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Department of Clinical Investigation

Annual Research Progress Report

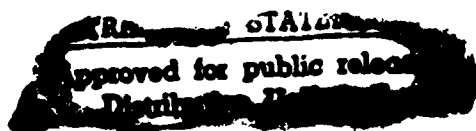
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Madigan Army Medical Center
Tacoma, Washington 98431-5000

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ANNUAL PROGRESS REPORT

30 SEPTEMBER 1992

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

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TABLE OF CONTENTS

Introduction	1
Acknowledgements.....	1
Foreword	2
Unit Summary.....	3
Committee Members.....	6
Bryon L. Steger Research Award	8
Wergeland Research Award	9
Publications.....	10
Theses	17
Presentations	18
Index To Protocols	24
Protocols...	
Department of Community Medicine.....	42
Clinical Psychology Service.....	45
Department of Clinical Investigation.....	48
Department of Dentistry.....	64
Department of Emergency Medicine.....	76
Department of Family Practice.....	90
Department of Medicine.....	101
Department of Nursing.....	157
Nutrition Care Division.....	173
Department of OB/GYN	175
Preventive Medicine Service	193
Department of Pediatrics.....	199
Department of Radiology.....	221
Department of Surgery	226
Fort Ord MEDDAC	254
Fort Wainwright, Alaska.....	256
Letterman MEDDAC	258
U.S. Department of Agriculture.....	260
Childrens Cancer Study Group	262
Gynecology Oncology Group	274
National Cancer Institute	319
Pediatric Oncology Group.....	321
Puget Sound Oncology Group.....	323
Southwest Oncology Group	326
University of Washington.....	410
Index of Authors and Investigators	414
Index of Keywords	422

ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1992

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

INTRODUCTION

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

ACKNOWLEDGEMENTS

I would like to take this opportunity to thank Nancy Whitten and Troy Patience for the effort which is obvious in the compilation, preparation, and editing of this publication.

FOREWORD

FY 92 was eventful for the Department of Clinical Investigation as well as for MAMC, which moved into its new state-of-the-art facility. DCI essentially tripled the size of its bench space with this move, as well as adding two new ultra-modern surgical suites and supporting animal use facilities. In spite of the considerable time and effort expended in preparing for and making the move, the number of new protocols increased and total protocols supported remained essentially unchanged.

Personnel changes included the much-appreciated addition of CPT Keith Martin, who lent his expertise to the expanding molecular biology thrust of the department. DCI sponsored "Introduction to Research" courses were given to three departments during the year. MAMC continued its success in bringing extramural funding to the institution. MAMC nurses were recipients of grants from nursing research funds and MAMC investigators garnered two of the six grants awarded from the FY 92 MRDC breast cancer appropriation.

I wish to acknowledge the continued commitment to excellence by all DCI personnel during this period of time, as well as the vital support of BG Leslie Burger, Commander, and COLs Michael Weir and Al Buck, who served as DCCS during this period.

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, Clinical Investigation MOORE, Dan C., M.D., COL, MC	06	60P9A
C, Clinical Studies Service JONES, Robert E., M.D., COL, MC	06	61C9A
C, Surg & Animal Care Svc POWELL, Douglas, D.V.M., MAJ, VC	04	64C9B
C, Microbiology Svc STEWART, Robert S., Ph.D., MAJ, MS	04	68A9B
C, Biochemistry Svc MOORE, Katherine Hines, Ph.D., CPT, MS	03	68C00
C, Bioresearch Svc MARTIN, Keith, Ph.D., CPT, MS (June 92 -)	03	68C8Z
NCOIC HANDY, Kevin , SSG	E6	92B3M4
NCOIC ROBERTS, Teresa, SSG (Aug 92 -)	E6	91T30R
Vet Animal Spec HEATH, George, SGT	E5	91T20
Vet Animal Spec SPAHN, Shelley, SGT	E5	91T20
Vet Animal Spec VERZOSA, Neil , SGT (Oct 91 - July 92)	E5	91T20
Vet Animal Spec FULK, Terry, SPC (Dec 91 -)	E4	91T20
Vet Animal Spec CARREIRO, Frank, PFC (Jan 92 -)	E3	91T20

<u>Description</u>	<u>Rank</u>	<u>MOS</u>
Med Tech MATEJ, Louis A., B.S., M.T.	GS9	0644
Med Tech WRIGHT, James R., B.A., M.T.	GS9	0644
Med Tech STYNER, M. J., B.S., M.T.	GS9	0644
Med Tech THOMSON-ARCHER, Kelly, B.S., M.T. (Nov 91 -)	GS9	0644
Statistician Medical PATIENCE, Troy H., B.S.	GS9	1530
Edit Asst/Steno WHITTEN, Nancy J., B.A.	GS7	1087
Sec/Steno HOUGH, Eugenia R.	GS6	0318
Maintenance Worker KAE0, Curtis	WG7	4749

Funding FY 92

MEDCASE Equipment	\$163,582.00
Capital Equipment	8,021.00
Civilian Salaries	267,823.00
Military Salaries	541,338.00
Consumable Supplies	120,457.00
Contractual Services	18,537.00
TDY - departmental	7,170.00
TDY - presentations	19,799.00

Total \$1,146,727.00

GRANTS: AMOUNT: \$131,670

SOURCE: NIH

FOR: Protocol - Piglet Tracheal Epithelial Injury and Regeneration
Following Endotracheal Suctioning.

PRINICIPAL INVESTIGATOR: COL Barbara S. Turner, AN

EXTRAMURAL FUNDING:

	FACT	
Travel		\$3,810
Personnel		11,430
		<hr/>
	<u>Total</u>	\$15,240

3. Progress

During FY 92 there were 343 active protocols that received administrative and/or technical support during the year. Of these, 218 are presently on-going; 3 are in a suspended status, 86 were completed; and 36 were terminated.

There were 90 publications, 3 theses were completed and accepted from approved research studies, and there were 106 presentations at regional, national, or international meetings.

4. Fellowship/Residency Program Support

Fellowship/Residency programs supported by DCI: 26

Number of protocols with a fellow/resident as principal investigator: 63

Number of protocols with a fellow/resident as associate investigator: 105

5. Other training programs supported by DCI:

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

6. Other protocols supported:

129 protocols held by hospital staff members
145 group oncology protocols
1 Fort Wainwright, AK protocols
2 Letterman MEDDAC protocols
1 USDA protocols

COMMITTEE MEMBERS

Commander

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

Clinical Investigation Committee

Chairman

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

Chief or delegated representative of:

Department of Clinical Investigation
Department of Pediatrics
Department of OB/GYN
Department of Family Practice
Department of Emergency Medicine
Department of Nursing
Department of Medicine
Department of Surgery
Department of Pathology
Department of Radiology
Pharmacy Service
Clinical Psychology Service
Clinical Studies Service, DCI
Microbiology Service, DCI
Biochemistry Service, DCI
Bioresearch Service, DCI
Lab Animal and Surgery Service, DCI
Medical Statistician, DCI

Human Use Committee

Chairman

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

Chief or delegated representative of:

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

BRYON L. STEGER RESEARCH AWARD

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

Recipient of this award for 1992:

MAJ Charles R. Weber, DC	Evaluation of Dexamethasone in Reducing Postoperative Edema and Inflammatory Response After Orthognathic Surgery
--------------------------	--

Other nominees were:

MAJ Scott E. Cameron, MC	A Prospective Randomized Comparison of Open Versus Arthroscopically Assisted Anterior Cruciate Ligament Reconstructions
CPT Brian Divelbiss, MC	Cephalad Imbalance in Patients With Adolescent Idiopathic Scoliosis Treated With Cotrel-Dubousset Instrumentation
CPT Randal D. Robinson, MC	Adverse Pregnancy Outcome in Patients With Antiphospholipid Antibodies
CPT Vic Velanovich, MC	Decision Analysis in Surgery: Comparing the Treatment Options in Adult Blunt Splenic Trauma
CPT Vic Velanovich , MC	Preoperative Laboratory Screening Based on Age, Gender, and Concomitant Medical Diseases
CPT Vic Velanovich, MC	The Effects of Age, Gender, Race, and Concomitant Disease on Postoperative Complications

WERGELAND RESEARCH AWARD

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

Recipient of this award for 1992:

CPT R. Michael Tuttle	The Effect of 5-Alpha Reductase Inhibition and Adrenal Androgen Suppression on the Growth Characteristics and Intratumor Androgen Levels of the Human Prostate Cancer Cell Line PC-3
-----------------------	--

Other nominees were:

MAJ Robert Broadhurst, MC	Use of a Short Interview, the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), and Two Physical Observations for Identifying Obsessive Compulsive Disorder in Childhood
---------------------------	--

LCDR Evelyn Lewis, MC	Family Function, Communication, and Sociodemographic Characteristics: A Descriptive Analysis
-----------------------	--

MAJ Dawn E. Light, MC	A Pilot Study on the Use of the Zung Self-Rating Depression Scale as a Screening Tool During Pregnancy
-----------------------	--

MAJ Dawn E. Light, MC	Prevalence of Depression Among Pregnant Spouses of Deployed Servicemen
-----------------------	--

LTC Thomas Michels, MC	Barriers to Screening: A Pilot Study Applying the Theory of Reasoned Action to Mammography Use in a Military Beneficiary Populations
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PUBLICATIONS**FISCAL YEAR 92****CLINICAL PSYCHOLOGY SERVICE**

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|---|---|
| Brown FH, Dodrill CB,
Clark T, Zych KA | An Investigation of the Relationship Between Self-Report of Memory Functioning and Memory Test Performance. J Clinical Psychology 47(6): 772-777, 1991. |
| Hansen JE, Clingan TA,
Munsinger HL | Children's Self-Report of Attention Deficit Hyperactivity Disorder. Journal of US Army Med Dept 8(1): 18-20, 1992. |
| Lehman R, Hansen JE,
Munsinger HL | Crisis Management of Children During Desert Storm. Journal US Army Med Dept 8(3): 39-41, 1992. |

CLINICAL SERVICES/ADMIN RESIDENT

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| Pratt DH | Utilization Review in the Military Health Care Delivery System. Military Medicine 157(9): 476-479, 1992. |
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DEPARTMENT OF CLINICAL INVESTIGATION

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| Friedl KE, Nuovo JA,
Patience TH, Dettori JR | Factors Associated with Stress Fracture in Young Army Women: Indications for Further Research. Military Medicine 157: 334-338, 1992. |
| Hannan CJ, Friedl KE,
Zold A, Kettler TM,
Plymate SR | Psychological and Serum Homovanillic Acid Changes in Men Administered Androgenic Steroids. Psychoneuroendocrinology 16(4): 335-343, 1991. |
| Heath G | TBR/Technician of the Year Report. Nwsltr, WA Br Am Asso LAS Nov/Dec: 6, 1991. |
| Moore DC,
Ruvalcaba RHA | Late Onset Gynecomastia Associated with Oxandrolone Therapy in Adolescents with Short Stature. Jour Pediatric Endocrinology 4(4): 249-253, 1991. |
| Petra PH, Griffin PR,
Yates JR, Moore KH,
Zhang W | Complete Enzymatic Deglycosylation of Native Sex Steroid Binding Protein (SBP or SHBG) of Human and Rabbit Plasma. Effect on the Steroid Binding Activity. Protein Science 1(7): 902-09, 1992. |
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Paulsen CA,
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DEPARTMENT OF EMERGENCY MEDICINE

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| Alba E, Youngberg R | Occult Fractures of the Femoral Neck. Amer J Emergency Medicine 10(1): 64-68, 1992. |
| Foutch RG,
Magelssen MD,
MacMillan JG | The Esophageal Detector Device - A Rapid and Accurate Method for Assessing Tracheal Versus Esophageal Intubation in a Porcine Model. Annals of Emergency Medicine 21(9): 1073-1076, 1992. |

Frohna WJ

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Lagutchik MS,
Martin DG

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DEPARTMENT OF FAMILY PRACTICE

Brunader RE,
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Prevalence of Cocaine and Marijuana Use Among Pregnant Women in a Military Health Care Setting. *J Amer Board Family Practice* 4(6): 395-98, 1991.

Light DE

Organizational Diagnosis for Commanders and Clinic Administrators. *J US Army Medical Department*: 21-22, 1991.

Spaulding SA,
Kugler JP

Influenza Immunization: The Impact of Notifying Patients of High Risk Status. *Journal of Family Practice* 33(5): 495-98, 1991.

DEPARTMENT OF MEDICINE

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DEPARTMENT OF NURSING

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Rae RE, Spring WB,
Koenig TE

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Sexton DL Aerobic Exercise and Quality of Life in Women With Breast Cancer. *Oncology Nursing Forum* 18(4): 751-57, 1991.

DEPARTMENT OF OB/GYN

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Herpolsheimer AH, Compared with Spontaneous Vaginal Delivery in Term
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Brady WK, Milligan D, *Obstetrics and Gynecology* 79(4): 571-74, 1992.
Strampel W

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Krauss MR Program for Soldiers. *Military Medicine* 157(4): 214-18, 1992.
- Fleming JL, Opheim GS Warehouse Workers Headache. *Journal of Occupational Med* 34(9): 872, 1992.
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McNeil JG, Milazzo MJ, Cohort. *J Acquired Immune Defic Syn* 5(8): 782-93, 1992.
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Haberberger RL,
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Screening for Maternal Depression in Pediatric Clinics. *Amer Journal Diseases of Chil* 146(7): 876-78, 1992.

Kinney JB, Albano EA,
Krober MS,
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PHARMACY SERVICE

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MacMillan M, Ferrell R

Possible Short Term Memory Loss Associated With Nafarelin Acetate. *Annals of Pharmacotherapy* 26(2): 169-171, 1992.

DEPARTMENT OF RADIOLOGY

Bauman JM

Gallbladder Ejection Fraction - Still in Need of Validation. *Gastroenterology* 102(4): 1446, 1992.

Phillips WT,
Rudolph AS, Goins B,
Timmons JH, Klipper R,
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A Simple Method for Producing a Technetium-99m-Labeled Liposome Which is Stable In Vivo. *Nuc Med Biol Int J Rad Ap Inst* 19(5): 539, 1992.

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DEPARTMENT OF SURGERY

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Velanovich V,
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Beck RA, Mercado DL,
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Cardiovascular Effects of Pseudoephedrine in Medically Controlled Hypertensive Patients. *Archives of Internal Medicine* 152(6): 1242-45, 1992.

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Hodges GF, Belville WD,
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Mazzoli RA,
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Rowsey JJ
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Yarbrough LW
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Myectomy in the Swine Model. Diseases of the Colon &
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Wettlaufer JN,
Miller GJ
Primary Carcinoid Tumor of the Testicle: A Case Report and
Management Schema. The Journal of Urology 148(3): 880-82,
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Transureteroureterostomy and Terminal Loop Cutaneous
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McGahren E.,
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THESES

FISCAL YEAR 92

DEPARTMENT OF FAMILY PRACTICE

Lewis EL	Sociodemographic Characteristics: A Descriptive Analysis.
Michels TC	Reasoned Action Applied to Mammography Use in a Military Beneficiary Population.

DEPARTMENT OF PEDIATRICS

Smith PS	Separation on School-aged Children Due to Temporary Separation for Military Duty.
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PRESENTATIONS**FISCAL YEAR 92****DEPARTMENT OF CLINICAL INVESTIGATION**

Moore DC, Moore KH, Krober AS	LH Isoforms Vary with Age in Childhood.	Northwest Pediatric Endocrine Society, Seattle, WA, April 92.
Moore KH, Dunbar BS, Bousfield GR, Ward DN	Initial Characterization of Equine Inhibin.	The Endocrine Society, San Antonio, TX, June 92.
Moore KH, Matej LA, Petra P	Does the Physiological State Influence the Carbohydrate Composition of Sex Hormone Binding Globulin (SHBG)?	The Society of Armed Forces Medical Laboratory Scientists, San Antonio, TX, April 92.
Moore KH, Moore DC, Wright JR, Krober AS	Ontogeny of Luteinizing Hormone (LH) Isoforms from Puberty to Adulthood	Society for the Study of Reproduction, Raleigh, NC, July 92.

