts subperiosteally on the rabbits' snouts, and gross and histomorphometric analysis of the specimens after euthanasia. The implants will be manufactured by Dr. Hollinger as the US Army Institute of Dental Research and will be surgically implanted in the rabbit model. After 20 weeks, the animals will be euthanized and the implants harvested with the attached underlying bones, followed by gross and histomorphometric analysis. Two rabbits will be used for technique development. Twelve rabbits will be used and the relative positions of the graft and implants will be rotated so that they occupy each of the three possible positions in four rabbits per position. Analysis of variance and multiple variance tests will be used to determine the percent of change in volume between the three methods. Analysis of variance test will be used to compare the trabecular volume at 20 weeks between the three methods.

**Progress:** The protocol has been completed and a manuscript is being written for submission for publication.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/057                      **Status:** Terminated

**Title:** Evaluation of Ankyloglossia: A Prospective Study

**Start Date:** 05/20/88                      **Est. Completion Date:** Apr 91

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** CPT Ray E. Jensen, MC

<b>Associate Investigators:</b>	MAJ Newton O. Duncan, MC
LTC Donald B. Blakeslee, MC	COL Gerald R. Aaron, DC
LTC Jose D. Masi, MC	Mark J. Stephan, M.D.
Kenton L. Yockey, DAC	

**Key Words:** ankyloglossia, evaluation

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	09/15/89

**Study Objective:** To better define the natural history of congenital ankyloglossia in order to establish appropriate criteria for intervention and treatment.

**Technical Approach:** This will be a non-randomized prospective study of congenital ankyloglossia to include objective diagnosis with management based on multi-disciplinary input from otolaryngology, speech pathology, dentistry, and pediatrics. Electron microscopy will be included for completeness. Hereditary patterns will be investigated and reported when available. Indications will be speech disorders, swallowing problems, dental problems, and cosmetic/functional abnormalities all directly related to ankyloglossia. Consultations will be obtained on all patients from speech pathology, developmental pediatrics, and dentistry. Speech recordings will be obtained pre and post-treatment. Twenty-five patients <3 years will be entered and observed. Twenty-five patients > 3 years will be entered and considered for surgical repair if indicated. Periodic review of subject files will take place as needed to direct appropriate management and case gathering. Follow-up for surgical patients will be at two weeks post-operation and at 1 and two years for all patients. After a two to three year period, cases will be compiled and an attempt made to draw conclusions from the gathered data. Type of data analysis will be based on type of data obtained.

**Progress:** Thirty-six subjects were entered. The protocol was terminated in May 1991 because the principal investigator was reassigned and the investigators had been unable to obtain sufficient follow-up data for data analysis.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/091	<b>Status:</b> On-going
<b>Title:</b> Transurethral Prostatectomy and Associated Erectile Dysfunction		
<b>Start Date:</b> 08/16/91	<b>Est. Completion Date:</b> Sep 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Richard W. Knight, MC		
<b>Associate Investigators:</b> COL John N. Wettlaufer, MC		MAJ Kurt L. Hansberry, MC
<b>Key Words:</b> sexual function, prostatectomy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To use objective data to measure erectile function after transurethral prostatectomy.

**Technical Approach:** All patients who have medical indications for transurethral resection of the prostate (TURP) will be asked to participate in this study, with the expectation of from 100-200 consenting subjects. Prior to undergoing the surgery the subjects would be asked to answer a questionnaire concerning sexual function/dysfunction. They would then undergo three nights of NPT (nocturnal penile tumescence) measurements at home with a computerized device called the Rigiscan. This device measures the "hardness" (rigidity) of the erect penis and the size (width) of the erect penis and records duration and number of events (erections) each night. The subject would then undergo the TURP. Approximately three to six months after the surgery the subjects will again undergo NPT for three nights, just like the before surgery procedure. Pre-op and post-op NPT measurements will be compared to determine any objective change in erectile function. The questionnaire will also be used to determine any subjective change in function.

**Progress:** No patients have been entered as the equipment necessary to complete this study has only recently been received.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/017                      **Status:** Completed

**Title:** A Comparison of Silastic and Polydioxanone in Prevention of Adhesive Otitis Media in the Mongolian Gerbil

**Start Date:** 12/07/90                      **Est. Completion Date:** May 91

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** CPT Douglas A. Liening, MC

**Associate Investigators:**                      MAJ John H. McGath, MC  
LTC Luann McKinney, VC

**Key Words:** otitis media:prevention,silastic,polydioxanone,gerbil,Animal Study

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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**Study Objective:** To determine if a thin sheet of polydioxanone is as effective as silastic in preventing adhesive otitis media in an animal model.

**Technical Approach:** Thirty Mongolian gerbils will be randomly assigned to the silastic sheet implant (Group A) and thirty to the polydioxanone implant (Group B). Each animal will serve as its own control with one ear undergoing the implant and the other having only a tympanomeatal flap elevated. Each animal will undergo electrocautery of both Eustachian tube orifices on day one. In each group, one randomly assigned ear will remain unimplanted and will act as a control. Both ears will have the external auditory canal injected with local anesthetic and a tympanomeatal flap will be raised. A piece of synthetic material, either polydioxanone or silicone, will be placed into the middle ear cleft over the promontory in the noncontrol ear. The external auditory canal will then be packed with Gelfoam to hold the tympanomeatal flap in its normal position. The animals will then be recovered from anesthesia. On days 35, 70, and 105, ten animals from each group will be randomly selected and sacrificed. Both the operated and control temporal bones will be examined histologically for the presence of tympanic membrane retraction, durability of the implanted prosthetic material, and surrounding tissue reactions. Each operated ear will be compared to the control ear and the two groups compared to each other. The percentage of middle ear adhesions present at the time of sacrifice will be compared between Group A, Group B, and the controls. Group A and Group B will also be compared separately to the control ears. The Student's t test will be used for statistical analysis.

**Progress:** The protocol has been completed with 60 animals being studied as stated in the approach. Data analysis is complete and an abstract is being prepared for submission to the 1992 meeting of the Triologic Otolaryngology Society.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/003	<b>Status:</b> On-going
<b>Title:</b> Videx (2',3',-dideoxyinosine, ddi) AIDS Treatment Program		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b> Indefinite	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Rodney A. Michael, MC		
<b>Associate Investigators:</b>		LTC Ronald H. Cooper, MC
<b>Key Words:</b> AIDS, Videx, treatment		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	11/01/91

**Study Objective:** To make ddi (Videx) available to patients with advanced HIV infection who are either intolerant of zidovudine (AZT) or who are deteriorating in spite of AZT, who otherwise are ineligible for the Phase II ddi protocol.

**Technical Approach:** Currently, the only approved drug for treating HIV infection is AZT, which inhibits viral reverse transcriptase. It is approved for use in patients with CD4 cell counts of  $<200/\text{mm}^3$  and/or in patients who have suffered from Pneumocystis carinii pneumonia. Though prolonging life, AZT has clinical toxicity that limits its use in some patients. Many patients who have developed intolerance to AZT are suitable for inclusion in this Treatment IND for ddi. This will be an open label, uncontrolled evaluation of oral ddi administered orally twice a day in dosages of 375, 250, or 167 mg depending on the patient's body weight. Complications of AIDS or AIDS-related complex will not be a basis for exclusion from the protocol. Information will be collected during drug therapy to evaluate safety and tolerance. Data collection will include: incidence of opportunistic infections and HIV associated neurological complications, development or change in Kaposi's sarcomas, performance status, weight changes, hospitalization, and survival. Measurement of CD4 counts and p24 antigen levels will be performed at each visit.

**Progress:** Three patients have been entered on this study. It is too early for any conclusions as to treatment efficacy.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/042	<b>Status:</b> On-going
<b>Title:</b> The Effect of Catheter Tunnelling With and Without Addition of a Subcutaneous Cuff on Catheter-Related Sepsis		
<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Michael J. Mooney, MC		
<b>Associate Investigators:</b>		
MAJ John C. Schilhab, MS	LTC Anthony S. Sado, MC	SGT Gregory James
<b>Key Words:</b> catheter sepsis, catheter tunnelling, subcutaneous cuff		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To study the effect of adding a subcutaneous cuff, with or without the addition of a subcutaneous tunnel, on venous catheter-related sepsis.

**Technical Approach:** Ninety-nine (99) ICU patients will be studied. Patients who are candidates for a 3-lumen central line and have subclavian punctures will be eligible. Patients who are clinically septic, in shock, or unstable at the time of line placement will be excluded. Group I will be a control group with current standard placement, care, and line changes. Group II will contain cuffed catheters, placed in the standard fashion. Group III will contain cuffed catheters placed through a subcutaneous tunnel. All groups will undergo standard central line care. Lines in Group I will be changed every 72 hours, with a culture of the intracutaneous portion performed. Lines in Groups II and III will be changed for evidence of sepsis or removed when no longer clinically indicated. Cultures will be done on the intracutaneous portion of all catheters with >1000 colonies on a quantitative culture being indicative of catheter-related sepsis.

**Progress:** Five subjects have been enrolled. Study enrollment has been limited due to multiple TDY on part of the principal investigator.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/005	<b>Status:</b> On-going
<b>Title:</b> An Epidemiological Study of Nasopharyngeal Cancer		
<b>Start Date:</b> 10/21/88	<b>Est. Completion Date:</b> Jan 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Michael R. Morris, MC		
<b>Associate Investigators:</b> Thomas L. Vaughan, M.D.		
<b>LTC Donald B. Blakeslee, MC</b>		
<b>Key Words:</b> cancer, nasopharyngeal		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To test the hypothesis that occupational and residential exposure to formaldehyde increases the risk of nasopharyngeal cancer, to determine if any increase in risk is modified by smoking status, dietary intake of beta-carotene and vitamin C, and other potential risk factors, and to identify other medical, environmental, and lifestyle factors associated with risk of the disease in a low-incidence population.

**Technical Approach:** Eligible cases will be all persons aged 18-74 years who develop nasopharyngeal cancer between 1 Jan 87 and 30 Jun 91, who reside in areas covered by six population-based cancer registries in the United States. A random digit dialing technique will be used to select one control per case from among residents of the same area in which each case resides. Subjects will be interviewed by phone using a standardized questionnaire and interviewer manual to determine occupational and residential histories, along with other factors suspected to be associated with risk of nasopharyngeal cancer, including medical, tobacco, alcohol, chemical exposure, and dietary histories. Blood specimens will be collected from nasopharyngeal cancer cases and controls. These specimens will be analyzed for histocompatibility type as well as antibodies to Epstein-Barr virus. Using exposure assessment methods already developed in a preliminary study, indices of formaldehyde exposure, both from home and workplace sources, will be calculated. Both stratified and multivariate analysis will be used to estimate relative risks of nasopharyngeal cancer in relation to the various environmental factors considered.

**Progress:** Eight patients have been entered in the protocol from MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/051	<b>Status:</b> Terminated
<b>Title:</b> Sonolith 3000 Clinical Study for Gallbladder Stones (For Use Alone or in Combination with Actigall Therapy)		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Nov 90	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Michael J. O'Reilly, MC		
<b>Associate Investigators:</b> MAJ Christopher R. Kaufmann, MC		
LTC William E. Eggebrotten, MC		
<b>Key Words:</b> gallbladder stones, lithotripter, actigall therapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	

**Study Objective:** To determine if extracorporeal shockwave lithotripsy (ESWL) is a safe and effective means for elimination of gallstones, with or without adjuvant Actigall therapy.

**Technical Approach:** This study is being conducted in over 30 sites, utilizing approximately 600 patients. Subjects will be 18-100 yrs old, anesthesia class I, II, or III, functioning gallbladder, 1-3 gallstones, largest stone <30 mm, total stone aggregate <46mm, and radiolucent stones <20% calcium. Patients will have pretreatment laboratory and screening evaluations to determine patency of the cystic duct, functionality of the gallbladder, and verification of stone burden. Treatment A will consist of ESWL with subsequent evaluation of need for Actigall therapy. Treatment B will consist of Actigall therapy for a minimum of 10 days followed by ESWL treatment followed immediately with continued Actigall therapy. In both treatments, each patient will be evaluated at 7-45 days postESWL for fragmentation success and the need for a possible second ESWL treatment. Patients with gallstone fragments >5 mm will be administered a second ESWL treatment, provided liver function tests are <2.5 times the upper limit of normal, there is no evidence of edema of the gallbladder wall, and the gallbladder is functioning. In Treatment A, Actigall will be administered if two ESWL treatments do not result in fragments <5 mm or the gallbladder is not clearing fragments <5 mm. Any patient with a clear gallbladder for 3 months will be considered a success and Actigall therapy will be discontinued at that time. Patients will be evaluated immediately posttreatment, at hospital discharge, and at 1, 3, and 6 month intervals after the last ESWL treatment. Any patient that continues to have symptoms will be taken off study and followed to investigate potential remaining effects of ESWL on future outcome. Demographic and baseline characteristics will be evaluated for comparability to determine the validity of combining data for pooled analysis. Analysis will include evaluation of patient symptoms, stone size, number of stones, presence/absence of fragmentation, and gallbladder clearing of remaining fragments.

**Progress:** This study has been terminated because the lithotripter which this study was to utilize has not been purchased and all of the investigators have been reassigned.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/001	<b>Status:</b> Completed
<b>Title:</b> Effects of Common Arthroscopic Irrigating Solution on Adult Rabbit Articular Cartilage Proteoglycan Synthesis: An <i>In Vivo</i> Study and an Animal Model to Stimulate Arthroscope Induced Trauma		
<b>Start Date:</b> 10/21/88	<b>Est. Completion Date:</b> Jan 89	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Jerome J. Perra, MC		
<b>Associate Investigators:</b> MAJ Charles J. Hannan, MC		LTC Bruce R. Wheeler, MC
<b>Key Words:</b> articular cartilage, rabbit, arthroscope induced trauma, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$1720.00	04/05/91

**Study Objective:** To assess the effects of commonly used arthroscopic irrigating solutions on articular cartilage proteoglycan synthesis using an animal model to simulate arthroscope-induced trauma to the articular surface which violates the lamina splendens.

**Technical Approach:** One control and three experimental groups of 10 adult male New Zealand white rabbits, weighing 2.0-3.0 kg, will be properly anesthetized. Both knee joint capsules will be exposed by surgical dissection and a small arthrotomy created in the capsule. A series of superficial lacerations 1.0 mm in depth will be made across the condyles with a controlled depth device. After repair of the arthrotomy, the knees will be irrigated continuously for two hours, using normal saline, Ringer's lactate, sterile H<sub>2</sub>O, or nothing (control group). After the irrigation is completed, the incision will be closed. Twenty-four hours after irrigation the animals will be re-anesthetized and infused intravenously with 200 mg of <sup>35</sup>SO<sub>4</sub>. One hour later the cartilage from the right knee will be excised and two hours post infusion the cartilage from the left knee will be excised. The samples will be blotted, weighed, and washed three times in distilled water for one hour and then overnight to remove unincorporated radioactivity. Samples will be placed in Aquasol for 24 hours and counted in a liquid scintillation spectrometer. The scintillant will be aspirated and counted separately to ensure that only incorporated <sup>35</sup>SO<sub>4</sub> is being counted. Counts/minute/gram cartilage will be plotted against time and graphed linearly. The one hour and two hour counts will be plotted against time and forced through the origin. Data with correlation coefficient <0.8 will be rejected. Standard deviations will be calculated and the means of the different groups compared using the Mann-Whitney non-parametric test.

**Progress:** The protocol has been completed and a paper is being written.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/036                      **Status:** On-going

**Title:** Influence of Baricity on the Elimination of Local Anesthetics from the Subarachnoid Space in a Swine Model

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

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** LTC Michael J. Sborov, MC

**Associate Investigators:**  
MAJ David M. Colonna, MC                      MAJ Frederick W. Burgess, MC  
LTC Douglas M. Anderson, MC                      LTC Joseph J. Mancuso Jr., MC

**Key Words:** anesthesia, subarachnoid space, baricity, swine, Animal Study

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To develop an operational quantitative high performance liquid chromatography assay for the local anesthetic, bupivacaine, and to study the influence of baricity on the clearance of bupivacaine from the subarachnoid space by monitoring peripheral blood plasma levels.

**Technical Approach:** The first phase of the protocol will be to establish an operational HPLC system for the determination of bupivacaine plasma levels and evaluate it in at least one animal using the protocol which follows. Five immature female Duroc-crossbred swine will undergo surgical insertion of a left carotid catheter and insertion of a continuous subarachnoid catheter under general endotracheal anesthesia. On postoperative days 3-5, each animal will receive IV sedation and light general anesthesia followed by injection of 0.29 mg/kg of 0.75 % bupivacaine in either saline (isobaric), dextrose (hyperbaric), or mannitol (hyperbaric) via the implanted subarachnoid catheter. Arterial blood samples will be withdrawn at 10 min intervals for the first 70 min and then at 90, 120, and 180 minutes for the determination of plasma bupivacaine levels by HPLC. The peak level of anesthesia will be determined by delivery of a 50 Hz subcutaneous electrical stimulus delivered with a peripheral nerve stimulator through 26 gauge needles inserted at 5 cm intervals along the midline above the umbilicus. Hemodynamic alterations will be monitored continuously via the arterial line. Heart rate and blood pressure measurements will be made at baseline and at 5 minute intervals thereafter. The primary focus of the protocol will be the comparison of the time to peak plasma concentration with each treatment. Analysis of variance will be employed to determine if there is a significant difference between the three treatments. If a difference is identified, between group comparisons will be performed using the Student-Neuman-Keuls test for multiple comparisons.

**Progress:** The HPLC assay is currently operational. A chronically instrumented animal model to study the pharmacokinetic disposition of subarachnoid bupivacaine has entered the data collection phase. To date only one animal has been studied.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/015		<b>Status:</b> On-going	
<b>Title:</b> Investigation of Cryotreatment on the Epiphysis of Growing Rabbit Bone					
<b>Start Date:</b> 02/16/90			<b>Est. Completion Date:</b> Jan 91		
<b>Department:</b> Surgery			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT James S. StLouis, MC					
<b>Associate Investigators:</b> COL D. Scott Smith, MC MAJ Michael Tidwell, MC			CPT Harvey Montigo, MC COL Roberto Barja, MC		
<b>Key Words:</b> bone,epiphysis,cryotreat,rabbit,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$150.00		03/01/91	

**Study Objective:** To determine if cryotreatment to the epiphysis of 6 week old rabbits will stunt growth, slow growth, or cause deformity.

**Technical Approach:** Number of rabbits studied: 15 The lateral aspect of the distal femur of the right leg will be exposed and the CT-73 cryosurgical system will be applied with a microprobe to freeze the area. The left rear leg will be operated in the same manner, except the cryoprobe will not be applied. After a six week period for bone growth, the animals will be euthanized. A pathologist will then determine the gross effect on growth plates and any deformities present on the right versus the left femur. Microscopic specimens of the cryotreated epiphyses will be examined to evaluate remaining potential growth of microvascular structures and uniformity of cryological effects. Data will be evaluated using a paired t test between right and left sides to compare the legs at an alpha level of .05.

**Progress:** This study has not been implemented due to the renovation of the laboratory animal facilities at MAMC and also because the cryoprobe equipment has not been received to date.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/041	<b>Status:</b> Terminated
<b>Title:</b> Urinary D-Lactate as an Indicator of Bowel Ischemia		
<b>Start Date:</b> 05/20/88	<b>Est. Completion Date:</b> Aug 88	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Barbara L. Tylka, MC		
<b>Associate Investigators:</b> COL Charles A. Andersen, MC		
<b>CPT Jon C. Bowersox, MC</b>		
<b>Key Words:</b> ischemia, bowel, D-lactate		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$400.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To determine whether urinary D-lactate levels can be used as non-invasive indicators of bowel ischemia in critically ill patients.

**Technical Approach:** Patients >18 years of age with hypovolemia, Ogilvie's syndrome, or a hemodynamically significant cardiac event requiring pressor support will be studied. Daily urine samples will be collected for analysis of urinary D-lactate until discharge from the ICU or CCU or death. The D-lactate concentration will be determined via the enzymatic conversion of D-lactate to pyruvate by the enzyme D-lactate dehydrogenase. To correct for variations in urine concentration, the urine creatinine will also be measured and results expressed as the D-lactate/creatinine ratio. If operative intervention is deemed necessary on clinical grounds, the bowel will be examined at surgery or, in the event of death, at autopsy for evidence of ischemia. The determination of ischemia will be made by the operating surgeon and any resected specimens will be examined by the pathologist. Subjects discharged from the ICU or CCU without operative intervention will be considered to not have experienced any clinically significant bowel ischemia and will form the control population. Based on previous studies, it is estimated that 20-30 patients, with a minimum of 10 with clinically proven bowel ischemia, will be required to determine a difference in urinary D-lactate levels between control and ischemic populations. Results will be analyzed by Student's paired t-test.

**Progress:** This protocol has been terminated. Three controls and three patients with bowel ischemia were entered in FY 88. No further patients have been entered due to logistical problems with the laboratory and other commitments of the principal investigator.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/021	<b>Status:</b> Completed
<b>Title:</b> Provocative Androgen Testing in Patients at High Risk for Persistent Carcinoma After Radical Prostatectomy		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jan 92	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC John A. Vaccaro, MC		
<b>Associate Investigators:</b> MAJ Rodney C. Davis, MC		
<b>Key Words:</b> cancer:prostate,PSA,androgen,prostatectomy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$500.00	<b>Periodic Review:</b> 04/05/91

**Study Objective:** To develop a test to identify those patients, with PSA (prostate-specific antigen) within normal limits after radical prostatectomy, who have persistent disease.

**Technical Approach:** This study will be done in conjunction with the University of Washington. Approximately 30 males, ages 40-75 will be studied. To be eligible, patients must be fully recovered from radical prostatectomy performed at least 3 months previously, have a serum PSA <0.4 ng/ml, and have had no additional therapy. Patients will be high risk for persistent disease, i.e., Stage B tumor confined to the capsule but with Gleason combined grade higher than 8, pathological stage C1 (capsular perforation), C2 (positive surgical margins), C3 (positive seminal vesicles), or D1a (microscopic lymph node involvement). The patient will undergo clinical restaging, including digital rectal exam, abdominal pelvic CT scan, bone scan, cystoscopy, and transrectal biopsy of the urethral vesicle anastomosis. Patients without evidence of persistent disease will then be given 100-300 mg of testosterone enanthate every week for 8 weeks. PSA levels will be determined each week. Should the patient's PSA level become >0.4 ng/ml, the patient will be immediately restaged (while on testosterone stimulation) and then the stimulation will be stopped and the PSA and testosterone values observed until testosterone nadir (approximately one month). If PSA levels rise further (>0.3 ng/ml) at any time during this withdrawal, treatment will be immediately started. If PSA stabilizes or falls during testosterone withdrawal and a lesion was demonstrated, the patient will be restaged. If no lesion is found during testosterone stimulation, the patient will also be restaged prior to treatment. Treatment will consist of either pelvic or prostatic bed radiation or hormone ablation therapy either by orchiectomy, LH-RH agonists, or diethylstilbestrol (3 mg/day), according to patient preference and established medical criteria. Patients without PSA elevation during the 8 week period will also be restaged at the end of testosterone stimulation but thereafter will be followed (without further treatment) by PSA and testosterone levels monthly for six months and every 3 months thereafter. Bone scans will be determined every 6 months for a year.

**Progress:** This protocol was terminated at MAMC due to the difficulty in finding patients that were eligible and would agree to participate and due to the impending reassignment of the principal investigator. No patients were entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 86/094                      **Status:** Terminated

**Title:** A Prospective Evaluation of Testicular Shielding in Preventing Hypogonadism in Prostate Cancer Patients Receiving External Beam Radiotherapy

**Start Date:** 10/17/86                      **Est. Completion Date:** May 87

**Department:** Surgery                      **Facility:** MAMC

**Principal Investigator:** LTC John A. Vaccaro, MC

<b>Associate Investigators:</b>	CPT Christopher P. Evans, MC
COL Victor J. Kiesling, MC	COL Stephen R. Plymate, MC
COL Donald H. Kull, MC	MAJ Pushpa M. Patel, MC
COL Gary L. Treece, MC	MAJ Rahul N. Dewan, MC

**Key Words:** cancer:prostate,hypogonadism,radiotherapy

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$1500.00	09/16/88

**Study Objective:** To assess a possible protective effect on testicular function of a lead testicular shield during the radiation treatment period.

**Technical Approach:** Twenty prostate cancer patients >18 years will be randomized into two groups to wear a lead gonadal shield during radiation therapy or to wear no shield during the therapy. Patients with prior radiation or hormonal therapy will be excluded. Blood to entry blood will be drawn for basal FSH, LH, testosterone, TeBG, prolactin, and diol levels. An LHRH stimulation test will be done with 30 and 60 minute levels drawn. Blood will again be drawn during mid-course of therapy and at 1 and 12 weeks post-therapy for these same determinations. Comparison of group results will be performed by standard statistical methodology.

**Progress:** This study has been terminated because all of the investigators have left MAMC and did not leave a status report. The staff at DCI has been unable to contact any of the investigators. Nine subjects had been enrolled but accrual was very slow during the time that it was open. The study had also been approved at WRAMC, but DCI at MAMC has been unable to obtain any information regarding that study.

DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/065	<b>Status:</b> Completed
<b>Title:</b> Retrospective Evaluation of the Rate of Avascular Necrosis Formation Following Austin Bunionectomy		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> Jul 91	
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Stephen V. Wilkinson, MS		
<b>Associate Investigators:</b> MAJ Leonard D. Sisks, MC		MAJ Richard O. Jones, MS MAJ John W. Van Manen, MC
<b>Key Words:</b> bunionectomy:Austin,necrosis formation		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**Study Objective:** To perform a chart review of the postoperative care and evaluation findings of Austin and McBride Bunionectomy patients to determine the rate of first metatarsal head avascular necrosis following bunion surgery.

**Technical Approach:** Records from 20 patients receiving the Austin (Head Osteotomy) and 5 patients receiving the Mod McBride (Non-osteotomy/control) bunionectomies will be reviewed. All patients at Madigan having bunion surgery receive preoperative physical examination and radiographic evaluation. Following surgery, patients without retained metallic implants receive postoperative serial radiographic evaluations, serial physical examinations, and a single MRI evaluation to determine the physiologic status of the first metatarsal head, following metaphyseal osteotomy. This is done in order to determine the presence or absence of avascular necrosis. Records of all patients receiving either the Mod McBride or the Austin bunionectomy techniques (procedures without retained metallic implants) will be reviewed to determine if radiographic, MRI, or physical examination evidence of avascular necrosis exists. The parameters to be studied are range of motion change after surgery, joint pain development, radiographic findings, MRI findings, and anatomic distribution of avascular necrosis. Descriptive statistics will be used to describe the results.

**Progress:** The protocol has been completed and a paper is being written.

**DETAIL SHEETS FOR PROTOCOLS**

**CHILDRENS CANCER STUDY GROUP**



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/093	<b>Status:</b> On-going
<b>Title:</b> CCG 134P: Therapy of Acute Lymphoblastic Leukemia in High Risk Patients		
<b>Start Date:</b> 09/18/87	<b>Est. Completion Date:</b> Jul 92	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b>		Maj Kip R. Hartman, MC
<b>Key Words:</b> leukemia:lymphoblastic		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To improve the treatment results for children with acute lymphoblastic leukemia (ALL) who possess poor prognostic features; to prevent the development of central nervous system (CNS) leukemia in these patients using a treatment regimen which includes both systemic high dose chemotherapy and intrathecal chemotherapy, but avoids cranial radiation; and to determine whether there is a difference in the outcome of poor prognosis patients with and without lymphomatous features treated on an identical treatment regimen.

**Technical Approach:** Previously untreated high risk patients with acute lymphoblastic leukemia will be treated. The induction phase of therapy will be 28 days in length and consist of treatment with vincristine, L-asparaginase, prednisone, daunomycin, and allopurinol. CNS therapy will consist of intrathecal cytosine arabinoside, methotrexate, and a high dose, protracted, systemic methotrexate infusion. Consolidation therapy will begin 7-10 days following completion of induction therapy and will last 35 days and will consist of vincristine, prednisone, and 6-mercaptopurine. CNS prophylaxis during consolidation will include both I.V. high dose methotrexate and intrathecal Ara-C. A 12-week intensification phase will begin 7-10 days after the last day of consolidation and will consist of cyclophosphamide, L-asparaginase, vincristine, daunomycin, and prednisone. CNS treatment will include periodic intrathecal methotrexate and cytosine arabinoside as well as systemic high dose Ara-C. Maintenance therapy will begin 7-10 days after the last day of consolidation and will consist of prednisone, vincristine, 6-mercaptopurine, L-asparaginase, and daunomycin. CNS treatment will include periodic intrathecal chemotherapy with methotrexate and Ara-C as well as systemic high dose methotrexate and high dose Ara-C. The chemotherapy will be given over a 24 week cycle, which will be repeated 4 times, after which all chemotherapy ceases. The first year off study, patients will have a physical exam and CBC every month and bone marrow and lumbar puncture every 4 months. The second year, they will have physical exam and CBC every 3 months and bone marrow and lumbar puncture every 6 months. The third and subsequent years off study, patients will receive routine follow-up per institutional guidelines.

**Progress:** No patients entered in FY 91. Two patients were entered in this protocol in previous years; one patient is still in the follow-up stage. The study is closed to patient entry.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/063	<b>Status:</b> On-going
<b>Title:</b> CCG 144: Treatment of Acute Lymphoblastic Leukemia in Average Risk Patients		
<b>Start Date:</b> 10/21/88	<b>Est. Completion Date:</b> Jul 93	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Maj Kip R. Hartman, MC		
<b>Key Words:</b> lymphoblastic		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To compare the efficacy of high dose, protracted intravenous methotrexate infusions versus intrathecal methotrexate as CNS preventive therapy for children with average risk lymphoblastic leukemia and to determine if there is a difference in the hematologic remission duration achieved using these different treatment approaches.

**Technical Approach:** Newly diagnosed average risk patients will be randomly allocated to receive one of two forms of CNS preventive therapy; either high dose protracted systemic methotrexate infusions or intrathecal methotrexate administered periodically during induction, consolidation, and maintenance. Systemic therapy will be identical for all patients. To insure similarity in the two treatment groups, patient randomization will be stratified to the prognostically significant variables of age and initial white blood cell count. Approximately 80 randomized patients will be required. It is anticipated that the required number of patients will be accrued within a 12-18 month period.

The induction phase for both arms will 28 days in length and will include chemotherapy in both groups with vincristine, l-asparaginase, prednisone, daunomycin, and allopurinol as well as the methotrexate and citrovorum factor rescue.

Consolidation (35 days in length) will begin 10 days after induction therapy is completed and will include vincristine, prednisone, and 6-mercaptopurine in addition to the methotrexate.

Maintenance therapy will begin 10 days after the consolidation phase is completed and will be divided into 6 cycles of therapy, each 22 weeks in length. In addition to the methotrexate, chemotherapy will include prednisone, vincristine, 6-mercaptopurine, and l-asparaginase, daunomycin given on a staggered schedule.

Patients who have an M3 bone marrow after completing at least 28 days of therapy or who manifest progressive disease will be removed from the study.

**Progress:** No patients entered in FY 91. One patient entered in FY 88 is in the following stage. The study is closed to patient entry.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/014	<b>Status:</b> On-going
<b>Title:</b> CCG 213: Treatment of Newly Diagnosed Acute Non-lymphoblastic Leukemia for Children Greater than One Month but Less than 21 Years of Age		
<b>Start Date:</b> 11/12/87	<b>Est. Completion Date:</b> Jan 94	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Maj Kip R. Hartman, MC		
<b>Key Words:</b> leukemia:nonlymphoblastic		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To improve the duration of complete remission in children with acute non-lymphocytic leukemia (ANLL).

**Technical Approach:** Induction will consist of two or three 14-day cycles of Denver Therapy (VP 16-213, daunomycin, Ara-C, 6-thioguanine, and dexamethasone) followed by two or three 14-day cycles of DNM/Ara-C (daunomycin and Ara-C) or given in the reverse order depending on randomization. If bone marrow is M1, ANC >750, and platelet count >75,000 after two cycles, the patient will start the alternate regimen. Patients with M1 marrow after the first regimen of induction or M1 or M2A marrow at any time after completion of induction will have a bone marrow transplant if a suitable donor is available and the patient/family wishes to pursue this course of action. At the end of induction, patients with remission and no donor will be entered in a consolidation phase which will consist of 2 cycles of high-dose Ara-C and L-asparaginase, followed by two cycles of 6thioguanine, vincristine, ara-C 5-azacytidine, and cyclophosphamide, and then one cycle of VP 16213, daunomycin, Ara-C, dexamethasone, and 6-thioguanine. Those with remission and no donor will then be randomized to no further therapy or eighteen 28-day cycles of 6-thioguanine, vincristine, Ara-C, 5-azacytidine, and cyclophosphamide. Those who have failed therapy will be taken off study. Intrathecal Ara-C prophylaxis will be given on day 0 of each cycle except for the regimen using high-dose Ara-C.

Children <2 years of age with acute monoblastic/monocytic leukemia will also be treated on this protocol using a 4-week induction phase of chemotherapy, followed by a four week consolidation phase of chemotherapy plus radiation therapy for CNS prophylaxis or involvement. The maintenance phase will consist of four 3-month chemotherapy courses plus radiation therapy for CNS prophylaxis or involvement. Drugs to be used are VM-26, VP-16, cyclophosphamide, intrathecal Ara-C, vincristine, prednisone, daunomycin, and 6-thioguanine. Patients will be taken off study if they are not in complete remission by Week 8 of the study.

**Progress:** No patients entered in FY 91. One patient previously entered has completed therapy and is being followed. The study is closed to patient entry.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/009		<b>Status:</b> On-going	
<b>Title:</b> CCG 321P4: "6 in 1" Chemotherapy for Children with Newly Diagnosed Advanced Stage Neuroblastoma					
<b>Start Date:</b> 11/18/88			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> CCG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Edythe A. Albano, M.D.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> neuroblastomachemotherapy					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		07/12/91	

**Study Objective:** To explore the novel "6 in 1" regimen in patients between 1 and 16 years of age with previously untreated advanced stage neuroblastoma. To assess the toxicity of this regimen and determine a maximum acceptable regimen by stepwise modification in cohorts of 5-10 patients.

**Technical Approach:** Patients will receive cycles of vincristine, cisplatin, cyclophosphamide, imidazole carboxamide (DTIC), Adriamycin, and VM-26, administered over 36 hours every 3-4 weeks for 8 cycles or until tumor progression. Patients will be evaluated for response following cycles 4 and 8 (weeks 12 and 24). Patients for whom surgical resection of residual primary tumor seems feasible will undergo such surgery after 4 or 8 cycles. Upon completion of chemotherapy, sites of original bulky tumor will be irradiated to 2000 rads or, at institutional option, patients may undergo ablative therapy with bone marrow rescue. Patients with progressive disease at any point after initiation of therapy will proceed to alternate therapy.

The initial cohort will receive a schedule that is more intense than that received by the ad hoc patients. The primary outcome index will be the mortality rate occurring in the first four cycles of treatment (approximately 3 months from start of treatment). If two or more deaths occur, then evaluation of the treatment schedule will be stopped with a conclusion of unacceptable mortality. Pending the outcome of this initial cohort and patient accrual, a second cohort of 10 patients will receive a schedule that will be an intensification or a reduction of this initial schedule. Efficacy will be assessed by comparison to historical experience of recent CCSG studies in this group.

The intended total duration of the study is two years of accrual and 6 to 12 months of follow-up to evaluate the outcome results.

**Progress:** No patients entered in this study at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/112	<b>Status:</b> On-going
<b>Title:</b> CCG 461: Intergroup National Wilms' Tumor Study - 4		
<b>Start Date:</b> 09/18/87	<b>Est. Completion Date:</b> Sep 97	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Hartman KR Maj Kip R. Hartman, MC		
<b>Key Words:</b> Wilms' tumor		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To compare the relapse-free and overall survival percentages of patients with: (1) Stages 1 and 2 favorable histology (FH) and Stage 1 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 chemor radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol.

Patients will be randomized as follows:

Stage I/FH & Stage I Ana	A + V (24 wks) <u>or</u> P/I A + V (18 wks)
Stage II/FH	A + V (22 vs 65 wks) <u>or</u> P/I A + V (60 wks)
Stages III & IV FH & clear cell (I-IV)	A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT
Stages II-IV Ana	A + V + D (65 wks) plus RT or A + V + D + C (65 wks) plus RT

A = actinomycin D                      V = vincristine  
D = doxorubicin (Adriamycin)      C = cyclophosphamide              RT = radiation therapy

**Progress:** A revised version of this protocol was approved in Sep 89. The main changes were to define specific parameters to be studied as opposed to a general information gathering protocol, a reduction in the length of treatment, and the addition of an arm to treat Stages 2-4 anaplastic tumor. Changes were made based on information gained in studies by other investigators as well as the information gained from this study to date. One patient was entered in FY 91 and one patient was entered in FY 89; both are being followed.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/008                      **Status:** Completed

**Title:** CCG 503: A Randomized Trial of COMP - Cyclophosphamide, Vincristine, Prednisone, and Methotrexate versus COMP & DAUNO - Cyclophosphamide, Vincristine, Methotrexate, Prednisone, Daunomycin for .....

**Start Date:** 04/21/89                      **Est. Completion Date:** Indef.

**Department:** CCG                      **Facility:** MAMC

**Principal Investigator:** Edythe A. Albano, M.D.

**Associate Investigators:** None

**Key Words:** lymphoma:non-Hodgkin's,cyclophosphamide,vincristine,prednisone,methotrexate,COMP,DAUNO,daunomycin

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91
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**Study Objective:** To improve the prognosis of children with disseminated nonlymphoblastic lymphomas by adding daunorubicin to COMP; to compare toxicity of this regimen with COMP alone; to examine the relationships between response to therapy, anatomic presentation, and histopathologic group; to improve the outcome for those patients with CNS disease at diagnosis or at risk for CNS relapse because of disease adjacent to the meninges; and to evaluate the relationship between cell surface markers, disease characteristics, and clinical course.

**Technical Approach:** Following initial evaluation, those patients without CNS or marrow involvement will be randomized to either COMP/ (cyclophosphamide, methotrexate, vincristine, prednisone) alone or to COMP plus daunorubicin. Patients with bone marrow or CNS involvement will be non-randomly assigned to COMP+DAUNO. The duration of chemotherapy for both regimens will be 18 months. Therapy will continue past 18 months if a minimum of 15 maintenance cycles has not been completed and will continue until the completion of 15 maintenance cycles. Radiation treatment will be given only to those patients with nervous system involvement, testicular involvement, bone involvement, or disease adjacent to the meninges.

**Progress:** This protocol was closed to patient entry, FY 91. One patient was entered in this study in FY 89 and died of the disease.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/076	<b>Status:</b> On-going
<b>Title:</b> CCG 521: Treatment of Newly Diagnosed Advanced Hodgkin's Disease - Pathologic Stages III(1) AS (macro), III(1)A Macromediastinum, III2A, IIIB, IVA, IVB, A Phase III, Group-wide Study		
<b>Start Date:</b> 05/15/87	<b>Est. Completion Date:</b> May 92	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b>		Hartman KR Maj Kip R. Hartman, MC
<b>Key Words:</b> Hodgkin's disease		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To improve the proportion of patients with advanced Hodgkin's Disease who are cured; to compare the relapse free survival and survival in advanced Hodgkin's disease in children utilizing an eight-drug (twelve cycle MOPP/ABVD) combination chemotherapy regimen versus a four drug (six cycle ABVD) chemotherapy regimen followed by low dose (2100 cGy rad) regional radiation therapy; and to compare the concurrent and long term toxicity of the two regimens.

**Technical Approach:** Patients <21 years with newly diagnosed Hodgkin's disease, pathologically staged as III1 ASmacro, III1A macromediastinum, III2A, IIIB, IVA, or IVB will be randomized to either Regimen A or Regimen B.

The drugs used in Regimen A are mustard, vincristine, prednisone, procarbazine (MOPP) and adriamycin, bleomycin, vinblastine, and DTIC (ABVD). Six courses of therapy will be given. Each course consists of alternating 28-day cycles of MOPP and ABVD. Each cycle of MOPP consists of two pulses of chemotherapy of mustard and vincristine given seven days apart and a fourteen day administration of prednisone and procarbazine. Each cycle of ABVD consists of two pulses of chemotherapy given two weeks apart. Treatment will be terminated at the end of the six courses of chemotherapy or upon disease progression.

Regimen B will consist of six cycles of ABVD. Each cycle consists of two pulses of chemotherapy given two weeks apart. All patients will receive six cycles of chemotherapy unless progressive disease is noted or unacceptable toxicity occurs. Regional irradiation of 2100 cGy in 12 fractions will then be given.

**Progress:** No patients have been entered in this study at MAMC.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/045	<b>Status:</b> Completed
<b>Title:</b> CCG 631: Intergroup Rhabdomyosarcoma Study - III. NCI Protocol #:INTERG-0032		
<b>Start Date:</b> 04/18/86	<b>Est. Completion Date:</b> Feb 92	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Potter AR LTC Allen R. Potter, MC                      Hartman KR Maj Kip R. Hartman, MC		
<b>Key Words:</b> Rhabdomyosarcoma		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To compare various forms of treatment of rhabdomyosarcoma and to determine: if various combinations of vincristine, dactinomycin, adriamycin, cyclophosphamide, cis-platin, and VP-16, with or without radiation therapy, will improve survival rates in both favorable and unfavorable histology tumors that have been completely or grossly, but incompletely, removed; if patients with localized orbit and head tumors will do well with vincristine and dactinomycin therapy limited to one year; patients with localized prostate, bladder, vagina, or uterus tumors can be treated successfully with cis-platin, adriamycin, vincristine, cyclophosphamide, and dactinomycin to avoid radical surgery and preserve the involved organ. Other objectives are to use second and third operations to see if the tumor is gone and, if not, to see if any remaining tumor can be surgically removed; to add other combinations of drugs when only partial response is obtained from the initial treatment; to use XRT and IT drugs to treat tumors extending or at risk of extension into the brain or spinal cord; and to do various studies of drug sensitivity and tumor typing on the removed tumor tissue to find new drugs for treatment and new ways of diagnosing cancer.

**Technical Approach:** Patients will be categorized as: Group I: localized disease, completely resected; Group II: total gross resection with evidence of regional spread; Group III: incomplete resection with gross residual disease; and group IV: distant metastatic disease present at onset. Patients will then be subcategorized into groups according to favorable or unfavorable histology and location of disease and treated with one of 8 regimens containing various combinations of actinomycin-D, adriamycin, cisplatin, cyclophosphamide, cytosine arabinoside, DTIC, hydrocortisone, leucovorin, vincristine sulfate, methotrexate, and VP-16, with or without the addition of radiation therapy and surgery.

**Progress:** The study was closed to patient entry FY 91. No patients have been entered at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/013	<b>Status:</b> Completed
<b>Title:</b> CCG 921: Unfavorable Medulloblastoma and Intracranial Primitive Neuroectodermal Tumors (PNET), Malignant Ependymoma, Ependymoblastoma, Pineoblastoma, and Central Neuroblastoma		
<b>Start Date:</b> 04/15/88	<b>Est. Completion Date:</b> Jan 94	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b>		Hartman KR Maj Kip R. Hartman, MC
<b>Key Words:</b> medulloblastoma, PNET, ependymoma, ependymoblastoma, pineoblastoma		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To define a more effective treatment for high risk medulloblastoma and other primitive neuroectodermal tumors of childhood.

**Technical Approach:** Patients <21 years old will have resection, intraoperative staging, and histopathologic assessment. If extent of disease evaluation demonstrates residual tumor >1.0x1.5 cm<sup>2</sup> in Stage T1-2 tumors or Stage T3-4 tumors and/or neuraxis or metastatic extension of tumor (M1-4), patients will be randomized to receive either Control Regimen A or Experimental Regimen B.

**Regimen A:** Standard radiation therapy plus vincristine once a week for 8 weeks followed by a 28-day rest period and then vincristine, prednisone, and CCNU maintenance chemotherapy given every 42 days for eight courses.

**Regimen B:** 8-drugs-in-1-day chemotherapy (cisplatin, procarbazine, CCNU, vincristine, cyclophosphamide, methylprednisolone, hydroxyurea, and cytosine arabinoside) for 2 courses on days 0 and 14. A rest period of 14 days will be followed by an extent-of-disease evaluation, then standard craniospinal radiation, and then 8-drugs in-1-day maintenance every 42 days for up to 8 courses. Patients will be followed for toxicity, time, sites of relapse, and survival for five years.

The end-point of this study will be time to disease recurrence or progression, as defined by both neuroradiological and clinical assessments, and overall survival.

**Progress:** This study was closed to patient entry FY 91. No patients have been entered in this study at MAMC.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/100                      **Status:** On-going

**Title:** CCG 1881: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Children Aged 2-9 Years Inclusive with White Blood Count <10,000/UL, Phase III

**Start Date:** 08/17/90                      **Est. Completion Date:** Indef.

**Department:** CCG                      **Facility:** MAMC

**Principal Investigator:** Edythe A. Albano, M.D.

**Associate Investigators:** None

**Key Words:** leukemia:lymphoblastic,chemotherapy,children:2-9 YO

Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	07/12/91

**Study Objective:** To assess the contribution of delayed intensification to event-free survival, disease-free survival, and overall survival rates in good prognosis patients with acute lymphoblastic leukemia (ALL) as well as to assess the toxicity of delayed intensification; to refine the current CCSG definition of what constitutes good prognosis ALL; to select out a group of less favorable good prognosis patients based upon blast cytogenetics at diagnosis and upon poor treatment response as assessed on the day 14 bone marrow; to assess event-free survival, disease-free survival, and overall survival for these less favorable patients after treating them with the addition of delayed intensification therapy to standard CCG "good prognosis" therapy; to assess the feasibility of collecting blast cell immunophenotypic and cytogenetic data in the context of a large cooperative group study; and to evaluate the prognostic significance of platelet counts <100,000/mm<sup>3</sup> and those >100,000/mm<sup>3</sup> at diagnosis in girls with good prognosis ALL.

**Technical Approach:** Patients will be induced with vincristine, prednisone, and L-asparaginase. CNS prophylaxis will be carried out using 6 doses of IT methotrexate during induction and consolidation, followed by maintenance doses every 12 weeks. Consolidation will consist of daily 6-mercaptopurine coupled with a 2-week taper of oral prednisone. Consolidation will be followed by an 8-week interim maintenance phase during which 2 pulses of vincristine and prednisone given at 4-week intervals will be administered along with daily 6-mercaptopurine and weekly methotrexate. At week 16, patients will be randomized to receive (Regimen B) or not receive (Regimen A) delayed intensification (a 4-week reinduction using vincristine adriamycin, L-asparaginase, and dexamethasone and a 3-week reconsolidation utilizing cyclophosphamide, cytosine arabinoside, 6-thioguanine and IT methotrexate). Maintenance therapy for both regimens will consist of monthly pulses of vincristine and prednisone, along with daily oral 6-mercaptopurine, weekly oral methotrexate, and IT methotrexate every 12 weeks. The duration of maintenance therapy will be two years for girls and three years for boys. Patients with favorable blast cell cytogenetics at diagnosis and patients with an early day 14 bone marrow response will be nonrandomly assigned to delayed intensification.

**Progress:** No patients were entered in this study in FY 91. One patient was entered in FY 90 and is still being followed.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/101	<b>Status:</b> On-going
<b>Title:</b> CCG 1882: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Children with A Poor Prognosis, Excluding Infants and Patients with Lymphoma-Leukemia or FAB L3 Blasts, Phase III		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> leukemia:lymphoblastic,chemotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	07/12/91

**Study Objective:** To show that the Berlin Frankfurt Munster (BFM) regimen without cranial radiation plus intensive intrathecal (IT) methotrexate will produce an approximate 80% event free survival in children with high risk acute lymphocytic leukemia (ALL) who have M1/M2 marrow response on day 7 of BFM induction; to improve event free survival in children with high risk ALL showing an M3 response on Day 7 of BFM therapy by intensifying standard BFM by (a) addition of non-myelosuppressive chemotherapy to consolidation, reconsolidation courses (vincristine, L-asparaginase), (b) addition of a second reinduction/reconsolidation course; (c) replacement of interim maintenance (oral 6-MP, oral methotrexate) with Capizzi I (vincristine, escalating parenteral methotrexate, L-asparaginase) intensification, (d) addition of a second Capizzi I intensification course following the first reinduction/reconsolidation course, (e) escalating 6-MP and methotrexate dosage during maintenance to maintain an absolute neutrophil count between 750-1500; to study further the impact of day 7 marrow status on outcome in children with high-risk ALL; and to obtain information concerning cytogenetic abnormalities and immunophenotype distribution in children with high-risk ALL.

**Technical Approach:** All patients entered on this study will be given BFM induction. A day 7 marrow will be performed and patients will be classified as either good responders (M1/M2) or poor responders (M3). Patients who are good responders and subsequently show an M1 marrow on day 29 will be randomized to receive either standard BFM (cranial RT and IT methotrexate) or BFM with only IT methotrexate as CNS prophylaxis. Patients who are poor responders and subsequently show an M1 marrow on day 28 will be nonrandomly assigned to an augmented BFM program which includes a second reinduction/reconsolidation course, additional vincristine and Lasparaginase during consolidation and reconsolidation, and two courses of Capizzi methotrexate in place of interim maintenance in an effort to improve disease free survival. Patients >10 years of age will be included on this high risk trial since CCG 105 showed that these patients had a worse outcome than younger patients, regardless of treatment regimen. Patients with lymphoma syndrome and/or FAB L3 morphology will be excluded.

**Progress:** No patients have been entered on this study at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/102	<b>Status:</b> On-going
<b>Title:</b> CCG 1883: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Infants Less Than 12 Months of Age, Phase III		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Dec 93	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> leukemia:lymphoblastic,chemotherapy,infant:(<1 YO)		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To prevent leukemic relapse and improve event free survival of infants <12 months with acute lymphoblastic leukemia (ALL) using intensive induction and consolidation therapy, followed by an intensification phase consisting of a reinduction, reconsolidation; to determine prospectively the prognostic significance and biologic implications of lymphoblast surface membrane immunophenotype and karyotypic analysis with respect to the treatment utilized in this study; to investigate the impact on duration of event-free survival of the addition of aggressive cytoreductive chemotherapy administered immediately following remission induction and again during intensification; to continue to investigate the efficacy of intensive intrathecal (IT) chemotherapy and very high-dose, protracted, systemic infusions of methotrexate in addition to highdose Ara-C as CNS prophylaxis in an effort to mitigate the potential neurotoxicity of conventional CNS prophylaxis incorporating whole brain radiotherapy in children of this age group; to include and standardize vigorous supportive care measures; to prospectively evaluate the effect of ALL and its treatment on development outcome and to identify children who may be at risk for later learning difficulties which may be responsive to early intervention efforts.

**Technical Approach:** Patients <12 months with newly diagnosed ALL will have immunophenotypic analysis, as well as karyotypic analysis of pretreatment bone marrow samples. All patients will receive intensive induction therapy consisting of vincristine, daunomycin, prednisone, L-asparaginase, and IT chemotherapy. Following remission induction, patients will receive consolidation therapy consisting of high-dose cytosine arabinoside with L-asparaginase, followed by 3 very high-dose, protracted (24 hr) systemic infusions of methotrexate with high-dose citrovorum factor rescue alternating weekly with IT cytosine arabinoside and cyclophosphamide. Consolidation therapy will be followed by an interim maintenance therapy consisting of IV methotrexate and L-asparaginase (Capizzi I) and IT chemotherapy. Following this, intensification therapy consisting of reinduction with vincristine, daunomycin, L-asparaginase, and reconsolidation therapy with high-dose cytosine arabinoside, very high-dose systemic methotrexate, and cyclophosphamide will be administered. Maintenance therapy will consist of oral 6-mercaptopurine and methotrexate with periodic vincristine and prednisone pulses, as well as IT chemotherapy.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/103	<b>Status:</b> On-going
<b>Title:</b> CCG 1884: A Comparison of Idarubicin to Daunomycin in A Multi-Drug Treatment of ALL in Marros Relapse		
<b>Start Date:</b> 09/21/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> ALL, idarubicin, daunomycin,		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$15000.00	07/12/91

**Study Objective:** To compare the efficacy and toxicities of Idarubicin (IDR) and Daunomycin (DNM) when used in combination with vincristine (V), prednisone (P), and L-asparaginase (L) to induce second marrow remission in children with acute lymphoblastic leukemia (ALL) who have experienced a first marrow relapse while on therapy or within one year of discontinuing therapy.

**Technical Approach:** A four-drug induction program with VPL and anthracycline will be used. In order to compare toxicity and efficacy, all patients will be randomized to receive either IDR or DNM. A rescue reinduction (Capizzi II) will be given to patients who do not enter remission with the four drugs, but these patients will not be evaluable for the maintenance vs bone marrow transplant question. All patients who achieve remission on VPL-IDR or VPLDNM will be consolidated with two cycles of Capizzi I. This will also provide a brief period to arrange for bone marrow transplant for those patients with a histocompatible sibling who will be treated on CCG-1006. Patients who do not have a suitable donor will remain on this study and receive maintenance therapy with Capizzi I and intermittent reinduction pulses of high-dose AraC and anthracycline. The anthracycline will be the same one used in induction and will be used in this phase either until a total cumulative lifetime anthracycline dose reaches 550 mg/m<sup>2</sup> (calculating each 12.5 mg/m<sup>2</sup> of IDR as 45 mg/m<sup>2</sup> of DNM equivalent) or until cardiotoxicity occurs (whichever occurs first). It is recommended that patients going to bone marrow transplant not receive more than 450 mg/m<sup>2</sup> total prior lifetime dose of anthracycline. Maintenance therapy will be continued for 2 1/2 years if the patient remains disease free.

**Progress:** No patients have been entered on this study at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/067	<b>Status:</b> On-going
<b>Title:</b> CCG 8602: Idarubicin for Remission Induction in Patients with Leukemia in Children in Second or Subsequent Marrow Relapse		
<b>Start Date:</b> 05/15/87	<b>Est. Completion Date:</b> May 91	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Hartman KR Maj Kip R. Hartman, MC		
<b>Key Words:</b> leukemia;marrow relapse,idarubicin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To refine the determination of the maximal tolerated dose of intravenous idarubicin and to determine the pharmacokinetics of intravenous idarubicin and idarubicinol in children with acute leukemia when treated with two schedules, weekly x 3 and daily x 3; and to determine the effects of scheduling of idarubicin on remission induction rates for children with acute lymphoblastic leukemia and acute non-lymphoblastic leukemia.

**Technical Approach:** Children who have had a second or subsequent marrow relapse will be randomized to a weekly x 3 schedule or a daily x 3 schedule. Since the maximal tolerated dose (MTD) has been reported as both 40 mg/m<sup>2</sup> and as 30 mg/m<sup>2</sup>, when given IV in equally divided doses daily for three days, the MTD for dosing on the daily schedule will be further refined and the MTD for a weekly schedule in children determined. A dose intermediate between the reported MTD's will be selected to evaluate first. If toxicity is acceptable, the dosages of drug given each week or each day will be escalated after three evaluable patients have been treated. Subsequent escalations in dose will also require acceptable toxicity in three evaluable patients. The dose will not be escalated in individual patients. Each patient will receive only one dosage throughout treatment. Once the MTD for each schedule is determined, the dose will be used in six additional patients to confirm acceptable toxicity. If acceptable toxicity is confirmed, additional patients will be entered at this dose level to assess remission induction rates. Remission induction rates will be determined at 21 days from initiation of therapy. If remission is not obtained following the three doses of idarubicin, the leukemia has not responded, and toxicity from the first course was acceptable, patients will be treated with a second course of the drug, using the same dose and schedule. Remission status will again be evaluated 21 days from the start of the second course of treatment. For patients attaining a complete remission, maintenance therapy will be at the discretion of the investigator.

**Progress:** No patients have been entered at MAMC.

Dr. Hartman original PI

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/068	<b>Status:</b> Completed
<b>Title:</b> CCG 8603: Phase I Study of the Combination of 5 Days Intravenous 5-Fluorouracil and 6 Days of High Dose Oral Leucovorin in Pediatric Patients		
<b>Start Date:</b> 05/15/87	<b>Est. Completion Date:</b> May 91	
<b>Department:</b> CCG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b> Hartman KR Maj Kip R. Hartman, MC		
<b>Key Words:</b> 5-Fluorouracil,leucovorin:high dose		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3000.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To determine the maximally tolerated dose of 5-fluorouracil (5-FU) administered as a daily x 5 bolus dose in combination with high dose oral folinic acid (leucovorin) in pediatric patients with cancer; to investigate the effects of 5-FU in combination with high dose folinic acid on the inhibition and recovery of thymidylate synthase in leukemic cells; and to determine the pharmacokinetics of oral folinic acid in pediatric patients.

**Technical Approach:** Patients with leukemia and solid tumors, ages 1-21 years, will be studied. Leucovorin will be administered orally at 0, 1, 2, and 3 hours daily for six days, commencing 24 hours prior to the first dose of 5-FU. Patients will be treated by IV bolus infusion over 15 minutes of 5-FU for five days (days 2-6), within one hour after the fourth dose of leucovorin each day. Second and subsequent courses will be administered no more frequently than three weeks or when the patient has recovered from the toxic effects of the therapy. The daily dose for leucovorin will be 500 mg/m<sup>2</sup> divided into four equal doses. The starting dose of 5-FU will be 300 mg/m<sup>2</sup>/day.