DEPARTMENT OF EMERGENCY MEDICINE

Burke T	An Unusual Case of Back Pain and Spinal Cord Compression.	Society for Academic Emergency Medicine, Toronto, Canada, May 92.
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DEPARTMENT OF MEDICINE

Bernier RM	Obstructive Purpura as a Clue to the Diagnosis of Seizures.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Bunner DL, Morris ER, Mereish KA	Effects of Anthrax Lethal Toxin (Protected Antigen and Lethal Factor Combined) on Human Monocytes and Polymorphonuclear Leukocytes.	American College of Physicians Regional Meeting (Army chapter), San Francisco, CA, October 91.
Ellingson AR, Lyons MF, Schlepp GE, Tsuchida AM	Sucralfate Causes Aluminum Deposition in Patients With Normal Renal Function Following Standard Six Week Oral Ingestion.	Washington State Chapter, American College of Physicians, December 91.
Ellingson AR, Lyons MJ, Schlepp GE, Tsuchida AM	Sucralfate Causes Aluminum Deposition in Subjects with Normal Renal Function Following Standard Six Week Oral Ingestion.	American Gastroentero- logical Association Meeting, San Francisco, CA, May 92.
Elliott	Delayed Occurrence of Myasthenia Gravis Following Recurrent Thymoma.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.

PRESENTATIONS - MAMC - FY 92

Flynn FG	Selegiline Treatment for Probable Diffuse Lewy Body Variant of Alzheimer's Disease.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Flynn FG, May E	The Acute Onset of Geschwind's Personality Syndrome with a Left Temporal Lobe Infarction.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Flynn FG, McBurney JW	Behavior and Juvenile Myoclonic Epilepsy.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Flynn FG, Warden D, Spector J	Neurobehavior Clinic: Model for Assessment and Management of Cognitive and Neuropsychiatric Disorders.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Flynn FG, Warder D, Joslin S	ECT Treatment in a Patient with Progressive Supranuclear Palsy.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Jones RE, Bell BK, Plymate SR	Comparison of Ether Versus Ester Lipid Synthesis in Ejaculated Human Sperm.	American College of Physicians Regional Meeting (Army Chapter), San Francisco, CA, October 91.
Jones RE, Wright JR	Direct Incorporation of Hexadecanol Into the Phosphatidylethanolamine Fraction of Human Sperm.	Society for the Study of Reproduction, Raleigh, NC, July 92.
Keenan LM	4 Hour and 6 Hour Urine Urea Nitrogens vs 24 Hour Urine Urea Nitrogens for Assessing Nitrogen Balance.	Army American College of Physicians Meeting, San Francisco, CA, October 91.
Lodato R, Tsuchida AM, Schlepp GE, Lyons MF	How Well Does Laparoscopy Predict Histology in Nonfocal Liver Disease?	19th Annual William Beaumont Gastrointestinal Symposium, El Paso, TX, October 91.
Lodato RJ, Lyons MF, Schelpp GE, Tsuchida AM	How Well Does Laparoscopy Predict Histology in Nonfocal Liver Disease.	American College of Gastroenterology, 56th Annual Scientific Meeting, Boston, MA, October 91.
Lombardo MA, McBurney JW	Onset of Typical Generalized Absence Epilepsy in an Adult Following Trauma.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Lyons MF, Tsuchida AM, Schlepp GE	Association of Colonic Neoplasia with Barrett's Esophagus vs. Esophageal Reflux Patients with Strictures.	American College of Gastroenterology, 56th Annual Scientific Meeting, Boston, MA, October 91.
Marden LA, Lombardo MA	Status Epilepticus Following Low Dose Self-Administration of Local Anesthetic.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.

PRESENTATIONS - MAMC - FY 92

McBurney JW, Lombardo MA	Hajdu-Cheney Syndrome, the "ET" Finger Disease.	1991 AMEDD Neurology Meeting, Washington, DC, November 91.
Roth BJ, Plymate SR, Kushner JP, Grover BS	Hypogonadism and Chronic Obstructive Pulmonary Disease.	American Thoracic Society/American Lung Association, International Conference, Miami Beach, FL, May 92.
Schlepp GE, Lyons MF, Tsuchida AM	Correlation of the ALT/AST Ratio to Liver Histology in Chronic Amino- Transferase Elevation.	American College of Gastroenterology, 56th Annual Scientific Meeting, Boston, MA, October 91.
Tsuchida AM, Schlepp GE, Lyons MF	Does Significant Liver Disease Exist in Young Healthy Asymptomatic Individuals with Incidental Alanine Transferase (ALT) Elevations?.	American College of Gastroenterology, 56th Annual Scientific Meeting, Boston, MA, October 91.
Tuttle RM, Bell BK, Moore KH, Jones RE, Plymate SR	The Effect of Insulin Induced Hypoglycemia on the Hypothalamic- Pituitary-Gonadal Axis.	Endocrine Society Meeting, San Antonio, TX, June 92.
Tuttle RM, Renfer LG, Loop S, Lewis SM, Ostenson RC, Jones RE, Plymate SR	The Effect of the 5-Alpha Reductase Inhibitor, 4-MA, on Human Prostate Cancer Cell Line Implanted in Athymic Nude Mice.	Army American College of Physicians Regional Meeting (Army Chapter), San Francisco, CA, October 91.
Willadsen DS, Lyons MF, Schlepp GE, Tsuchida AM	Dietary Supplementation of Folic Acid is Associated with Lack of Dysplasia in Patients with Chronic Inflammatory Bowel Disease.	American College of Gastroenterology, 56th Annual Scientific Meeting, Boston, MA, October 91.

DEPARTMENT OF OB/GYN

Dyksterhouse DL, Downey GO, Bayliss PM, Kopelman JN	Role of Color Flow Doppler in the Evaluation of Patients with Persistent Trophoblastic Disease.	American College of Obstetricians/Gynecologist, Las Vegas, NV, May 92.
Larsen WI, Brady K, Kopelman JN	Twelve Hour Urine Collections in Comparison to Twenty Four Hour Urine Collections in Patients with Preeclampsia.	American College of Obstetricians and Gynecologists Meeting, Las Vegas, NV, April 92.
Thorne ME	Objective Measurement of Thyroid Volume During Pregnancy.	Military District, American College of Obstetricians and Gynecologists, Cincinnati, OH, October 91.
Thorne ME, Brady K, Treece GL	Objective Measurement of Thyroid Volume During Pregnancy.	American College of Obstetrics and Gynecology, Cincinnati, OH, October 91.

DEPARTMENT OF PEDIATRICS

Broadhurst RB, Kelly P	Use of a Short Screening Interview and the Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) for Identifying Obsessive Compulsive Disorder (OCD).	Northwest Developmental Pediatric Society, Vancouver, BC, Canada, April 92.
Broadhurst RB, Stephan M	Unknown Familial Syndrome with Multiple Congenital Anomalies.	Northwest Genetics Society, Seattle, WA, May 92.
Kemper K, Greteman A, Bennett E, Babonis TR	Screening Mothers of Young Children for Substance Abuse.	Ambulatory Pediatric Association, Carmel, CA, February 92.

DEPARTMENT OF RADIOLOGY

Phillips WT, Goins B, Timmons JH, Klipper R, Blumhardt R	A Stable Technetium-99M-Labeled Liposome for Use in Biodistribution Studies.	Southwest Regional American College of Surgeons Meeting, October 91.
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DEPARTMENT OF SURGERY

Anderson P, Velanovich V, Kaufmann CL, Carter P	Late Perforation of the Distal Roux-en-Y Anastomosis in a Patient with Biliopancreatic Diversion.	Washington State Chapter of American College of Surgeons, Chelan, WA, June 92.
Armstrong PJ, Kaufmann CR	The Peritoneal Dialysis Catheter: Simple and Safe.	Washington State Chapter of American College of Surgeons, Chelan, WA, June 92.
Boehm B, Plymate S, Davis R	Inhibin and Its Association with Varicoceles.	Washington State Chapter of American College of Surgeons, Lake Chelan, WA, June 92.
Burgess FW, Brooks DE, Wade CE, Perkins D, Rodkey WG	Influence of Continuous Epidural Bupivacine on Perioperative Fluid Shifts.	American Society of Anesthesiologists, San Francisco, CA, October 91.
Burgess FW, Snodgrass G, Sborov MJ, Helman JD, Anderson M	Combined Epidural/General Anesthesia and the Hemodynamic Response to Moderate Hemorrhage.	Association of University Anesthesiologists, Palo Alto, CA, May 92.
Cameron S	Prospective Randomized Comparison of Arthroscopic versus Open Anterior Cruciate Ligament (ACL) Reconstructions.	59th Annual Meeting of the American Academy of Orthopaedic Surgeons, Washington, DC, February 92.

PRESENTATIONS - MAMC - FY 92

Danielson RW, Donahue A	15 Years Revisited: The Prevalence of Hearing Loss Among Selected US Army Branches.	Joint 1992 Hearing Conservation Conference, Cincinnati, OH, April 92.
Dietz JW	Does Obesity Affect Outcome After Lumbar Fusions.	25th Annual American Orthopaedic Association Meeting, Ann Arbor, MI, March 92.
Helman J, Bellows W, Leung J, Velasco W, Mangano D	Anesthetic Induction of High Risk Patients: Effects of Desflurane on Hemodynamics and Echocardiographic Measures of Ischemia.	1991 American Society of Anesthesiologists Annual Meeting, San Francisco, CA, October 91.
Helman J, Browner W, Li J, Mangano D	Prognostic Importance of Preoperative Hypertension.	1991 American Society of Anesthesiologists Annual Meeting, San Francisco, CA, October 91.
Helman J, Leung J, Bellows W, Pineda N, Mangano D	Desflurane Anesthesia and Myocardial Ischemia: Comparative Risk vs. Sufentanil Anesthesia in Patients Undergoing Coronary Artery Bypass Graft Surgery.	1991 American Society of Anesthesiologists Annual Meeting, San Francisco, CA, October 91.
Hetherington HE, Hollinger JO, Morris MR	Onlay Bone Augmentation with a Xenogenetic Osteoinductive Protein in a Biodegradable Matrix.	American Academy of Facial, Plastic, and Reconstructive Surgery, Washington, DC, September 92.
Mader TH	Ocular Injuries of the Persian Gulf War - Preliminary Report.	Lasers on the Modern Battlefield Conference, San Francisco, CA, October 91.
Mader TH, Yuan R, Lynn MJ, Stulting RD, Wilson LA, Waring GO	Astigmatic Change Following Suture Removal More Than One Year After Penetrating Keratoplasty.	American Academy of Ophthalmology Annual Meeting, Anaheim, CA, October 91.
Perkins JA, Morris MR, Canonica DM	Neuropeptide Levels in the Nasal Secretions and Nasal Mucosa of Patients with Chronic Sinusitis and Nasal Polyposis.	American Rhinologic Society, Washington, DC, September 92.
Place R, Velanovich V, Carter P	Breast Fine Needle Aspiration: Utility in Clinical Management.	Washington State Chapter of American College of Surgeons, Lake Chelan, WA, June 92.
Tran L, Velanovich V, Kaufman C	Familial Multiple Glomus Tumors: Report of a Pedigree and Literature Review.	Washington State Chapter of the American College of Surgeons, Lake Chelan, WA, June 92.

PRESENTATIONS - MAMC - FY 92

Velanovich V	Predictive Value of Preoperative EKG Findings for Cardiac Complications.	Pacific Northwest Vascular Society Meeting, Portland, OR, November 91.
Velanovich V	Predicting Wound Complications After Elective Surgery: Are There Clinical Risk Factors.	Forum on Wound Repair/Symposium on Advanced Wound Care, New Orleans, LA, April 92.
Velanovich V	The Effects of Age, Gender, Race and Concomitant Disease on Postoperative Complications.	Washington State Chapter of the American College of Surgeons, Lake Chelan, WA, June 92.
Velanovich V, Kaufmann C	Two Pitfalls of Laparoscopic Balloon Cholangiography: Recognition and Correction.	Washington State Chapter of the American College of Surgeons, Lake Chelan, WA, June 92.
Weber SE, Williard W	Do Patients with Colorectal Carcinoma Under the Age of Forty Have A Worse Prognosis.	Washington State Chapter of American College of Surgeons, Lake Chelan, WA, June 92.
Williard WC, Hajdu SI, Casper ES, Brennan MF	The Role of Amputation in Extremity Soft Tissue Sarcoma.	American College of Surgeons Clinical Congress, Chicago, IL, October 91.
Winkler T, Tollefson D	Late Aortic Prosthetic Graft After Dental Hygiene.	Washington State Chapter of American College of Surgeons, Lake Chelan, WA, June 92.

FORT WAINWRIGHT, ALASKA

Levine ME, Milliron AN, Duffy LK	Melatonin and Cortisol Secretion in the Arctic: Effects of Photoperiod on Circadian Rhythms and Mood.	Fourth Annual Meeting of Society for Light Treatment and Biological Rhythms, Bethesda, MD, May 92.
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PRESENTATIONS - MAMC - FY 92

PRESENTATIONS (Addendum)

FISCAL YEAR 92

DEPARTMENT OF CLINICAL INVESTIGATION

Stewart RS	Molecular Microbiology - Bug Wars IV (The Next Generation).	The Society of Armed Forces Medical Laboratory Scientists, San Antonio, TX, April 92.
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DEPARTMENT OF EMERGENCY MEDICINE

Frohna WJ	Neurogenic Pulmonary Edema Secondary to Traumatic Hydrocephaly in Minor Head Injury.	American College of Emergency Physicians Scientific Assembly, September 92.
Guertler AT	Effects of an Anti-Cyanide Treatment on Sheep Exercise Performance.	Joint Services Symposium on Emergency Medicine, April 92.
Pace SA	Oral Morphine Study.	American College of Emergency Physicians Scientific Assembly, September 92.
Rice MM	Medical/Legal Issues in Emergency Medicine.	Government Services Chapter of the American College of Emergency Physicians, May 92.
Rice MM	Medical/Legal Issues in Emergency Medicine Services/Prehospital Care.	Indian health Services EMS Conference, June 92.
Rice MM	Prehospital Care (EMS).	American College of Emergency Physicians Scientific Assembly, September 92.
Taillac P	The Incidence, Type, and Severity of Pediatric Gunshot Wound in A Large Urban Center.	American College of Emergency Physicians Scientific Assembly, September 92.

DEPARTMENT OF FAMILY PRACTICE

Brown ER, Lillegard WA	The Efficacy and Safety of Strength Training in Children Using Free Weights.	American College of Sports Medicine, Dallas, TX, May 92.
Ellis DD	Infectious Etiologies in Patients With Inflammatory PAP Smears.	Uniformed Services Academy of Family Practice Annual Meeting, Oakland, CA, May 92.

PRESENTATIONS - MAMC - FY 92

Kiser WR	Career Development for Family Practitioners.	43rd Military Medical Surgical Clinical Congress, Willingen, Germany, May 92.
Kiser WR	Tuberculosis Update.	43rd Military Medical Surgical Clinical Congress, Willingen, Germany, May 92.
Kiser WR	Rheumatic Fever Update.	43rd Military Medical Surgical Clinical Congress, Willingen, Germany, May 92.
Kiser WR, Nusbaum MRH, Michels TC, Light DE, Lovins DE, Kugler JP	Wellness in Family Practice Departments.	United Services Academy of Family Physicians Annual Meeting, Oakland, CA, May 92.
Kugler JP	A Study of Various Sociodemographic, Family Function, and Logistic Variation and Prenatal Care Utilization in A Military Setting.	Uniformed Services Academy of Family Physicians Annual Meeting, Oakland, CA, May 92.
Lillegard WA	The Exercise and Nutrition Prescriptions for Family Physicians.	Hawaiian Academy of Family Physicians, ,February 92.
Lillegard WA	The Family Physician as Team Physician.	Uniformed Services Academy of Family Physicians, Oakland, CA, April 92.
Lillegard WA	Sports Nutrition.	Uniformed Services Academy of Family Physicians, Oakland, CA, April 92.