The maximum tolerated dose (MTD) will be investigated for leukemia and solid tumors separately. For each of these two disease categories, three evaluable patients will be required at each dose level examined. Dose escalation will proceed at 25% of the previous dose until a dose is reached at which there is evidence of Grade III or IV toxicity which is attributable to the treatment. Three patients will then be enrolled at the penultimate dose and evaluated. If there is no evidence of life threatening toxicity among these three patients, this dose will be considered the MTD. If evidence of such toxicity is noted, the dose level will be reduced in single steps by the original increments and three evaluable patients enrolled. The first dose at which no life threatening toxicities are noted will be considered the MTD.

**Progress:** This study was closed to patient entry in FY 91. No patients were enrolled at MAMC.

Dr. Hartman original PI

**DETAIL SHEETS FOR PROTOCOLS**

**GYNECOLOGY ONCOLOGY GROUP**



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 82/073		<b>Status:</b> On-going	
<b>Title:</b> GOG 26A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies					
<b>Start Date:</b> 11/20/81			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> malignancy:pelvic					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**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 evaluable 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  $>1500/\text{mm}^3$ , platelet count  $>100,000/\text{mm}^3$ , 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 91. Protocol 26Y was closed to patient accrual in FY 91 due to sufficient numbers of patients.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 82/007	<b>Status:</b> On-going
<b>Title:</b> GOG 26C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies		
<b>Start Date:</b> 11/20/81	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:pelvic,cisplatinum		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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<sup>2</sup> 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 new patients were entered in FY 91. Three patients were entered in previous years and have died of their disease.

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/067                      **Status:** On-going

**Title:** GOG 26DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies

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

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** None

**Key Words:** cancer:pelvic,amonafide

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	03/01/91

**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 nonrandomized cases. Amonafide will be administered as a slow intravenous infusion over an hour at an initial dose of 300 mg/m<sup>2</sup> daily for five days. A serial dose escalation up to 450 mg/m<sup>2</sup> 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 entered at MAMC.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/082	<b>Status:</b> On-going
<b>Title:</b> GOG 26EE: A Phase II Trial of Didemnin B (NSC #325319) in Patients with Advanced Pelvic Malignancies		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:pelvic,didemnin B		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

**Technical Approach:** Patient must demonstrate a normal prothrombin time to be eligible for this protocol. Didemnin B will be administered at a dosage of 4.2 mg/m<sup>2</sup> every four weeks. The dosage will be calculated using the GOG standard monogram. Prophylaxis against nausea and vomiting using metoclopramide, diphenhydramine, and dexamethasone will be required. Dose modifications will be permitted. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of Didemnin B and demonstrating progression more than or equal to four weeks from study entry will be considered evaluable for response and progression. Toxicity, however, may be assessed as soon as drug is given. Each patient should remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 90/023		<b>Status:</b> On-going	
<b>Title:</b> GOG 26GG: 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					
<b>Start Date:</b> 01/20/90			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix,fazarabine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**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  $>1500/\text{mm}^3$ , platelet count  $>100,000/\text{mm}^3$ , BUN  $<25 \text{ mg}\%$ , creatinine  $<1.5 \text{ mg}\%$ , bilirubin  $<1.1 \text{ mg}$ , and SGOT  $<5 \text{ IU}$ .

Fazarabine will be administered at a dose of  $40 \text{ mg}/\text{m}^2/\text{day}$  for five days. Cycles of therapy will be repeated every 28 days.

Patients with a response or stable disease will continue therapy until progression of disease is documented or adverse effects prohibit further therapy. Patients with progressive disease will have Fazarabine discontinued. Patients will be monitored for adverse effects and dose levels modified as necessary.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/024	<b>Status:</b> On-going
<b>Title:</b> GOG 26HH: A Phase II Trial of 5-Fluorouracil and Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies		
<b>Start Date:</b> 01/20/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:pelvic,5-Fluorouracil,leucovorin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**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  $>1500/\text{mm}^3$ , platelet count  $>100,000/\text{mm}^3$ , BUN  $<25 \text{ mg}\%$ , creatinine  $<1.5 \text{ mg}\%$ , bilirubin  $<1.1 \text{ mg}$ , and SGOT  $<5 \text{ IU}$ .

Leucovorin will be given in a dose of  $20 \text{ mg}/\text{m}^2$  daily for 5 days and repeated at 4 and 8 weeks and thereafter every 5 weeks.

5-FU will be infused in a dose of  $425 \text{ mg}/\text{m}^2$  daily for 5 days immediately after the Leucovorin has been given and will be repeated at 4 and 8 weeks and thereafter every 5 weeks.

An adequate trial will be one course of treatment and living four weeks for additional tumor assessment provided death is not due to tumor progression. All patients entered on study will be evaluable for toxicity. Patients will remain on study and continue receiving the drugs until disease progression or until toxicity prevents further treatment.

**Progress:** No patients entered at MAMC.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/008	<b>Status:</b> On-going
<b>Title:</b> GOG 26II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> pelvic malignancy,5-Fluorouracil,leucovorin:high dose		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$4000.00	//

**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<sup>2</sup> 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<sup>2</sup>/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 evaluable for toxicity. Patients will remain on study and continue receiving chemotherapy until disease progression or until toxicity prevents further treatment.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/085	<b>Status:</b> On-going
<b>Title:</b> GOG 26KK: A Phase II Trial of Merbarone (NSC336628) in Patients with Advanced and Recurrent Epithelial Ovarian Carcinoma		
<b>Start Date:</b> 08/02/91	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:ovarian:epithelial,merbarone		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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  $\leq 1.5$  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<sup>2</sup>/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 entered at MAMC.



**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 83/024		<b>Status:</b> On-going	
<b>Title:</b> GOG 26N: A Phase II Trial of Diahydroxyanthracenedione (DHAD) (NSC #30179) (CL232315) in Patients with Advanced Pelvic Malignancies					
<b>Start Date:</b> 11/19/82			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:pelvic,DHAD,diahydroxyanthracenedione					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**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<sup>2</sup> 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 new patients were entered in FY 91 at MAMC. In previous years three patients have been entered. All died of their disease.

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 83/026                      **Status:** On-going

**Title:** GOG 26Q: 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 Gordon O. Downey, MC

**Associate Investigators:**  
COL William L. Benson, MC                      COL Roger B. Lee, MC

**Key Words:** cancer:pelvic,aminothiadiazole

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	03/01/91

**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<sup>2</sup> I.V. once a week. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

**Progress:** No entries in FY 91. One patient was entered in FY 85 and died from squamous cell carcinoma of the cervix.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 84/064		<b>Status:</b> On-going	
<b>Title:</b> GOG 26S: A Phase II Trial of Teniposide in Patients with Advanced Pelvic Malignancies					
<b>Start Date:</b> 06/15/84			<b>Est. Completion Date:</b> Jun 89		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:pelvic,teniposide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**Study Objective:** To determine the efficacy of Teniposide in patients whose advanced malignancies have been resistant to high priority methods of treatment.

**Technical Approach:** Teniposide will be administered at a dosage of 100 mg/m<sup>2</sup> every week. The patients will be followed for toxicities to the drug and the drug dosages will be modified according to the severity of the toxicities. Response to the drug will be followed. Progression of disease and/or excessive toxicities will terminate the study for the patient.

**Progress:** No new patients entered in FY 91. Two patients were entered in previous years and died of the disease.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 85/087                      **Status:** On-going

**Title:** GOG 26U: A Phase II Trial of Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #25232) in Patients with Advanced Pelvic Malignancies

**Start Date:** 10/18/85                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

**Key Words:** cancer:pelvic,ifosfamide,uroprotector mesna

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**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<sup>2</sup> daily for five days and mesna will be given 400 mg/m<sup>2</sup> t.i.d every four weeks. Patients will be followed for toxicities to the drug and the drug dosage will be modified according to the severity of the toxicities. Response to the drug will be followed; progression of disease and/ or excessive toxicities will terminate the study for the patient.

**Progress:** No patients entered at MAMC.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/075	<b>Status:</b> On-going
<b>Title:</b> GOG 26W: A Phase II Trial of Echinomycin in Patients with Advanced Pelvic Malignancies		
<b>Start Date:</b> 07/18/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		
COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:pelvic,echinomycin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Echinomycin will be administered at a dosage of 1500 mcg/m every 4 weeks. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of drug and demonstrating progression < 4 weeks from study entry will be considered evaluable for response and toxicity. Each patient will remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/058                      **Status:** On-going

**Title:** GOG 26X: A Phase II Trial of Gallium Nitrate (NSC #15200) in Patients with Advanced Pelvic Malignancies

**Start Date:** 05/20/88                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

**Key Words:** cancer:pelvic,gallium nitrate

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**Study Objective:** To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

**Technical Approach:** Gallium nitrate will be given as a slow intravenous infusion over 30-60 minutes at a dose of 750 mg/m<sup>2</sup>. The dose will be repeated once every three weeks. Patients will be hydrated with at least three liters of fluid the day prior to treatment. An additional 500 cc normal saline will be infused in the two hours prior to administration of gallium nitrate. Hydration of three liters of fluid orally or intravenously will be continued during the first 24 hours after therapy.

Patients receiving concurrent radiotherapy are ineligible for this study.

An adequate trial will be defined as receiving one course of therapy and living three weeks. Each patient will continue receiving gallium nitrate until disease progression or death or until adverse effects prohibit further therapy.

**Progress:** No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/062	<b>Status:</b> Completed
<b>Title:</b> GOG 26Y: A Phase II Trial of Vinblastine (NSC 049842) in Patients with Advanced Pelvic Malignancies		
<b>Start Date:</b> 03/20/87	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:pelvic,vinblastine		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**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:** Vinblastine will be administered at a dosage of 9 mg/m<sup>2</sup>, I.V. push, on day 1 every three weeks with dose escalation to 12 mg/m<sup>2</sup> if minimal or no toxicity. An adequate trial is defined as receiving one course of therapy and alive for evaluation at three weeks. Patients will remain on study until progression of disease or adverse effects prohibit further therapy.

**Progress:** No patients entered at MAMC. The protocol has been closed to patient entry in FY 91.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 81/012                      **Status:** Completed

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**Title:** GOG 33: A Clinical Pathologic Study of Stage I and Stage II Carcinoma of the Endometrium

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**Start Date:** 11/21/80                      **Est. Completion Date:** Nov 83

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**Department:** GOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

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**Key Words:** cancer:endometrium

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**Study Objective:** To determine the incidence of pelvic and aortic lymph node metastases associated with Stages I and II adenocarcinoma of the endometrium and the relationship of the node metastases to other important prognostic factors. These findings will then be used as a guide for treatment protocols.

**Technical Approach:** Patients will receive standard treatment; this protocol is only for data collection purposes. Patients with histologically proven endometrial carcinoma, clinical FIGO Stages I (grades 2 and 3) and Stage II (all grades) who have undergone total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling are eligible. The following histologic types of endometrial carcinoma are acceptable: adenocarcinoma, adenocarcinoma with squamous metaplasia, adenoacanthoma, and adenosquamous carcinoma. Patients who have received preoperative radiotherapy are ineligible. Pathologic evaluation will include: (a) peritoneal washing will be evaluated for malignant cells; (b) the uterus will be evaluated in regard to location of tumor, depth of myometrial invasion, differentiation of tumor, size of uterus; (c) the adnexa will be evaluated for presence of metastasis (d) the lymph nodes (total number indicated) will be evaluated as to metastasis and location and number of lymph nodes involved. After surgery, all patients will be entered into the appropriate protocol or receive appropriate treatment if no protocol is available.

**Progress:** This protocol has been terminated; therefore no more data is being collected on patients. No patients were entered in FY 91. In previous years, eight patients were entered on the protocol.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 81/079	<b>Status:</b> On-going
<b>Title:</b> GOG 40: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas		
<b>Start Date:</b> 05/15/81	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		
<b>COL Roger B. Lee, MC</b>		
<b>Key Words:</b> sarcoma:uterine		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To determine the incidence of pelvic and aortic lymph node metastases associated with Stages I and II uterine sarcomas, the relationship of these node metastases to other important prognostic factors such as mitotic index of the tumor, and the complication rate of the procedures. These findings will then be used as a guide for treatment protocols.

**Technical Approach:** Patients with histologically proven uterine sarcoma clinical Stages I or II who undergo total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, peritoneal cytology sampling and omentectomy (optional) as described in the protocol are eligible. Patients who have had prior preoperative adjuvant pelvic radiation or chemotherapy will be ineligible. The following pathologic evaluation will be done:

- a. Peritoneal cytology will be evaluated for malignant cells.
- b. The uterus will be evaluated at least in regard to:
  - (1) location of tumor;
  - (2) depth of myometrial invasion;
  - (3) differentiation of tumor;
  - (4) size of uterus;
  - (5) number of mitoses per 10 HPF;
  - (6) histologic type of tumor.
- c. The adnexa will be evaluated for presence of metastasis.
- d. The lymph nodes will be evaluated as to metastasis and location and number of involved lymph nodes.

After surgical staging, patients may be transferred to an appropriate treatment protocol if all criteria are met. If no protocol is available, further treatment will be at the discretion of the physician.

**Progress:** No new patients were entered at MAMC in FY 91. This protocol has been closed to patient entry. Six patients have been entered in previous years, with three of them still being followed.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 81/035		<b>Status:</b> On-going	
<b>Title:</b> GOG 41: Surgical Staging of Ovarian Carcinoma					
<b>Start Date:</b> 01/16/81			<b>Est. Completion Date:</b> Jan 86		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,surgical staging					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	03/01/91	

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 is closed to patient entry. Nine patients were entered in the study. One has died of the disease; one has been entered on another study; two have been lost to follow-up; and five are still being followed.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 81/025                      **Status:** Completed

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**Title:** GOG 44: Evaluation of Adjuvant Vincristine, Dactinomycin, and Cyclophosphamide Therapy in Malignant Germ Cell Tumors of the Ovary After Resection of all Gross Tumor, Phase III

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**Start Date:** 12/17/80                      **Est. Completion Date:** Jun 83

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**Department:** GOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

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**Key Words:** tumor:germ cell:ovary,vincristine,dactinomycin,cyclophosphamide

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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Study Objective: To evaluate the effect of combined prophylactic vincristine, dactinomycin, and cyclophosphamide (VAC) chemotherapy in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (Grades 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovary, Stages I and II, after total removal of all gross tumor; to evaluate the role of serum markers, especially alpha-feto-protein and human chorionic gonadotropin (beta-HCG), when these are present in predicting response and relapse; to determine the role of restaging laparotomy in determining response, predicting relapse, and planning further therapy.

Technical Approach: Patients with histologically confirmed malignant germ cell tumors of the ovary, Stage I or II, if previously untreated and completely resected, (excluding patients with pure dysgerminoma) will be eligible. Patients with Grade 2 or 3 immature teratoma are eligible. After adequate recovery from required surgery, patients will receive 6 courses of VAC chemotherapy. If progression is noted during chemotherapy, patients will be transferred to the appropriate protocol. Patients with no evidence of disease after 6 courses will then undergo a restaging laparotomy. Those showing evidence of progression will be transferred. If laparotomy reveals no evidence of disease, patients will receive an additional 3 courses of VAC and then be followed on no further therapy.

Progress: This protocol has been closed to patient entry; no new entries in FY 91. Two patients were entered at MAMC in previous years; one died of the disease and the other has been lost to follow-up; therefore, the protocol has been closed at MAMC.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 81/105                      **Status:** Completed

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**Title:** GOG 52: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma

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**Start Date:** 08/21/81                      **Est. Completion Date:** Aug 86

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**Department:** GOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

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**Key Words:** cancer:ovarian,cyclophosphamide,adriamycin,platinol

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	03/01/91

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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 chemoor 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 is closed to patient entry. No patients were entered in FY 91. Six patients were entered in previous years. Five patients died of the disease and one has been lost to follow-up; therefore, the study has been closed at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 82/008	<b>Status:</b> Completed
<b>Title:</b> GOG 56: A Randomized Comparison of Hydroxyurea vs Misonidazole as an Adjunct to Radiation Therapy in Patients with Stage IIB, II, & IVA Carcinoma of the Cervix & Negative Para-Aortic Nodes (Phase III)		
<b>Start Date:</b> 11/20/81	<b>Est. Completion Date:</b> Jul 86	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC COL Donald H. Kull, MC
<b>Key Words:</b> cancer:cervix,hydroxyurea,misonidazole		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To determine whether hydroxyurea or misonidazole is superior as a potentiation of radiation therapy in advanced cervical cancer; and to compare the toxicity of hydroxyurea versus misonidazole when given concurrently with radiotherapy.

**Technical Approach:** All patients with invasive squamous cell carcinoma of the cervix, Stages IIB through IVA will undergo preoperative clinical staging. This will include traditional staging as permitted by FIGO rules. Extended clinical staging utilizing lymphangiography, computerized transaxial tomography, and/or sonography is required. Subsequently, patients will undergo a paraaortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides histologic proof of metastasis to the aortic nodes. All patients with cancer confined to the pelvis are eligible for treatment. They will receive pelvic irradiation and will be randomly assigned to receive concomitant hydroxyurea or misonidazole. Patients with metastasis outside the pelvis are not eligible for treatment.

**Progress:** No new entries at MAMC in FY 91. In previous years, five patients have been entered. One died of the disease and four are alive. The protocol was terminated by GOG; therefore; no more data will be collected on these patients.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91      **Protocol No.:** 81/117      **Status:** Completed

**Title:** GOG 59: A Randomized Comparison of Extended Field Radiation Therapy and Hydroxyurea Followed by Cisplatin or No Further Therapy in Patients with Cervical Squamous Cell Carcinoma Metastatic to High Common Iliac and/or Para-aortic Lymph Nodes, Phase III

**Start Date:** 09/18/81      **Est. Completion Date:** July 86

**Department:** GOG      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:**  
COL William L. Benson, MC      COL Roger B. Lee, MC  
COL Donald H. Kull, MC

**Key Words:** cancer:cervix:squamous cell,cisplatin,hydroxyurea,radiotherapy

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	03/01/91

**Study Objective:** To determine if cis-diamminedichlorplatinum, cisplatin, given in an adjuvant setting will decrease the risk of geographic failure or improve the survival rate of progression-free interval in patients who have squamous carcinoma of the cervix with metastases to high common iliac and/or para-aortic lymph nodes, proven by either histologic or cytologic means; to evaluate the role of scalen fat pad biopsy in this group of patients before initiation of extended field irradiation therapy; to accumulate clinical/surgical pathologic data on this high risk group of patients to expedite development of further protocols.

**Technical Approach:** Eligibility: patients with primary, previously untreated, histologically confirmed, invasive squamous cell carcinoma of the uterine cervix, all clinical stages, with metastasis to high common iliac or para-aortic lymph nodes proven by cytologic or histologic means. Patients will undergo preoperative clinical staging utilizing lymphangiography, computerized axial tomography, and/or sonography as well as traditional methods. Subsequently, the patients will undergo a para-aortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides cytologic proof of metastasis to extrapelvic nodes. All patients with para-aortic metastasis and negative scalene node biopsies are eligible for treatment. They will receive pelvic and para-aortic irradiation and hydroxyurea and will be radnomly assigned to receive cisplatin or no further therapy. An adequate trail will be defined as completion of the prescribed radiation therapy, completion of one course of cisplatin and survival of four weeks, or survival of eight weeks after radiation therapy for the no-further-treatment regimen. Patients will be followed quarterly for two years and every six months for three additional years.

**Progress:** The protocol is closed to patient entry. One entry at MAMC (FY 84) on the cisplatin arm is alive with no evidence of disease

The protocol has been terminated by GOG which means that no more data are being collected on this patient and the protocol has been closed at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 81/118	<b>Status:</b> On-going
<b>Title:</b> GOG 60: A Phase III Randomized Study of Doxorubicin Plus Cyclophosphamide Plus Cisplatin versus Doxorubicin Plus Cyclophosphamide Plus Cisplatin Plus BCG in Patients with Advanced Suboptimal Ovarian Adenocarcinoma, Stage III & IV		
<b>Start Date:</b> 09/18/81	<b>Est. Completion Date:</b> Sep 84	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:ovarian,chemotherapy:multiple,doxorubicin,cyclophosphamid		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To determine if the addition of BCG to doxorubicin plus cyclophosphamide plus cisplatin improves remission rate, remission duration, or survival in suboptimal Stages III and IV ovarian adenocarcinoma; to determine the frequency and duration of true complete remission using these regimens as judged at second-look laparotomy.

**Technical Approach:** Eligibility: Patients with established suboptimal Stage III or Stage IV ovarian epithelial cancer. Patients must have optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue for histologic evaluation. Patients with measurable or nonmeasurable disease will be evaluated. Patients with histologically confirmed serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, or mixed epithelial carcinoma will be eligible. Patients who have received previous chemotherapy or radiotherapy will be ineligible. Patients will be randomized to receive either doxorubicin, cyclophosphamide, and cisplatin every 3 weeks for 8 courses; or the above regimen plus BCG (days 8 & 15 for 8 courses). Patients with complete response will have a second look laparotomy and will be taken off therapy if complete response is confirmed. Patients who have partial response of stable disease will be considered for a second look if, in the opinion of the investigator, significant tumor reduction may have been achieved. If residual tumor is detected, patients will be taken off study and placed on GOG #61. Patients with progressive disease at any time will be removed from the chemotherapy on this study, but will be followed.

**Progress:** The protocol is closed to patient entry. Five patients were entered in this study. One is alive and is still being followed.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 82/036	<b>Status:</b> On-going
<b>Title:</b> GOG 63: A Clinical Pathologic Study of Stages IIB, III, and IVA Carcinoma of the Cervix		
<b>Start Date:</b> 03/19/82	<b>Est. Completion Date:</b> Mar 88	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC                      COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:cervix,pathologic study		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To evaluate the sensitivity and specificity of non-invasive procedures such as sonography, computerized transaxial tomography and lymphangiography in detection of metastases; to better understand the significance of various surgical and pathologic factors involved in staging and therapy for advanced cervical cancer. The accumulated clinical/surgical/pathological data may then play a role in modification or design of future protocols; to determine by observations of five-year survival and disease-free interval, the validity of current FIGO staging in comparison to histopathologic prognostic factors such as size of lesion, location of lesion, histology, grade, pelvic lymph node metastases, and aortic lymph node metastases, in patients with Stages II<B>, III, and IV<A> carcinoma of the cervix.

**Technical Approach:** All eligible patients with invasive carcinoma of the cervix, Stages II<B> through IV<A>, will undergo preoperative clinical staging, including traditional staging as permitted by FIGO rules. Extended clinical staging utilizing sonography, lymphangiography, and computerized transaxial tomography are mandatory. When these tests reveal an aortic nodal metastasis, the patient will have a fine needle biopsy; however, if the tests are negative, the patient will have an aortic lymphadenectomy. Patients who have a positive fine needle biopsy or positive aortic lymphadenectomy will undergo scalene node biopsy before consideration for a GOG treatment protocol. It is anticipated that all patients will be considered for entry into a GOG protocol for which they are suitable when such protocols are available.

**Progress:** This study is closed to patient entry. Four patients were entered and are alive without evidence of disease.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 83/041	<b>Status:</b> On-going
<b>Title:</b> GOG 71: Treatment of Patients with Suboptimal Stage IB Carcinoma of the Cervix: A Randomized Comparison of Radiation Therapy & Post-Treatment Para-Aortic & Common Iliac Lymphadenectomy vs Radiation...		
<b>Start Date:</b> 02/18/83	<b>Est. Completion Date:</b> Jun 86	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC COL Donald H. Kull, MC
<b>Key Words:</b> cancer:cervix,radiotherapy,lymphadenectomy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To evaluate the role of adjunctive extrafascial hysterectomy in the treatment of suboptimal Stage IB carcinoma of the cervix, the survival and patterns of failure in bulky IB cervix cancer, and the prognostic value of pretreatment endometrial sampling in suboptimal Stage IB carcinoma of the cervix; and to study the toxicity of a combined radiation and surgical therapeutic program.

**Technical Approach:** Eligible patients: patients with primary, untreated, histologically confirmed invasive carcinoma of the uterine cervix, FIGO Stage IB, as confirmed by cervical biopsy and endometrial sampling.

Regimen I: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration.

Regimen II: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration plus total extrafascial hysterectomy.

All patients will be followed for five years. Patients found to have more extensive disease (i.e., positive para-aortic nodes, intra-abdominal metastasis) will be treated at the discretion of the physician and will be followed for five years.

**Progress:** No patients entered at MAMC in FY 91. One patient entered at MAMC in FY 86 and has been lost to follow-up.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 84/033                      **Status:** On-going

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**Title:** GOG 72: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease

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**Start Date:** 02/17/84                      **Est. Completion Date:** Dec 88

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**Department:** GOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

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**Key Words:** tumor:ovarian,melphalan,cisplatin

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**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 cis-platin 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:** Three patients entered in FY 91 for a total of ten entries. None of these patients has died to date.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 84/074	<b>Status:</b> On-going
<b>Title:</b> GOG 78: 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 .....		
<b>Start Date:</b> 08/17/84	<b>Est. Completion Date:</b> Jul 89	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		
COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,teratoma,tumor:sinus,chemo,bleomycin,cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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 evaluable a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted.

Per addendum of Jan 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** One patient entered at MAMC in FY 91.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 85/090                      **Status:** On-going

**Title:** GOG 83: A Clinico-Pathologic Study of Simultaneous Endometrial and Ovarian Carcinomas

**Start Date:** 09/20/85                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

**Key Words:** cancer:ovarian,cancer:endometrial,clinico-pathologic study

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**Study Objective:** To determine the natural history of patients with synchronous adenocarcinoma presenting in both the enometrium and the ovary; to obtain estimates of mortality at five years; to determine whether histologic criteria or pattern of spread can be used to distinguish subsets of patients with differing prognoses; to determine whether these criteria would be appropriate to direct therapy in different patients to that appropriate for Stage III endometrial carcinoma, Stage I or II ovarian carcinoma with endometrial metastases, or Stage I or II endometrial and ovarian carcinoma.

**Technical Approach:** Patients will have had no prior pelvic radiation or chemotherapy and will have no previous or conomitant malignancy except of skin (excluding melanoma). Surgery will be carried out as specified in the protocol to include TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy, peritoneal cytology, pelvic cytology, pelvic and peritoneal biopsy, and washing, scraping, and biopsy of the right hemidiaphragm. Since no further treatment by protocol is available, further treatment will be at the discretion of the investigator. All patients will be followed for five years. Principal parameters employed to examine the natural history of these patients will be survival time, histologic type, histologic grade, and depth of myometrial invasion.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/089	<b>Status:</b> Completed
<b>Title:</b> GOG 85: 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 ....		
<b>Start Date:</b> 09/19/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:cervix,chemotherapy,hydroxyurea,5-Fluorouracil,cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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:** The protocol has been closed to patient entry. Two patients were entered at MAMC in FY 90 and have died of their disease.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/024	<b>Status:</b> Completed
<b>Title:</b> GOG 87A: Master Protocol for Phase II Drug Studies in the Treatment of Recurrent or Advanced Uterine Sarcomas		
<b>Start Date:</b> 01/17/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		
COL Roger B. Lee, MC		
<b>Key Words:</b> sarcoma:uterus,drug studies		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To identify new agents and combinations for treating this malignancy and to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy.

**Technical Approach:** The study design will involve treating an average sample size of 30 evaluable patients per drug studied for each of the following cell type categories:

Mixed mesodermal tumor

Leiomyosarcoma

Other sarcomas

Patients will have had no prior drug therapy. Since this is a Phase II study, no randomization is involved. The principal parameters employed to evaluate the efficacy of each agent are:

The frequency and duration of objective response.

The frequency and severity of observed adverse effects.

Survival time for all patients.

Duration of progression-free interval for all patients.

In order to estimate the true response rate and be 90% certain that the estimate is within +15%, 30 evaluable patients per histologic category will be needed (group wide). Reviews will be held at least twice yearly. Consequently, on at least two occasions, early termination can be considered if the results do not warrant conducting the study to completion. Although the exact number of potential subjects cannot be forecast at this time, the relatively slow accrual rates guarantee that inactive agents will be expeditiously recognized. The active phase of this study for each drug should be approximately:

Mixed mesodermal tumor 1 to 1 1/4 years

Leiomyosarcoma 3 years

Other sarcomas 6 years

**Progress:** No entries at MAMC. All sections of this protocol that were active at MAMC have been closed to patient entry.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 87/102		<b>Status:</b> Completed	
<b>Title:</b> GOG 87C: A Phase II Trial of Hydroxyurea, Decarbazine (IC4DTIC) and Etoposide (VP-16) in Patients with Advanced or Recurrent Uterine Sarcomas					
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> sarcoma:uterus,hydroxyurea,DTIC,VP-16,etoposide,decarbazine					
<b>Accumulative MEDCASE Cost:</b>		\$0.00	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 03/01/91

**Study Objective:** To identify new agents and combinations for treating this malignancy and to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The agents to be studied in protocol are hydroxyurea, dacarbazine (DTIC), and etoposide (VP-16).

**Technical Approach:** The treatment regimen combines hydroxyurea, a chemotherapeutic agent with a known cell-cycle synchronizing effect with DTIC, an antimetabolite, and VP-16, a premitotic inhibitor.

On Day 1, Hydroxyurea, 500 mg capsules, will be given p.o. every 6 hours with no restrictions on diet or activity. On Day 2, VP16, 100 mg/m<sup>2</sup>, diluted in 250 cc NS will be infused over one hour beginning at exactly 24 hours after the start of hydroxyurea, followed by DTIC, 700 mg/m<sup>2</sup>, diluted in 500 cc D5W, infused over four hours. On Day 3, VP-16, 100 mg/m<sup>2</sup>, diluted in 250 cc NS will be infused over one hour. On Day 4, VP-16, 100 mg/m<sup>2</sup>, diluted in 250 cc NS will be infused over one hour. Premedication with anti emetic regimens will be given on Day 2. The treatment course will be administered every four weeks, if toxicity permits and will continue for 12 courses unless progression occurs.

An adequate trial is defined as receiving one course of treatment and living four weeks. If the patient suffers progressive disease before four weeks elapse, this indicates treatment failure. Patients will remain on study and continue to receive therapy for 12 months unless there is progression or adverse effects which prohibit further therapy. Patients who die of drug-related complications prior to having their disease re-evaluated will be considered inevaluable for response but evaluable for toxicity.

**Progress:** No entries at MAMC. This study has been closed to patient entry.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/090	<b>Status:</b> Completed
<b>Title:</b> GOG 88: A Randomized Study of Radical Vulvectomy and Bilateral Groin Dissection versus Radical Vulvectomy and Bilateral Groin Radiation		
<b>Start Date:</b> 09/19/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL Roger B. Lee, MC COL William L. Benson, MC		
<b>Key Words:</b> cancer:vulva,vulvectomy,groin radiation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

Study Objective: To evaluate the comparative efficacy and morbidity of groin radiation therapy in lieu of groin dissection for selected patients with invasive squamous cell carcinoma of the vulva and to monitor patterns of recurrence and survival of patients treated with groin radiation therapy in lieu of groin dissection.

Technical Approach: Patients with invasive squamous cell carcinoma of the vulva who meet eligibility criteria as listed in the protocol will be randomized between radical vulvectomy and groin dissection and radical vulvectomy and groin radiation therapy. Complete clinical and radiographic evaluation will be performed prior to randomization. Needle aspiration cytology will be performed if there is concern over groin node status.

Progress: The study has been closed to patient entry. No entries at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 87/013		<b>Status:</b> On-going	
<b>Title:</b> GOG 90: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors					
<b>Start Date:</b> 11/21/86			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> tumor:germ cell:ovary,cisplatin,etoposide,bleomycin,VAC,vincristine,dactinomycin,cyclophosphamide,BEP					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**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 entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91      **Protocol No.:** 87/104      **Status:** On-going

**Title:** GOG 92: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

**Start Date:** 08/21/87      **Est. Completion Date:** Indef.

**Department:** GOG      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, 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:** 03/01/91

**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:** No entries in FY 91 at MAMC. One patient was entered in FY 88 and is still being followed.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/036	<b>Status:</b> On-going
<b>Title:</b> GOG 93: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)		
<b>Start Date:</b> 05/19/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:ovarian,chromic phosphate,laparotomy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$2416.00	<b>Periodic Review:</b> 03/01/91

**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 entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/048	<b>Status:</b> On-going
<b>Title:</b> GOG 94: A Phase II Study of the Treatment of Papillary Serous Carcinoma of the Endometrium Stages I and II and Maximally Debulked Advanced Endometrial Carcinoma with Total Abdominal Radiation Therapy		
<b>Start Date:</b> 02/27/87	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC                      COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:endometrial,papillary,debulked,radiation		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To determine the survival and progression-free interval of patients with maximally debulked advanced endometrial carcinoma treated with abdominal radiation and to determine the progression-free interval and site of recurrence in patients with Stage I or II papillary serous carcinoma of the endometrium treated with abdominal radiation therapy with pelvic boost.

**Technical Approach:** Following surgery, the whole abdomen will be irradiated with opposed fields to a total dose of 3000 cGy in 20 fractions of 150 cGy each. If the treatment is not tolerated because of GI symptoms or leukopenia, the daily fraction will be decreased to 125 cGy per day. Whole abdominal radiation will require four to five weeks. Following whole abdominal radiation, the pelvis will be boosted to a midplane dose of 980 cGy at 180 cGy per fraction for eleven treatments. The combined whole abdominal radiation and the total pelvic field radiation will require a total time of approximately six to seven weeks.

Patients will be followed quarterly for the first two years after completion of therapy and semi-annually for an additional three years.

Patients will continue on protocol until disease progression or adverse effects necessitates removal from the study. An adequate trial will consist of receipt of any protocol therapy.

**Progress:** No entries at MAMC in FY 91. Two patients were entered in FY 88. Both died of the disease.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/028	<b>Status:</b> On-going
<b>Title:</b> GOG 95: 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		
<b>Start Date:</b> 11/21/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:ovarian,cyclophosphamide,cisplatin,P32		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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 progressionfree 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<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m<sup>2</sup> IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** One patient entered in FY 91. Four patients were entered in previous years and have died of the disease.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/040                      **Status:** Completed

**Title:** GOG 97: Phase III Randomized Study of Cyclophosphamide (NSC 26271) and Cisplatin (NSC #119875) in Patients with Suboptimal Stage III and Stage IV Epithelial Ovarian Carcinoma Comparing Intensive and Nonintensive Schedules

**Start Date:** 01/16/87                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

**Key Words:** cancer:ovarian,chemotherapy,cyclophosphamide,cisplatin

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	03/01/91

**Study Objective:** To determine response rate, response duration and survival in suboptimal Stages III and IV ovarian carcinoma treated with Cytoxan and cisplatin administered by two different schedules, one intense and the other standard; to determine the relative toxicities of the two schedules; the therapeutic index of the two schedules; to evaluate if dose intensity is directly correlated with tumor response, response duration, and survival; to examine quality of life through the use of the FLIC questionnaire, and examine the ability of CA-125 levels to predict tumor response.

**Technical Approach:** Following optimal initial surgery, patients will be stratified according to whether or not measurable disease is present. They will then be randomized to cyclophosphamide, 1000 mg/m<sup>2</sup> and cisplatin 100 mg/m<sup>2</sup> every 21 days for four courses or to cyclophosphamide, 500 mg/m<sup>2</sup> and cisplatin 50 mg/m<sup>2</sup>, every 21 days for eight courses. Patients with partial response, stable disease, or increasing disease will then go off study. Patients with no clinical evidence of disease will have second look surgery. Those with residual disease will go off study. Those with no evidence of disease will be followed every month for six months, then every three months for four years, and yearly thereafter. The FLIC quality of life evaluation will be completed by the patient when the consent form is signed, prior to each course of therapy, and six weeks after the last course of therapy or at the time of the second reassessment, whichever comes first. CA-125 levels will be recorded prior to admission, immediately after the initial course of therapy, after each course, on completion of therapy and at each follow-up for three years. Adequate trial to evaluate response is defined as receiving one course of therapy and living three weeks for repeat lesion measurement. Adequate trial to evaluate toxicity is defined as receiving one course of therapy and receiving any follow-up information for observation of toxicity.

**Progress:** The protocol has been closed to patient entry. No patients entered at MAMC in FY 91. Two patients entered in previous years have died of the disease.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/091	<b>Status:</b> On-going
<b>Title:</b> GOG 99: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma		
<b>Start Date:</b> 07/17/87	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:endometrial,radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**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 entered at MAMC in FY 91. Two patients were entered in FY 87. Both are still being followed.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/105                      **Status:** On-going

**Title:** GOG 100: Monoclonal Antibody Against Free Beta HCG to Predict Development of Persistent Gestational Trophoblastic Disease (PGTD) in Patients with Hydatidiform Mole

**Start Date:** 08/21/87                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** COL Roger B. Lee, MC  
COL William L. Benson, MC

**Key Words:** hydatidiform moles, monoclonal antibody, free beta HCG, PGTD

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	03/01/91

**Study Objective:** To measure the serum concentration of free beta HCG and total beta HCG in patients with molar pregnancies in order to determine whether the ratio of free beta HCG to total beta HCG may be of value in predicting which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent gestational trophoblastic disease.

**Technical Approach:** Patients with gross and microscopically verified diagnosis of hydatidiform mole, either classic (true) or partial (incomplete), obtained by evacuation of the uterus with uterine conservation will be eligible. Patients will have a pelvic ultrasound within two weeks of evacuation and the first serum will be drawn within 48 hours (prior to if at all possible) of evacuation for beta HCG and free beta HCG determinations. Following histologic confirmation of the hydatidiform mole (within one week of evacuation) the patient will be placed on study. Serum samples will be obtained weekly until a negative assay is attained or until a plateau or rise in titer is observed. All patients will remain on study for a minimum of twelve weeks after primary evacuation of the molar pregnancy. After spontaneous remission, patients will have beta HCG titers monthly for six months (free beta HCG assay is not necessary). After persistent disease, the patient will remain on study until remission. The principle parameters employed to investigate the prediction of which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent trophoblastic disease are free beta HCG, total HCG concentration, ratio of free beta HCG to total HCG, and remission of disease as determined by weekly titers.

**Progress:** No patients have been entered at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/106	<b>Status:</b> On-going
<b>Title:</b> GOG 101: A Phase II Evaluation of Preoperative Chemoradiation for Advanced Vulvar Cancer		
<b>Start Date:</b> 08/21/87	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b>		
COL William L. Benson, MC	COL Roger B. Lee, MC	COL Donald H. Kull, MC
<b>Key Words:</b> cancer:vulva,chemoradiotherapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To determine: the feasibility of using preoperative chemoradiotherapy to obviate the need for pelvic exenteration 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 T<sub>3</sub> 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 N<sub>3</sub> 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 T<sub>4</sub> or unresectable T<sub>3</sub> primary tumor and NO or N<sub>1</sub> groin nodes will receive a split course of radiation therapy to the vulva by AP-PA fields. Twice daily fractions of 150 cGY will be given on days 1-4 and 1'-4'; once daily fractions of 180 cGY will be given on days 5, 8-12 and 5', 8'-12'. A 1 1/2 to 2 1/2 week split will be allowed between the two courses. Total midplane dose will be 4560 cGY.

During the twice daily radiation (days 1-4 and 1'-4'), patients will receive concurrent chemotherapy of 5-FU, 1000 mg/m<sup>2</sup> over 24 hours, allopurinol, 300 mg p.o., and cisplatin, 50 mg/m<sup>2</sup> 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 nodes. Total dose will be the same.

**Progress:** No patients have been entered at MAMC.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 88/060		<b>Status:</b> Completed
<b>Title:</b> GOG 102A: Master Protocol for Phase II Intraperitoneal drug studies in Treatment of Minimal Residual Ovarian Malignancies Documented at Second-Look Surgery				
<b>Start Date:</b> 05/20/88		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> ovarian malignancy, drug studies, intraperitoneal				
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0.00	\$0.00	03/01/91		

**Study Objective:** To determine the activity of various drugs or biologic response modifiers (BRM's) alone or in combination when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy and to evaluate further the toxicity (systemic and local) of drugs and BRM's or combinations used.

**Technical Approach:** Eligible patients: those with primary histologically documented epithelial carcinoma of the ovary; partial or incomplete responses to combination chemotherapy or minimal residual disease (<1.0 cm maximum tumor diameter) at second-look surgery; a history of complete response followed by a recurrence with no nodule >1 cm in diameter, GOG performance grade of 0, 1, or 2; at least three weeks from last treatment with chemotherapy or radiation, WBC >3000, platelet count >100,000, serum creatinine >2.0 mg%, and bilirubin and SGOT > two times normal. Ineligible patients: those with borderline tumors; leptomeningeal or cerebral metastases; current evidence of disease outside the peritoneal cavity; serious infection, septicemia, or pneumonia; major or extensive intra-abdominal adhesions or other factors which would impair surgical placement of the intraperitoneal catheters; prior whole abdominal radiation therapy; or other specific criteria as detailed in the individual sections of the protocol.

Chemotherapy will start within 12 weeks of second-look surgery. The drug or drugs will be administered intraperitoneally through an implantable peritoneal dialysis catheter. The catheter will be placed at the time of second-look laparotomy or at a subsequent operation. Ovarian tumor tissue will be studied for sensitivity against various chemotherapeutic agents utilizing in vitro clonogenic assays. Patients who receive one or more courses of drug and live at least three weeks will be evaluable for response. Patients who receive one or more courses of drug are evaluable for adverse effects regardless of subsequent survival.

**Progress:** No patients entered in this master protocol at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/025	<b>Status:</b> Completed
<b>Title:</b> GOG 102E: Intraperitoneal Administration of Cisplatin (NSC #119875) and Etoposide (VP-16) (NSC #141540) in Patients with Residual Ovarian Carcinoma		
<b>Start Date:</b> 01/20/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:ovarian,chemo,cisplatin,etoposide		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To determine the activity of Cisplatin and Etoposide when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy, and to evaluate further the toxicity of this combination of drugs.

**Technical Approach:** Eligible patients: those with primary histologically documented epithelial carcinoma of the ovary; partial or incomplete responses to combination chemotherapy or minimal residual disease (<1.0 cm maximum tumor diameter) at second-look surgery; a history of complete response followed by a recurrence with no nodule >1 cm in diameter, GOG performance grade of 0, 1, or 2; at least three weeks from last treatment with chemotherapy or radiation; WBC >3000; platelet count >100,000; and bilirubin and SGOT > two times normal. A special eligibility requirement for this protocol is that patients have creatinine < 1.5 mg.

Cisplatin, 100 mg/m<sup>2</sup>, and Etoposide, 200 mg/m<sup>2</sup>, will be given intraperitoneally and repeated at four week intervals or as soon thereafter as toxicity has resolved. If more than six weeks pass from the time of the last treatment and toxicity has not resolved, the patient will go off study. Dosage of medications will be modified if required by toxicity. Appropriate antiemetics, hydration, and Mannitol diuresis will be administered.

Treatment will continue for a total of six cycles in responding patients or in patients with nonevaluable disease. Patients with progressive disease will go off study. Following the completion of six cycles of therapy, patients with nonevaluable disease and those in a clinically-defined complete remission will undergo an exploratory laparotomy to further define the status of disease and the nature of the response. If the patient is found to be in a surgically-defined complete response, the patient will be followed without further treatment. If residual disease is present, the patient will go off study to receive alternative treatment.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/081	<b>Status:</b> On-going
<b>Title:</b> GOG 106: Evaluation of the Serum Marker, CA-125, in the Management of Carcinoma of the Endometrium		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:endometrial,CA-125,serum marker		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** To evaluate the sensitivity of CA-125 for endometrial carcinoma; to correlate CA-125 levels with surgicalpathologic criteria (stage, grade, sites); to evaluate the efficacy of CA-125 in monitoring response to therapy (surgery, radiation, chemo, hormonal) in endometrial carcinoma; and to evaluate the efficacy of CA-125 in predicting survival and/or recurrence in endometrial cancer.

**Technical Approach:** Patients with endometrial carcinoma who are eligible for designated concurrently active GOG treatment protocols for endometrial cancer will be eligible. Specific protocols are selected to obtain a population of patients with tumor burdens and risks for recurrence appropriate to accomplish the study objectives. Serum for CA-125 will be collected according to a schema individually developed for each treatment protocol to be consistent with the regimen and anticipated findings. The collection schedules developed will follow the general schema below, modified as appropriate:

1. prior to surgery, if surgery is needed
2. prior to initiation of therapy
3. prior to each chemotherapy treatment
4. monthly during hormonal therapy
5. prior to initiation of postoperative radiation and at two week intervals during therapy
6. at the completion of therapy
7. at regular follow-up intervals, approximately every three months for the first year, every four months the second year, and every six months thereafter, on patients who are free of disease
8. in patients who progress, follow-up blood samples will not be required after progression is well documented and sera at those time points has been obtained

The duration of this study will be determined by the designated concurrently active GOG treatment protocols with five years of follow-up thereafter

Patients are entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/037	<b>Status:</b> On-going
<b>Title:</b> GOG 107: A Randomized Study of Doxorubicin (NSC #123127) versus Doxorubicin Plus Cisplatin (NSC #119875) in Patients with Primary Stage III and IV Recurrent Endometrial Adenocarcinoma		
<b>Start Date:</b> 05/19/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:endometrial,doxorubicin,cisplatin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**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<sup>2</sup> IV every three weeks to a maximum total dose of no greater than 500 mg/m<sup>2</sup>.

Regimen II: doxorubicin 60 mg/m<sup>2</sup> IV every three weeks plus cisplatin, 50 mg/m<sup>2</sup> IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m<sup>2</sup>.

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 entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/052	<b>Status:</b> On-going
<b>Title:</b> GOG 108: 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		
<b>Start Date:</b> 04/21/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> tumor:uterus,ifosfamide,cisplatin,uuroprotector mesna		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To confirm reported high response rates of advanced or recurrent mixed mesodermal tumors of the uterus to Ifosfamide/ Mesna; to determine the toxicity and whether the addition of Cisplatin to Ifosfamide/Mesna improves response rates or survival in patients with these tumors.

**Technical Approach:** Patients will be randomized to either Regimen I or to Regimen II.

Regimen I: Ifosfamide 1.5 g/m<sup>2</sup>/d IV for 5 days plus Mesna 120 mg/2 IV bolus 15 minutes prior to Ifosfamide, first day only; then 1.5 g/m<sup>2</sup>/d infusion over 5 days; repeated every 21 days.

Regimen II: cisplatin 20 mg/m<sup>2</sup>/d IV for five days before administration of Ifosfamide as given in Regimen I; repeated every 21 days.

The Ifosfamide starting dose will be 1.2 g/m<sup>2</sup> if the patient has had prior radiotherapy.

One course of chemotherapy and living three weeks for repeat lesion measurement will be the minimal trial to evaluate response.

One course (or part of one course) of therapy and receiving any follow-up information for observation of toxicity will be the minimal trial to evaluate toxicity.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/086		<b>Status:</b> On-going	
<b>Title:</b> GOG 109 (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 ...					
<b>Start Date:</b> 08/02/91			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix,5-Flourouracil,cisplatin,radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		//	

**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:** One patient was entered in this study (FY 91).

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/009	<b>Status:</b> On-going
<b>Title:</b> GOG 110: 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 ....		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:cervix,squamous cell,chemotherapy,cisplatin,dibromodulcitol		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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<sup>2</sup> every three weeks.

Regimen II: cisplatin 50 mg/m<sup>2</sup> plus dibromodulcitol, 180 mg/m<sup>2</sup> daily x 5, every three weeks

Regimen III: cisplatin 50 mg/m<sup>2</sup> plus ifosfamide 5 gm/m<sup>2</sup> infused over 24 hours plus mesna 6 gm/m<sup>2</sup> during and for 12 hours following ifosfamide, every three weeks

Therapy will continue for 6 courses or until cumulative adverse effects dictate cessation of therapy.

**Progress:** No patients entered at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/010	<b>Status:</b> On-going
<b>Title:</b> GOG 111: 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 ....		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:ovarian,chemotherapy,cyclophosphamide,cisplatin,taxol		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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 greater than 100. A 21 item patient self-report questionnaire and a five item nurse neurologic 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:** Two patients have been entered in this study (both in FY 91).

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/011	<b>Status:</b> On-going
<b>Title:</b> GOG 112: A Randomized Comparison of Chemoprophylaxis Using Methotrexate versus Routine Surveillance in the Management of the High Risk Molar Pregnancy		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> molar pregnancy, methotrexate, routine surveillance		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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 mgm/m<sup>2</sup> IM weekly x 3 courses) will be initiated within 14 days after evacuation and prior to obtaining the day 15 post-evacuation titer. If remission occurs, patients will have monthly beta HCG titers for 12 months, then every three months for one additional year. The principal parameters employed to examine the relative therapeutic value of chemoprophylaxis are the frequency of post molar trophoblastic disease after evacuation and the frequency and degree of toxicity associated with chemoprophylaxis.

**Progress:** No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/064	<b>Status:</b> On-going
<b>Title:</b> GOG 113: 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 Para-aortic Nodes		
<b>Start Date:</b> 07/12/91	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:cervix,hydroxyurea,5-Fluorouracil,cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**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:** Two patients were entered in this study; both in FY 91.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/074                      **Status:** On-going

**Title:** GOG 115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, and Unclassified Sex Cord Stroma Tumor)

**Start Date:** 7/12/91                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** None

**Key Words:** tumor:ovarian stroma,chemo,bleomycin,etoposide,cisplatin

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma of the ovary as a first-line regimen.

**Technical Approach:** Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa 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 entered in the study in FY 91.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/038		<b>Status:</b> On-going	
<b>Title:</b> GOG 8803: Flow Cytometrically Determined Tumor DNA Content in Advanced Epithelial Ovarian Cancer					
<b>Start Date:</b> 03/17/89			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian:epithelial,DNA,flow cytometry					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		03/01/91	

**Study Objective:** To determine if ploidy and cell proliferation: (1) can be correlated to accepted tumor and host factors, including patient age, tumor histology, and grade, stage, and amount of residual disease; (2) can be correlated to tumor response, second look laparotomy findings, relapse, and survival; and (3) are consistent between primary and metastatic sites and stable before and after combination chemotherapy.

**Technical Approach:** Pre-chemotherapy paraffin-embedded ovarian tumor blocks will be obtained from patients with advanced (Stage III or IV) epithelial ovarian cancer who were previously entered on GOG protocols 47, 52, or 60. To be eligible patients must have received enough chemotherapy on protocol to be considered evaluable for response and have adequate follow-up information including second look laparotomy findings (if done) or time to progression, as well as follow-up after negative second look laparotomy and survival. If possible, blocks will be analyzed from both the primary ovarian tumor as well as 1 to 3 metastatic sites to look at the inter-tumor variability. When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:327-33, 1985).

**Progress:** Blocks are being submitted to GOG for analysis.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/039                      **Status:** On-going

**Title:** GOG 8809: Flow Cytometrically Determined Tumor DNA Content in Ovarian Tumors of Low Malignant Potential

**Start Date:** 03/17/89                      **Est. Completion Date:** Indef.

**Department:** GOG                      **Facility:** MAMC

**Principal Investigator:** LTC Gordon O. Downey, MC

**Associate Investigators:** None

**Key Words:** tumor:ovarian,low malignant potential,DNA,flow cytometry

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**Study Objective:** To determine if the DNA content of borderline ovarian tumors (carcinoma of low malignant potential) can be correlated with extent/stage of tumor, potential for recurrence, and patient survival.

**Technical Approach:** This study proposed to determine the DNA content in paraffin-embedded tumor specimens in patients with any stage of disease entered on GOG Protocol #72. These data will be correlated with stage of disease at entry, as well as recurrence/ progression of disease. Specimens of recurrent tumor will also be analyzed to determine the effect of treatment on DNA content.

At least one representative paraffin-embedded ovarian tumor specimen from the pretreatment laparotomy must be available as well as follow-up information including second look laparotomy findings (if done) or time to progression and follow-up after negative second look laparotomy and survival.

When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:32733, 1985).

**Progress:** Blocks are being submitted to GOG for analysis.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/041	<b>Status:</b> On-going
<b>Title:</b> GOG 8810: Flow Cytometrically Determined DNA Content in Endometrial Carcinoma		
<b>Start Date:</b> 03/17/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:endometrial,DNA,flow cytometry		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	03/01/91

**Study Objective:** o determine the DNA content of primary, recurrent, and metastatic endometrial adenocarcinoma and to identify whether the presence of aneuploid cell populations is related to histologic cell type, histologic grade, or stage of disease; to determine if tumor ploidy is related to the probability of lymph node or distant metastasis, extended progression free interval, or five year survival; and to determine whether tumor ploidy is consistent when primary tumors are compared with their metastases.

**Technical Approach:** The investigators will study the DNA content of primary, recurrent, and metastatic endometrial adenocarcinomas of patients entered on GOG Protocol ##, using nuclei obtained from conventionally processed paraffin blocks. At least one paraffin block containing endometrial adenocarcinoma obtained at D&C or hysterectomy must be available. If metastatic tumor was histologically confirmed in that patient, then one paraffin block of metastatic tumor also would be highly desirable.

When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:32733, 1985).

**Progress:** Blocks are being submitted to GOG for analysis.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/072	<b>Status:</b> On-going
<b>Title:</b> GOG 8902: Correlation of Specific HPV Types and Amplification and Expression of the C-MYC Gene with the Behavior of Squamous Carcinoma of the Cervix		
<b>Start Date:</b> 07/28/89	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:cervix,HPV,C-MYC,gene expression		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91

**Study Objective:** To determine if HPV (human papilloma virus) types correlate with lymph node metastasis, survival, and other pathologic factors such as histologic diagnosis, grade, capillary-like space invasion, etc, in Stage I carcinoma of the cervix; to determine if C-MYC gene amplification and overexpression correlate with lymph node metastasis, survival, and other pathologic factors in Stage I carcinoma of the cervix; and to determine if HPV type, c-myc amplification and overexpression are independent or interrelated prognostic factors for cervical cancer.

**Technical Approach:** Paraffin blocks from evaluable patients with cervical cancer (squamous, adenocarcinoma, or adenosquamous carcinoma) who were entered on GOG Protocol 49 will be obtained. There must also be adequate follow-up information on these patients. The blocks should correspond to the slides from the primary tumor and lymph node metastasis that were originally reviewed for entry onto Protocol 49. If these particular blocks are not available, another representative block from the tumor will be used.

An H&E section and six sections for PCR (polymerase chain reaction) analysis will be prepared from each paraffin block. Analysis will be performed for HPV's 6, 11, 16, 18, 31, 33, 35, and c-myc gene sequences. HPV DNA will be extracted from the paraffin blocks and analyzed. Positive controls, negative controls, and controls to measure the sensitivity of the test will be included in each test. PCR analysis will be performed using oligomer primers complementary to sequences 100 base pairs apart within the third exon of the cmyc gene. PCR will be performed under conditions wherein the amount of amplified product is linearly related to complementary DNA in starting material. The amplified DNA sequences will be subjected to electrophoresis. In situ hybridization using 3H labelled antisense RNA probes for c-myc transcript will be performed to correlate c-myc expression with cellular morphology in tissue sections. A c-myc sense probe and ribosomal RNA antisense will be used as negative and positive type controls, respectively.

**Progress:** Blocks are being submitted to GOG for analysis.



## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 90/026                      **Status:** On-going

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**Title:** GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia

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**Start Date:** 01/20/90                      **Est. Completion Date:** Indef.

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**Department:** GOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Gordon O. Downey, MC

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**Associate Investigators:** None

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**Key Words:** trophoblastic neoplasia, DNA, hydatidiform moles

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 03/01/91
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**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 postmolar 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 postmolar 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:** Blocks are being submitted to GOG for analysis.

# **DETAIL SHEETS FOR PROTOCOLS**

**NATIONAL CANCER INSTITUTE**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 81/033		<b>Status:</b> On-going	
<b>Title:</b> NCI 7602: All Stage IC and II 9A,B,C) and Selected Stage IAii and IBii Ovarian Cancer					
<b>Start Date:</b> 01/16/81			<b>Est. Completion Date:</b> Jun 85		
<b>Department:</b> NCI			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,surgery,melphalan,radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	11/17/89	

**Study Objective:** To define the natural history of patients treated with surgery plus either chemotherapy or radioisotope; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to determine the patterns of relapse for each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

**Technical Approach:** All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 2A, 2B, 2C, IAii, IBii, or IAi or IBi with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If IIB, IIC, residual disease is found, will be randomized to pelvic radiotherapy plus melphalan alone. If after 18 months of therapy, the patient remains free of disease, chemotherapy will be discontinued. Second look will be done if the patient is free of disease after 18 months of chemotherapy.

**Progress:** This protocol was closed to patient entry September 1986. Data is still being collected on some patients.

# **DETAIL SHEETS FOR PROTOCOLS**

## **PEDIATRIC ONCOLOGY GROUP**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/077	<b>Status:</b> On-going
<b>Title:</b> POG 8850 (ccsg #7881): Evaluation of Vincristine, Adriamycin, Cyclophosphamide, and Dactinomycin With or Without the Addition of Ifosfamide and Etoposide in the Treatment of Patients With Newly Diagnosed Ewing's Sarcoma or Primitive Neuroectodermal Tumor of Bone, A Phase III Intergroup Study		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Edythe A. Albano, M.D.		
<b>Associate Investigators:</b>		LTC Howard Davidson, MC
<b>Key Words:</b> bone, Ewing's sarcoma, tumor: neuroectodermal, chemo		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 07/12/91

**Study Objective:** To determine the event-free survival (EFS) and survival of patients with Ewing's sarcoma and primitive neuroectodermal tumor (PNET) of the bone who are treated with etoposide and ifosfamide in combination with standard therapy; and to compare their EFS and survival rates with those of patients treated with standard therapy alone.