DEPARTMENT OF MEDICINE

Harford R, Reed L, Morris M, Sapien I, Warden R, Kowalski K, Lopez A, D'Alesandro M	Alterations in Thyrotropin, Total and Lipoprotein Cholesterol With Antarctic Residence.	1992 Federation of American Society of Experimental Biologists, Anaheim, CA, April 92.
Jones RE	Characterization and Regulation of Fatty Acid Utilization in Sperm - Implications for Phospholipis Synthesis.	Society of Uniformed Endocrinologists, Endocrine Society, San Antonio, TX, June 92.

PRESENTATIONS - MAMC - FY 92

Kern J	Utility of Bronchoscopy in Evaluation of the Solitary Pulmonary Nodules.	American Thoracic Society, Miami Beach, FL, May 92.
Kowalski K, Reed HL, VanTuyt M, Harford R, Homer L	Change in Oxygen Consumption in Cold Climate Assessed With a Submaximal Cycle Ergometer Test.	1992 Federation of American Society of Experimental Biologists, Anaheim, CA, April 92.
Landry FJ	A Controlled Trial to Improve Medical Student Attitudes, Knowledge, and Use of the Medical Literature.	1992 Meeting of the Society of General Internal Medicine, Washington, DC, April 92.
LeMar H, Georgitis W, Mercill	Thyroid Cell Line Derived From A Papillary Thyroid Cancer With Marked TSH Sensitivity.	American Thyroid Association, Rochester, MN, September 92.
Quesada MH, Reed HL, Cosgrove S, Licaucio G, Castro S, D'Alesandro M, Homer L, Young B	Changes in Porcine Triiodothyronine Distribution After Prolonged Cold Exposure Versus a Short Term Exposure.	1992 Federation of American Society of Experimental Biologists, Anaheim, CA, April 92.
Reed HL, Harford R, Morris M, Sapien L, Warden R, Lopez A, D'Alesandro M, Homer L	Time Course of Changing Serum Triiodothyronine Kinetics and Circulating Thyrotropin With Extended Antarctic Residence.	The Endocrine Society, San Antonio, TX, June 92.
Reed HL, Quesada M, Cosgrove S, D'Alesandro M, Harford R, Castro S, Turner B, Christopherson R	Changes in Porcine Serum Triiodothyronine (T3) Kinetics With Prolonged Exposure to Cold Air.	1992 Federation of American Society of Experimental Biologists, Anaheim, CA, April 92.
Robson ME	The Role of Guanosine-Nucleoside-Binding Proteins in the Regulation of Development of the Liver in the Fetal Rat.	American Association for the Study of Liver Disease, Mackinaw, MI, June 92.
Rone JK, Dons RF, Reed HL	The Effect of Endurance Training on Serum Triiodothyronine (T3) Kinetics in Man: A Proposed Physiologic Role for Thyroid Hormone Action in Physical Training.	Endocrine Society, San Antonio, TX, June 92.

PRESENTATIONS - MAMC - FY 92

Roth BJ,
Plymate SR,
Kushner JP,
Grover BS

Hypogonadism and Chronic
Obstructive Pulmonary Disease.

Regional ACP Meeting,
October 91.

DEPARTMENT OF OB/GYN

Robinson RD,
Polzin WJ,
Kozakowski MH,
Kopelman JN,
Carlson M,
McGlasson DS,
Read JA, Brady WK

Adverse Pregnancy Outcome in
Patients with Antiphospholipid
Antibodies.

American College of
Obstetricians and
Gynecologists, Las Vegas,
NV, April 92.

DEPARTMENT OF RADIOLOGY

Bauman JW

The Use of Bone Scans in the
Diagnosis of Athletic Injuries.

National Athletic Trainers
Association Annual
Meeting and Clinical
Symposium, Denver, CO,
June 92.

Timmons JH

Interventional Ultrasound.

Present Concept in
Diagnostic Radiology
Meeting, San Francisco,
CA, May 92.

DEPARTMENT OF SURGERY

Burgess FW,
Anderson DM,
Colonna DM,
Cavanaugh DG

Can the Addition of Bupivacaine to
Thoracic Epidural Fentanyl
Infusions Decrease Fentanyl
Requirements for Post-thoracotomy
Pain Control.

American Society for
Regional Anesthesia, 17th
Annual Meeting, March 92.

Burgess FW,
Colonna DM,
Anderson DM,
Sborov MJ

Post-thoracotomy Pain; Not All Chest
Wall.

American Society for
Regional Anesthesia, 17th
Annual Meeting, March 92.

Canonico DM,
Morris MR

Arginine Vasopressin in Secreting
Esthesioneuroblastoma.

American Academy of
Otolaryngology - Head and
Head Surgery,
Washington, DC, September
92.

Kruse RW

Posterior Dislocation of Radial Head:
Congenital or Traumatic.

Pediatric Orthopaedic
Trauma Symposium, A.I.
dePont Institute,
Wilmington, DE, February
92.

PRESENTATIONS - MAMC - FY 92

Kruse RW	Reflex Sympathetic Pain in Children: Earlier Diagnosis of a Perplexing Problem.	American Academy of Orthopaedic Surgeons, 59th Annual Meeting, Washington, DC, February 92.
Morris MR	Difficult Surgical, Clinical, and Reconstructive Problems in Otolaryngologic Surgery.	Sixth Annual Reconstructive Surgery Seminar, Tacoma, WA, August 92.
Morris MR, Morris WJ	Esthesioneuroblastoma - An Unusual Presentation Complicating the Surgical Approach.	Third International Congress on Head and Neck Cancer, San Francisco, CA, July 92.
Simmang CL	Anal Spincter Reconstruction in the Elderly: Does Advancing Age Affect Outcome.	American Society of Colon and Rectal Surgeons, June 92.
Taylor GW	21 Year Results of Charnley Total Hip Replacements.	International meeting of the Charnley Low Friction Society, London, England, September 92.
Williard WC	The Role of Amputation in Soft-Tissue Extremity Sarcoma.	Gary Wratten Surgical Symposium, April 92.

INDEX TO PROTOCOLS

O = Ongoing T = Terminated
C = Completed S = Suspended

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
DEPARTMENT OF COMMUNITY MEDICINE			
Provencher MA #92/089	C	A Clinical Comparison of Subjective Autorefractors to Conventional Refraction	43
Vaccaro AR #92/038	C	Low Back Pain - A Retrospective Descriptive Study	44
CLINICAL PSYCHOLOGY SERVICE			
Parkison SC #91/056	C	Use of Psychometric Procedures in Assessing ADHD and the Effects of Stimulant Medication	46
Zych KA #90/049	T	Establishment of Normative Data for Neuropsychological Instruments with a Military Population	47
DEPARTMENT OF CLINICAL INVESTIGATION			
Moore DC #87/100	O	Thyroid Size in Children and Adolescents	49
Moore DC #90/091	O	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...	50
Moore DC #91/092	O	Characterization of LH Isoforms in Treated and Untreated Precocious Puberty	51
Moore DC #92/048	O	Treatment use of Oxandrin (Oxandrolone) in Boys with Constitutional Delay of Growth and Puberty	52
Moore DC #91/060	O	Thyroid Volume in Adolescents as Determined by Ultrasound	53
Moore KH #92/058	O	Is Sex Hormone Binding Globulin Locally Produced in Breast Cancer Tissue?	54
Moore KH #91/043	O	Sex Hormone Binding Globulin (SHBG): Carbohydrate Function and Characterization	55
Moore KH #91/019	C	Mechanisms for Sex-Hormone-Binding-Globulin (SHBG) Regulation of Prostate Carcinoma	57
Moore KH #90/109	O	Characterization of Equine Inhibin: Sequence Analysis and Carbohydrate Composition	58
Powell DA #92/005	O	Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine, Goat, Rabbit, Ferret, Rat, Mouse)	59
Stewart RS #92/074	O	Microbiological Analysis of Male NGU Specimens by Polymerase Chain Reaction: A Retrospective Study	60
Stewart RS #92/075	O	Precise Tissue Distribution of DNA and Hormone Receptors in Breast Biopsies as Clinical Prognosticators: A Retrospective Study	61
Stewart RS #92/073	O	Molecular Microbiology Assay Development	62
Styner MJ #92/034	O	Insulin-Like Growth Factor Binding Proteins in Prostate Carcinoma Cell-Lines	63

DEPARTMENT OF DENTISTRY

Brown CR #91/063	C	Survey of Drugs Utilized by Pediatric Medical Patients and Their Potential Dental Implications	65
Dorsett CR #91/059	O	The Influence of Prophylactic Administration of Intravenous Ondansetron on Post Operative Nausea and Vomiting and Length of Stay in the Post Anesthesia Care Unit	66
Engibous PJ #92/062	O	Postoperative Complications in Operating Room Dentistry for Children	67
Jones HL #90/032	T	An Assessment of Parental Desire to Accompany Their Child in the Dental Operatory	68
Kittle PE #90/068	O	Parental Recall of Informed Consent for General Anesthesia Dental Procedures	69
Kittle PE #91/037	C	The Presence of Human Immunodeficiency Virus (HIV) in the Saliva of Pediatric Acquired Immunodeficiency Syndrome (AIDS) Patients	70
Kittle PE #92/098	O	Waste Anesthetic GAS (WAG) Exposure of Pediatric Dentists During Operating Room Dental Procedures	71
Meadors LW #91/038	C	The Effect of Dentists' Attire on Initial Anxiety Levels in Children	72
Page MG #92/063	O	Common Behavior Management Techniques Used in Pediatric Dentistry: Why Parents Accept or Object to Them	73
Weber CR #90/081	C	Determination of Optimum Dose and Schedule of Intravenous Dexamethasone for Prevention of Postsurgical Edema After Orthognathic Surgery	74
Wygonski RJ #91/061	O	Comparison of Induction and Recovery From Propofol-Nitrous Oxide versus Methohexital-Isoflurane-Nitrous Oxide Anesthesia in Ambulatory Oral Surgery Patients	75

DEPARTMENT OF EMERGENCY MEDICINE

Brantner RD #92/011	C	A Double Blind Placebo Controlled Study of Intramuscular Ketorolac Tromethamine in the Rescue Treatment of Headache	77
Brantner RD #92/100	O	The Randomized Use of Helium-Oxygen Mixture for the Administration of Bronchodilator Therapy in the Treatment of Bronchial Asthma	78
Butcher JD #91/062	C	The Physiologic Toll of Internship	79
Conley LD #91/025	C	Evaluation of a Urine Pregnancy Test Kit in the Emergency Department	80
Frohna WJ #91/012	C	Diagnostic Value and Clinical Significance of the Electrocardiogram During Chest Pain	81
Guertler AT #92/035	C	An Evaluation of the Frequency and Magnitude of Benzocaine-Induced Methemoglobinemia in Humans	82
Holmes KD #90/078	O	Oral Versus Intravenous Steroid: A Prospective Study in Acute Asthma	83
Johnson KR #92/097	O	Pediatric Pain Assessment Survey	84
May TC #91/027	C	Determination of Effectiveness of the Esophageal Detector Device in Young Porcine Animal Models	85

PI and No.	Status	Title	Page
Rice MM #82/025	C	Emergency Room Procedure Training	86
Rice MM #90/016	O	Pediatric Intubation Training Utilizing the Ferret Model	87
Rusinko JB #91/079	C	Effects of Trendelenburg's Position on Oxygen Consumption and Cerebral Perfusion Pressure in the Adult Pig	88
Vanderlinde J #92/039	O	Treatment of Corneal Abrasions: Is Eye Patching Necessary?	89

DEPARTMENT OF FAMILY PRACTICE

Grajcar MS #92/096	O	The Impact of Low Back Pain on Medical Facilities of Fort Lewis	91
Johnson JJ #92/085	S	Diagnoses Which Stimulate Physician Initiated Discussions About Advance Directives: A Survey of Practicing Physicians	92
Kiser WR #92/077	C	Empathy and Specialty Choice in a Population of Army Interns	93
Kiser WR #92/083	O	The Effect of Internship on Moral Reasoning	94
Lewis EL #91/058	O	An Analysis of Selected Elements of Family Function and Related Variable in Adolescent Pregnancy	95
Light DE #91/048	C	Evaluation of Pre- and Postpartum Depression Among Pregnant Wives of Alerted and Deployed Soldiers	96
Lovins DE #92/084	O	Back Pain in Aviators: A Descriptive Study of the Type of Care Received/Sought and Implications for Flight Status - Part Two	97
Lovins DE #92/029	C	Back Pain in Aviators: A Descriptive Study of the Type of Care Received/Sought and Implications for Flight Status	98
Michels TC #92/030	C	Mammography Utilization in a Military Beneficiary Population	99
Uyemura MC #92/003	C	Child Abuse and Neglect Scale	100

DEPARTMENT OF MEDICINE

Andrade WP #89/055	O	Multicenter Clinical Evaluation of Penicillin Skin Testing	102
Bernier RM #92/066	O	A Prospective Study of Headache in Pregnancy	103
Bertram KA #92/009	O	Fluconazole Versus Amphotericin B as Empiric Therapy in Febrile, Neutropenic Patients. University of Washington	104
Bunner DL #92/020	O	Evaluation of the Efficacy and Safety of Glimepiride versus Glyburide in Subjects with Noninsulin-Dependent Diabetes Mellitus (NIDDM)	105
Chamusco RF #90/059	T	Acute Coronary Angiographic and Hemodynamic Response to Cigarette Smoking in Chronic Smokers With Coronary Artery Disease	106
Clayton WL #92/050	O	Effects of Valproic Acid on Semen Parameters in Male Epileptics	107
Cooper RH #91/099	O	Azithromycin in the Treatment of Nongonococcal Urethritis: A Multicenter Double-Blind, Double-Dummy Study Employing Doxycycline as A Comparative Agent	108

PI and No.	Status	Title	Page
Davidson H #92/103	O	Dolasetron Mesylate Protocol MCPR 0031: A Double Blind, Randomized, Parallel Study of the Antiemetic Effectiveness of IV Dolasetron Mesylate vs IV Zofran in Patients Receiving Cisplatin Chemotherapy	109
Davidson H #87/070	C	High Dose Cisplatin, VP-16 With or Without Radiation Therapy in Advanced Nonsmall Cell Lung Cancer	110
Ellingson AE #91/050	C	Sucralfate and Aluminum Absorption	111
Ellis RB #92/072	O	Prognostic Significance of Oncogene Amplification and Expression in Human Breast Cancer	112
Ellis RB #92/070	O	Comparison of TLC D-99 Doxorubicin Liposome Injection versus Doxorubicin Injection in Metastatic Breast Cancer	113
Irvin TL #92/019	O	The Efficacy and Safety of Misoprostol for the Prevention of NSAID-Induced GI Complications	114
Irvine TW #91/013	C	Is Continuous Enteral Feeding Alone Adequate Prophylaxis Against Gastroduodenal Bleeding of Stress Induced Mucosal Lesions	115
Jeffers DJ #89/062	O	Determination of the Sensitivity and Specificity of Light Reflection Rheography for the Diagnosis of Deep Venous Thrombosis in the Lower Extremity	116
Jones RE #92/069	O	Phospholipid Composition of Human Epididymal and Ejaculated Spermatozoa	117
Jones RE #87/023	O	Investigations into the Mechanisms of Phospholipid Synthesis in Human Spermatozoa	118
Jones RE #88/083	C	Influence of Calcium on Phosphatidylcholine Synthesis in Human Spermatozoa	119
Jones RE #85/084	T	Purification of Long Chain Fatty Acid: CoASH Ligase from Human Spermatozoa	120
Jones RE #90/038	O	Detailed Studies Into Membrane Lipid Synthesis in Human Sperm	121
Jones RE #83/081	O	Studies on Fatty Acid Activation in Spermatozoa: Kinetics and Localization	122
Jones RE #88/026	O	Neutral and Polar Lipid Synthesis in Human Spermatozoa: A Correlation with Morphology and Function	123
Jones RE #88/070	O	Characterization of Serovar-Specific Ureaplasma Antigens by Analysis with Monoclonal Antibodies	124
Keenan LM #92/059	O	Bleomycin vs. Minocycline in a Randomized Double Blind Prospective Trial of Intrapleural Therapy for Recurrent Malignant Pleural Effusions	125
Keenan LM #92/057	C	Do Not Resuscitate: Do Not Provide Care?	126
Lyons MF #90/098	O	Does Laparoscopy Add to the Diagnosis of Nonfocal Liver Disease?	127
Lyons MF #91/051	S	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 ...	128
McBurney JW #92/042	T	Safety and Efficacy of BID and QID Dosing with Tiagabine HCl Versus Placebo as Adjunctive Treatment for Complex Partial Seizures	129