**Technical Approach:** Patients with newly diagnosed (< 1 month) Ewing's sarcoma, PNET of bone, or a diagnosis compatible with primitive sarcoma of bone will be eligible. Patients will be randomized to one of two treatment regimens. One regimen will use drugs according to the standard regimen (vincristine, adriamycin, actinomycin D, and cyclophosphamide) and the other will add VP-16 and ifosfamide. Mesna will be given to prevent bleeding from the bladder. Patients will be treated with chemotherapy for 9 weeks and then evaluated. Those who have a response to treatment will be treated for 6 additional weeks with chemotherapy and radiation therapy and/or surgery. The necessity and extent of surgery will be determined based on the response to therapy and the site of the lesion. Patients will receive radiation therapy to the site of the primary lesion and to all sites of metastases which were present at the time of diagnosis, unless there has been complete resection of the primary lesion with a documented tumor-free margin of < 1 cm. At the end of this treatment period, patients will again be evaluated, and those who have shown a marked response to treatment will continue chemotherapy for another 34 weeks. Patients with no response or recurrent or progressive disease at any of the evaluation points will go off study.

**Progress:** No patients were entered in this study at MAMC in FY 91. Two patients were entered in previous years and are still being followed.

# **DETAIL SHEETS FOR PROTOCOLS**

**PUGET SOUND ONCOLOGY GROUP**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/079	<b>Status:</b> On-going
<b>Title:</b> PSOC 615: Intraperitoneal Consolidation Therapy Following Second-Look Operation in Ovarian Cancer		
<b>Start Date:</b> 06/19/87	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> PSOC	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gordon O. Downey, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> cancer:ovarian,P32,cisplatin,5-Flourouracil		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 11/17/89

**Study Objective:** To examine the effect of intraperitoneal therapy on disease free survival in patients with no disease or minimal residual disease following second-look surgery and to document the complication rate associated with the use of intraperitoneal chromic phosphate or chemotherapy in patients previously treated with systemic chemotherapy.

**Technical Approach:** Following standard induction chemotherapy, patients with Stage IIb, IIc, or III epithelial carcinoma of the ovary will have second-look laparotomy in the standard fashion. The second look procedure will include resection of any remaining female genital organs. If the patient has no evidence of gross persistent disease greater than 1.0 cm at the time of second look, a Tenckhoff catheter will be inserted. If the pathologic findings from the second look procedure show no evidence of persistent tumor, the patient will receive 15 millicuries of intraperitoneal P-32 in 1000-1500 ml of normal saline, with appropriate rotation of position to assure proper distribution of the P-32.

If the patient has positive disease within the peritoneal cavity, she will receive chemotherapy with cisplatin (100 mg/m<sup>2</sup>) and 5-FU (1000 mg/m<sup>2</sup>) through the Tenckhoff catheter every three weeks for a maximum of four doses unless there are unacceptable side effects.

**Progress:** No patients entered at MAMC in FY 91. One patient was entered in FY 87 at MAMC and is in the follow-up phase of the study.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** MAY 94

**Department:** PSOC                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ William A. Phillips	MAJ Luke M. Stapleton, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer I. Cadiz, MC	

**Key Words:** adriamycin, cefoperazone

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**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 re-evaluated 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 has been entered at MAMC with no adverse effects.



**DETAIL SHEETS FOR PROTOCOLS**

**SOUTHWEST ONCOLOGY GROUP**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 78/042	<b>Status:</b> Completed
<b>Title:</b> SWOG 7804: Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin, and Mitomycin-C (FAM) vs. Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma		
<b>Start Date:</b> 06/16/78	<b>Est. Completion Date:</b> Jun 80	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> Suresh B. Katakhar, M.D., DAC		COL Friedrich H. Stutz, MC LTC H. Irving Pierce, MC
<b>Key Words:</b> cancer:stomach,surgery,chemotherapy,5-fluorouracil,adriamycin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**Study Objective:** To determine the efficacy of adjuvant chemotherapy with FAM on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

**Technical Approach:** Patient Eligibility: patients must have TNM stage-group IB, IC, II, or III gastric adenocarcinoma and no microscopic or gross residual postoperatively; no prior chemotherapy or radiotherapy; no medical contraindications to chemotherapy with FAM; serum bilirubin <2.0 mg/100 ml; SGOT and SGPT <3 times the upper limit of normal values; creatinine clearance >75 cc/ min; BUN <25 mg%; serum creatinine <1.5 mg%; WBC >4,000; platelets >100,000. Treatment: After surgery, patients will be randomized to either: Treatment 1 (no further therapy) or Treatment 2: FAM 5-FU, 600 mg/m<sup>2</sup> IV days 1 & 8, 29 & 36; adriamycin, 30 mg/m<sup>2</sup> IV days 1 & 29; mitomycin-C, 10 mg/m<sup>2</sup> IV day 1.

A total of 6 courses, one every 8 weeks, will be administered. After 12 months, the active therapy phase is completed. The patient will be followed at six month intervals for five years if remission continues.

**Progress:** This protocol has been closed to patient entry. One patient was entered in FY 84 at MAMC and has died of the disease.

### DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 78/047	<b>Status:</b> On-going
<b>Title:</b> SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6		
<b>Start Date:</b> 07/31/78	<b>Est. Completion Date:</b> Jan 88	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> LTC H. Irving Pierce, MC		COL Friedrich H. Stutz, MC Suresh B. Katakhar, M.D., DAC
<b>Key Words:</b> Hodgkin's disease: Stages III & IV, chemotherapy, modality RX		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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:** Seven patients were entered in previous years and data is still being collected on two of the patients.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** COL Friedrich H. Stutz, MC  
Suresh B. Katakhar, M.D., DAC                      COL Irwin B. Dabe, MC

**Key Words:** cancer:breast,chemotherapy,modality therapy

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**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 1 yr 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:** The study was closed to patient entry, 15 Aug 89. Thirty-five subjects were entered in this study at MAMC. Data is still being collected on several patients at MAMC. Groupwide: 288 eligible patients have been entered. Toxicities have been similar for both arms. No fatal toxicities have been reported.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 84/018	<b>Status:</b> On-going
<b>Title:</b> SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer		
<b>Start Date:</b> 12/14/83	<b>Est. Completion Date:</b> Sep 85	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Friedrich H. Stutz, MC	COL William D. Belville, MC	COL Irwin B. Dabe, MC
MAJ Thomas M. Baker, MC	MAJ Alfred H. Chan, MC	MAJ Michael D. Stone, MC
MAJ Timothy J. O'Rourke, MC		
<b>Key Words:</b> cancer:bladder,BCG,adriamycin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**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:** The protocol was closed to new patient entry in FY 88. Three patients were entered at MAMC during FY 84 and data is still being collected on them.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 84/019                      **Status:** On-going

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**Title:** SWOG 8221: Treatment of Advanced Bladder Cancer with Preoperative Irradiation and Radical Cystectomy versus Radical Cystectomy Alone, Phase III

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**Start Date:** 12/14/83                      **Est. Completion Date:** Oct 85

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Howard Davidson, MC

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**Associate Investigators:**

COL Donald H. Kull, MC	COL William D. Belville, MC
COL Irwin B. Dabe, MC	COL Friedrich H. Stutz, MC
MAJ Alfred H. Chan, MC	MAJ Thomas M. Baker, MC
MAJ Michael D. Stone, MC	MAJ Timothy J. O'Rourke, MC

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**Key Words:** cancer:bladder,cystectomy,radiotherapy

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

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**Study Objective:** To compare survival and pelvic recurrence rates in patients with transitional cell bladder cancer treated with radical surgery alone versus patients treated with preoperative irradiation with 2,000 rads followed by cystectomy.

**Technical Approach:** Patients eligible to be entered, must have histologically proven transitional cell carcinoma of the urinary bladder, and must have one of the following characteristics:

1. Evidence of muscle invasion.
2. Rapidly recurring superficial high-grade tumors and/or diffuse carcinoma *in situ* not amenable to transurethral resection and/or intravesical chemotherapy.

Patients will be randomized to receive either surgery with radical cystectomy or radiation therapy plus radical cystectomy. Patients will be seen in follow-up every three months following the cystectomy. Patients with either local or distant recurrence will be removed from the study. Five-year survival rates and two-year recurrence rates will be the major objectives of this study.

**Progress:** This study was closed to patient entry in Nov 89. One patient was entered during FY 84 and was randomized to cystectomy alone, tolerated the procedure well, and is being followed.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 83/061                      **Status:** Completed

**Title:** SWOG 8229/30: Combined Modality Therapy for Multiple Myeloma, VMCP-VBAP for Remission Induction Therapy: VMCP + Levamisole vs Sequential Half-body Radiotherapy + Vincristine-Prednisone for Patients ..

**Start Date:** 04/15/83                      **Est. Completion Date:** Mar 85

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	LTC James E. Congdon, MC
COL Friedrich H. Stutz, MC	COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC	MAJ Alfred H. Chan, MC
MAJ Thomas M. Baker, MC	

**Key Words:** myeloma, chemotherapy, radiotherapy, levamisole, vincristine-prednis

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To compare the effectiveness of two intermittent pulse schedules of VMCP (vincristine, melphalan, cyclophosphamide, and prednisone) and VBAP (vincristine, BCNU, adriamycin and prednisone) for induction of remission in previously untreated patients with multiple myeloma. Results will also be compared with other combination regimens in previous SWOG studies. In patients proven to achieve remission, to compare the value of 12 months of chemo-immunotherapy maintenance (VMCP + levamisole) vs a consolidation program consisting of sequential half-body radiotherapy + vincristine and prednisone followed by unmaintained remission. In patients who only achieve improvement, to determine whether sequential half-body radiotherapy plus vincristine and prednisone will increase the remission rate. To determine if sequential half-body radiotherapy plus vincristine and prednisone can serve as an effective form of induction therapy for patients who fail to respond to chemotherapy or suffer early relapse.

**Technical Approach:** Patients with previously untreated multiple myeloma will be stratified as to tumor mass status and randomized to induction therapy on VMCP alternated every 3 wks with VBAP for a minimum of 6 months to a maximum of one yr or to VMCP for 3 cycles followed by 3 cycles of VBAP, repeated every 3 wks, for a minimum of 6 months to a maximum of one year. Upon completion of induction, patients with documented 75% regression with chemotherapy alone will be randomized to receive VMCP + levamisole, repeated every 3 wks or to sequential half-body radiotherapy and concomitant vincristine and prednisone. Partial responders or nonresponders following induction therapy will receive sequential half-body radiotherapy, vincristine, and prednisone for 6 wks.

**Progress:** This study was closed to patient entry, 15 Nov 88. Five patients were entered on the study and all have now died of their disease.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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

<b>Associate Investigators:</b>	LTC James E. Congdon, MC
COL Friedrich H. Stutz, MC	COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC	MAJ Alfred H. Chan, MC
MAJ Thomas M. Baker, MC	

**Key Words:** cancer:breast,surgery,biological parameters

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**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 diseasefree 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 cms 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:** No patients were entered in FY 91. Eleven patients have been entered at MAMC in previous years. The protocol was closed to patient entry in May 88, but data collection has not been completed.

Preliminary group-wide data indicate that this has proven to be a positive study; the CMFP arm has shown superior disease free survival.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 85/008	<b>Status:</b> On-going
<b>Title:</b> SWOG 8300: Treatment of Limited Non-small Cell Lung Cancer: Radiation versus Radiation Plus Chemotherapy (FOMi/CAP), Phase III		
<b>Start Date:</b> 11/16/84	<b>Est. Completion Date:</b> Oct 86	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	COL Irwin B. Dabe, MC
MAJ Timothy J. O'Rourke, MC	MAJ Michael D. Stone, MC	
CPT David R. Bryson, MC		
<b>Key Words:</b> cancer:lung:non-small cell,radiation,chemotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**Study Objective:** To compare combination chemotherapy (FOMi-CAP:5-FU, vincristine, and mitomycin-C alternating with cyclophosphamide, Adriamycin, and cis-platinum) plus radiotherapy to radiotherapy alone for patients with limited, non-small cell lung cancer (NSCLC) in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; to determine the toxicity of radiotherapy plus FOMi-CAP relative to radiotherapy alone for patients with limited NSCLC; to evaluate the responsiveness of smaller tumor burdens (less than metastatic disease) to FOMi-CAP; to determine the pattern of relapsing disease in each treatment arm and in subgroups of patients determined by histology and response to FOMi-CAP; and to determine if prophylactic brain irradiation will decrease the chances for brain metastasis and influence toxicity or survival.

**Technical Approach:** Patients will be randomized to four treatment arms: (1) radiation alone to the chest; (2) radiation therapy to the chest and prophylactic radiation to the brain; (3) chemotherapy with FOMi-CAP followed by radiation therapy to the chest (those patients showing some response will receive two additional cycles of chemotherapy after completion of radiation therapy); (4) same treatment as in #3 with the addition of concomitant prophylactic brain irradiation to 3750 rads.

**Progress:** No entries in FY 91. Three patients were entered at MAMC in previous years. Two of the patients have expired of the disease and one patient is still in follow-up at MAMC. The study was closed to patient entry in March 1988.

Group-wide data show that none of the regimens has been highly toxic. A significant difference has been shown among the four arms. A difference has been noted in favor of the two arms not receiving prophylactic cranial irradiation.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 84/072                      **Status:** Completed

**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:**  
COL Friedrich H. Stutz, MC                      MAJ Thomas M. Baker, MC  
MAJ Timothy J. O'Rourke, MC                      COL Irwin B. Dabe, MC  
MAJ Michael D. Stone, MC

**Key Words:** cancer:breast,endocrine therapy,megestrol acetate

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90
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**Study Objective:** To determine if combination hormonal therapy with aminoglutethimide and hydrocortisone + megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased 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 the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

**Technical Approach:** Patients who have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for 6 months with documented disease progression and clear-cut bone scan evidence of cortical bone metastases will be randomized to: Arm I megestrol acetate given alone until there is documented evidence of disease progression; Arm II aminoglutethimide plus hydrocortisone; or Arm III megestrol acetate plus aminoglutethimide and hydrocortisone. 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 study was closed to patient entry 15 Nov 90. No patients were entered at MAMC in FY 87. One patient entered at MAMC in FY 86 was died of the disease.

Group wide 235 eligible patients have been entered. There has been one treatment related death on the combination arm from bacteremia secondary to leukopenia.

Seventeen of 61 patients had toxicities of Grade 3 or greater, compared to 8 of 63 on aminoglutethimide and 3 of 69 on megestrol.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 84/059	<b>Status:</b> On-going
<b>Title:</b> SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III		
<b>Start Date:</b> 05/18/84	<b>Est. Completion Date:</b> May 86	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Irwin B. Dabe, MC	COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC
MAJ Timothy J. O'Rourke, MC	MAJ Michael D. Stone, MC	
<b>Key Words:</b> cancer:breast,chemotherapy,emergency room		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**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 postmastectomy 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:** No patients were entered in FY 90. Three have been entered in previous years. Two of these patients have died of progressive breast cancer. The study was closed to patient entry 15 June 1990.

The quality of life component of this study was discontinued in January 1989 because of poor compliance in completing questionnaires.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/016                      **Status:** Completed

**Title:** SWOG 8325: Combination Chemotherapy with O,P'-DDD and Cis-platinum in Metastatic Adrenal Carcinoma, Phase II

**Start Date:** 12/11/87                      **Est. Completion Date:** Oct 90

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	COL Irwin B. Dabe, MC
COL Gary L. Treece, MC	LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC	MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC	CPT Denis Bouvier, MC

**Key Words:** cancer:adrenal gland,O P'-DDD,cisplatinum

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$365.00	10/19/90

**Study Objective:** To study the responsiveness of adrenocortical carcinoma to combination chemotherapy consisting of cis-platinum and Mitotane (O,P'-DDD); to study the prognostic features of patients with metastatic and/or resectable adrenal carcinoma receiving chemotherapy; and to document the toxicity of chemotherapy in this group of patients.

**Technical Approach:** Patients with metastatic or residual adrenocortical carcinoma in whom further surgical removal of disease is not possible will be eligible. Prior radiotherapy or chemotherapy other than cis-platinum is allowed. Patients will be divided into good and poor risk categories with poor risk defined as the presence of one or more of the following criteria: (1) age >65 years, (2) poor tolerance to prior chemotherapy, and (3) extensive prior radiation therapy to over 30% of the bone marrow bearing areas.

Regimens: Good risk patients: cis-platinum, 100 mg/m<sup>2</sup> IV, repeated every three weeks, if recovery from toxicities occurs) plus O,P'-DDD, 1000 mg PO, three times a day. Poor risk patients: cisplatinum, 75 mg/m<sup>2</sup> IV, repeated every three weeks (if recovery from toxicities occurs, plus O,P'-DDD, 1000 mg PO, four times a day, continuously. In the absence of a complete response, chemotherapy will be continued until progressive disease or unacceptable toxicity occurs. If complete response occurs, chemotherapy will be continued for 18 months or until progressive disease occurs. An adequate trial will be defined as one course of chemotherapy with both drugs followed by three weeks of observation.

**Progress:** This protocol was closed to patient entry 1 Jul 89. Two patients were entered at MAMC in FY 88; both have now expired.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 88/032		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8326/27: Evaluation of Combination Chemotherapy Using High Dose Ara-C in Adult Acute Leukemia and Chronic Granulocytic Leukemia in Blastic Crisis, Phase III					
<b>Start Date:</b> 02/19/88			<b>Est. Completion Date:</b> Feb 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Thomas M. Baker, MC			MAJ David M. Dunning, MC		
MAJ Ruben D. Sierra, MC			CPT Denis Bouvier, MC		
<b>Key Words:</b> leukemia:acute,chronic granulocytic,chemotherapy,Ara-C					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0.00</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
					<b>Periodic Review:</b> 10/19/90

**Study Objective:** To compare the effectiveness of three different drug combinations, using high dose Ara-C or high dose Ara-C in combination with m-AMSA or mitoxantrone for remission induction in relapsed adult leukemias including both acute non-lymphocytic leukemia, chronic granulocytic during accelerated or blastic phase, and untreated secondary acute leukemias, and to monitor the side effects of the above combination chemotherapy schedules.

**Technical Approach:** Patients will be randomized to ARM I: Ara-C, 3 gm/m<sup>2</sup>, IV infusion every 12 hrs for 6 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/m<sup>2</sup>/day on days 7, 8, and 9; or ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/m<sup>2</sup>/day on days 7, 8, and 9. Bone marrow aspiration and biopsy will be performed on day 14, following induction therapy, with subsequent aspirations and biopsies performed every 7-10 days to determine when marrow recovery has occurred to start the next course of therapy. Patients with complete response will receive consolidation therapy. Consolidation therapy will consist of Arm I: Ara-C, 3 gm/m<sup>2</sup>, IV infusion every 12 hrs for 3 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/m<sup>2</sup>/day on day 1; and ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/m<sup>2</sup>/day on day 1. Three courses of consolidation therapy will be given, administered every 28 days. A bone marrow aspiration and biopsy will be done prior to each consolidation course. No further treatment will be given after consolidation therapy. Pyridoxine will be given for 10 days during induction and 5 days during consolidation for control of neurotoxicity. Patients whose bone marrow remains A3 at day 14, those who relapse after the attainment of a complete or partial remission, and those who develop potentially fatal nonmyelosuppressive toxicity will be taken off study.

**Progress:** No patients were entered at MAMC in FY 91. Two patients were entered at MAMC in FY 88 with no unexpected reactions. Both have died of the disease.

Group-wide: Arm II was closed at the end of 1987 because of unacceptable toxicity.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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

<b>Associate Investigators:</b>	COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC	LTC Howard Davidson, MC
MAJ Thomas M. Baker, MC	MAJ Michael D. Stone, MC
CPT David R. Bryson, MC	

**Key Words:** leukemia:lymphoblastic,consolidation regimens

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**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, 6mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 wk for 36 mth or until relapse. An adequate trial will be the completion of remission induction.

**Progress:** No patients were entered at MAMC in FY 91. Six patients were entered in previous years, all of which have expired from their disease. No adverse effects reported at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/033	<b>Status:</b> On-going
<b>Title:</b> 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 ....		
<b>Start Date:</b> 02/28/87	<b>Est. Completion Date:</b> Dec 89	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Irwin B. Dabe, MC	MAJ Thomas M. Baker, MC	LTC Lauren K. Colman, MC
MAJ David M. Dunning, MC	MAJ Ruben D. Sierra, MC	COL Roger B. Lee, MC
CPT David R. Bryson, MC		
<b>Key Words:</b> cancer:ovarian,chemotherapy,IP,IV cyclophosphamide,cisplatinum		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup> every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup>, 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:** No entries at MAMC in FY 91. One patient was entered in FY 87 and refused second-look surgery; therefore he was taken off study. Group-wide: 363 eligible patients have been entered. There have been no fatal toxicities reported. Granulocytopenia has been the predominant toxicity reported on both arms.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/107                      **Status:** On-going

**Title:** SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III

**Start Date:** 03/19/88                      **Est. Completion Date:** Aug 90

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	COL Irwin B. Dabe, MC
COL William D. Belville, MC	COL Victor J. Kiesling, MC
LTC Lauren K. Colman, MC	MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC	MAJ Ruben D. Sierra, MC
CPT Denis Bouvier, MC	

**Key Words:** cancer:bladder,BCG,immunotherapy

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**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 diseasefree 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:** The study was closed to patient entry 12/15/88. Ten subjects were entered at MAMC. One patient was taken off study due to severe urticarial reactions to BCG; another had severe hematuria attributed to BCG and was taken off study. Data is still being collected on several patients.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 88/053		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8515: Evaluation of Menogaril (NSC 269148) in Non-Hodgkin's Lymphoma, Phase II					
<b>Start Date:</b> 05/20/88			<b>Est. Completion Date:</b> Apr 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Thomas M. Baker, MC			MAJ David M. Dunning, MC		
MAJ Ruben D. Sierra, MC			CPT Denis Bouvier, MC		
<b>Key Words:</b> lymphoma:non-Hodgkin's,menogaril					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0.00</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
					<b>Periodic Review:</b> 10/19/90

**Study Objective:** To estimate the response rate and response duration for favorable and unfavorable histology Non-Hodgkin's lymphoma (NHL) treated with menogaril and to define the qualitative and quantitative toxicities of menogaril administered in a Phase II study.

**Technical Approach:** Patients will be stratified at initial registration by histology (favorable versus unfavorable).

Menogaril 160 mg/m<sup>2</sup> will be administered over 1 hour in 500 ml of 50% dextrose in water once every 28 days, provided the patient has a total absolute granulocyte count >2000 m l and a platelet count >100,000/ m l.

Treatment with menogaril will continue until disease progression. Patients with documented progression of disease or unacceptable toxicity will be removed from the study. All patients will be followed until death.

Doses will be modified in subsequent courses based on nadir counts. Patients experiencing granulocytopenia <1000/ m l or thrombocytopenia <50,000/ m l, following two dosage reductions will be taken off protocol treatment unless they have achieved a partial response, in which case one further dose reduction will be attempted.

Menogaril will be discontinued in the event of clinically detectable evidence of congestive heart failure. Patients who have received prior Adriamycin will undergo a follow-up MUGA scan prior to every third course of menogaril. The drug will be discontinued if the ejection fraction drops by more than 15% from baseline.

**Progress:** No patients entered at MAMC in FY 91. One patient was entered in this study in FY 88 and has expired from the disease. Drug-induced phlebitis was reported in this patient.

**Group-wide:** Forty-four eligible patients have been registered on this protocol. There have been no fatal toxicities.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 86/080	<b>Status:</b> Completed
<b>Title:</b> SWOG 8516: A Phse III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma		
<b>Start Date:</b> 09/19/86	<b>Est. Completion Date:</b> Jul 89	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> COL Irwin B. Dabe, MC MAJ David M. Dunning, MC	MAJ Thomas M. Baker, MC LTC Lauren K. Colman, MC CPT David R. Bryson, MC	
<b>Key Words:</b> lymphoma:non-Hodgkin's,chemotherapy,CHOP,m-BACOD,MACOP-B,ProMACE-CytaBOM		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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, doxorubicin, vincristine, and prednisone. Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide, doxorubicin, vincristine, bleomycin, dexamethasone, methotrexate, and calcium leucovorin rescue after each MTX dose. Arm III (ProMACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide, doxorubicin, VP-16, prednisone, Ara-C, bleomycin, vincristine, methotrexate, calcium leucovorin rescue after each MTX dose, and trimethoprim-sulfamethoxazole. Arm IV (MACOP-B will be given over 12 weeks): methotrexate, calcium leucovorin rescue after each MTX bolus, doxorubicin, cyclophosphamide, vincristine, bleomycin, prednisone, and trimethoprim-sulfa. 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 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 by SWOG, 16 Jun 91. No entries at MAMC.

Group-wide: 735 eligible patients have been entered. There is a reasonable balance across treatment arms by stratification factors and by the type of institution.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 88/003		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8520: Cis-Diamminedichloroplatinum (II), Methotrexate and Bleomycin in the Treatment of Advanced Epidermoid Carcinoma of the Penis, Phase II					
<b>Start Date:</b> 12/11/87			<b>Est. Completion Date:</b> Sep 90		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>					
COL Irwin B. Dabe, MC		MAJ Thomas M. Baker, MC			
MAJ David M. Dunning, MC		LTC Lauren K. Colman, MC			
CPT Denis Bouvier, MC		MAJ Ruben D. Sierra, MC			
		COL William D. Belville, MC			
<b>Key Words:</b> cancer:penis,cis-diamminedichloroplatinum,methotrexate,bleomycin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0.00		\$0.00		10/19/90	

**Study Objective:** To determine the response rate in patients with advanced epidermoid carcinoma of the penis treated with cisplatin, methotrexate, and bleomycin and to evaluate the toxicity of this three-drug combination in this patient population.

**Technical Approach:** Cis-platinum, 75 mg/m<sup>2</sup>, 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<sup>2</sup>, IV bolus on days 1 and 8 and bleomycin, 10 units/m<sup>2</sup>, IV bolus on days 1 and 8. Courses will be repeated every 21 days provided absolute granulocyte count is >1500/ m l 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<sup>2</sup> has been reached.

Two cycles of chemotherapy will constitute an adequate trial. Patients with stable or responding disease will continue on treatment beyond two cycles until evidence of disease progression or unacceptable toxicity. Patients who have achieved a complete remission will discontinue all chemotherapy after six cycles. Patients who achieve a complete response will receive 6 courses of treatment.

**Progress:** No patients entered at MAMC. Group-wide: Nineteen eligible patients have been entered. Six patients have experienced toxicities of Grade 3 or worse (33%).

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 86/072                      **Status:** Completed

**Title:** SWOG 8573: Treatment of Limited Small Cell Lung Cancer with Concurrent Chemotherapy, Radiotherapy, and Intensification with High Dose Cyclophosphamide, Phase II Pilot

**Start Date:** 06/20/86                      **Est. Completion Date:** Jun 89

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC	COL Irwin B. Dabe, MC
MAJ David M. Dunning, MC	CPT David R. Bryson, MC

**Key Words:** cancer:lung:small cell,chemo,radiotherapy,cyclophosphamide

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To estimate the response rate and survival of patients with limited small cell lung cancer when treated with concurrent chemo-radiotherapy followed by chemotherapy and late intensification with high dose cyclophosphamide and to assess the toxicity of this treatment program.

**Technical Approach:** Patients treated previously with chemo or radiotherapy are ineligible, except if radiation was given for localized, controlled skin cancer. Only patients with limited disease will be eligible. Patients will be taken off study for nonresponse or increasing disease after induction therapy, increasing disease at any time, inability to tolerate the lowest prescribed dose of chemotherapy, or to deliver the radiotherapy within the allowable time.

**Induction (days 1-36):**             VP-16, 60 mg/m<sup>2</sup>, days 1-5, 22-26

    CDDP, 50 mg/m<sup>2</sup>, days 1,8,22, & 29

    Chest XRT 4500 rads (180/day) days 1-36

**Consolidation (days 64-92):**    VP-16, 60 mg/m<sup>2</sup>, days 64-66 & 85-87

    CDDP, 50 mg/m<sup>2</sup>, days 64 & 85

    Adriamycin, 50 mg/m<sup>2</sup>, days 64 & 85

    Vincristine, 2 mg, days 64,71,85, and 92

**Late intensification (days 113-141):**    cyclophosphamide 50 mg/kg,  
    days 113-115

    Brain XRT, 3000 rads, 200/day, days 120-141

**Progress:** This study was closed 1 May 88 due to sufficient patient accrual. Three patients were entered at MAMC, all have died of their disease.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 85/073                      **Status:** On-going

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**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 Study, EST  
2382)

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**Start Date:** 08/23/85                      **Est. Completion Date:** May 87

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Howard Davidson, MC

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<b>Associate Investigators:</b>	MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC	COL Irwin B. Dabe, MC
COL William J. Gernon, MC	MAJ Timothy J. O'Rourke, MC
MAJ Michael D. Stone, MC	CPT David R. Bryson, MC
LTC Donald B. Blakeslee, MC	

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**Key Words:** head & neck,surgery,chemotherapy,radiotherapy

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

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**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 cis-platinum 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 at MAMC. One patient is still being followed.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 85/064	<b>Status:</b> On-going
<b>Title:</b> 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		
<b>Start Date:</b> 06/28/85	<b>Est. Completion Date:</b> Apr 87	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
MAJ Jens A. Strand, MC	COL Irwin B. Dabe, MC	
MAJ Michael D. Stone, MC	MAJ Timothy J. O'Rourke, MC	
	CPT David R. Bryson, MC	
<b>Key Words:</b> cancer:colon,levamisole,5-Fluorouracil		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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 entered in previous years with no unexpected toxicities. Data collection is still in progress on several of these patients.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/032	<b>Status:</b> On-going
<b>Title:</b> SWOG 8956: A Phase II Study of Cisplatin and 5-Fluorouracil Infusion for Treatment of Advanced and/or Recurrent Metastatic Carcinoma of the Urinary Bladder		
<b>Start Date:</b> 05/03/91	<b>Est. Completion Date:</b> Jan 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Luke M. Stapleton, MC	MAJ William A. Phillips	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	MAJ Robert L. Sheffler, MC	
MAJ Robert B. Ellis, MC	CPT Jennifer L. Cadiz, MC	
<b>Key Words:</b> cancer:bladder,cisplatin,5-Fluorouracil		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To assess efficacy and feasibility of utilizing cisplatin (CDDP) and 5-fluorouracil infusion (5-FU-I) in patients with advanced and/or recurrent carcinoma of the urinary bladder and to evaluate the toxicity of cisplatin and 5-FU in this group of patients.

**Technical Approach:** Bladder cancer is the sixth most common cancer in the United States, accounting for 10,000 deaths per year. Treatments have been developed which provide 15% long term disease-free survival equated with cure. However, the toxicities have been profound, including treatment related mortalities. As a consequence, this potential less toxic regimen has been devised for evaluation in metastatic bladder cancer. In this study, all patients will receive the same treatment which includes cisplatin on the first day of treatment and continuous infusion of 5-FU on each of the first five days of treatment. These treatments will be repeated every 21 days. Patients' response to treatment will be assessed every other course (every six weeks). The patients will continue on therapy until they have progression of disease.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/109                      **Status:** On-going

**Title:** SWOG 8598: (RTOG-85-01): Prospective Trial for Localized Cancer of the Esophagus: Comparing Radiation as a Single Modality to the Combination of Radiation Therapy and Chemotherapy, Phase III, .....

**Start Date:** 09/18/87                      **Est. Completion Date:** Aug 90

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	MAJ Mark H. Kozakowski, MC
COL Irwin B. Dabe, MC	LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC	MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC	CPT Denis Bouvier, MC
LTC Howard Davidson, MC	

**Key Words:** cancer:esophagus,radiation,chemotherapy

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To determine the role of chemotherapy for a potentially curable subset of patients with squamous cell cancer of the esophagus. Specifically, to determine if the combination of chemotherapy and radiation will add to the overall survival and cure of patients treated with the combination when compared to patients treated by radiation alone. To determine if the patterns of recurrence for patients treated with chemotherapy plus radiation differs from those patients treated with radiation alone.

**Technical Approach:** Patients with squamous cell or adenocarcinoma of the thoracic esophagus, no evidence of disseminated cancer, negative bone scan, and WBC >4,000/mm, platelets >100,000/mm, creatinine <1.5 mg%, BUN <22 mg%, and/or creatinine clearance >60 cc/min are eligible. Patients will be stratified according to weight loss, lesion size, and histology. Patients will be randomized to arms I or II.

(I) Cisplatinum, 75 mg/m<sup>2</sup> the first day of weeks 1, 5, 8, and 11, 5-FU, 1000 mg/m<sup>2</sup> 96-hr continuous fusion, weeks 1, 5, 8 and 11; Radiotherapy, 2 Gy five days a week for three weeks followed by boost of 2 Gy five days a week for five weeks.

(II) 2 Gy for five days a week for five weeks followed by a boost of 2 Gy five days a week for 1.4 weeks If 12 weeks after therapy is completed, tumor remains in the esophagus or there is recurrence, the patient has failed therapy but continues to be followed for survival. Patients with no evidence of tumor upon esophagoscopy and esophagram will be considered response to therapy and followed until relapse or death.

**Progress:** This study was closed to patient entry 1 May 91. One entry at MAMC in FY 90 who is alive and well; one patient was entered in FY 88 and died of his disease 13 months later.



## DETAIL SUMMARY SHEET

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<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/045	<b>Status:</b> On-going
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**Title:** SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia

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<b>Start Date:</b> 02/27/87	<b>Est. Completion Date:</b> Feb 90
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<b>Department:</b> SWOG	<b>Facility:</b> MAMC
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**Principal Investigator:** MAJ Paul C. Sowray, MC

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<b>Associate Investigators:</b> LTC Lauren K. Colman, MC MAJ Thomas M. Baker, MC MAJ Ruben D. Sierra, MC	 COL Irwin B. Dabe, MC LTC Howard Davidson, MC MAJ David M. Dunning, MC CPT David R. Bryson, MC
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**Key Words:** leukemia:non-lymphocytic,Ara-C,daunorubicin,cytosine arabinoside

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90
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**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:** One patient was entered at MAMC in FY 91 for a total of six entries, four have expired from the disease.

Group-wide: 570 eligible patients have been entered. The accrual goal is 600 patients.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 87/110                      **Status:** Completed

**Title:** SWOG 8616: Intergroup Phase III Randomized Study of Doxorubicin and Decarbazine With or Without Ifosfamide and Mesna in Advanced Soft Tissue and Bone Sarcoma (INT #0072)

**Start Date:** 09/18/87                      **Est. Completion Date:** Aug 90

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, MC	COL Irwin B. Dabe, MC
LTC Howard Davidson, MC	MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC	CPT Denis Bouvier, MC

**Key Words:** sarcoma:bone,ifosfamidem,doxorubicin,decarbazine

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To determine if the addition of ifosfamide to doxorubicin and dacarbazine significantly changes the response rate, survival, and toxicity.

**Technical Approach:** Patients with histologically documented metastatic or unresectable sarcoma will be eligible. Metastatic osteogenic (OGS), Ewing's (ES), and rhabdomyosarcoma (RMS) will be assigned to Arm II (doxorubicin/DTIC plus ifosfamide) and will be analyzed separately. Kaposi's sarcoma and mesothelioma will be excluded. Patients will have had no prior chemotherapy for sarcomas and no prior doxorubicin. Patients will be stratified by stage, grade, and radiotherapy history. Patients will be randomized to receive either doxorubicin/DTIC or doxorubicin/DTIC + ifosfamide. Doxorubicin, 15 mg/m<sup>2</sup>, will be given by continuous infusion, Days 1-4. DTIC, 250 mg/m<sup>2</sup>, will be given by continuous infusion, Days 1-4. Ifosfamide, 2500 mg/m<sup>2</sup>, will be given by continuous infusion, Days 1-3. Mesna will be infused continuously Days 1-4 to counteract urotoxicity. Each regimen will be given every 21 days. OGS, ES, and RMS patients will be removed from study and crossed to a standard regimen after four cycles if response is documented. Complete responders will continue combination chemotherapy for six cycles after documentation of response. Partial response and stable disease patients will continue treatment at the highest tolerable dose for a least two cycles after the maximum response or until disease progression. Patients with rapid disease progression will be removed from the study. Otherwise, there will be a minimum of two cycles of chemotherapy before removal.

**Progress:** This protocol was closed to patient entry 1 Jul 90. Four patients were entered at MAMC and all have expired.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/045	<b>Status:</b> On-going
<b>Title:</b> SWOG 8621: Chemohormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III		
<b>Start Date:</b> 03/17/89	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	COL Irwin B. Dabe, MC	MAJ Everardo E. Cobos Jr., MC
CPT Denis Bouvier, MC	MAJ Kenneth A. Bertram, MC	
<b>Key Words:</b> cancer:breast,postmenopausal,chemohormonal therapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$2316.00	<b>Periodic Review:</b> 10/19/90

**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:** This study was closed to patient entry, 1 Aug 91. The Tamoxifen Arm was closed 1 Jul 90. One patient was entered at MAMC in May 91 and is alive and well.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 87/060                      **Status:** Completed

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**Title:** SWOG 8624: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma. (1) Comparison of VMCP/VBAP to VAD or VMCPP/VBAPP for Induction; (2) Alpha-2b Interferon or No Therapy for Maintenance; and (3) Alpha-2b Interferon + Dexamethasone for Incomplete or Non-Responders

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**Start Date:** 03/20/87                      **Est. Completion Date:** Sep 90

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Howard Davidson, MC

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**Associate Investigators:**  
LTC Lauren K. Colman, MC                      COL Irwin B. Dabe, MC  
MAJ David M. Dunning, MC                      MAJ Thomas M. Baker, MC  
CPT David R. Bryson, MC                      MAJ Ruben D. Sierra, MC

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**Key Words:**

myeloma:multiple,chemotherapy,VMCP,VBAP,VAD,VMCPP,VBAPP,alpha-2b interferon

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90
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**Study Objective:** To compare the effectiveness in achieving remission of the three regimens; to determine if interferon alpha-2b prolongs remission duration and survival compared to no maintenance therapy for patients achieving remission; to determine if dexamethasone plus interferon alpha-2b will enable patients achieving only improvement with the chemotherapy induction to achieve remission, and to study various proposed prognostic factors in multiple myeloma.

**Technical Approach:** Agents to be used are Adriamycin (A), BCNU (B), cyclophosphamide (C), dexamethasone (D), melphalan, (M), prednisone (P), vincristine (V), and alpha-2b interferon. Patients previously untreated with chemotherapy with the diagnosis of multiple myeloma are eligible. Patients will be stratified as to tumor mass, prior radiation therapy, and risk category. Patients will be randomized to induction therapy as follows: Arm I VMCP alternating with VBAP every 3 weeks; Arm II VAD every 3 weeks; or Arm III VMCPP alternating with VBAPP every 3 weeks. Induction therapy on arms I and III will be given for a minimum of 9 cycles and a maximum of 18 cycles. Arm II (VAD) induction therapy will be given for a minimum of 6 cycles and a maximum of 9 cycles. Arms I and III will require a minimum of 9 cycles of induction therapy and Arm II a minimum of 6 cycles before beginning maintenance therapy. At the appropriate time, responding patients will be randomized for maintenance to alpha-2b interferon or no maintenance. Evaluable patients failing to achieve 75% tumor regression will be ineligible for remission maintenance but will be registered on a non-randomized trial of dexamethasone plus alpha 2b interferon to determine if this therapy can convert the patient to a remission status.

**Progress:** The study was closed to patient entry 1 Oct 90; no entries at MAMC. Group-wide: 458 patients have been entered. Two patients on the VAD arm died of leukopenia and one died of gastrointestinal bleeding.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/047	<b>Status:</b> Completed
<b>Title:</b> SWOG 8691: A Randomized Comparison of Deoxycoformycin versus Alpha-Interferon in Previously Untreated Patients with Hairy Cell Leukemia		
<b>Start Date:</b> 03/20/87	<b>Est. Completion Date:</b> Feb 90	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
LTC Lauren K. Colman, MC	COL Irwin B. Dabe, MC	
MAJ David M. Dunning, MC	MAJ Thomas M. Baker, MC	
CPT David R. Bryson, MC	MAJ Ruben D. Sierra, MC	
<b>Key Words:</b> leukemia:hairy cell,alpha-interferon,deoxycoformycin		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To compare deoxycoformycin (dCF) versus alpha-interferon ( $\alpha$ -IFN) in terms of relative efficacy in hairy cell leukemia patients who have not had splenectomy and to evaluate toxicities of both.

**Technical Approach:** Patients will be stratified according to performance status and randomized to either Arm I or Arm II.

Arm I:  $\alpha$ -IFN,  $3 \times 10^6$  IU, subcutaneously, 3 times a wk for 6 mon. Complete or partial remissions will continue treatment for 6 more months. Non-responders will be crossed over to dCF. After the second 6 months of treatment, if either a complete or partial remission has been achieved, therapy will be discontinued and the patient will be observed on a monthly basis to document duration of response.

Arm II: dCF, IV, every 2 weeks for 6 months. Performance status 0, 1, or 2 patients will receive  $4 \text{ mg/m}^2$  and status 3 patients will receive  $2 \text{ mg/m}^2$  and escalated as permitted by toxicity. If a complete remission is achieved, 2 additional doses of dCF will be given, treatment will then be stopped and the patient observed at monthly intervals. If a complete or partial remission has not been achieved by 6 months, the patient will be crossed over to the  $\alpha$ -IFN arm. If a partial remission is achieved, dCF will be continued. When a complete remission is documented, 2 additional doses of dCF will be given and then treatment will be stopped. At 12 months on either therapy, if the best response is a partial remission, therapy will be discontinued and the patient will be observed at monthly intervals.

**Progress:** The study was closed to patient entry 1 Oct 90; no entries at MAMC. Group-wide: 325 patients have been entered. There have been no fatal nonhematological toxicities (histological toxicity evaluation is incomplete). In general, flu-like symptoms are more common with IFN, while infections and nausea/vomiting/anorexia are more common with DCF.

**DETAIL SUMMARY SHEET**

**Date:** 30 Sep 91                      **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:** Jun 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**  
MAJ Mark H. Kozakowski, MC                      COL Irwin B. Dabe, MC  
MAJ Kenneth A. Bertram, MC                      MAJ Everardo E. Cobos Jr., MC  
CPT Denis Bouvier, MC

**Key Words:** cancer:breast,surgical oophorectomy,Zoladex,ER,PgR positive

<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**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 assess 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 entered at MAMC. Group-wide: 62 eligible patients have been entered, with slow accrual being a problem.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 87/111	<b>Status:</b> On-going
<b>Title:</b> SWOG 8694 (CALGB 8582): A Comparison of Pentostatin (NSC-218321) and Alpha-Interferon (NSC-377523) in Splenectomized Patients With Active Hairy Cell Leukemia		
<b>Start Date:</b> 08/21/87	<b>Est. Completion Date:</b> Aug 90	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	COL Irwin B. Dabe, MC	LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC	MAJ David M. Dunning, MC	CPT Denis Bouvier, MC
MAJ Ruben D. Sierra, MC		
<b>Key Words:</b> leukemia:hairy cell,pentostatin,alpha-interferon,splenectomized		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To compare the frequency of response between pentostatin and alpha-interferon treatment in patients with hairy cell leukemia who following splenectomy manifest active or progressive disease; to compare time to response, response duration, and toxicity of these two treatments; and to determine if pentostatin salvages nonresponders to alpha-interferon treatment and if alpha-interferon salvages nonresponders to pentostatin treatment.

**Technical Approach:** Patients will have had splenectomy at least 3 months prior to treatment, with no prior treatment with pentostatin or interferon. Patients will be randomized to either interferon or pentostatin.

Interferon ( $2 \times 10^6$  IU/m<sup>2</sup>) will be given by injection (s.c.) 3 times a week. Patients will be assessed at 3 months but will continue interferon treatment. Patients will be assessed at 6 months and those with complete (CR) or partial remission (PR) or stable disease (SD) will continue treatment for 6 months more. Non-responders will be crossed over to pentostatin. Patients will be assessed at 12 months, and those with CR, PR, or SD will be followed with no further therapy. If progression occurs, patients will be retreated with interferon.

Pentostatin, 4 mg/m<sup>2</sup>, will be given IV on days 1 and 15, and repeated every 4 weeks with dosage adjusted for performance status. Patients will be assessed at 3 months and the pentostatin will be reduced to once every 4 weeks. At the 6 month assessment, patients with CR, PR, or SD will continue treatment for 6 more months. Nonresponders will be crossed over to interferon. Patients will be assessed at 12 months and those with CR, PR, or SD will be followed with no further therapy. If progression occurs, patients will be retreated with pentostatin.

**Progress:** No entries at MAMC. Group-wide: Approximate accrual is 86 subjects. No fatal toxicities have been reported.

## DETAIL SUMMARY SHEET

Date: 30 Sep 91

Protocol No.: 89/030

Status: Completed

**Title:** SWOG 8697 (EST 3185; INT 0077): Phase III Combination Chemotherapy of Predominantly Hormone Insensitive Metastatic Breast Cancer: An Evaluation of CAF versus Rotating Regimens of CAF and TSAVBH Induction Therapy Followed by Observation or Maintenance Therapy with CMF(P)TH or CMFH Intergroup

**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

CPT Denis Bouvier, MC

COL Irwin B. Dabe, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Kenneth A. Bertram, MC

**Key Words:** cancer:breast,hormone insensitive,chemotherapy,CAF,TSAVBH

**Accumulative**

**MEDCASE Cost:** \$0.00

**Est. Accumulative**

**OMA Cost:** \$0.00

**Periodic Review:**

10/19/90

**Study Objective:** To investigate the induction efficiency and impact on time to treatment failure and survival of CAF\* vs CAF-TsAVbH\*\* used in a rotating schedule; to investigate the value of CMF(P)TH\*\*\* vs no maintenance treatment in duration of complete response and survival; and to evaluate on-study disease characteristics and patient discriminants with respect to prognostic use of the above objectives.

**Technical Approach:** All patients with ER negative tumors are eligible unless they have responded to prior hormone manipulation therapy. ER positive or ER unknown patients are eligible only if they have had prior therapeutic hormone manipulation and did not respond to this therapy. Patients must have a performance status of 0-3, adequate bone marrow, renal, and hepatic function, and a blood sugar <170 mg/dL. Patients will be stratified by ER status, prior adjuvant therapy (yes vs no); dominant metastatic site; disease free interval; and menopausal status. Patients will be randomized to either CAF for six cycles or to CAF alternating with TsAVbH (three cycles of CAF alternating with three cycles of TsAVbH). Patients with a partial response or stable disease will be registered to receive CMFH\*\*\*\* and those with progressive disease will go off study. Patients with a complete response will be randomized to either CMF(P)TH or to observation. Cycles will be repeated every 29 days until relapse.

**Progress:** The study was closed to patient entry 13 Feb 91. No patients were entered at MAMC.

\*CAF Cytosan, Adriamycin, 5-FU

\*\*TsAVbH thiotepa, Adriamycin, vinblastine, halotestin

\*\*\*CMF(P)TH cyclophosphamide, methotrexate, 5-FU, prednisone, tamoxifen, halotestin

\*\*\*\*CMFH Cytosan, methotrexate, 5-FU, halotestin



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/039	<b>Status:</b> On-going
<b>Title:</b> SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Mar 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC John A. Vaccaro, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Mark H. Kozakowski, MC	
CPT Denis Bouvier, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
<b>Key Words:</b> cancer:bladder,cystectomy,M-VAC		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** In patients with locally advanced bladder cancer: to compare the survival of those treated with cystectomy alone to those treated with M-VAC, followed by cystectomy in a randomized phase III neoadjuvant trial and to quantify the tumor down-staging effect on neoadjuvant M-VAC.

**Technical Approach:** Patients must have a histologically proven diagnosis of T2-T4a, N0, M0 transitional cell carcinoma of the bladder with or without squamous differentiation and with normal organ function documented by careful pretreatment staging, including a pathologic assessment of tumor grade and depth of invasion, within 6 weeks prior to protocol entry. Patients will be randomized to either radical cystectomy (Arm I) or to M-VAC (methotrexate, vinblastine, adriamycin, cisplatin) plus radical cystectomy (Arm 2). Patients will be stratified according to age (>65 years old vs <65 years old) and stage: T2 vs T3, T4a. Patients will be followed every three months for the first year after cystectomy, every six months the second year, and yearly thereafter. Arm II patients will be removed from the study if unacceptable toxicity develops or if there is documented disease progression. Arm I and Arm II patients will be removed from the study if tumor recurs. The primary endpoint for comparison of treatment arms will be survival. The secondary endpoint is to evaluate changes in clinical staging parameters in Arm II patients and, specifically, whether down-staging to pCR, documented from cystectomy specimens, carries any positive survival prognosis in Arm II.

**Progress:** No patients entered at MAMC. Groupwide, the accrual rate continues to be a significant problem since it is below the target accrual rate of 6.2 patients per month.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/084	<b>Status:</b> On-going
<b>Title:</b> SWOG 8719: Evaluations of Didemnin B or Ifosfamide/Mesna in Endocrine Resistant Prostate Cancer and of Ifosfamide/Mesna in Patients Without Prior Endocrine Manipulation, Phase II		
<b>Start Date:</b> 06/15/90	<b>Est. Completion Date:</b> May 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Everardo E. Cobos Jr., MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> cancer:prostate,Didemnin B,Ifosfamide,Mesna,endocrine resistance		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To evaluate the likelihood of response for each regimen in order to assess whether either treatment should be advanced to further studies; to evaluate the qualitative and quantitative toxicities of the regimens; and to explore the response rate, toxicity, and time to progression of patients with no prior or concomitant endocrine treatment who are treated with Ifosfamide/ Mesna for measurable Stage D2 prostatic cancer.

**Technical Approach:** Patients must have a histologically confirmed diagnosis of adenocarcinoma of the prostate and advanced (Stage D2) disease with objective evidence of progression following prior endocrine treatment. Newly diagnosed Stage D2 patients without prior endocrine manipulation will be placed directly on Arm II.

Patients will be randomized to either Arm I (Didemnin B, IV, once every 28 days) or to Arm II (Ifosfamide and Mesna, IV, days 1-5, every 21 days). After two courses of treatment, patients will be evaluated, and will continue on the same arm until progression of disease.

**Progress:** No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 89/031                      **Status:** Completed

**Title:** SWOG 8721: A Phase II Trial of Trimetrexate in the Treatment of Esophageal Cancer

**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:esophagus,trimetrexate

**Accumulative**

**MEDCASE Cost:**

\$0.00

**Est. Accumulative**

**OMA Cost:**

\$0.00

**Periodic Review:**

10/19/90

**Study Objective:** To determine the response rate, response duration, and toxicity of trimetrexate given on a daily x 5 schedule every three weeks to patients with esophageal cancer.

**Technical Approach:** Patients must have a biopsy proven epidermoid carcinoma that is measurable. Patients may have had previous surgical therapy. If patients have had previous radiotherapy, they must have recovered from toxicities of radiotherapy, have demonstrated progressive disease with measurable disease outside of the previous radiation therapy port, and must have received radiotherapy to less than 25% of the bone marrow. Patients must have a performance status of 0-2 and adequate bone marrow, renal, and hepatic function. Patients may not be a candidate for potentially curative resection of tumor nor a candidate for potentially curative radiation therapy. They may not have received more than one prior combination chemotherapy and must not have ascites or pleural effusions.

Patients will receive trimetrexate, IV bolus daily for five days, every three weeks. Treatment with trimetrexate will continue until progression of disease.

**Progress:** The study was closed to patient entry, 1 Sep 91. No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/065	<b>Status:</b> On-going
<b>Title:</b> SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy		
<b>Start Date:</b> 11/18/88	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
CPT Denis Bouvier, MC	COL Irwin B. Dabe, MC	MAJ Steven S. Wilson, MC
MAJ Rahul N. Dewan, MC		
<b>Key Words:</b> lymphoma:non-Hodgkin's,radiotherapy,CHOP,chemotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**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 nonHodgkin'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<sup>2</sup> IV, day 1.

Doxorubicin, 50 mg/m<sup>2</sup> IV, day 1.

Vincristine, 1.4 mg/m<sup>2</sup> IV, day 1

Prednisone 100 mg/day po, days 1-5

**Progress:** One patient was entered in FY 91 for a total of four subjects.

**Group-wide:** 153 eligible patients have been entered with a good balance between the treatment arms. Grades 3 and 4 granulocytopenia or leukopenia have been common.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/076	<b>Status:</b> On-going
<b>Title:</b> 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		
<b>Start Date:</b> 09/16/88	<b>Est. Completion Date:</b> Sep 91	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	COL Irwin B. Dabe, MC	CPT Denis Bouvier, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> cancer:lung:non-small cell,cisplatin,mitomycin-C		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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:

- Arm I: standard dose cisplatin (50 mg/m<sup>2</sup>, IV) every four weeks for a maximum of eight cycles,
- ARM II: high dose cisplatin alone (100 mg/m<sup>2</sup>, IV) every four weeks for a maximum of four cycles,
- ARM III: high dose cisplatin (100 mg/m<sup>2</sup> IV) plus mitomycin-C (8 mg/m<sup>2</sup> 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 protocol was closed to patient entry, 1 Jun 90. Five patients were entered at MAMC. Three have died of the disease.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 05/18/90                      **Est. Completion Date:** Apr 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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

**Key Words:** tumor:germ cell,etoposide,cisplatin,carboplatin,CBDCA

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90
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**Study Objective:** To determine in a randomized trial the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens; etoposide + cisplatin 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 was closed to patient entry 15 Dec 89. One patient was entered at MAMC in FY 90.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/053                      **Status:** Completed

**Title:** SWOG 8791 (INT-0087): Adjuvant Trial of Soft Tissue Sarcomas, Phase III

**Start Date:** 03/16/90                      **Est. Completion Date:** Dec 92

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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

**Key Words:** sarcoma:soft tissue,chemotherapy

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$12000.00	10/19/90

**Study Objective:** To assess whether adjunctive chemotherapy with Adriamycin, DTIC, and Ifosfamide/Mesna can improve the survival and disease-free survival of selected patients with soft tissue sarcomas and to establish a repository of frozen sarcoma tissues to be used for ancillary genetic and flow cytometric analysis.

**Technical Approach:** As a consequence of several studies which show conflicting results as to further treatment after surgery and radiation for local control of the disease, most clinicians advise these patients to either undergo no further therapy or to enter on clinical trials such as this. Since the completion of the aforementioned trials, Ifosfamide has been demonstrated to be an extremely active agent in advanced soft tissue sarcoma. Therefore, it would seem logical to combine this new effective agent with the best alternative old regimen which consists of DTIC and Adriamycin. This combination stands the best chance of showing improvement in survival if used in the adjuvant setting. In this study, patients will receive local treatment and then be randomized to either standard therapy (which is observation) or to combination chemotherapy with Adriamycin, DTIC, Ifosfamide, and Mesna, to be given by continuous infusion in the hospital over 4 days once every 21 days for a total of 6 courses.

**Progress:** This protocol was closed to patient entry, 1 Dec 90. No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/021                      **Status:** On-going

**Title:** SWOG 8792 (EST 2886, INT 0079): Phase III Study of Alfa-nl (Wellferon) as Adjuvant Treatment for Resectable Renal Cell Carcinoma

**Start Date:** 01/15/88                      **Est. Completion Date:** Dec 90

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**  
COL Irwin B. Dabe, MC                      MAJ Thomas M. Baker, MC  
MAJ Ruben D. Sierra, MC                      MAJ David M. Dunning, MC  
COL William D. Belville, MC                      CPT Denis Bouvier, MC

**Key Words:** cancer:renal cell, resectable Alfa-nl, adjuvant treatment

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To assess in a controlled fashion the effectiveness of interferon alfa-nl (Wellferon) as a surgical adjuvant in patients with renal cell carcinoma. Study endpoints will be patient survival and time to recurrence.

**Technical Approach:** Patients must have histologic proof of adenocarcinoma of the kidney where complete resection of the primary tumor has been performed with neither gross nor microscopic evidence of residual disease. The primary kidney cancer must show at least one of the following indicators of poor prognosis: tumor invading perinephric fat; invasion of renal vein or vena cava; regional lymph node metastases, or contiguous metastases resected. Surgical margins must be free of tumor and radical nephrectomy and lymphadenectomy must have been performed. Performance status must be 0 or 1. Patients with prior or concurrent radiotherapy, chemotherapy, or systemic corticosteroid therapy are ineligible. Patients with impaired hepatic or renal function, angina, or active congestive heart failure, and seizure disorders as well as pregnant or lactating females are ineligible. Patients will be randomized to Wellferon or observation following definitive surgery. Adjuvant treatment will be started no later than 30 days after resection of the primary and regional nodes. Patients will be stratified according to modified TNM classification for renal tumors, tumor invasion of neighboring structures, and tumor involving regional nodes. Patients randomized to observation only will be followed at 3, 6, 9, 12, 18, and 24 months and every 6 months thereafter. Patients randomized to observation only will be taken off study on recurrence. Patients on the treatment arm will receive Wellferon as an intramuscular injection daily x 5 days every 3 weeks for a total of 12 cycles (nine months), unless recurrence of renal cell carcinoma is documented or intolerable toxicity occurs. These patients will be followed at 12, 18, and 24 months after entry and at six month intervals thereafter.