PI and No.	Status	Title	Page
McBurney JW #91/073	T	Vagal Nerve Stimulation via Neurocybernetic Prosthesis for the Control of Chronic Epilepsy	130
McCarty JP #92/094	O	Effects of Carnitine on Measures of Cognition, Mood, and Sleep in Adolescents with Epilepsy Treated with Valproate	131
Michael RA #91/003	C	Videx (2',3',-dideoxyinosine, ddi) AIDS Treatment Program	132
Michael RA #92/018	C	Open Label, Compassionate Clearance Treatment of Aids-Related Cryptosporidial Diarrhea with Diclazuril (R64,433)	133
Peele ME #91/097	O	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	134
Reed HL #92/068	O	The Time Course for Metabolic Responses to Thyroid Hormone: Specific Contributions of Muscle Efficiency and Resting Oxygen Utilization	136
Reed HL #92/032	C	The Relationship Between Circulating Androgens and Declining Body Weight During Extended Cold Weather Operations	137
Riordan KK #91/082	T	Iontophoresis Therapy for Rheumatoid Arthritis	138
Riordan KK #91/083	O	Iontophoresis Therapy for Bursitis and Tendinitis	139
Roth BJ #90/099	O	Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure	140
Roth BJ #91/015	O	Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure	141
Roth BJ #89/043	O	The Effects of Testosterone Replacement in Hypogonadal, Malnourished Patients with Chronic Obstructive Pulmonary Disease (COPD)	142
Roth BJ #92/024	O	Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging	143
Saltiel D #90/036	C	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	144
Schwartz PS #90/035	C	Home Intravenous Antibiotic and Heparin Therapy in a Military Setting	145
Sowray PC #90/082	O	A Pilot Study of Carboplatin and Daily Oral Etoposide in the Treatment of Advanced Non-Small Cell Lung Cancer	146
Sowray PC #90/007	O	Treatment of Thrombocytopenia, Hemolytic Anemia, or Neutropenia with Ascorbic Acid	147
Sowray PC #91/044	T	Fludarabine Phosphate in Patients with Refractory Chronic Lymphocytic Leukemia and non-Hodgkin's Lymphoma	148
Treece GL #84/040	T	Treatment of Graves' Ophthalmopathy with Cyclosporin	149
Treece GL #81/056	C	The Effect of Nephrosis on Treated Hypothyroidism	150
Treece GL #82/005	T	The Utility of Urinary Free Cortisol to Monitor Replacement Therapy for Adrenal Insufficiency	151

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
Tsuchida AM #92/045	T	Randomized Trial of Interferon Versus Ursodeoxycholic Acid in the Treatment of Non-A, Non-B, Type C Hepatitis	152
Tuttle RM #91/039	C	Investigation Into the Acute Decline in Serum Testosterone Levels in Healthy Men Exposed to Acute Stress	153
Tuttle RM #91/081	O	The Effect of Thyroid Hormone Suppression on Thyroid Nodules Found to be Indeterminate by Fine Needle Aspiration	154
Tuttle RM #91/080	O	A Prospective Evaluation of Gonadal Damage in Thyroid Cancer Patients Treated with Radioactive Iodine	155
Willadsen DS #92/043	O	Utility of Sinus Tenderness as a Diagnostic Sign in Sinusitis	156

DEPARTMENT OF NURSING

Conway BC #91/026	T	The Primary Needs of Relatives of Critically Ill Patients	158
Hellman S #92/082	O	Evaluation of Aftacare Videotaped Programs on Diabetes, Cancer & Heart Disease for Patient Education as an Intervention in Secondary Prevention of Complications Associated with These Chronic Diseases	159
Loan LA #91/031	C	Tracheal Epithelial Injury and Body Core Temperature Changes Related to Ventilator Inspired Gas Temperatures in Piglets	160
Mittelstaedt EA #92/088	C	Maternal Adaptation: Concerns, Perceived Social Support, and Health Care Utilization	161
Renaud MT #92/102	O	The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants	162
Rich IM #91/046	O	Pregnancy Attitudes, Ambivalence, and Symptom Distress	163
Schultz CK #91/084	C	A Study to Evaluate the Effects of Heparinized and Non-heparinized Flush Solutions on the Patency of Arterial Pressure Monitoring Lines	164
Smith PS #91/075	C	The Effects of Prolonged Parental-Child Separation on School-Aged Children Due to Military Deployment	165
Turner BS #89/028	O	The Effect of Two Levels of Hyperoxygenation Given via a Manual Resuscitation Bag and Ventilator During Endotracheal Suctioning of Premature Infants	166
Turner BS #92/086	O	Physiologic Responses to Exogenous Surfactant	167
Turner BS #90/072	O	Piglet Tracheal Epithelial Injury and Regeneration Following Endotracheal Suctioning	168
Turner BS #91/034	O	Impact of Continuous vs Intermittent Negative Pressure on Tracheal Trauma and Regeneration	169
Turner BS #92/036	C	Transition of the Preterm Infant to an Open Crib	170
Yackel EE #92/078	C	Nurses vs. Patients: Views on Nurses Smoking and Its Influence on Patient Health Practice	171
Young-McCaughan SB #91/047	C	The Relationship of the Sense of Coherence and Hardiness to the Nutritional Status of Anorectic Head and Neck Cancer Patients Currently Undergoing Radiation Therapy	172

NUTRITION CARE DIVISION

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
Charney PJ #91/041	C	Dental Liquid Ration Evaluation	174

DEPARTMENT OF OB/GYN

Armstrong AY #92/010	O	Predictors of Response to Ovulation Induction with Clomiphene Citrate in the Overweight Patient	176
Armstrong AY #92/093	O	Hyperactivation in Cryopreserved Spermatozoa Effects of Progesterone and Various Membrane-Active Agents	177
Bayliss PM #89/022	T	Preterm Delivery Prevention	178
Boley TJ #92/021	O	Amniotic Fluid Index: A Comparison Between Real Time Ultrasound and Color Flow Doppler Ultrasound in its Determination	179
Boley TJ #92/071	O	The Establishment of the Doubly Perfused, Placental Cotyledon Model for the In Vitro Investigation of the Umbilical-Placental Circulation	180
Boley TJ #92/023	O	A Comparison of Amniotic Fluid Collected by Amniocentesis versus Amniotic Fluid Collected Via an Intrauterine Pressure Catheter in the Diagnosis of Chorioamnionitis in Laboring Patients at Term	181
Boley TJ #92/022	O	Continuous Infusion Epidural Analgesia: Its Effects on the Doppler Velocimetry of the Umbilical Arteries of Normotensive and Preeclamptic Patients in Labor	182
Boley TJ #92/090	O	The Effects of Estradiol and Progesterone on Vasoactive Substances in the Dually Perfused Cotyledon Model	183
Dyksterhouse DL #92/064	C	Role of Color Flow Doppler in Evaluation of Patients with Persistent Trophoblastic Disease	184
Foos CC #92/041	O	Correlation of Vaginal Ultrasonographic Findings with Pathology in GYN Surgical Patients	185
Kopelman JN #92/060	O	A Randomized Prospective Evaluation of Bladder Flap Closure at Time of Cesarean Section	186
Kopelman JN #90/034	T	Cordocentesis in an Animal Model	187
Kopelman JN #92/101	O	Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy	188
Larsen WI #90/106	C	Evaluation of Efficacy of Twelve Hour Urine Collections in the Diagnosis of Pre-eclampsia	189
Nelson KM #91/024	T	The Evaluation of an Endocervical Brush Device in a Population of Pregnant Patients	190
Potter ME #89/017	O	Surgical Management of the Bowel and Urinary Tract in Gynecologic Surgery (Swine Model)	191
Read JA #92/091	C	Quantitative Evaluation of Blood Loss in Parturients With and Without Clinical Chorioamnionitis	192

PREVENTIVE MEDICINE SERVICE

Baird CP #92/027	C	Immunization Status Among Two Year Olds and the Role of Missed Opportunities	194
Davidson DR #92/028	C	Epidemiology of Unintentional Injuries in Infant and Toddler Age Children in a Military Population	195
Fuery HA #92/076	O	Early Identification of and Assistance to Pregnant Women Subjected to Domestic Violence	196

PI and No.	Status	Title	Page
Krauss MR #90/014	O	Assessment of Risk Factors for HIV Infection Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion - Incident Cases	197
Rubertone MC #92/033	C	STD Recidivism Study	198

DEPARTMENT OF PEDIATRICS

Babonis TR #91/004	T	Tympanometry Guidance for Treatment of Otitis Media	200
Babonis TR #91/093	C	Health Habits and Lifestyles in Families of Children Less Than Two Years of Age	201
Babonis TR #92/049	C	Perceptions of Discipline and Child Physical Abuse Among Blacks and Whites	202
Beachy JC #90/058	O	Neonatal Emergency Procedure Training in the Rabbit Model	203
Broadhurst RB #91/055	O	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	204
Brooks KL #92/004	O	Incidence of Group A Beta Hemolytic Streptococcus Colonization and Infection in Association with Varicella	205
Dubravec VA #90/079	O	Use of Metoclopramide With Chloral Hydrate for Sedation	206
Kahn CA #92/044	O	Lead Levels and Their Relationship to Attention Deficit Hyperactivity Disorder and Developmental Delay	207
Krober MS #90/071	O	Pyridoxine as Specific Therapy and Prophylaxis in the Treatment of Theophylline-Induced Seizures in Mouse and Rabbit Models	208
Krober MS #90/108	T	Role of Anticonvulsants in Theophylline Toxicity	210
Krober MS #91/053	O	Role of Glutamine and 4-aminobutyraldehyde in Pyridoxine-Treated Theophylline Toxicity	211
Krober MS #91/052	T	Role of Anticonvulsants with Pyridoxine in Theophyllin Toxicity in Rabbits	212
Krober MS #89/076	O	Protective Role of Pyridoxine in Gentamicin Nephrotoxicity	213
Krober MS #92/007	O	A Comparative Study of the Safety and Efficacy of Clarithromycin and Eryped (Erythromycin Ethylsuccinate) Suspensions in the Treatment of Children with Community-Acquired Pneumonia	214
Krober MS #90/092	O	Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses	215
Krober MS #90/093	O	Epidemiology of HIV in Pediatric and Perinatal Patients: A Natural History Study	216
Krober MS #90/107	O	Perinatal HIV Infection: Epidemiology and Natural History	217
Krober MS #91/018	O	Role of Pyridoxine in Gentamicin-Lasix Nephrotoxicity in Rabbits	218
Scott JS #89/071	O	Comparison of Effectiveness of Lidocaine HCL vs Hyaluronidase in the Early Treatment of Soft Tissue Extravasation Injuries in Swine	219

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
Stafford EM #92/067	O	Cervical Human Papillomavirus Infection Prevalence in Female ROTC College Cadets	220
DEPARTMENT OF RADIOLOGY			
Bender GN #92/012	T	Nasogastric Tissue Sampling of the Upper Alimentary Tract	222
Bender GN #92/013	T	Nasogastric (Gastric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Stomach (Feasibility Study)	223
Bender GN #92/014	T	Nasogastric (Gastric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Stomach (Validation for Detection of Gastric Carcinoma)	224
Bender GN #92/015	T	Nasogastric (Gastaric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Pancreas	225
DEPARTMENT OF SURGERY			
Burgess FW #91/028	O	The Influence of Prophylactic Administration of Intravenous Crystalloid and Colloid Solutions on the Incidence of Hypotension Following Subarachnoid Anesthesia	227
Burgess FW #91/029	T	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 ...	228
Burgess FW #91/030	C	Determination of the Ideal Bupivacaine/Fentanyl Concentration for Continuous Thoracic Epidural Infusion for Postoperative Analgesia in Thoracotomy Patients	229
Burgess FW #91/035	C	The Effects of Combined General and Epidural Anesthesia on the Physiologic Response to Hemorrhagic Shock in Swine: II	230
Burgess FW #91/090	O	Selective Blockade of the Vagus Nerve to Relieve Referred Shoulder Pain Associated with Pulmonary Surgery in Human Subjects	232
Burgess FW #92/008	O	Influence of Phrenic Nerve Blockade on the Incidence of Referred Shoulder Pain in Patients Undergoing Thoracic Surgery for Pneumonectomy	233
Burgess FW #92/047	O	Identification of the Optimal Bupivacaine Concentration for Epidural Analgesia in Combination with Patient Controlled Epidural Fentanyl Analgesia	234
Burgess FW #92/061	O	A Double Blind, Placebo-Controlled Comparison Between 0.125%, 0.25%, and 0.5% Ropivacaine, When Used for Post-operative Infiltration in Herniorrhaphies: A Dose Resposne Study	235
Canonico DM #92/026	S	Shoulder Morbidity in Head and Neck Surgery	236
Chismire KJ #79/064	C	Implantation of Intraocular Lenses	237
Cosio MQ #86/016	O	Teaching Program for Practical Microsurgery	238
Davis SM #92/099	O	The Implantation of Bone Morphogenic Protein Using Vascularized Omentum in a Predetermined Size and Shape in Swine	239
Grace TS #92/037	C	Metatarsus Proximus: Its Association with Interdigital Neuromas	240
Gridley GD #92/046	O	Can the Combination of Intramuscular Ketorolac and Continuous Epidural Bupivacaine Eliminate the Need for Narcotic Analgesia Post-Thoracotomy	241

PI and No.	Status	Title	Page
Hansberry KL #91/098	O	Randomized Prospective Study Comparing Intermittent Pneumatic Compression of the Calf to Intermittent Sequential Pneumatic Compression of the Whole Leg	242
Helman JD #92/087	O	Patient-Controlled Analgesia and the Risk of Postoperative Myocardial Ischemia	243
Kaufmann CR #85/021	O	Advanced Trauma Life Support Course	244
Knight RW #91/091	O	Transurethral Prostatectomy and Associated Erectile Dysfunction	245
Mooney MJ #91/042	T	The Effect of Catheter Tunnelling With and Without Addition of a Subcutaneous Cuff on Catheter-Related Sepsis	246
Morris MR #89/005	C	An Epidemiological Study of Nasopharyngeal Cancer	247
Neary MT #92/031	C	Evaluation of the Rate of Avascular Necrosis Formation Following Austin Bunionectomy: A Follow-up Study	248
Parmley VC #92/092	O	Gram Negative Endotoxin Monoclonal Antibody as an Adjunct to Treating Gram Negative Endophthalmitis in the Rabbit	249
Perkins JA #92/025	C	Neuropeptide Levels in Nasal Secretions and Mucosa of Patients with Chronic Sinusitis and Nasal Polyposis	250
Sborov MJ #91/036	C	Influence of Baricity on the Elimination of Local Anesthetics from the Subarachnoid Space in a Swine Model	251
Simmang CL #87/007	O	General Surgery Stapling Familiarization Lab (Swine Model)	252
StLouis JS #90/015	O	Investigation of Cryotreatment on the Epiphysis of Growing Rabbit Bone	253

FORT ORD MEDDAC

Carter PM #92/081	C	A Benefit-Cost/Utility Analysis of Cervical Cytology During Pregnancy	255
----------------------	---	---	-----

FORT WAINWRIGHT, ALASKA

Levine ME #91/054	O	Melatonin and Cortisol Secretion in the Arctic, Effects of Photoperiod on Circadian Rhythms and Mood	257
----------------------	---	--	-----

LETTERMAN MEDDAC

Tobin LM #92/085	O	Racial Differences in Responses to the Rorschach Inkblot Test in a Psychiatric Population	259
---------------------	---	---	-----

U.S. DEPARTMENT OF AGRICULTURE

Burri BJ #92/001	O	Methods for Assessing Vitamin A Status in Healthy Adults	261
---------------------	---	--	-----

CHILDREN'S CANCER STUDY GROUP

Albano EA #89/009	T	CCG 321P4: "6 in 1" Chemotherapy for Children with Newly Diagnosed Advanced Stage Neuroblastoma	263
Albano EA #90/100	T	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	264

PI and No.	Status	Title	Page
Albano EA #90/100	T	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	264
Albano EA #90/101	T	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	265
Albano EA #90/102	T	CCG 1883: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Infants Less Than 12 Months of Age, Phase III	266
Albano EA #90/103	T	CCG 1884: A Comparison of Idarubicin to Daunomycin in A Multi-Drug Treatment of ALL in Marros Relapse	267
Albano EA #87/076	T	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	268
Albano EA #87/093	T	CCG 134P: Therapy of Acute Lymphoblastic Leukemia in High Risk Patients	269
Albano EA #88/063	T	CCG 144: Treatment of Acute Lymphoblastic Leukemia in Average Risk Patients	270
Albano EA #88/014	T	CCG 213: Treatment of Newly Diagnosed Acute Non-lymphoblastic Leukemia for Children Greater than One Month but Less than 21 Years of Age	271
Albano EA #87/112	T	CCG 461: Intergroup National Wilms' Tumor Study - 4	272
Albano EA #87/067	T	CCG 8602: Idarubicin for Remission Induction in Patients with Leukemia in Children in Second or Subsequent Marrow Relapse	273

GYNECOLOGY ONCOLOGY GROUP

Downey GO #88/067	O	GOG 26DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies	275
Downey GO #88/082	O	GOG 26EE: A Phase II Trial of Didemnin B (NSC #325319) in Patients with Advanced Pelvic Malignancies	276
Downey GO #90/023	O	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	277
Downey GO #90/024	C	GOG 26HH: A Phase II Trial of 5-Fluorouracil and Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies	278
Downey GO #90/026	O	GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia	279
Downey GO #91/008	O	GOG 26II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies	280
Downey GO #91/009	O	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 ...	281
Downey GO #91/010	O	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 ...	282
Downey GO #91/011	O	GOG 112: A Randomized Comparison of Chemoprophylaxis Using Methotrexate versus Routine Surveillance in the Management of the High Risk Molar Pregnancy	283

PI and No.	Status	Title	Page
Downey GO #89/036	O	GOG 93: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)	285
Downey GO #88/081	O	GOG 106: Evaluation of the Serum Marker, CA-125, in the Management of Carcinoma of the Endometrium	286
Downey GO #89/037	O	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	287
Downey GO #89/052	O	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	288
Downey GO #89/038	C	GOG 8803: Flow Cytometrically Determined Tumor DNA Content in Advanced Epithelial Ovarian Cancer	289
Downey GO #89/039	O	GOG 8809: Flow Cytometrically Determined Tumor DNA Content in Ovarian Tumors of Low Malignant Potential	290
Downey GO #89/041	C	GOG 8810: Flow Cytometrically Determined DNA Content in Endometrial Carcinoma	291
Downey GO #89/072	C	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	292
Downey GO #91/074	O	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,	293
Downey GO #91/085	O	GOG 26KK: A Phase II Trial of Merbarone (NSC336628) in Patients with Advanced and Recurrent Epithelial Ovarian Carcinoma	294
Downey GO #91/086	O	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 ...	295
Downey GO #82/073	O	GOG 26A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies	296
Downey GO #82/007	O	GOG 26C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies	297
Downey GO #83/024	O	GOG 26N: A Phase II Trial of Dihydroxyanthracenedione (DHAD) (NSC #30179) (CL232315) in Patients with Advanced Pelvic Malignancies	298
Downey GO #83/026	O	GOG 26Q: A Phase II Trial of Aminothiadiazole in Patients with Advanced Pelvic Malignancies	299
Downey GO #84/064	C	GOG 26S: A Phase II Trial of Teniposide in Patients with Advanced Pelvic Malignancies	300
Downey GO #85/087	O	GOG 26U: A Phase II Trail of Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #25232) in Patients with Advanced Pelvic Malignancies	301
Downey GO #86/075	O	GOG 26W: A Phase II Trial of Echinomycin in Patients with Advanced Pelvic Malignancies	302
Downey GO #88/058	O	GOG 26X: A Phase II Trial of Gallium Nitrate (NSC #15200) in Patients with Advanced Pelvic Malignancies	303
Downey GO #81/079	O	GOG 40: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas	304

PI and No.	Status	Title	Page
Downey GO #81/079	O	GOG 40: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas	304
Downey GO #84/033	O	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	305
Downey GO #84/074	O	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 ...	306
Downey GO #87/048	C	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	307
Downey GO #87/028	O	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	308
Downey GO #87/091	O	GOG 99: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma	309
Downey GO #87/105	O	GOG 100: Monoclonal Antibody Against Free Beta HCG to Predict Development of Persistent Gestational Trophoblastic Disease (PGTD) in Patients with Hydatidiform Mole	310
Downey GO #81/035	O	GOG 41: Surgical Staging of Ovarian Carcinoma	311
Downey GO #81/118	C	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...	312
Downey GO #82/036	C	GOG 63: A Clinical Pathologic Study of Stages IIB, III, and IVA Carcinoma of the Cervix	313
Downey GO #85/090	C	GOG 83: A Clinico-Pathologic Study of Simultaneous Endometrial and Ovarian Carcinomas	314
Downey GO #83/041	C	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...	315
Downey GO #87/104	O	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	316
Downey GO #87/106	O	GOG 101: A Phase II Evaluation of Preoperative Chemoradiation for Advanced Vulvar Cancer	317
Downey GO #87/013	O	GOG 90: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors	318
NATIONAL CANCER INSTITUTE			
Downey GO #81/033	O	NCI 7602: All Stage IC and II 9A,B,C) and Selected Stage IAii and IBii Ovarian Cancer	320

PEDIATRIC ONCOLOGY GROUP

PI and No.	Status	Title	Page
Albano EA #89/077	T	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 ...	322
PUGET SOUND ONCOLOGY GROUP			
Downey GO #87/079	O	PSOC 615: Intraperitoneal Consolidation Therapy Following Second-Look Operation in Ovarian Cancer	324
Sowray PC #91/066	O	PSOC 1007: Adriamycin and Cefoperazone for Treatment of Carcinoma and Sarcoma Refractory to Adriamycin	325
SOUTHWEST ONCOLOGY GROUP			
Bertram KA #92/006	C	SWOG 9016: Study of External Brain Irridation and Cisplatin/BCNU Followed by BCNU for the Treatment of Primary Malignant Brain Tumors	327
Bertram KA #92/052	O	SWOG 9031: A Double Blind Placebo Controlled Tiral of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Luekemia, Phase III	328
Bertram KA #91/094	O	SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary	329
Bertram KA #91/096	O	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...	330
Bertram KA #92/095	O	SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia	331
Cobos E #89/060	C	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 ...	332
Davidson H #90/087	C	SWOG 8910: Evaluation of Low Dose Continuous 5-Fluorouracil (5-FU) and Weekly Cisplatinum (CCDP) in Advanced Adenocarcinoma of the Stomach	333
Davidson H #90/047	O	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	334
Davidson H #88/003	O	SWOG 8520: Cis-Diamminedichloroplatinum (II), Methotrexate and Bleomycin in the Treatment of Advanced Epidermoid Carcinoma of the Penis, Phase II	335
Davidson H #87/033	O	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 ...	336
Davidson H #88/021	C	SWOG 8792 (EST 2886, INT 0079): Phase III Study of Alfa-nl (Wellferon) as Adjuvant Treatment for Resectable Renal Cell Carcinoma	337
Davidson H #85/073	O	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...	338

PI and No.	Status	Title	Page
Davidson H #85/008	C	SWOG 8300: Treatment of Limited Non-small Cell Lung Cancer: Radiation versus Radiation Plus Chemotherapy (FOMi/CAP), Phase III	339
Davidson H #85/064	O	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	340
Davidson H #84/019	C	SWOG 8221: Treatment of Advanced Bladder Cancer with Preoperative Irradiation and Radical Cystectomy versus Radical Cystectomy Alone, Phase III	341
Davidson H #84/018	O	SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer	342
Davidson H #91/069	O	SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study	343
Davidson H #90/084	O	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	344
Davidson H #83/056	O	SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study	345
Davidson H #88/032	C	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	346
Davidson H #88/053	C	SWOG 8515. Evaluation of Menogaril (NSC 269148) in Non-Hodgkin's Lymphoma, Phase II	347
Davidson H #87/107	O	SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III	348
Davidson H #88/066	O	SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)	349
Davidson H #88/065	O	SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy	350
Davidson H #88/076	O	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	351
Davidson H #89/021	O	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...	352
Davidson H #89/058	O	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	353
Davidson H #89/045	O	SWOG 8621: Chemohormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III	354
Davidson H #90/027	O	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....	355
Davidson H #90/029	O	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...	356

PI and No.	Status	Title	Page
Davidson H #90/056	O	SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide	357
Davidson H #90/065	C	SWOG 8906: Evaluation of Merbarone in Hepatoma, Phase II	358
Davidson H #90/086	O	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	359
Davidson H #89/080	O	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...	360
Davidson H #92/079	O	SWOG 8925: Evaluation of Cisplatin + VP-16 Followed by Mitotane at Progression if no Prior Mitotane or Cisplatin + VP-16 Only if Prior Treatment with Mitotane in Patients with Advanced and ...	361
Davidson H #84/059	O	SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III	362
Davidson H #79/096	O	SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III	363
Davidson H #78/047	O	SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6	364
Davis RC #90/039	O	SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)	365
Davis RC #90/040	O	SWOG 8793 (EST-3883): Randomized Phase III Evaluation of Hormonal Therapy versus Observation in Patients with Stage D1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prost	366
Gomez PL #91/067	O	SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients	367
Gomez PL #90/054	O	SWOG 8810: Six Courses of 5-Fluorouracil & Cisplatin with Correlation of Clinical & Cellular DNA Parameters in Patients with Advanced, Untreated, & Unresectable Squamous Cell Carcinoma of the...	368
Gomez PL #90/055	O	SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III	369
Gomez PL #90/110	C	SWOG 8915: A Phase II Study of 6-Thioguanine Administered as 120 Hour Continuous Infusion for Refractory or Recurrent Small Cell Carcinoma	370
Gomez PL #91/007	O	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	371
Gomez PL #91/070	C	SWOG 9046: Evaluation of 10-EdAM in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck	372
Gomez PL #92/017	O	SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma	373
Phillips WA #91/006	O	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	374

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
Phillips WA #91/021	O	SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver	375
Phillips WA #91/045	O	SWOG 9028: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD to VAD/Verapamil/Quinine for Induction	376
Rearden TP #92/104	O	SWOG 9110: A Phase II Evaluation of Diademnin B in Central Nervous System Tumors	377
Sowray PC #92/002	O	SWOG 9045: Evaluation of Quality of Life in Patients with Advanced Colorectal Cancer Enrolled on SWOG 8905	378
Sowray PC #87/045	O	SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia	379
Sowray PC #86/007	O	SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III	380
Sowray PC #89/065	O	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	381
Sowray PC #87/111	C	SWOG 8694 (CALGB 8582): A Comparison of Pentostatin (NSC-218321) and Alpha-Interferon (NSC-377523) in Splenectomized Patients With Active Hairy Cell Leukemia	382
Sowray PC #91/078	O	SWOG 9111: Post-Operative Adjuvant Interferon Alpha 2 in Resected High-Risk Primary and Regionally Metastatic Melanoma, Intergroup	383
Sowray PC #90/041	O	SWOG 8828: A Phase II Trial of Carboplatin (CBDCA) in Relapsed or Refractory Acute Myeloid Leukemia	384
Sowray PC #90/063	O	SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors	385
Sowray PC #90/064	O	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	386
Sowray PC #90/088	C	SWOG 8923: "Neo-Fac" for Poor Prognosis Stage IV Breast Cancer, A Phase II Pilot Study	387
Sowray PC #90/112	O	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..	388
Sowray PC #91/068	O	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)	389
Sowray PC #91/076	C	SWOG 8936: Evaluation of Piroxantrone in Gastric Carcinoma, Phase II	390
Sowray PC #91/077	O	SWOG 9039: Evaluation of Quality of Life in Patients with Stage D2 Cancer of the Prostate Enrolled on SWOG 8894	391
Sowray PC #91/033	O	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	392

<u>PI and No.</u>	<u>Status</u>	<u>Title</u>	<u>Page</u>
Sowray PC #92/053	O	SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II	393
Sowray PC #92/056	O	SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients	394
Sowray PC #92/054	O	SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II	395
Sowray PC #92/080	O	SWOG 9151: Evaluation of Topotecan in Hepatoma, Phase II	396
Sowray PC #92/055	O	SWOG 8842: Dihydroxyazacytidine in Malignant Mesothelioma, Phase II Study	397
Sowray PC #91/088	C	SWOG 8900: A Phase II Pilot of VAD and VAD/Verapamil for Refractory Multiple Myeloma	398
Sowray PC #91/095	C	SWOG 9012: Evaluation of Low Dose Alpha-Interferon in Patients with Advanced Renal Cell Carcinoma, Phase II	399
Sowray PC #92/016	C	SWOG 9009: Pilot Study for Analysis of Lymphocyte Sub-Set in Natural Killer Activity After Treatment with Levamisole	400
Sowray PC #92/040	O	SWOG 9030: Phase II Study of High Dose Ara-C/Mitoxantrone for the Treatment of Relapsed/Refractory Acute Lymphocytic Leukemia	401
Sowray PC #91/087	O	SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol	402
Stapleton LM #91/089	O	SWOG 8947: Central Lymphoma Serum Repository Protocol	403
Sowray PC #87/109	C	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,...	404
Sowray PC #90/030	O	SWOG 8905: Phase II/III Study of Fluorouracil and Its Modulation in Advanced Colorectal Cancer	405
Sowray PC #90/028	C	SWOG 8857: Alternating Cisplatin/VP-16 with Continuous CAV and Consolidation Chemotherapy for Extensive Small Cell Lung Cancer with PCI for Complete Responders	406
Sowray PC #91/020	O	SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II	407
Sowray PC #91/032	O	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	408
Stapleton LM #92/051	O	SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II	409

UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

Davidson H #89/013	O	UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System	411
Davidson H #88/073	O	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	412
Davidson H #88/017	O	UWNG 87-01: Phase II Study of TPDCHF for Recurrent Malignant Brain Tumor	413

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF COMMUNITY MEDICINE

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/089	Status: Completed
Title: A Clinical Comparison of Subjective Autorefractors to Conventional Refraction		
Start Date: 08/03/92	Est. Completion Date:	
Department: Community Medicine	Facility: MAMC	
Principal Investigator: MAJ Marc A. Provencher, MS		
Associate Investigators: LTC Merlin C. Johns, MC		COL Robert H. Pinson, MC Tony Bentley, M.D.
Key Words: optometry, autorefractors		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective : To determine the accuracy and cost effectiveness of two autorefractors with subjective refinement capability, the Allergan Humphrey Model 570 and the Marco Technologies AR1600G.