**Progress:** No patients entered at MAMC. Group-wide: 171 patients have been entered. There have been no Grade 5 toxicities. One patient experienced a Grade 4 neurologic reaction, two experienced extreme fatigue and became bedridden, and one experienced Grade 4 neutropenia.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/040	<b>Status:</b> On-going
<b>Title:</b> SWOG 8793 (EST-3883): Randomized Phase III Evaluation of Hormonal Therapy versus Observation in Patients with Stage D <sub>1</sub> Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prostate Following Pelvic Lymphadenectomy and Radical Prostatectomy		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Feb 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC John A. Vaccaro, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC
CPT Denis Bouvier, MC		
MAJ Robert L. Sheffler, MC		
<b>Key Words:</b> cancer:prostate,hormonal therapy,lymphadenectomy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To determine the time to progression and survival in patients with histologically confirmed Stage D<sub>1</sub> adenocarcinoma of the prostate, following radical prostatectomy and pelvic lymphadenectomy, treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy; to determine the effect of early hormone therapy on local control of D<sub>1</sub> prostate cancer; to determine whether the effects of hormonal manipulation on progression or patterns of failure are modified by tumor grade, prior TUR, number and grade of involved nodes; to determine if an initially elevated acid phosphatase level predicts a poor response to therapy; to determine whether pretreatment hypogonadism is predictive of a poor response to hormonal therapy; and to evaluate the role of the prostate specific antigen in assessing response, progression, and survival.

**Technical Approach:** Patients must have undergone a radical prostatectomy within 12 weeks prior to randomization and must have no evidence of disease. Patients with a history of previous hormonal, radiation, systemic or intravesical chemotherapy, a history of other neoplasms in the past 5 years, and those previously treated for prostate cancer (except for prostatectomy and/or pelvic lymph node dissection) are ineligible.

Patients will be randomized to hormonal therapy (Zoladex or orchiectomy) or to observation. The treating physician, after consultation with the patient, will determine if the patient receives Zoladex or orchiectomy therapy. Patients randomized to observation, who subsequently progress systemically, will have hormonal management instituted within 6 weeks of systemic progression. Patients randomized to hormonal therapy or who are later put on hormonal therapy will be taken off study if disease progression occurs.

**Progress:** No patients entered at MAMC. Groupwide mild renal toxicity, hot flashes, and neurologic toxicity have been common toxicities.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 89/060	<b>Status:</b> On-going
<b>Title:</b> SWOG 8795 (INT-0094, EST-1888): Randomized Prospective Comparison of Bacillus Calmette-Guerin and Mitomycin-C Therapy and Prophylaxis in Superficial Transitional Cell Carcinoma of the Bladder With DNA Flow Cytometric Analysis. Phase III		
<b>Start Date:</b> 05/19/89	<b>Est. Completion Date:</b> Jun 92	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Everardo E. Cobos Jr., MC		
<b>Associate Investigators:</b>		
COL William D. Belville, MC	COL Irwin B. Dabe, MC	COL Victor J. Kiesling, MC
LTC John A. Vaccaro, MC	LTC Howard Davidson, MC	MAJ Kenneth A. Bertram, MC
MAJ Mark H. Kozakowski, MC		
CPT Denis Bouvier, MC		
<b>Key Words:</b> cancer:bladder,bacillus Calmette-Guerin,DNA,mitomycin-C		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To compare the efficacy of mitomycin-C to that of BCG in preventing recurrence of superficial Stage Ta and T1 transitional cell carcinoma of the bladder and to compare treatments with respect to differences in flow cytometry histogram findings of tumors at the time of recurrence.

**Technical Approach:** Patients must have a diagnosis of Stage Ta or T1 (Grades 1-4) transitional cell carcinoma of the bladder that has been completely resected. Concurrent unresectable carcinoma in situ (CIS) is allowed. Histologic confirmation of the disease must come from a transurethral resection done within 4 weeks prior to registration. A random biopsy done 1-4 weeks prior to registration is required. Patients must be judged to be at increased risk for tumor recurrence as demonstrated by 2 occurrences of tumor within 12 months prior to registration. Patients must not have received any prior systemic chemotherapy. Patients may have had treatment with any intravesical agent other than mitomycin-C or BCG; however, the treatment must not have been within 4 weeks prior to registration. Patients must not have received radiation therapy for treatment of bladder tumor within one year prior to registration. Patients must not have a history of another primary malignancy or CIS at any site other than the bladder. Patients must have adequate bone marrow reserve, adequate renal and liver function, and a performance status of 0-2. Patients will be stratified by CIS involvement: Stage Ta or T1 without concurrent CIS vs Stage Ta or T1 with concurrent CIS. Patients will be randomized to BCG, 50 mg weekly x 6, then at wks 8 and 12 and then monthly for months 4-12 or mitomycin-C, 20 mg on the same schedule. Cystoscopy, cytology, biopsy, and flow cytometry will be done prestudy at 3, 6, 9, and 12 months.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/066	<b>Status:</b> On-going
<b>Title:</b> SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)		
<b>Start Date:</b> 07/15/88	<b>Est. Completion Date:</b> Jun 91	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> CPT Denis Bouvier, MC		COL Irwin B. Dabe, MC
<b>Key Words:</b> Hodgkin's Disease, chemotherapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**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<sup>2</sup> IV, days 1 and 8  
Vincristine, 1.4 mg/m<sup>2</sup> IV, days 1 and 8  
Procarbazine, 100 mg/m<sup>2</sup> PO per day x 14 days  
Prednisone 40 mg/m<sup>2</sup> PO per day x 14 days

**ABVD:** Adriamycin, 25 mg/m<sup>2</sup> IV, days 1 and 15  
Bleomycin, 10 units/m<sup>2</sup> IV, days 1 and 15  
Vinblastine, 6 mg/m<sup>2</sup> IV days 1 and 15  
DTIC, 375 mg/m<sup>2</sup> IV, days 1 and 15

The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m<sup>2</sup> IV, day 8; bleomycin, 10 units/m<sup>2</sup> IV day 8; and vinblastine, 6 mg/m<sup>2</sup> IV, day 8.

**Progress:** The study was closed to patient entry, 1 Aug 89. One patient entered at MAMC (FY 89) is in the followup stage.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 05/18/90                      **Est. Completion Date:** Apr 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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

**Key Words:** lymphoma,alpha-interferon,ProMACE-Mopp,chemo

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**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 histologies. 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:** One patient was entered in this study at MAMC in Jul 91 for a total of two entries. Groupwide, two toxicities have been reported and Grade 4 toxicity was common

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 90/054                      **Status:** On-going

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**Title:** SWOG 8810: Six Courses of 5-Fluorouracil & Cisplatinum with Correlation of Clinical & Cellular DNA Parameters in Patients with Advanced, Untreated, & Unresectable Squamous Cell Carcinoma of the Head and Neck, Phase II, Pilot Study

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**Start Date:** 04/20/90                      **Est. Completion Date:** Mar 93

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** ; MAJ Patrick L. Gomez, MC

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<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ Mark H. Kozakowski, MC
MAJ Everardo E. Cobos Jr., MC	CPT Denis Bouvier, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Michael R. Morris, MC	

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**Key Words:** cancer:head & neck,DNA,5-Fluorouracil,cisplatinum

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$8200.00	10/19/90

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**Study Objective:** To evaluate, following three and six courses of treatment, the likelihood of increased numbers of patients achieving complete response rates when given three additional courses of the same regimen; to evaluate the qualitative and quantitative toxicities of 5-fluorouracil and cisplatinum following three and six courses of treatment; and to evaluate by serial biopsy and flow cytometry the correlation of the cellular DNA parameters of degree of aneuploidy (DNA index) and proliferative activity (SPF) with the patients clinical characteristics, tumor morphology, cytotoxic response, disease free interval, and survival.

**Technical Approach:** Patients must have a histologically confirmed diagnosis of advanced unresectable squamous cell carcinoma of the head and neck, Stage IV, and not be eligible for SWOG protocol of higher priority. Nasopharyngeal primary tumor will be excluded. Biopsy specimens for flow cytometry will be taken before treatment. Patients will be treated with three courses of 5-FU and cisplatinum combination chemotherapy. Patients achieving a partial response or complete response will continue for an additional three courses of therapy. Patients who have no response after three courses will be taken off study and a biopsy will be taken for flow cytometry. Patients will have a triple endoscopy and re-biopsy of the primary site and lymph nodes for flow cytometry analysis within four weeks of completion of treatment following the full six courses of therapy or at any time that disease recurs. All patients will be followed until death.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 07/28/89

**Est. Completion Date:** Jun 92

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

**Associate Investigators:**

LTC Howard Davidson, MC

MAJ Kenneth A. Bertram, MC

MAJ Mark H. Kozakowski, MC

COL Irwin B. Dabe, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

**Key Words:** cancer:lung:small cell,chemo,radiotherapy,GM-CSF,interferon

**Accumulative  
MEDCASE Cost:**

\$0.00

**Est. Accumulative  
OMA Cost:**

\$0.00

**Periodic Review:**  
10/19/90

**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:** Two patients were entered at MAMC in FY 91 for a total of three entries. One patient has died from his disease. This study was temporarily closed in November 1989 due to excessive toxicity and reopened in December 1989 with reduced doses of CDDP and VP-16.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 10/20/89                      **Est. Completion Date:** Sep 99

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

<b>Associate Investigators:</b>	MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC

**Key Words:** cancer:breast,chemoendocrine therapy,CAF,tamoxifen

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$8692.00	10/19/90

**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:** Three patients were entered at MAMC, all in FY 90.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 05/02/91                      **Est. Completion Date:** Nov 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	MAJ William A. Phillips
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** mycosis fungoides, retinoic acid, interferon-A

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To evaluate the response rate of mycosis fungoides treated with the drug combination of 13-cis retinoic 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,  $3 \times 10^6$   $\mu\text{g}/\text{m}^2$  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:** No patients entered at MAMC.



## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC	MAJ Patrick L. Gomez, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Robert L. Sheffler, MC
MAJ Robert B. Ellis, MC	MAJ Richard Tenglin, MC
CPT Jennifer L. Cadiz, MC	CPT James Hu, MC
MAJ Kenneth A. Bertram, MC	

**Key Words:** lymphoma:tissue procurement

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**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:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/041                      **Status:** On-going

**Title:** SWOG 8828: A Phase II Trial of Carboplatin (CBDCA) in Relapsed or Refractory Acute Myeloid Leukemia

**Start Date:** 02/16/90                      **Est. Completion Date:** Feb 92

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

**Associate Investigators:**

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

**Key Words:** leukemia:myeloid,carboplatin,CBDCA

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To evaluate the complete remission rate of carboplatin (CBDCA) in patients with relapsed or refractory acute myeloid leukemia (AML); to assess the qualitative and quantitative toxicities of these patients; and to identify the pattern of treatment failure by the criteria of Preisler.

**Technical Approach:** Patients must have a bone marrow aspiration and biopsy demonstrating AML with FAB subtype M1-M7. Patients must be in relapse or must have had a treatment failure of Preisler type 1 or 2 on the most recent induction attempt. Patients must have received only one prior remission induction regimen for AML. Patients with prior CML or myelodysplastic syndrome or those who have received prior radiotherapy or chemotherapy for non-AML conditions are ineligible.

**Induction:** Carboplatin, 300 mg/m<sup>2</sup>/day continuous intravenous infusion daily for 5 days.

**Second induction course:** If the bone marrow on Day 21 shows >10% blasts and cellularity >30%, patients will be treated with carboplatin 300 mg/m<sup>2</sup>/day continuous intravenous infusion daily for 5 days beginning Day 22.

Patients who do not achieve a remission after two induction courses will be removed from protocol treatment.

**Consolidation:** If A-1 marrow is achieved: carboplatin 210 mg/m<sup>2</sup>/day continuous intravenous infusion daily for 5 days. Patients will receive only one consolidation course.

There will be no maintenance treatment.

Patients will be removed from the protocol at any time unacceptable toxicity occurs.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/027	<b>Status:</b> On-going
<b>Title:</b> SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor-Positive Breast Cancer--Intergroup		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Dec 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:breast,chemotherapy,chemohormonal therapy,premenopausal		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$8200.00	<b>Periodic Review:</b> 10/19/90

**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:** Two patients were entered in this study in FY 91 for a total of three entries.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 90/047                      **Status:** On-going

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**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

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**Start Date:** 03/16/90                      **Est. Completion Date:** Mar 98

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Howard Davidson, MC

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**Associate Investigators:** None

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**Key Words:** cancer:breast,DNA,cytometry,postmenopausal

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<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90
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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: Two patients were entered at MAMC; both in FY 91.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/067	<b>Status:</b> On-going
<b>Title:</b> SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> June 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Robert L. Sheffler, MC	MAJ Everardo E. Cobos Jr., MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> cancer:head & neck,cytometry,DNA		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	//

**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 been entered in this study at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/028                      **Status:** On-going

**Title:** SWOG 8857: Alternating Cisplatin/VP-16 with Continuous CAV and Consolidation Chemotherapy for Extensive Small Cell Lung Cancer with PCI for Complete Responders

**Start Date:** 01/19/90                      **Est. Completion Date:** Nov 92

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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

**Key Words:** cancer:lung:small cell,chemotherapy,PCI,CAV,cisplatin,

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To assess response rate, especially rate of complete response (CR), and toxicity of a dose-intensive approach to induction chemotherapy in which cisplatin/VP-16 is alternated with cyclophosphamide, adriamycin, and vincristine; consolidation therapy will be given to responders with one cycle of each induction regimen, coupled with prophylactic brain irradiation in CR patients; and to measure survival in patients so treated.

**Technical Approach:** All patients must have extensive disease (Stage 4 by the international staging system).

**Regimen A:**            Cisplatin 50 mg/m<sup>2</sup> days 1 and 8 (IV)  
                         VP-16 50 mg/m<sup>2</sup>/day for 14 days (PO)

**Regimen B:**            Cytoxan 60 mg/m<sup>2</sup>/day for 21 days (PO)  
                         Adriamycin 20 mg/m<sup>2</sup>/week for 3 weeks (IV)  
                         Vincristine 2 mg on day 1 of cycle (IV)

Patients will be entered on Regimen A, followed by a two week rest period. They will then be entered on Regimen B, which will be followed by a one week rest period. Regimen A will be repeated at weeks 9 and 24. Regimen B will be repeated at weeks 13 and 28.

Patients will be restaged after completion of the second cycle of Regimen B (week 17).

Patients who have a clinical CR by week 17 at restaging will be administered prophylactic whole brain irradiation on week 24. For patients presenting with brain metastases, radiation will be given on day 1 rather than beginning at day 162 (week 24).

Patients with progression of disease or unacceptable toxicity will be removed from the study. All patients will be followed until death.

**Progress:** This study was closed to patient entry, 15 May 91. One patient was entered in FY 91 at MAMC for a total of three entries; two have died of their disease.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/055	<b>Status:</b> On-going
<b>Title:</b> SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III		
<b>Start Date:</b> 04/20/90	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Everardo E. Cobos Jr., MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
MAJ Michael R. Morris, MC		
<b>Key Words:</b> cancer:nasopharyngeal,5-Fluorouracil,cisplatin,radiotherapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$3900.00	<b>Periodic Review:</b> 10/19/90

**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 entered at MAMC in FY 91.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 90/086                      **Status:** On-going

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**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

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

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** LTC Howard Davidson, MC

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**Associate Investigators:**

MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC
LTC John A. Vaccaro, MC	MAJ Robert L. Sheffler, MC

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**Key Words:** cancer:prostate,orchiectomy,flutamide

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

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**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:** One patient has been entered at MAMC in FY 91 for a total of two entries. Group-wide, the study has accrued rapidly with an average of 31 patients per month.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/029	<b>Status:</b> On-going
<b>Title:</b> 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...		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jan 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:breast,chemotherapy,endocrine therapy		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$5000.00	<b>Periodic Review:</b> 10/19/90

**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:** One patient was entered at MAMC in FY 91 for a total of four entries. Groupwide over 800 patients have been entered. Grade 4 toxicities include granulocytopenia and nausea on the CMF arms; granulocytopenia, leukopenia, vomiting, and stomatitis on the CAF arms.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91      **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 Selected Patients with Duke's B and C Colon Cancer

**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      COL Irwin B. Dabe, MC  
MAJ Kenneth A. Bertram, MC      CPT Denis Bouvier, MC  
MAJ Everardo E. Cobos Jr., MC

**Key Words:** cancer:colon,resection,chemotherapy,leucovorin,levamisole

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$50.00	10/19/90

**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<sup>2</sup> + 5-FU 425 mg/m<sup>2</sup>; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses
  - (3) Leucovorin 500 mg/m<sup>2</sup> + 5-FU 600 mg/m<sup>2</sup>; 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); no new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

**Progress:** Four patients entered at MAMC in FY 91 for a total of thirteen subjects. One patient has died of the disease.

Groupwide: 471 subjects accrued with no unexpected toxicities.

## DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 91/088                      **Status:** On-going

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**Title:** SWOG 8900: A Phase II Pilot of VAD and VAD/Verapamil for Refractory Multiple Myeloma

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**Start Date:** 08/02/91                      **Est. Completion Date:** Aug 94

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** MAJ Paul C. Sowray, MC

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<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Robert B. Ellis, MC	MAJ Richard Tenglin, MC
CPT Jennifer L. Cadiz, MC	CPT James Hu, MC
MAJ Patrick L. Gomez, MC	

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**Key Words:** myeloma, Verapamil, VAD

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

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**Study Objective:** To estimate the response rate and response duration with chemotherapy alone (VAD) and chemotherapy plus the chemomodifier, Verapamil (VAD/V), in patients who have failed previous combination chemotherapy; to investigate the toxicities of these two treatments; and to evaluate the presence and prognostic significance of Ki-67 and P-glycoprotein in multiple myeloma.

**Technical Approach:** Patients with refractory multiple myeloma have a high response rate to continuous infusion of Vincristine and Adriamycin with Dexamethasone. However, patients often develop what is termed multiple drug resistance which is a way that the cancer cells have of rapidly excreting chemotherapeutic agents from the cell. In this study, patients will be randomized to either VAD (standard therapy) or VAD plus Verapamil since Verapamil has been shown to overcome the multiple drug resistance on some occasions. Both regimens will be given every 21 days. Patients will be stratified by the following variables: tumor mass status, risk category, prior vincristine/adriamycin, response to previous therapy, number of prior treatments. For patients with response to therapy or stable disease, therapy will be given for a maximum of 18 cycles. Patients with disease progression will be taken off study.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/030                      **Status:** On-going

**Title:** SWOG 8905: Phase II/III Study of Fluorouracil and Its Modulation in  
Advanced Colorectal Cancer

**Start Date:** 01/19/90                      **Est. Completion Date:** Jun 92

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

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

**Key Words:** cancer:colorectal,5-Fluorouracil,leucovorin,PALA

Accumulative	Est. Accumulative	Periodic Review:
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$20780.00	10/19/90

**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:** One patient was entered at MAMC in FY 91.

**DETAIL SUMMARY SHEET**

**Date:** 30 Sep 91                      **Protocol No.:** 90/065                      **Status:** On-going

**Title:** SWOG 8906: Evaluation of Merbarone in Hepatoma, Phase II

**Start Date:** 05/15/90

**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

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

**Key Words:** hepatoma,merbarone

**Accumulative**

**MEDCASE Cost:**

\$0.00

**Est. Accumulative**

**OMA Cost:**

\$0.00

**Periodic Review:**

10/19/90

**Study Objective:** To evaluate the response rate and response duration of hepatomas treated with merbarone, given as a five day continuous intravenous infusion, every 21 days, and to evaluate the qualitative and quantitative toxicities of merbarone administered on this schedule.

**Technical Approach:** All patients must have a histologically proven diagnosis of hepatoma. Patients will receive treatment as stated above. While the patient is receiving merbarone, objective disease status will be assessed every six weeks. Patients will continue treatment with merbarone until progression of disease or unacceptable toxicity requiring discontinuation of chemotherapy. Patients will be followed until death.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/087	<b>Status:</b> On-going
<b>Title:</b> SWOG 8910: Evaluation of Low Dose Continuous 5-Fluorouracil (5-FU) and Weekly Cisplatinium (CCDP) in Advanced Adenocarcinoma of the Stomach		
<b>Start Date:</b> 06/15/90	<b>Est. Completion Date:</b> Jun 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Everardo E. Cobos Jr., MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
CPT Denis Bouvier, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
<b>Key Words:</b> cancer:stomach,5-Fluorouracil,cisplatinium		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**Study Objective:** To evaluate response to low dose continuous 5-FU and weekly cisplatinium in patients with advanced adenocarcinoma of the stomach and to assess the qualitative and quantitative toxicities of this regimen.

**Technical Approach:** Patients must have a histologically confirmed diagnosis of advanced gastric adenocarcinoma which is objectively measurable. Patients may not have CNS metastases. Patients may not have had prior chemotherapy but may have received prior immunotherapy. Patients who have had prior surgery and radiotherapy are eligible as long as they have recovered from associated toxicities and complications. Patients will be classified by performance status: 0-1 vs 2. Patients will be given a continuous infusion of 5-FU daily plus cisplatinium weekly for 8 weeks, then every other week. At eight weeks, patients with complete or partial response or stable disease will continue treatment until disease progression. Patients with disease progression at eight weeks will go off study.

Twenty patients will be accrued. If three, four, or five responses are seen, an additional 15 patients will be accrued.

**Progress:** No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/110	<b>Status:</b> On-going
<b>Title:</b> SWOG 8915: A Phase II Study of 6-Thioguanine Administered as 120 Hour Continuous Infusion for Refractory or Recurrent Small Cell Carcinoma		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Apr 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Everardo E. Cobos Jr., MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> cancer:small cell,6-thioguanine,continuous infusion		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To assess the response rate of 6-thioguanine and the qualitative and quantitative toxicities of this drug administered as a 120 hour continuous infusion in patients with refractory (progression while on treatment) or recurrent small cell lung cancer.

**Technical Approach:** Patients must have recurrent or refractory small cell lung cancer after treatment with one first line combination chemotherapy regimen. Patients must not have received more than one prior treatment regimen. Limited disease patients must have also failed prior radiotherapy. All patients must have measurable disease. Patients must have adequate renal and hepatic function and a SWOG performance status of 0-2. Patients will be classified by performance status: 0-1 vs 2. A course of 6-thioguanine will consist of a 120 hour infusion followed by a rest period of four weeks. Patients will be treated with 35 mg/m<sup>2</sup>/day on days 1-5, every 35 days. Patients may not receive concurrent hormonal, biologic, or cytotoxic therapy or concurrent palliative radiation therapy to the measurable lesions being followed for response. Treatment will continue until progression of disease. The accrual rate is anticipated to be 24 patients per year. Thus the study should be completed in about 15 months from activation.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/066                      **Status:** Completed

**Title:** SWOG 8916: Evaluation of Merbarone in Pancreatic Adenocarcinoma, A Phase II Study

**Start Date:** 05/18/90

**Est. Completion Date:** Apr 93

**Department:** SWOG

**Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

**Associate Investigators:**

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

LTC Howard Davidson, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

**Key Words:** cancer:pancreatic,merbarone

**Accumulative**

**MEDCASE Cost:**

\$0.00

**Est. Accumulative**

**OMA Cost:**

\$0.00

**Periodic Review:**

10/19/90

**Study Objective:** To evaluate the response rate and response duration in pancreatic adenocarcinoma treated with merbarone given as a five day continuous intravenous infusion, every 21 days and to evaluate the qualitative and quantitative toxicities of merbarone administered on this schedule.

**Technical Approach:** Patients must have a pathologically verified diagnosis of adenocarcinoma of the exocrine pancreas that is advanced, recurrent, or progressive, and not amenable to surgery or radiotherapy.

Merbarone will be given 1000 mg/m<sup>2</sup> IV continuous infusion days 1-5, every 21 days. While the patient is receiving merbarone, objective disease status will be assessed every six weeks. Patients will continue treatment with merbarone until progression of disease or unacceptable toxicity. All patients will be followed to death.

**Progress:** This study was closed to patient entry, 15 Jun 91. No patients were entered at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/111	<b>Status:</b> Completed
<b>Title:</b> SWOG 8921: Phase II Trials of Cyclophosphamide/IL2, DTIC/IL2, and DTIC/Cisplatinum/Tamoxifen in Stage IV Melanoma		
<b>Start Date:</b> 10/19/90	<b>Est. Completion Date:</b> Sep 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ William A. Phillips	LTC Howard Davidson, MC	
MAJ Luke M. Stapleton, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Everardo E. Cobos Jr., MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> melanoma,IL2,cyclophosphamide,cisplatinum,tamoxifen,DTIC		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To evaluate the response rates and assess the qualitative and quantitative toxicities associated with each of the three regimens: cyclophosphamide (CTX) and IL-2; dacarbazine (DTIC) and IL-2; and DTIC, cisplatin (CDDP), and tamoxifen (TAM).

**Technical Approach:** Patients must have histologically proven Stage IV malignant melanoma which is measurable. Patients must not have symptomatic pleural effusions or ascites. Patients must have had no prior chemotherapy or IL-2 therapy for Stage IV disease. Patients may have received other prior immunotherapy for Stage IV disease, adjuvant therapy for melanoma (not including IL-2, DTIC, or cisplatin), or prior surgery and/or radiation therapy provided 21 days have elapsed since the completion of treatment and they have recovered from all side effects. Patients who have received prior adjuvant therapy that included IL-2, DTIC, or cisplatin are eligible provided relapse did not occur while the patient was on treatment and at least six months have elapsed since the end of treatment. Patients will be stratified by sites of active disease (skin and/or lymph nodes only versus any other sites), performance status, and prior treatment for disseminated disease.

The treatment regimens are not designed to be compared in a randomized fashion but rather as three simultaneously evaluable treatment regimens. Arm I utilizes cyclophosphamide and IL-2 given every three weeks until maximum response. Arm II utilizes DTIC and IL2 given every four weeks. Both Arms I and II are using IL-2 in a fashion designed to minimize toxicity and allow the drugs to be given as an outpatient. Arm III utilizes DTIC and cisplatin, given every three weeks in conjunction with tamoxifen, given daily. Treatment on Arms II and III is given until disease progression.

**Progress:** This study was closed to patient entry, 1 Sep 91. No patients were entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/088	<b>Status:</b> On-going
<b>Title:</b> SWOG 8923: "Neo-Fac" for Poor Prognosis Stage IV Breast Cancer, A Phase II Pilot Study		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b> Apr 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	LTC Howard Davidson, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> cancer:breast,Neo-Fac		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To assess complete response and toxicity of a dose-intensive approach to treatment of metastatic breast cancer with a combination of daily oral Cytoxan, weekly Adriamycin, and 5-FU by continuous infusion on a low-dose continuous basis, followed by weekly Methotrexate; and to measure time to treatment failure and survival in patients so treated.

**Technical Approach:** Patients must have histologically confirmed diagnosis of breast cancer with recurrent or metastatic disease with at least one measurable or evaluable site. Patients may have had no prior chemotherapy for disseminated or recurrent breast cancer. Prior adjuvant chemotherapy is permitted, if it was completed.

Patients will be stratified according to ER+ vs ERvs ER unknown; Pgr+ vs PgRvs PgR unknown; prior adjuvant chemotherapy; prior hormonal therapy, performance status, and brain metastases.

Patients will be treated with 5-FU given on a continuous basis via an ambulatory pump through a permanently placed central venous catheter. In addition, patients will receive Adriamycin once a week, Cytoxan pills daily, and Prednisone pills daily for seven weeks. If more than 25 weekly doses of Adriamycin are needed, the Adriamycin will be changed to weekly Methotrexate. Once the patient progresses, this chemotherapy regimen will be discontinued and an alternate treatment plan determined by the primary physician.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/031	<b>Status:</b> Completed
<b>Title:</b> SWOG 8926: Evaluation of Low Dose Continuous Infusion 5-Fluorouracil in Patients with Advanced and Recurrent Renal Cell Carcinoma		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jan 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	LTC Howard Davidson, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:renal cell,5-Fluorouracil		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To evaluate the likelihood of response in order to assess whether low dose continuous infusion 5-FU should be advanced to further studies and to assess the qualitative and quantitative toxicities.

**Technical Approach:** Patients not eligible for higher priority SWOG studies with histologically proven renal cell carcinoma, which is advanced and/or recurrent, are eligible for this study. Patients may not have received prior cytotoxic chemotherapeutic regimens. No prior malignancy is allowed except for adequately treated basal cell skin cancer or other cancer for which the patient has been disease-free for five years.

Patients will receive 5-FU, 300 mg/m<sup>2</sup>/day, IV by continuous infusion via a semi-permanent infusion device. Patients will also receive pyridoxine, 150 mg PO daily. Patients will be examined and graded weekly for subjective/objective evidence of developing toxicities according to the SWOG toxicity criteria. Patients will be assessed every four weeks for disease response. Patients with a complete or partial response or stable disease will continue on treatment for six months. Patients with progressive disease or unacceptable toxicity will be taken off study. Patients who develop an intercurrent illness which would affect assessments of clinical status to a significant degree or require discontinuation of the drug will also be taken off study. If there is tumor progression at any time following the six months of treatment and response, therapy may be reinstated.

**Progress:** This study was closed to patient entry, 15 Feb 91. There were no patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 90/112                      **Status:** On-going

**Title:** SWOG 8931 (EST-3189): Phase III Comparison of Cyclophosphamide, Doxorubicin, and 5-Fluorouracil (CAF) and 1 16-Week Multi-drug Regimen as Adjuvant Therapy for Patients with Hormone Receptor Negative..

**Start Date:** 10/19/90                      **Est. Completion Date:** Sep 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ William A. Phillips	MAJ Patrick L. Gomez, MC
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** cancer:breast,cyclophosphamide,doxorubicin,5-Fluorouracil

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	10/19/90

**Study Objective:** To compare disease-free and overall survival and toxicities in node positive receptor-negative breast cancer patients receiving adjuvant CAF or a 16-week multidrug chemotherapy regimen.

**Technical Approach:** Patients must be female and must have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma, and must have one or more pathologically involved axillary nodes. Prior malignancies are limited to a curatively treated basal or squamous cell carcinoma of the skin, carcinoma in situ of the cervix, or other cancer if the patient has been disease-free > five years. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible.

Patients will be stratified by the number of positive axillary nodes, menopausal status, and pathologic size of the primary tumor at the largest dimension. Patients will be randomized to CAF (cyclophosphamide, doxorubicin, and 5-FU), given every 28 days for six cycles or a 16-week multidrug regimen: cyclophosphamide, doxorubicin, vincristine, methotrexate, 5-FU (600 mg/m<sup>2</sup>), and leucovorin, given weeks 1, 3, 5, 7, 9, 11, 13, and 15, with 5-FU, 300 mg/m<sup>2</sup>, given on alternate weeks.

**Progress:** No patients entered at MAMC.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 91/005		<b>Status:</b> Completed							
<b>Title:</b> SWOG 8932: Evaluation of Piroxantrone in Patients with Recurrent and Metastatic Squamous Cell Carcinoma of the Head and Neck, Phase II											
<b>Start Date:</b> 04/05/91			<b>Est. Completion Date:</b> Oct 93								
<b>Department:</b> SWOG			<b>Facility:</b> MAMC								
<b>Principal Investigator:</b> ; MAJ Patrick L. Gomez, MC											
<b>Associate Investigators:</b>											
MAJ Paul C. Sowray, MC		LTC Howard Davidson, MC									
MAJ Luke M. Stapleton, MC		MAJ William A. Phillips									
MAJ Robert L. Sheffler, MC		MAJ Everardo E. Cobos Jr., MC									
CPT Jennifer L. Cadiz, MC		MAJ Robert B. Ellis, MC									
				MAJ John H. McGath, MC							
<b>Key Words:</b> cancer;head & neck,piroxa <tr><td colspan="2"><b>Accumulative MEDCASE Cost:</b> \$0.00</td><td colspan="2"><b>Est. Accumulative OMA Cost:</b> \$0.00</td><td colspan="2"><b>Periodic Review:</b> //</td></tr>						<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> //	
<b>Accumulative MEDCASE Cost:</b> \$0.00		<b>Est. Accumulative OMA Cost:</b> \$0.00		<b>Periodic Review:</b> //							

Study Objective: To assess the response rate of patients with recurrent and metastatic squamous cell carcinoma of the head and neck to treatment with Piroxantrone and to evaluate the toxicities of Piroxantrone in this patient population.

Technical Approach: Piroxantrone is a compound, whose mechanism of action is incompletely understood, that has demonstrated a broad spectrum of activity in experimental tumor systems. It most likely involves DNA binding with induction of strand breaks and inhibition of DNA, RNA, and protein synthesis. Based on prior Phase I clinical trials, the starting dose of this Phase II trial will be 150 mg/m<sup>2</sup>, repeated every 21 days for patients with no prior treatment and a starting dose of 120 mg/m<sup>2</sup> repeated every 21 days for patients with prior treatment. Patients with squamous cell carcinoma of the head and neck region that has persisted or recurred despite surgery or radiation, as well as those with newly diagnosed metastatic disease are eligible for this study.

Progress: No patients entered at MAMC. The protocol was closed to patient entry on 15 Jul 91.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/076                      **Status:** On-going

**Title:** SWOG 8936: Evaluation of Piroxantrone in Gastric Carcinoma, Phase II

**Start Date:** 07/12/91                      **Est. Completion Date:** July 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ William A. Phillips	MAJ Luke M. Stapleton, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** cancer:gastric,piroxantrone

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To assess the response rate and response duration of gastric carcinoma treated with Piroxantrone and to evaluate the qualitative and quantitative toxicities of Piroxantrone administered in a Phase II study.

**Technical Approach:** Once advanced gastric carcinoma occurs or is deemed surgically unresectable, it is an incurable disease. In this study, patients must have a histologically proven diagnosis of adenocarcinoma of the stomach with gross unresectable residual disease (locally advanced or metastatic). Patients may not have had prior chemotherapy, hormonal therapy, or biologic response modifier therapy. All patients will receive the investigational drug, Piroxantrone, to be given once every three weeks and continued indefinitely until the tumor progresses. The study is designed to permit termination of patient accrual after the first 20 patients in the event that extreme results (either positive or negative) are observed. If such extreme results are not observed, a maximum of 35 patients will be studied unless undue toxicity or other medical considerations warrant termination.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 90/042	<b>Status:</b> Completed
<b>Title:</b> SWOG 8943: Evaluation of Merbarone in Advanced Soft Tissue Sarcomas, Phase II		
<b>Start Date:</b> 02/16/90	<b>Est. Completion Date:</b> Feb 91	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	LTC Howard Davidson, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> sarcoma:soft tissue,merbarone		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> 10/19/90

**Study Objective:** To assess the response rate of advanced soft tissue sarcomas treated with Merbarone and to evaluate the qualitative and quantitative toxicities of Merbarone administered in a Phase II Study.

**Technical Approach:** Patients must have histologic diagnosis of unresectable or metastatic soft tissue sarcoma. Ineligible histologies include Kaposi's sarcoma, Ewing's sarcoma, lymphoma, and extraskeletal chondrosarcoma. Patients must not have received more than one prior biologic or chemotherapy regimen and must have been off previous chemotherapy or radiation therapy for at least 4 weeks.

Patients will be stratified by performance status (0-1 vs 2); prior chemotherapy regimens (0 vs 1); prior biologic regimens (0 vs 1); and prior radiotherapy (yes vs no).

Patients will be treated with Merbarone, 1000 mg/m<sup>2</sup>, IV, continuous infusion on days 1-5, repeated every 21 days, with disease assessment every 6 weeks. Patients with complete response, partial response, or stable disease will continue this treatment until progression of disease or unacceptable toxicity occur.

**Progress:** This study was closed to patient entry, 1 Jul 91. No patients were entered at MAMC. Toxicity has been mild to moderate.

### DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** Aug 95

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC	MAJ Patrick L. Gomez, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Robert L. Sheffler, MC
MAJ Robert B. Ellis, MC	MAJ Richard Tenglin, MC
CPT Jennifer L. Cadiz, MC	CPT James Hu, MC
MAJ Kenneth A. Bertram, MC	

**Key Words:** lymphoma:serum repository

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	/  /

**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:** One patient from SWOG protocol 8736 was registered on this study.



### DETAIL SUMMARY SHEET

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**Date:** 30 Sep 91                      **Protocol No.:** 91/006                      **Status:** On-going

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**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

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**Start Date:** 04/05/91                      **Est. Completion Date:** May 93

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**Department:** SWOG                      **Facility:** MAMC

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**Principal Investigator:** MAJ William A. Phillips

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<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ Patrick L. Gomez, MC
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

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**Key Words:** Hodgkin's disease, ABVD, MOPP, ABV Hybrid

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<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

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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 entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 04/05/91                      **Est. Completion Date:** Oct 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Patrick L. Gomez, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ William A. Phillips
MAJ Luke M. Stapleton, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	

**Key Words:** cancer:head & neck,radiotherapy,cisplatin,5-Fluorouracil

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$9130.00	//

**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<sup>2</sup>, 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<sup>2</sup>, day 1 every 21 days for three courses and 5-FU, 1000 mg/m<sup>2</sup>, days 1-14 every 21 days for three courses.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/021	<b>Status:</b> On-going
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**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 .....

<b>Start Date:</b> 04/05/91	<b>Est. Completion Date:</b> Nov 93
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<b>Department:</b> SWOG	<b>Facility:</b> MAMC
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**Principal Investigator:** MAJ William A. Phillips

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ Luke M. Stapleton, MC
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC	COL Joseph F. Homann, MC

**Key Words:** cancer:colorectal,resection,chemotherapy,liver

<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //
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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 whether 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 surgery 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<sup>2</sup>/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<sup>2</sup>/day IV continuously for 14 days and repeated every 28 days for eight more cycles.

Progress: No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 04/20/90                      **Est. Completion Date:** Mar 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

**Associate Investigators:**

MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC
LTC John A. Vaccaro, MC	MAJ Robert L. Sheffler, MC

**Key Words:** cancer:testicular,chemotherapy,cisplatin,bleomycin,ifosfamide

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$12862.00	10/19/90

**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.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/022	<b>Status:</b> Completed
<b>Title:</b> SWOG 8999: Evaluation of Radiation Treatment Following Surgical Resection of Solitary Brain Metastasis, Phase II		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b> Nov 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> ; MAJ Luke M. Stapleton, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	MAJ William A. Phillips	MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC	MAJ Robert L. Sheffler, MC	
MAJ Robert B. Ellis, MC	CPT Jennifer L. Cadiz, MC	
<b>Key Words:</b> brain:metastasis,radiation,resection		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To evaluate the response rate, duration of response, neurological improvement and survival of patients with solitary brain metastasis treated with surgery and radiation therapy; to look at patterns of failure; and to assess the possibility of conducting a future randomized, phase III study.

**Technical Approach:** A significant number of solid tumors result in central nervous system (CNS) metastases, in particular non-small cell carcinoma of the lung. While radiation therapy to the whole brain has been a standard approach, several studies suggest benefit to surgical resection of solitary brain metastases. Patients will be stratified by either non-small cell bronchogenic tumor and no other metastases other than solitary brain or other than non-small cell bronchogenic tumor with solitary brain metastasis. Non-small cell bronchogenic will be further stratified by no evidence of primary disease or recurrent or persistent primary disease. All patients will receive surgical resection followed by whole brain radiation therapy consisting of 4,000 rads in 16 fractions plus a boost dose of 250 rads/fraction times four to the tumor site for a total of 5,000 rads in four weeks. Once treatment is completed, patients will be followed at two month intervals. The appropriate blood counts, chemistry, and radiologic studies to monitor the systemic treatment of primary disease will be performed at the discretion of the individual investigator.

**Progress:** This protocol was closed to patient entry, 15 Dec 90. No patients were entered at MAMC.

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/094	<b>Status:</b> On-going
<b>Title:</b> SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary		
<b>Start Date:</b> //	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, MC	MAJ Luke M. Stapleton, MC	
MAJ Robert B. Ellis, MC	MAJ Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard Tenglin, MC	
	CPT James Hu, MC	
<b>Key Words:</b> cancer:leukemia,cytogenetic studies		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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. Marrow specimens will be submitted whenever possible, unless the 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 one protocol. Data will be collected by major categories of leukemia: first line AML, 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.

DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/095	<b>Status:</b> On-going
<b>Title:</b> SWOG 9012: Evaluation of Low Dose Alpha-Interferon in Patients with Advanced Renal Cell Carcinoma, Phase II		
<b>Start Date:</b> 09/06/91	<b>Est. Completion Date:</b> Sep 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Kenneth A. Bertram, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert B. Ellis, MC	MAJ Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard Tenglin, MC	
	CPT James Hu, MC	
<b>Key Words:</b> cancer:renal cell,alpha-interferon		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To evaluate in this Phase II study of low dose alpha-interferon the likelihood of response in order to assess whether low dose alpha-interferon should be advanced to further studies and to evaluate the qualitative and quantitative toxicities.

**Technical Approach:** Patients with either metastatic or recurrent renal cell cancer usually have incurable disease. A variety of therapies has been used with minimal effectiveness. Alpha-interferon has been used with some degree of effectiveness in this setting, but the toxicities using high doses are quite severe. In this study, all patients with recurrent or metastatic renal cell cancer will be treated with low dose alpha-interferon, which is usually associated with no side effects, to see if some patients can benefit by having their tumor shrink. Patients will self administer one dose a day of alpha-interferon subcutaneously until the disease progresses. Patients who progress on low dose interferon therapy may at the discretion of the treating physician be treated with conventional doses of interferon. Data will be analyzed after 20 response-evaluable patients have been entered. If zero responses are observed, the study will be permanently closed. If any responses are observed, 20 additional patients will be accrued. If 4 or fewer response are observed in the final 40 patients, it will be concluded that this regimen is disappointing. If 5 or more response are observed, it will be concluded that this regimen warrants further study.

**Progress:** This is a newly approved study and no patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** 05/03/91                      **Est. Completion Date:** Jan 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
MAJ William A. Phillips	MAJ Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC	MAJ Robert L. Sheffler, MC
MAJ Robert B. Ellis, MC	CPT Jennifer L. Cadiz, MC
COL Joseph F. Homann, MC	COL Daniel G. Cavanaugh, MC
MAJ Everardo E. Cobos Jr., MC	

**Key Words:** cancer:esophagus,chemotheray,surgery,modality therapy

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**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.

All patients have been enrolled in this study at MAMC.



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/045	<b>Status:</b> On-going
<b>Title:</b> SWOG 9028: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD to VAD/Verapamil/Quinine for Induction; (2) Alpha-2b Interferon or Alpha-2b Interferon Plus ..		
<b>Start Date:</b> 05/03/91	<b>Est. Completion Date:</b> Jan 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ William A. Phillips		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	MAJ Luke M. Stapleton, MC
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<b>Key Words:</b> myeloma, alpha 2b interferon, VAD, VMCP		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To determine if multidrug resistance can be prevented during remission induction by adding chemosensitizers (verapamil or quinine) to the VAD (vincristine, adriamycin, and dexamethasone); to determine if interferon alone or plus VMCP (vincristine, melphalan, cytoxan, and prednisone) represents better maintenance therapy for myeloma; to examine the prognostic significance of pretreatment LDH level, Ki-67 level, and presence of P-glycoprotein; and to evaluate the relationship between the magnitude of cytoreduction and survival.

**Technical Approach:** Previously untreated patients with all stages of multiple myeloma are eligible.

Protein criteria must be present but patients with IgM myeloma are not eligible. Patients must not have symptoms of congestive heart failure and may not be on digitalis preparations, beta blockers, or calmodulin inhibitors. Cardiac ejection fraction must be at least 50%, the EKG must be free of serious cardiac arrhythmias, and systolic blood pressure must be >90 mm/Hg. Patients who have had a prior malignancy within the last five years except for basal or squamous cell carcinoma or in situ cervical cancer are not eligible. Patients will be randomized to VAD every 21 days or to VAD plus verapamil and quinine every 21 days. Patients with >75% disease regression and at least 6 months of treatment and those with at least 50% regression after 9 months of treatment will be randomized to maintenance therapy. Maintenance therapy will consist of either alpha-2B interferon 3 times weekly or to alpha-2B interferon plus VMCP 3 times weekly every 3 months until relapse.

**Progress:** No patients have been entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 91/068                      **Status:** On-going

**Title:** SWOG 9037: Prediction of Recurrence and Survival in Node-Negative Breast Cancer Patients Using a Panel of Prognostic Factors: A Companion Protocol to SWOG 8897 (EST-2188, CALGB-8897, INT-0012)

**Start Date:** 06/14/91                      **Est. Completion Date:** May 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
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CPT Jennifer L. Cadiz, MC	

**Key Words:** cancer:breast,prognostic factors,recurrence,survival

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** To measure histologic and nuclear grade, estrogen and progesterone receptors, HER-2 oncogene, cathepsin D, EGF receptor, PS2, and hsp 27, 70, and 90 in paraffin-embedded histopathological specimens; and to correlate the above factors with biological and clinical features including recurrence and survival in patients entered on SWOG 8897.;

**Technical Approach:** There is now evidence in prospective randomized clinical trials that adjuvant endocrine therapy and adjuvant chemotherapy can be of benefit in axillary node-negative (ANN) breast cancer patients. This study will be done in concert with a current prospective trial (SWOG 8897) of ANN good risk patients assigned to observation or chemo plus or minus endocrine therapy based upon low and high proliferative rate and in tumors too small for estrogen receptor measurement. In the paraffin-embedded histopathological specimens submitted to the laboratory for DNA flow cytometry, extra 5 microgram sections will be cut for measurement of histological and nuclear grade, estrogen and progesterone receptors; HER-2 oncogene; cathepsin D; EGF receptor; PS2; and hsp 27, 70, and 90. This represents the most popular proposed prognostic factors for predicting recurrence and survival in ANN patients. A critical aspect of this study will be the multivariate analysis (Cox model) which will indicate the relative importance of these factors as well as tumor size and DNA flow cytometry in predicting recurrence and survival in good risk ANN patients. This study should help decide if prognostic factors can and should be used in treatment decisions in ANN patients.

**Progress:** 130 patients entered at MAMC.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/077	<b>Status:</b> On-going
<b>Title:</b> SWOG 9039: Evaluation of Quality of Life in Patients with Stage D2 Cancer of the Prostate Enrolled on SWOG 8894		
<b>Start Date:</b> 07/12/91	<b>Est. Completion Date:</b> July 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
MAJ William A. Phillips	LTC Howard Davidson, MC	
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MAJ Robert L. Sheffler, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
<b>Key Words:</b> cancer:prostate,quality of life		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**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:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** May 93

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** ; MAJ Everardo E. Cobos Jr., MC

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**Key Words:** cancer:rectum,5-Fluorouracil,leucovorin,levamisole

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**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:** One patient entered at MAMC; too early to evaluate.

DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/070	<b>Status:</b> On-going
<b>Title:</b> SWOG 9046: Evaluation of 10-EdAM in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b> June 94	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC		
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<b>Key Words:</b> cancer:head & neck,squamous cell,10-EdAM		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b> //

**Study Objective:** To evaluate the likelihood of response in order to assess whether 10-EdAM should be advanced to further studies in patients with histologically confirmed recurrent or metastatic squamous cell carcinoma of the head and neck and to evaluate the qualitative and quantitative toxicities of 10-EdAM.;

**Technical Approach:** Recurrent squamous cell carcinoma of the head and neck responds poorly to chemotherapy. Combination therapy is probably more effective than single agents. However, complete responses in recurrent and/or metastatic patients are still below the level at which survival benefit might be expected. A new agent for the treatment of advanced head and neck squamous cell carcinoma is 10-ethyl-1 deaza-aminopterin (10-EdAM) which is an analogue of methotrexate. In this Phase II study, 10-EdAM will be given once weekly at a dose of 80 mg/m<sup>2</sup> IV to patients with squamous cell carcinoma of the head and neck region that has persisted or recurred following definitive surgery and/or radiation therapy.

The disease measurements will be assessed every 8 weeks. In the absence of progression, therapy will continue at weekly intervals.

**Progress:** No patients entered at MAMC.

**DETAIL SUMMARY SHEET**

**Date:** 30 Sep 91                      **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:** Aug 94

**Department:** SWOG                      **Facility:** MAMC

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

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
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CPT Jennifer L. Cadiz, MC	CPT James Hu, MC

**Key Words:** cancer:leukemia,B-cell,fludarabine phosphate,chlorambucil

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	//

**Study Objective:** To compare in previously untreated CLL patients the response rates and progression free survival with the following three therapeutic regimens: (1) fludarabine phosphate, (2) chlorambucil, and (3) fludarabine phosphate plus chlorambucil; to determine whether the quality of life (need for transfusions, incidence of infections, and performance status) is superior using any of the three regimens; and to determine whether these two drugs are non-cross-resistant by a crossover design for patients failing to respond to the single agent to which they were initially randomized.

**Technical Approach:** B-cell chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. This study is designed to compare a new drug, fludarabine, (Arm I) to standard therapy, chlorambucil (an alkylating agent, Arm II), and to the combination of fludarabine and chlorambucil (Arm III). The drugs will be administered every four weeks until patients reach a complete remission or maximally beneficial response (up to one year of treatment). Patients with progressive disease on Arm I or II will crossover to the other single agent arm. After completing the prescribed treatment arm, patients may be re-entered if they relapse. Patients will be randomly assigned, with equal probabilities, to one of the three treatment arms. Randomization will be stratified by risk group and duration of disease with treatment allocations being adjusted as necessary to avoid treatment imbalance within institutions.

**Progress:** New study; no patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **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:** July 94

**Department:** SWOG                      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	LTC Howard Davidson, MC
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**Key Words:** melanoma,interferon alpha 2

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	//

**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 log rank 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 entered at MAMC.

# **DETAIL SHEETS FOR PROTOCOLS**

**UNIVERSITY WASHINGTON**  
**NEURO-ONCOLOGY GROUP**



## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 88/073	<b>Status:</b> On-going
<b>Title:</b> UWNG 86-01: Phase II Study of External Brain Irradiation and Hydroxyurea Followed by Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Primary Malignant Brain Tumors		
<b>Start Date:</b> 08/19/88	<b>Est. Completion Date:</b> Jul 91	
<b>Department:</b> UWNG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> COL Irwin B. Dabe, MC CPT Denis Bouvier, MC		Robert Goodkin, M.D. MAJ Joseph H. Piatt, MC
<b>Key Words:</b> tumor:brain,irradiation,PCV,procarbazine,CCNU,vincristine		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	10/19/90

**Study Objective:** To evaluate radiation therapy plus hydroxyurea and PCV in terms of the following parameters: time to progression from start of therapy, response rates and stabilization rate, survival time from start of therapy, and quality of life and activity level (Karnofsky).

**Technical Approach:** Patients must have a primary intracranial malignant glioma. Most patients will have had some form of surgery. Treatment will begin within four weeks of the operation at which the current diagnosis was made or within four weeks of clinical diagnosis. No prior cytotoxic, chemotherapy, or radiation therapy will be permitted. Local field radiotherapy will be employed. Only one course of radiotherapy will be given. The total dose to the tumor will be 5940 cGy delivered in a period of 6-7 weeks. The tumor volume will include at least the enhanced portion of tumor based on CT scan and a 2-3 cm margin of normal tissue in all directions. Every other day during radiotherapy, beginning day 1, patients will receive hydroxyurea, 300 mg/m<sup>2</sup> every six hours. PCV treatment will begin within two weeks after radiotherapy. CCNU, 110 mg/m<sup>2</sup> po, will be given on day one of each course. Procarbazine, 60 mg/m<sup>2</sup> po will be given days 8-14. Vincristine, 1.4 mg/m<sup>2</sup>, will be given IV push on days 8 and 29. Patients will be evaluated and courses given at six to eight week intervals in the absence of irreversible toxicity. Patients will remain on protocol until the completion of two full courses of PCV. If tumor progression is documented after the second course, the patient will be taken off protocol. If tumor progression is not demonstrated, PCV will be given for one year or a minimum of 6 courses (not to exceed 8 courses) and then stopped. All patients will be followed for survival. Patients who expire from tumor progression early in the course of therapy will be evaluable for analysis if one full course of PCV was administered.

**Progress:** No patients entered at MAMC.

## DETAIL SUMMARY SHEET

**Date:** 30 Sep 91                      **Protocol No.:** 88/017                      **Status:** On-going

**Title:** UWNG 87-01: Phase II Study of TPDCFH for Recurrent Malignant Brain Tumor

**Start Date:** 01/15/88                      **Est. Completion Date:** Sep 90

**Department:** UWNG                      **Facility:** MAMC

**Principal Investigator:** LTC Howard Davidson, MC

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**Key Words:** tumor:brain,chemotherapy,TPDCFH

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$100.00	10/19/90

**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 confirmed recurrence of a malignant supratentorial glioma; liver and renal function are not seriously impaired (liver enzymes and serum creatinine within 1.5 x normal for laboratory; Karnofsky performance 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 scans will serve as an additional criterion of recurrence. All patients will receive the following schedule:

- 0-66 hr: 6-thioguanine, 30 mg/sq.m., q. 6 hr p.o. x 12 doses
- 60-78 hrs: procarbazine, 50 mg/sq.m., q. 6 hr p.o. x 4 doses
- 60 hrs: dibromodulcitol, 400 mg/sq.m., p.o.
- 72 hrs: CCNU, 100 mg/sq.m., p.o.
- Days 14 & 15: 5-FU, 1 g/sq.m. continuous infusion over 48 hrs
- Day 15, hydroxyurea, 1 g/sq.m. p.o., 4 hours before the 5-FU infusion ends and at 4 hr intervals for a total of 3 doses

The cycle will be restarted on day 37-48, depending on toxicity level. In general WBC and platelets should increase to WBC >4000/cu mm and platelets >125,000/cu mm before the next cycle is made to restart when WBC >3600/cu mm for patients with granulocyte depressed bone marrow.

**Progress:** No patients entered at MAMC.

**DETAIL SUMMARY SHEET**

<b>Date:</b> 30 Sep 91		<b>Protocol No.:</b> 89/013		<b>Status:</b> On-going	
<b>Title:</b> UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System					
<b>Start Date:</b> 09/15/89			<b>Est. Completion Date:</b> Nov 92		
<b>Department:</b> UWNG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
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MAJ Everardo E. Cobos Jr., MC			MAJ Kenneth A. Bertram, MC		
<b>Key Words:</b> lymphoma:central nervous system,chemoradiotherapy,methotrexate					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$328.00	10/19/90	

**Study Objective:** To evaluate this regimen; the endpoints of analysis will be time to progression of disease from beginning of therapy; response rates and disease stabilization rates; survival time measured from the beginning of therapy; quality of life and activity level measured by Karnofsky performance status.

**Technical Approach:** Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver functions and a performance status of >70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m<sup>2</sup>, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses parenterally on an every 6 hour basis following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate, and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time the patient will be removed from the protocol and can be treated with other therapy as indicated. Patients will be followed until death.

**Progress:** One patient entered at MAMC in FY 88; none in FY 91.

# **DETAIL SHEETS FOR PROTOCOLS**

**FORT WAINWRIGHT, ALASKA**

## DETAIL SUMMARY SHEET

<b>Date:</b> 30 Sep 91	<b>Protocol No.:</b> 91/054	<b>Status:</b> On-going
<b>Title:</b> Melatonin and Cortisol Secretion in the Arctic, Effects of Photoperiod on Circadian Rhythms and Mood		
<b>Start Date:</b> 03/15/91	<b>Est. Completion Date:</b> May 92	
<b>Department:</b> Fort Wainwright	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Matthew E. Levine, MC		
<b>Associate Investigators:</b>		Lt Lawrence K. Duffy, USNR
<b>Key Words:</b> melatonin,arctic,photoperiod,circadian rhythm,mood		
<b>Accumulative MEDCASE Cost:</b> \$0.00	<b>Est. Accumulative OMA Cost:</b> \$0.00	<b>Periodic Review:</b>

**Study Objective:** To establish basic knowledge and understanding of the effects of extreme latitude on the circadian secretory patterns of the primary hormones of the pineal and adrenal glands, and to determine possible effects on mood and behavior.

**Technical Approach:** Melatonin and serum cortisol levels will be determined on approximately 100 individuals on a quarterly basis, as close to the solstices and equinoxes as practical, at 0200, 0800, 1030, and 1700 hours on those days. Sufficient blood will be obtained for additional endocrine studies, such as reproductive hormones, and possibly thyroid hormones. Subjects will be screened verbally for recent acute stress or geographic changes, and, if either is present, the blood draw will be delayed by one week to allow for diminution of physiologic stress response or readjustment to arctic photoperiod. On the day of the first sampling, a Seasonal Pattern Assessment Questionnaire will be administered. The Beck Depression Inventory will administered to each subject at each sampling period. Data will be compared with that from other studies at similar and different latitudes.

Seasonal variations in hormone levels and mood rating scores will be compared in individual subjects, as well as in the study group. Relationships between mood behavior, endocrine physiology, and season will be subject to statistical analysis using a repeated measures ANOVA with season and sex as factors, and age as a covariate. A posteriori multiple contrasts will be made with Bonferroni tests.

**Progress:** Forty two subjects have been screened with the Seasonal Pattern Assessment Questionnaire. Blood samples were obtained and the Beck Depression Inventory administered at the summer solstice and the autumnal equinox.

## Investigators/Authors

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