Technical Approach : Patients (n=100) presenting for vision care will be given an autorefraction with subjective refinement using the two autorefractors as part of the routine pre-exam procedures. Using each instrument, a technician will perform an autorefraction and then refine it by showing the patient various targets and asking questions. These results will be compared to the results obtained by an optometrist following the same procedure. The data gathered will be objective autorefraction and visual acuity, subjective refinement and visual acuity with the autorefractor, time elapsed from positioning the patient at the autorefractor until the print out of the data to the nearest minute; and the patients age and any medical/ocular conditions affecting vision. Autorefractor measurements will be compared to the subjective best visual acuity refraction to the nearest 0.25 diopter using frequency histograms, scattergrams, and simple descriptive statistics. Cost effectiveness will be assessed using a simple cost analysis. Military pay grades will be used using the pay grade E/5 for the technician and O/4 for the optometrist. Equipment cost will be determined using manufacturer's retail price and accepted accounting principles to determine yearly cost plus the cost of a yearly service contract.

Progress : One hundred twenty subjects were studied. A complete statistical analysis is in progress. Preliminary data analysis indicates minimal improvement in refraction accuracy using subjective autorefraction when compared to the autorefraction. Subjective autorefraction is probably not cost effective in the military health care environment.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/038	Status: Completed
Title: Low Back Pain - A Retrospective Descriptive Study		
Start Date: 02/07/92	Est. Completion Date:	
Department: Community Medicine	Facility: MAMC	
Principal Investigator: CPT Alfonso R. Vaccaro, MC		
Associate Investigators: CW4 Charles Gorie		
LTC James L. Fleming, MC		
Key Words: Low back pain, management		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To identify delays in treatment of soldiers with low back pain to identify subspecialties that are being misutilized in the care of low back pain patients to identify the subspecialty performing the majority of medical boards for low back pain and to identify any specific demographic profile associated with low back pain patients presenting to a medical board.

Technical Approach: This low back pain management study will be a retrospective descriptive study of 49 active-duty Army and National Guard personnel who completed a formal medical board at Madigan in 1990, specifically for low back pain. Data will be collected from the patient's medical board files, inpatient and outpatient medical records. Data collection will include: demographics type(s) of treatment utilized subspecialties utilized and the timetables in which these treatments and consultations were performed. Demographic data will be collected to detect any trends in the selected patient population. Information or findings from this study will have no impact on the studied population. Simple descriptive statistical analysis will be utilized. Results will be presented to the MAMC Healthy Back Committee.

Progress: The results were reported to the QA Committee as a QA study. No paper is being written.

DETAIL SHEETS FOR PROTOCOLS

CLINICAL PSYCHOLOGY SERVICE

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/056 **Status:** Completed

Title: Use of Psychometric Procedures in Assessing ADHD and the Effects of Stimulant Medication

Start Date: 04/05/91

Est. Completion Date: Feb 91

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

Principal Investigator: MAJ Steven C. Parkison, MS

Associate Investigators:
Thomas A. Clinghan, M.D.
CPT Robert A. Byrne, MS

LTC Thomas R. Babonis, MC
LTC Patrick C. Kelly, MC

Key Words: ADHD, psychometric procedures, stimulant medication

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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: No further work was done on this study in FY 92 due to a shortage of personnel and time constraints. Twenty subjects were entered previously. The results suggest that the Stroop Color Test is helpful in distinguishing ADHA children from normal children.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/049

Status: Terminated

Title: Establishment of Normative Data for Neuropsychological Instruments with a Military Population

Start Date: 06/15/90

Est. Completion Date: Mar 91

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

Principal Investigator: LTC Kenneth A. Zych, MS

Associate Investigators:
Timothy S. Clark, Ph.D.

Alberta Klaus-Hagen, Ph.D.

Key Words: neuropsychological instruments, military population

Accumulative
MEDCASE Cost:

\$0.00

Est. Accumulative
OMA Cost:

\$200.00

Periodic Review:
04/05/91

Study Objective: To collect normative data on standardized neuropsychological 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: No patients were entered on this protocol. It was never implemented because of personnel shortages and patient load of the investigators.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/100	Status: On-going
Title: Thyroid Size in Children and Adolescents		
Start Date: 08/21/87	Est. Completion Date: Nov 91	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: None		
Key Words: thyroid size, adolescents		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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: 246 patients have been entered (27 in FY 92). Data collection continues.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/091	Status: On-going
Title: A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp ⁽⁶⁾ -Des-Gly ⁽¹⁰⁾ -N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing Factor (Deslorelin)		
Start Date: 08/17/90	Est. Completion Date: Nov 92	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: None		
Key Words: precocious puberty, deslorelin, LH		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	07/02/92

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: No new patients entered in FY 92. One patient has dropped out of the study and two others continue. There has been no progression of puberty in these patients.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 91/092		Status: On-going
Title: Characterization of LH Isoforms in Treated and Untreated Precocious Puberty				
Start Date: 09/06/91		Est. Completion Date: Jun 92		
Department: Clinical Investigation		Facility: MAMC		
Principal Investigator: COL Dan C. Moore, MC				
Associate Investigators: MAJ Jim Hansen, MC		CPT Katherine H. Moore, MS		
Key Words: precocious puberty,LH:isoforms				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$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 0.025 M Tris (pH=9.3) for 2 hours and then applied to a 1.0 x 20 cm Mono P HR 5/20 column (4 ml column volume), which has been equilibrated with 15 column volumes of 0.025 M Tris (pH=9.3). The sample is eluted with 50 ml Polybuffer 96 (diluted 1:10 with water, pH=6.0) at 1 ml/min and collected in 2 ml fractions. To study LH isoforms which are present between pH 7 and 4, similar procedures will be used, substituting Polybuffer 74 and Tris protein precipitation with 0.5 ml of 1% BSA and 2.8 g of powdered ammonium sulfate. After thorough mixing and incubating at 20 deg C for 2 hr. the fractions are centrifuged at 1500 g for 30 minutes. Supernatant is discarded and precipitates are washed once with saturated ammonium sulfate and then reconstituted in 0.5 ml of assay buffer for LH RIA and bioassay. Aliquots of fractions which contain LH activity will be pooled for each chromatofocusing peak and analyzed for LH immunoactivity and bioactivity. Changes in bioactivity correlating with changes in chromatofocusing pattern will be sought in pre and post treatment sera.

Progress: Samples were received for 12 patients in August 1992. The one patient analyzed in FY 92 had precocious puberty and a chromatofocusing pattern that looked pubertal.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/048	Status: On-going
Title: Treatment use of Oxandrin (Oxandrolone) in Boys with Constitutional Delay of Growth and Puberty		
Start Date: 06/05/92	Est. Completion Date:	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: COL Dan C. Moore, MC		
Associate Investigators: MAJ Robert A. Newman, MC		
Key Words: delayed maturation and growth, boys, oxandrin		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: No patients have yet met the eligibility criteria.

Detail Summary Sheet

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

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

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

Progress: Thirty-six patients were entered in FY 92 for a total of 73 subjects. Enrollment continues. No data have been analyzed yet.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/058	Status: On-going
Title: Is Sex Hormone Binding Globulin Locally Produced in Breast Cancer Tissue?		
Start Date: 05/01/92	Est. Completion Date: Jun 94	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: CPT Katherine H. Moore, MS		
Associate Investigators: Louis A. Matej, B.S.		MAJ Kenneth A. Bertram, MC
Key Words: SHBG, breast cancer		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: In preliminary experiments, we have isolated mRNA from two breast cancer cell lines (MCF-7 and ZR75-1) and probed for SHBG using Northern blot procedures. SHBG mRNA was identified in the ZR75-1 cell line, but not in the MCF-7. The SHBG mRNA identified in the ZR75-1 cells contained multiple transcripts, similar to what has been identified in prostate cancer cells. It remains to be determined if the ZR75-1 cells are producing functional SHBG or if this mRNA is coding for a functional protein.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/043

Status: On-going

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

Start Date: 03/01/91

Est. Completion Date: May 92

Department: Clinical Investigation

Facility: MAMC

Principal Investigator: CPT Katherine H. Moore, MS

Associate Investigators:

MAJ John E. van Hamont, MS

Louis A. Matej, B.S.

Philip H. Petra, Ph.D.

CPT Robert M. Tuttle, MC

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

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

08/07/92

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 ¹²⁵I 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 ¹²⁵I label) and the clearance measured by IRMA. The animals will have chronically implanted cannulas, allowing repeated sampling from individual animals. Samples will be collected for 6 days.

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

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

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/019	Status: Completed
Title: Mechanisms for Sex-Hormone-Binding-Globulin (SHBG) Regulation of Prostate Carcinoma		
Start Date: 11/16/90	Est. Completion Date: Dec 93	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: CPT Katherine H. Moore, MS		
Associate Investigators: MAJ Curtis J. Hobbs, MC CPT Brenda K. Bell, MC Geoffrey Hammond, M.D. M. J. Styner, B.S.	LTC John A. Vaccaro, MC COL Stephen R. Plymate, MC Steve Loop CPT Rita C. Hoop, MC James R. Wright, M.T.	
Key Words: cancer:prostate,SHBG:regulation		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: The investigators were able to confirm the effects of thyroxine, estradiol, testosterone, insulin, and epidermal growth factor on SHBG mRNA production in ALVA 101 and DU 145 cell lines. The effect of these hormones and growth factors in HepG2 cells served as a positive control. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/109		Status: On-going	
Title: Characterization of Equine Inhibin: Sequence Analysis and Carbohydrate Composition					
Start Date: 10/19/90			Est. Completion Date: Oct 92		
Department: Clinical Investigation			Facility: MAMC		
Principal Investigator: CPT Katherine H. Moore, MS					
Associate Investigators:			Kristine M. Wiren, Ph.D.		
Key Words: equine inhibin,sequence,carbohydrate composition,Animal Study					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$8870.00	08/07/92	

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: The rat pituitary cell bioassay was used to detect inhibin activity during purification. Equine follicular fluid was equally potent to porcine follicular fluid in this assay (v/v). Western blot analysis was used to study the size heterogeneity of the inhibin alpha and beta subunits. The alpha subunit antibody was against porcine alpha subunit and the beta-a subunit antisera (rabbit anti 93-105 beta, a porcine inhibin). These studies determined the following: inhibin is present in good yield in equine follicular fluid a higher proportion of the total activity is present in larger molecular weight forms than with porcine inhibin inhibin was detected at 90 kDa, 56 kDa, and 32 kDa. Alpha subunit only bands were detected at 40 kDa and 80 kDa. The lower molecular weight form of equine inhibin was similar to porcine inhibin in size and pattern of 2-D PAGE.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/005

Status: On-going

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

Start Date: 12/06/91

Est. Completion Date:

Department: Clinical Investigation

Facility: MAMC

Principal Investigator: MAJ Douglas A. Powell, VC

Associate Investigators: None

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

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$125.00

Periodic Review:
08/07/92

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

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

Progress: Seven training sessions were held in FY 92, using two rabbits, one pig, and thirteen rats.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/074		Status: On-going	
Title: Microbiological Analysis of Male NGU Specimens by Polymerase Chain Reaction: A Retrospective Study					
Start Date: 06/05/92			Est. Completion Date: Aug 92		
Department: Clinical Investigation			Facility: MAMC		
Principal Investigator: MAJ Robert S. Stewart, MS					
Associate Investigators:			MAJ Margot R. Krauss, MC		
Key Words: urethritis, polymerase chain reaction					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:		
\$0.00		\$0.00	//		

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

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

Progress: Primers for polymerase chain reaction amplification of DNA have been prepared for Chlamydia trachomatis, Mycoplasma genitalium, Trichomonas vaginalis, and herpes simplex virus, as well as human papillomavirus. Oligonucleotide probes for each of these have also been prepared. Testing of stored samples will begin as soon as the last set of primer sequences is received from Dr. Vito del Vecchio for Ureaplasma urealyticum.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/075

Status: On-going

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

Start Date: //

Est. Completion Date: Jun 93

Department: Clinical Investigation

Facility: MAMC

Principal Investigator: MAJ Robert S. Stewart, MS

Associate Investigators:

Troy H. Patience, B.S.

Key Words: breast biopsy, DNA, hormone receptors

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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

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

Progress: This study has not been implemented. The investigators have applied for MRDC grant funding and are awaiting a decision on the funding.

Detail Summary Sheet

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

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

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

Progress: An in vitro method for the detection of human papillomavirus DNA by polymerase chain reaction (PCR) was developed with sensitivity to 30 viral genomes per sample achieved. Primers for testing samples by self-sustained sequence replication reaction (3SR) have also be prepared but evaluation has not yet begun. A nonradiometric procedure for genotyping HPV using biotinylated oligonucleotide probes was evaluated and discarded as too insensitive (Millipore, PolarPlex System). Another system utilizing digoxigenin-labeled probes coupled with chemiluminescent detection is under evaluation and appears to be much more sensitive. (Boehringer Mannheim, Genius System with LumiPhos 530).

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 92/034**Status:** On-going**Title:** Insulin-Like Growth Factor Binding Proteins in Prostate Carcinoma Cell-Lines**Start Date:** 01/03/92**Est. Completion Date:****Department:** Clinical Investigation**Facility:** MAMC**Principal Investigator:** M. J. Styner, B.S.**Associate Investigators:**

CPT Katherine H. Moore, MS

James R. Wright, M.T.

COL Stephen R. Plymate, MC

Louis A. Matej, B.S.

Kelly L. Thomsen-Archer, B.S.

Key Words: protein, growth factor, prostate carcinoma**Accumulative****MEDCASE Cost:**

\$0.00

Est. Accumulative**OMA Cost:**

\$0.00

Periodic Review:

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

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

Progress: The IGF-BP's 1-5 have been shown to be present in total RNA extracts in the prostate cell lines ALVA 41 and ALVA 101, using Northern analysis with ALVA 41 showing a very strong signal for BP3. Bands for the control cells HEPG2 have yielded consistent results for the binding proteins as was expected, and the commercially purchased DU145 has consistently shown RNA bands for all the binding proteins except BP5 which shows a very weak signal. Messenger RNA has been selected from total extracts and has been detected with the above cell lines using BP's 1 and 2. The other binding proteins are currently in the process of being hybridized to Northern membranes and awaiting autoradiography. Total genomic DNA has been extracted from the prostate cell lines and the HEPG2 cells and digested with restriction enzymes. Southern analysis has been started and has yet to yield any results. Ligand blots have been performed on the media conditioned with the prostate cell lines and the ALVA 101 and 41 lines show a large abundance of protein for the BP 4 and nothing for the other BP's.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF DENTISTRY

Detail Summary Sheet

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

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: Seventy-three medical conditions were noted from the records (approximately 500) reviewed. However, only 31 of these medical conditions required medications. Forty-seven possible side effects of dental consequence from the medications taken orally were determined. There were 44 different medications prescribed to treat 31 conditions. Twenty percent of these medications did not have a potential side effect of dental consequence, 27% had a single potential side effect, and 53% had multiple potential side effects of dental consequence. It was discovered that there were dental consequences to some of the medications prescribed that were not common knowledge and that did not have references readily available in the pediatric dentistry literature. Furthermore, it was found that there was often a variety of medications prescribed for the same medical condition, some of which had dental consequences and others which had different dental consequences or no dental consequence at all.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/059 **Status:** On-going

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

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

Department: Dentistry **Facility:** MAMC

Principal Investigator: MAJ Cecil R. Dorsett, DC

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

Key Words: postoperative nausea, postoperative vomiting, ondansetron

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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. Antiemetic rescue will be provided if subjects experience three episodes of emesis in one hour or if the intensity of nausea and emesis requires immediate treatment. The administration of a rescue antiemetic will be considered to indicate insufficient efficacy of the antiemetic treatment. Subjects will be evaluated 18-24 hours postoperatively and again at a follow-up appointment within 4-7 days from surgery. Data analysis will be primarily focused on the difference in the incidence of vomiting occurring between the placebo and ondansetron treatment groups using chi-square analysis. Times to discharge from the postanesthesia care unit will be assessed for significance with the unpaired t test.

Progress: An additional 18 patients was entered in FY 92 for a total of 38. To date, it appears that ondansetron is highly effective at preventing postoperative nausea and vomiting.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/062

Status: On-going

Title: Postoperative Complications in Operating Room Dentistry for Children

Start Date: 05/01/92

Est. Completion Date:

Department: Dentistry

Facility: MAMC

Principal Investigator: MAJ Paul J. Engibous, DE

Associate Investigators:

LTC Herschel L. Jones, DE

Key Words: dentistry, children, postoperative complications

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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

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

Progress: Forty-two patients have been studied. The results show minor postoperative complications as expected. Without statistical evaluation, no discernible trends can be seen and no conclusions drawn. Data collection continues and will be terminated at 50 subjects.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/032		Status: Terminated	
Title: An Assessment of Parental Desire to Accompany Their Child in the Dental Operatory					
Start Date: 02/16/90			Est. Completion Date: Feb 91		
Department: Dentistry			Facility: MAMC		
Principal Investigator: LTC Herschel L. Jones, DE					
Associate Investigators: LTC Paul E. Kittle Jr., DE			COL Gerald R. Aaron, DC		
Key Words: dental, parental desire					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
				Periodic Review: 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: It has been very difficult to find subjects that meet the criteria for this study. Therefore, the protocol was terminated due to the departure of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/068

Status: On-going

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

Start Date: 04/20/90

Est. Completion Date: Feb 91

Department: Dentistry

Facility: MAMC

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

Associate Investigators:
LTC Herschel L. Jones, DE

COL Gerald R. Aaron, DC

Key Words: informed consent,dental

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
05/03/91

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

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

Progress: Thirty-eight subjects have been entered and data collection is complete. Data analysis is in process.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/037	Status: Completed
Title: The Presence of Human Immunodeficiency Virus (HIV) in the Saliva of Pediatric Acquired Immunodeficiency Syndrome (AIDS) Patients		
Start Date: 02/07/92	Est. Completion Date: Feb 92	
Department: Dentistry	Facility: MAMC	
Principal Investigator: LTC Paul E. Kittle Jr., DE		
Associate Investigators: Dr. Sandra Burchett, M.D. James R. Wright, M.T.		
LTC Paul E. Kittle Jr., DE MAJ John E. van Hamont, MS		
Key Words: HIV,AIDS,pediatric patients		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 Stilness (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: The study sample consisted of 20 pediatric patients between the ages of 18 and 156 months who were both seropositive and blood culture positive for HIV-1 and they were all on Zidovudine treatment. No DNA-associated genome was isolated from the samples. RNA-associated genome was found in only one sample. Lack of HIV-1 in the samples indicates that the saliva of pediatric AIDS patients is apparently not a mode of transmission. It is hypothesized that the RNA-associated genome isolated in the single patient was due to the patient's short duration (1 week) of Zidovudine treatment. The principal investigator was changed to Dr. Paul Kittle upon the departure of Dr. House.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/098		Status: On-going	
Title: Waste Anesthetic GAS (WAG) Exposure of Pediatric Dentists During Operating Room Dental Procedures					
Start Date: //			Est. Completion Date:		
Department: Dentistry			Facility: MAMC		
Principal Investigator: LTC Paul E. Kittle Jr., DE					
Associate Investigators:			MAJ Curtis D. Goho, DC		
Key Words: waste anesthetic gas, pediatric dentists					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
				Periodic Review: //	

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

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

Progress : Ten subjects have been studied.

Detail Summary Sheet

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

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: Two hundred forty children were evaluated using a graphic rating scale to assess levels of anxiety induced by dentists' attire with all other factors standardized. It was found that dentists' attire does have an effect on a child's feelings, but that the effect is not statistically significant for any particular attire. The exception was that the dentist dressed in the clown attire caused statistically significant negative feelings in 7 to 9 years old children who had extensive prior dental treatment ($P < .001$).

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/063

Status: On-going

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

Start Date: 05/01/92

Est. Completion Date:

Department: Dentistry

Facility: MAMC

Principal Investigator: MAJ Michael G. Page, DE

Associate Investigators:

LTC Paul E. Kittle Jr., DE

Key Words: pediatric dentistry, behavior

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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

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

Progress: The filming and editing of the vignettes have been completed. Twelve of the 75 surveys have been completed. Data collection is on-going. It is too early to make any conclusions.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/081		Status: Completed	
Title: Determination of Optimum Dose and Schedule of Intravenous Dexamethasone for Prevention of Postsurgical Edema After Orthognathic Surgery					
Start Date: 08/17/90			Est. Completion Date: Jul 91		
Department: Dentistry			Facility: MAMC		
Principal Investigator: MAJ Charles R. Weber, DC					
Associate Investigators: COL Douglas B. Boyd, DC			CPT Michael C. Daines, MC		
Key Words: orthognathic surgery,edema:prevention,dexamethasone:optimum dose					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$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: The paper written from the data collected on this protocol won The Steger Award at Madigan for 1992. A paper has also been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/061

Status: On-going

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

Start Date: 07/12/91

Est. Completion Date: Apr 92

Department: Dentistry

Facility: MAMC

Principal Investigator: MAJ Robert J. Wygonski, DC

Associate Investigators:
COL Douglas B. Boyd, DC

MAJ Frederick W. Burgess, MC
COL Jerre M. Griffin, DE

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

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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

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

Progress: Forty eight subjects have been entered with testing completed on 36 of them.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/011	Status: Completed
Title: A Double Blind Placebo Controlled Study of Intramuscular Ketorolac Tromethamine in the Rescue Treatment of Headache		
Start Date: 02/07/92	Est. Completion Date:	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: CPT Richard D. Brantner, MC		
Associate Investigators: MAJ William J. Snuffin, MC		MAJ John W. McBurney, MC
Key Words: headache, ketorolac tromethamine		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$500.00	//

Study Objective: To determine the therapeutic role of a new injectable non-steroidal anti-inflammatory in the rescue treatment of moderate to severe headache.

Technical Approach: Patients presenting to the emergency room with a complaint of headache/migraine will pass through the routine established routes of triage. Consenting patients will then be randomized to either a placebo or to ketorolac tromethamine. Patients will receive either normal saline or ketorolac tromethamine intramuscularly. At times 0, 30, and 60 minutes, vital signs will be obtained along with a report of pain level using a visual analog scale. During this period subjects will complete a demographic and headache evaluation sheet. The treatment phase of the study will terminate 60 minutes after entry. The patient will either be discharged home or given further medication to relieve pain. Patients will be asked to rate their pain at 24 and 48 hours and requested to list all additional headache medications taken from time of discharge to follow-up visit. All patients will be seen in a follow-up at the Neurology Clinic within five working days and the Headache Classification Committee criteria will be used to establish type of headache. Chi square analysis will be used to analyze the data.

Progress: Fifty-six (56) subjects were entered in the study. Forty-eight were used in the statistical evaluation. Both groups were statistically similar 24 subjects in each group with six in each group showing significant improvement in symptoms in 60 minutes. Original PI: Dr. William Snuffin, changed to Dr. Brantner in July 1992.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/100	Status: On-going
Title: The Randomized Use of Helium-Oxygen Mixture for the Administration of Bronchodilator Therapy in the Treatment of Bronchial Asthma		
Start Date: //	Est. Completion Date: Jul 93	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: CPT Richard D. Brantner, MC		
Associate Investigators: CPT David Della-Giustina, MC		MAJ William T. Hurley, MC MAJ Linda M. Brantner, MC
Key Words: asthma, helium-oxygen mixture, bronchodilator		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$315.00	//

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

Technical Approach : Each patient (n=150) will be evaluated using peak flow rates and given supplemental oxygen. Patients with peak flow rates <180 L/m will be given prednisone, 60 mg, by mouth. Patients will then be randomized to a nebulized albuterol treatment administered either by the air driven method or by Heliox at a rate of 8 L/min. Albuterol treatment will continue as above every 30 minutes for a total of four treatments. Patients will be on continuous pulse oximetry monitoring. Repeat evaluations will consist of vital signs and physical examination to include respiratory rate and lung auscultation every 30 minutes. Peak flow/FEV₁ measurements will be obtained at entry and at 10 minutes after each nebulized bronchodilator treatment. A final peak flow/FEV₁ will be obtained 20 minutes after the last nebulizer treatment. Patients will be asked to respond to a questionnaire indicating the severity of presenting symptoms, the time to feeling improvement in respiratory effort, and the decrease in objective wheezing. Patients will be contacted by phone 48 hours after discharge to repeat the questionnaire. Groups will be compared for age, sex, history of severity of disease, initial pulse oximetry, and respiratory rate, using the t-test. Initial FEV₁ will be determined and percent predicted will be determined using the patient's age, sex, height, and weight, and groups compared as to severity using the t-test. Subjective rate of improvement in symptoms will be analyzed using the Mann-Whitney U Test. Both peak flow and FEV₁ measurements will be plotted and percentage of improvement from baseline determined. The percentage improvement in FEV₁ will be compared between the two groups using the t-test.

Progress : This is a new study which has not yet been implemented.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/062

Status: Completed

Title: The Physiologic Toll of Internship

Start Date: 02/07/92

Est. Completion Date: Jun 92

Department: Emergency Medicine

Facility: MAMC

Principal Investigator: CPT Janus D. Butcher, MC

Associate Investigators:

Mark S. Grajcar, MC

Marilyn P. Johnson, MC

MAJ Wade A. Lillegard, MC

CPT Thomas W. Irvine, MC

Key Words: internship, stress, physiologic toll

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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: VO2max, push-ups, sit-ups, grip strength, sit and reach technique (flexibility), skin fold (for body fat determination), FVC, FEV1, FEF25-75, 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 Wilcox rank sum test.

Progress: Forty-five subjects were entered in this study. A paper is being prepared for possible presentation at the American College of Sports Medicine.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/025	Status: Completed
Title: Evaluation of a Urine Pregnancy Test Kit in the Emergency Department		
Start Date: 07/12/91	Est. Completion Date:	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: LCDR Laurence D. Conley		
Associate Investigators: CPT William T. Hurley, MC		
Key Words: pregnancy test,urine,emergency room		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 colorimetric determination, and tests requiring a dilutional procedure. Results of the three tests will be compared for reliability using KAPPA statistics.

Progress: A paper has been submitted to the Annals of Emergency Medicine. The investigators conclude that monoclonal antibody immunoassay (Wampole One-Step hCG) is a reliable and rapid technique for urine pregnancy testing by Emergency Department personnel. It can also result in time and cost savings when substituted for the serum assay.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/012	Status: Completed
Title: Diagnostic Value and Clinical Significance of the Electrocardiogram During Chest Pain		
Start Date: 06/14/91	Est. Completion Date:	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: CPT William J. Frohna, MC		
Associate Investigators: MAJ Alice M. Mascette, MC		Steven A. Pace, MD
Key Words: chest pain, ECG		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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. 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: Fifty subjects were entered in this study. Data are being analyzed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/035		Status: Completed	
Title: An Evaluation of the Frequency and Magnitude of Benzocaine-Induced Methemoglobinemia in Humans					
Start Date: 04/03/92			Est. Completion Date:		
Department: Emergency Medicine			Facility: MAMC		
Principal Investigator: MAJ Andrew T. Guertler, MC					
Associate Investigators:			CPT William A. Pearce, MC		
Key Words: methemoglobinemia, benzocaine-induced					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:		
\$0.00		\$0.00	//		

Study Objective: To evaluate the effect of a benzocaine-containing spray (Hurricane) on methemoglobin (MHb) induction in a human population.

Technical Approach: One hundred patients undergoing an endoscopic procedure will be studied. Baseline MHb levels (prior to benzocaine application) will be measured and subsequent MHb levels will be determined at 20, 40, and 60 min after benzocaine dosing. Benzocaine will be applied via a spray using Hurricane and standardized by timing the application period. Since G-6-PD deficiency is frequently recognized only after exposure to an oxidative agent, red cell G-6-PD deficiency will be qualified on all patients who develop methemoglobinemia following benzocaine exposure.

Progress: Fifty-six males and 34 females (median age of 52) were studied. There was a significant increase in percent MHb between baseline and 20, 40, and 60 min measurements. There were no differences between the 20, 40, and 60 min levels. Data were analyzed with one-way ANOVA. Post-hoc testing used Fishers PLSD. The investigators conclude that a 2 second spray of 20% benzocaine applied to the oropharynx of humans induces a slight but statistically significant increase in MHb levels between baseline and measurements obtained at 20, 40, and 60 min after dosing.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/078		Status: On-going
Title: Oral Versus Intravenous Steroid: A Prospective Study in Acute Asthma				
Start Date: 11/01/91		Est. Completion Date: Feb 92		
Department: Emergency Medicine		Facility: MAMC		
Principal Investigator: LCDR Kyle D. Holmes, MC				
Associate Investigators: LCDR Richard S. Perren		MAJ Kirin M. Russell, MC CPT David C. White, MC		
Key Words: asthma:acute,steroids:oral,steroids:IV				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		11/01/91

Study Objective: To compare the efficacy of oral prednisone and intravenous methylpredisone in the treatment of adults with an acute asthma exacerbation by comparing FEV1, patient's subjective index, and physician evaluation of clinical course.

Technical Approach: The patient sample will be 100 patients, ages 18-45 years, presenting to the Emergency Room with exacerbation of asthma, unrelieved by the usual home treatment. Each patient will be evaluated by the physician and tested with a portable spirometer. Oxygen saturations will be recorded per pulse oximetry. Arterial blood gases may be used in place of pulse oximetry if the clinical situation dictates. The patient will then be randomized in a double blind fashion to receive either IV methylprednisolone and oral grape Tang or oral prednisolone mixed with grape Tang and normal saline IV. All patients will receive oxygen and a beta-agonist as per emergency room protocol, three treatments, 20 minutes apart. Patients will be evaluated with spirometry for FEV1 on arrival and every hour for three hours. Patients will be discharged or admitted as clinical circumstances warrant. Discharge steroid dosing will be left to the discretion of the treating physician. Follow-up evaluation will consist of repeat vital signs (every 30 minutes), physician examination (after every treatment), patient symptom scale of 1 to 10 (every hour), and spirometry (every hour). Patients who are discharged will be contacted the following day for evaluation of subjective complaints and will be asked to rate themselves on the patient symptom scale. FEV1 and FVC will be analyzed with repeated measures analysis of variance. Analog scaled variables like physician exam and subjective index will be analyzed with appropriate non-parametric methods.

Progress: Thirty patients have been entered. The investigators will now review the data to estimate the number of patients required.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/097	Status: On-going
Title: Pediatric Pain Assessment Survey		
Start Date: //	Est. Completion Date:	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: MAJ Kerry R. Johnson, MC		
Associate Investigators: Cami Tier, AN		
Key Words: pediatric pain, acute injuries, parental preferences		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress : Approximately 20 children and 20 parents have completed the questionnaire.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/027

Status: Completed

Title: Determination of Effectiveness of the Esophageal Detector Device in Young Porcine Animal Models

Start Date: 04/05/91

Est. Completion Date:

Department: Emergency Medicine

Facility: MAMC

Principal Investigator: LCDR Timothy C. May

Associate Investigators:
LTC Blake P. Gendron, MC

CPT Marc D. Magelssen, MC

Key Words: endotracheal tube placement, EDD, porcine, Animal Study

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
08/07/92

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: The data were inconclusive. There was a trend towards large animals being more accurate with regard to the EDD. A larger population should be studied.

Detail Summary Sheet

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

Title: Emergency Room Procedure Training

Start Date: 02/19/82

Est. Completion Date: Feb 87

Department: Emergency Medicine

Facility: MAMC

Principal Investigator: LTC Matthew M. Rice, MC

Associate Investigators:

MAJ Steven C. Dronen, MC

MAJ Mel D. Robinson, MC

MAJ Stanley P. Liebenberg, VC

LTC Cloyd B. Gatrell, MC

COL Frederick Burkle, MC

LTC Samuel T. Coleridge, MC

Key Words: emergency room, training protocol, Animal Study

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$1360.00

08/07/92

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

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

Progress: Two sessions using two goats each (4 total) were held in FY 92.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/016

Status: On-going

Title: Pediatric Intubation Training Utilizing the Ferret Model

Start Date: 03/16/90

Est. Completion Date: Indef.

Department: Emergency Medicine

Facility: MAMC

Principal Investigator: LTC Matthew M. Rice, MC

Associate Investigators:
LTC Patrick C. Kelly, MC

LTC Cloyd B. Gatrell, MC

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

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$400.00

Periodic Review:
08/07/92

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 sessions were held during FY 92. The ferrets survived the procedure so the same six ferrets were used for both sessions.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/079	Status: Completed
Title: Effects of Trendelenburg's Position on Oxygen Consumption and Cerebral Perfusion Pressure in the Adult Pig		
Start Date: 02/07/92	Est. Completion Date: Jan 92	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: MAJ Joseph B. Rusinko, MC		
Associate Investigators: MAJ John E. Reed, MC		
Key Words: oxygen consumption, cerebral perfusion, position, pig, Animal Study		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: 08/07/92

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: Fourteen animals were studied. Data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/039	Status: On-going
Title: Treatment of Corneal Abrasions: Is Eye Patching Necessary?		
Start Date: 02/07/92	Est. Completion Date:	
Department: Emergency Medicine	Facility: MAMC	
Principal Investigator: CPT Jan Vanderlinde, MC		
Associate Investigators: CPT Lee E. Payne, MC, USAF		MAJ Andrew T. Guertler, MC
Key Words: corneal abrasion, patching		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: Thirty patients have been enrolled in the study.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF FAMILY PRACTICE

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/096	Status: Completed
Title: The Impact of Low Back Pain on Medical Facilities of Fort Lewis		
Start Date: //	Est. Completion Date:	
Department: Family Practice	Facility: MAMC	
Principal Investigator:	S. Grajcar, MC	
Associate Investigators: MAJ John W. Dietz, MC	MAJ Wade A. Lillegard, MC	
Key Words: low back pain, impact on facility		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective : To assess the utilization of medical resources in the diagnosis and treatment of low back pain in a military community.

Technical Approach : Patients 15 years and older who are seen for low back pain in the Emergency Room Acute Illness Clinic, Troop Medical clinics 1, 2, 3, 5, 6, and 13, and the Family Practice, Orthopedics, Neurology, Neurosurgery, Pediatrics, Obstetrics, Physical Therapy, and Physical Medicine clinics will be asked to fill out a questionnaire to provide the information that will be assessed as stated below. At the end of three months, the total number of low back pain visits will be compared to the total number of patient visits in the clinics surveyed and a percentage calculated. The number of diagnostic and treatment modalities will also be assessed for each subject. Demographic information, job description, low back pain history, and severity of pain will be measured. Common characteristics of the subjects will be evaluated. Correlations will then be made between patient characteristics and the extent of the medical resources utilized. Actual costs of these medical resources will not be included. The data will be analyzed primarily with descriptive statistics. This will specifically involve the calculation of percentages, proportions, and rates. Some potential associations will be tested by chi-square for categorical data, non-parametric tests for ordinal data, and t-test for interval data.

Progress : Four hundred thirty men and 161 women were surveyed. Eighty-five percent reported prior episodes of back pain; 53% claimed injury on the job and 32% felt that the injury was the fault of their employer or someone else; 70% claimed that their pain significantly affected their job performance. Physicians in this study treated 47.6% of the patients with rest, 30% with physical therapy, 56% with nonsteroidals, and 33% with muscle relaxants. The data will be analyzed further to provide more information on the impact of low back pain on the medical facilities at Ft Lewis.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/085		Status: Suspended	
Title: Diagnoses Which Stimulate Physician Initiated Discussions About Advance Directives: A Survey of Practicing Physicians					
Start Date: 07/02/92			Est. Completion Date: Aug 92		
Department: Family Practice			Facility: MAMC		
Principal Investigator: CPT Jefferey J. Johnson, MC					
Associate Investigators:			Cliff A. Robertson, MD		
Key Words: advance directives, power of attorney, CPR					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		//	

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

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

Progress: This study has not been implemented and has been suspended until a new principal investigator can be assigned. The original principal investigator was reassigned before he could start the study and due to communication problems and rotations in other institutions the physician listed as the present investigator was not informed that he was to take over the study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/077		Status: Completed	
Title: Empathy and Specialty Choice in a Population of Army Interns					
Start Date: 06/05/92			Est. Completion Date: Aug 92		
Department: Family Practice			Facility: MAMC		
Principal Investigator: CDR W. R. Kiser, MC					
Associate Investigators: None					
Key Words: specialty choice					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
					Periodic Review: //

Study Objective: To examine the potential association of empathic makeup and specialty choice in an Army intern population.

Technical Approach: This will be a multicenter study with TAMC and DDEAMC participating along with MAMC. During the intern orientation session, the study will be explained and interns will be asked to participate. Those who participate will complete the Davis Interpersonal Reactivity Index (a 28 question self-reporting measure of empathy) and a short questionnaire seeking demographic information and each intern's specialty aspiration. The independent variable for data analysis will be empathy which will be measured via the use of the Davis Interpersonal Reactivity Index. The dependent variable will be specialty choice which will be grouped into two categories: primary care (family practice, pediatrics, and general internal medicine) and non-primary care (all others). This will be compared to the independent variable using two trait chi-square analysis in a contingency table. Comparison will also be made between the stated independent and dependent variables and the demographic information via chi square analysis, t-testing, and logistic regression analysis where appropriate.

Progress: Ninety-one interns participated. Empathy does have an association with specialty choice in women interns and in DO interns. A paper is being written for potential publication.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/083	Status: On-going
Title: The Effect of Internship on Moral Reasoning		
Start Date: 07/02/92	Est. Completion Date: Jun 93	
Department: Family Practice	Facility: MAMC	
Principal Investigator: CDR W. R. Kiser, MC		
Associate Investigators: LTC John P. Kugler, MC		
Donnie J. Self, Ph.D.		
Key Words: moral reasoning, internship		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: The DIT was administered to 20 interns in the first month of the internship. It will be repeated a month before completion of the internship.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/058	Status: On-going
Title: An Analysis of Selected Elements of Family Function and Related Variable in Adolescent Pregnancy		
Start Date: 04/05/91	Est. Completion Date:	
Department: Family Practice	Facility: MAMC	
Principal Investigator: LCDR Euelya L. Lewis		
Associate Investigators: None		
Key Words: pregnancy:adolescent,family function,adolescent:female,parent participation		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: 08/07/92

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

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

Progress: Data were gathered from 173 participants between the ages of 12 and 17. Parental (mother responses) were also used. A thesis was written as a partial fulfillment for the requirements for the degree of Master of Arts in Social Sciences. More patients are being entered in the study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/048	Status: Completed
Title: Evaluation of Pre- and Postpartum Depression Among Pregnant Wives of Alerted and Deployed Soldiers		
Start Date: 02/01/91	Est. Completion Date:	
Department: Family Practice	Facility: MAMC	
Principal Investigator: MAJ Dawn E. Light, MC		
Associate Investigators: MAJ Philip M. Bayliss, MC		
Key Words: depression, pregnancy, deployed soldiers		
Accumulative	Est. Accumulative	Periodic Review:
IEDCASE Cost: \$0.00	OMA Cost: \$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: 335 subjects were entered in the study. Spouses of deployed service members had a relative risk for depression of 1.38 compared to spouses of service members who were not affected. No difference was demonstrated in pregnancy outcomes. It is concluded that during a military conflict the risk for depression is increased for pregnant wives of deployed service members.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/084		Status: On-going	
Title: Back Pain in Aviators: A Descriptive Study of the Type of Care Received/Sought and Implications for Flight Status - Part Two					
Start Date: //			Est. Completion Date: Mar 93		
Department: Family Practice			Facility: MAMC		
Principal Investigator: LCDR Danell E. Lovins					
Associate Investigators: MAJ Daniel Fitzpatrick, MC			LTC John P. Kugler, MC		
Key Words: back pain, aviators					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		//	

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

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

Progress: Questionnaires have been mailed to subjects.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/029	Status: Completed
Title: Back Pain in Aviators: A Descriptive Study of the Type of Care Received/Sought and Implications for Flight Status		
Start Date: 01/03/92	Est. Completion Date:	
Department: Family Practice	Facility: MAMC	
Principal Investigator: LCDR Danell E. Lovins		
Sociate Investigators:		
MAJ Daniel Fitzpatrick, MC		LTC John P. Kugler, MC
Rita Altamore, M.D., MPH		Daniel Cherkin, Ph.D.
Key Words: back pain, aviators		
Accumulative		
EDCASE Cost:	Est. Accumulative	Periodic Review:
\$0.00	OMA Cost: \$0.00	//

Study Objective: This study addresses the nature of health care sought and received by military aviators for back pain and also the behaviors of aviators that may not be conducive to safe aviation.

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

Progress: The results of the study indicate that mission readiness, aviation safety, and health care services are affected by back pain in aviators in several different ways. Safety is impaired by using non-military care (not so much that it is inappropriate, but because of lack of communication between the military system and the civilian doctor regarding treatment and status) nearly 80% of the aviators avoid care for any reason and nearly 50% avoid care for back pain because of the possibility of being grounded. A thesis was written by Dr. Lovins as partial fulfillment of the requirements for the degree of Master of Public Health.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/030		Status: Completed	
Title: Mammography Utilization in a Military Beneficiary Population					
Start Date: 01/03/92			Est. Completion Date:		
Department: Family Practice			Facility: MAMC		
Principal Investigator: LTC Thomas C. Michels, MC					
Associate Investigators:			LTC John P. Kugler, MC		
Key Words: mammography, utilization, military population					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$225.00	//	

Study Objective: (1) To estimate the level of participation in mammography in Madigan's population, as well as utilization by source of care, and estimation of unmet need and (2) to apply schema of the Theory of Reasoned Action to measure the degree to which constructs of this theory correlate with mammography participation.

Technical Approach: A questionnaire will be mailed to a random sample of 500 eligible women. The questionnaire will obtain information on number of mammograms women have had in the past five years and where they had them, a history for breast cancer, and information on expense, embarrassment, inconvenience, discomfort, and opinions of family members on the need for a mammogram, whether the patient desires the availability of a mammogram on a regular basis, and the participant's knowledge regarding breast cancer and mammograms. According to the Theory of Reasoned Action constructs, the intention to obtain a mammogram will be used as the dependent variable in regression equations, with the other constructs of the TRA used as independent variables (attitude and norm). A regression would be done with past mammography behavior as the dependent variable with attitude, norms, and intention as independent variables. These will be separately analyzed for subgroups as well, including age, race/ethnic origin, socioeconomic status, and risk factors. The regression equations can be done with these demographic variables included. Correlations between these same variables would also be done in the process of analyzing the data. An estimate of the true population proportion not participating in mammography will be done using standard formulas for proportions and confidence intervals for single groups.

Progress: A substantial proportion of women eligible for care at Madigan age 40+ have never had a mammogram (19.6%) although this is better than the national average (40%). Of those women who have had a mammogram, a substantial proportion have had their last one done at a civilian facility (46%). Cost was the number one barrier cited by women to obtaining a mammogram. Constructs of the Theory of Reasoned Action are able to distinguish between women who have received an optimal number of mammograms and those who have not, but this theory is less useful in separating women who do and those who do not intend to get a mammogram.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/003 **Status:** Completed

Title: Child Abuse and Neglect Scale

Start Date: 10/04/91

Est. Completion Date: Jan 92

Department: Family Practice

Facility: MAMC

Principal Investigator: CPT Monte C. Uyemura, MC

Associate Investigators: MAJ Jon Davis, MS

Key Words: child abuse, child neglect, weighted scale, prediction

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

Study Objective: To devise a weighted scale to predict likelihood of substantiation of child abuse and/or neglect.

Technical Approach: Social Work Service will provide the CPS report on 100 cases of nonsexual abuse cases referred from Madigan clinics for investigation for child abuse or neglect, but blinded as to final judgment by Social Work. The primary investigator will review the report and outpatient chart and fill out a worksheet for each case obtaining information on the growth status of the child as well as immunization status and any broken bones, bruises, burns, etc. and previous investigation of family. When the data is obtained, the cases will be unblinded and the judgments of substantiated versus unsubstantiated cases revealed. Statistical analysis using odds ratio will be used to correlate variables with investigational decision. Variables will then be subjected to multivariate analysis based on stepwise addition of variable that had greatest correlation with substantiated child abuse or neglect. Factors will be weighted to develop a scale for "risk of substantiated child abuse or neglect". This will be a pilot for a prospective study testing the scale and getting valid percentages to correlate with the scale.

Progress: Ninety seven charts were reviewed with 57 cases of abuse or neglect. The numbers were not large enough to make any conclusions and the principal investigator PCS'd at this point.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF MEDICINE

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/055	Status: On-going
Title: Multicenter Clinical Evaluation of Penicillin Skin Testing		
Start Date: 03/16/90	Est. Completion Date: Jun 90	
Department: Medicine	Facility: MAMC	
Principal Investigator: COL W. Pierre Andrade		
Associate Investigators:		
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	
Key Words: penicillin skin testing		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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 penicilloate (MDM-B), in the usual concentrations, as well as routine histamine and diluent controls. The two penicilloates and the penicilloate 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: No new patients entered in this study in FY 92. Dr. Andrade has been reassigned and Dr. Brown will be the principal investigator at MAMC and enter more patients when he has had time to review the data collected to this point.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/066		Status: On-going
Title: A Prospective Study of Headache in Pregnancy				
Start Date: 05/01/92		Est. Completion Date:		
Department: Medicine		Facility: MAMC		
Principal Investigator: CPT Renee M. Bernier, MC				
Associate Investigators:		CPT Linda A. Marden, MC		
Key Words: headache, pregnancy				
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:		
\$0.00	\$0.00	//		

Study Objective: To prospectively characterize incidence, type, and outcome of headaches during pregnancy by following women from early first trimester to delivery.

Technical Approach: At the first obstetrics visit, patients (aged 15-45) in the first trimester of pregnancy will fill out a questionnaire regarding previous history of headaches and other related disorders prior to pregnancy. The questionnaire will cover frequency, duration, location, severity, associated symptoms, and type of pain of their headaches and will also cover headache occurrence from time of conception to time of first obstetrics visit. Patients will fill out a short follow-up questionnaire once a month as well as at the six weeks post-delivery appointment. The data will be studied first to determine overall incidence of headache in the study population. Reports of headache will then be analyzed to determine the class of headache and the frequency of each type will be determined. Time of onset will be studied to establish if certain classes of headache are more likely to occur during a particular segment of pregnancy. Subjects with new onset of migraine during pregnancy will be studied separately to determine if this group differs in time of onset and character. Outcome of pregnancy will then be studied in the headache and non-headache groups. These groups will be compared using a chi-square analysis to establish if there is any statistically significant increased morbidity associated with headache. Final outcome will be expressed as either increased morbidity or no increased morbidity associated with headache. Subtypes of headaches will be looked at for evidence of increased risk of morbidity within a specific subtype and new onset migraine will be studied separately for evidence of increased risk.

Progress: Initial entry into the study has been very good with 506 subjects filling out the initial questionnaire. However, participation via follow-up questionnaire has not been very good and adjustments are being made to improve follow-up response. Despite this, some good data have been obtained with the initial questionnaire.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/009	Status: On-going
Title: Fluconazole Versus Amphotericin B as Empiric Therapy in Febrile, Neutropenic Patients. University of Washington		
Start Date: 02/07/92	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Kenneth A. Bertram, MC		
Associate Investigators:	LTC Howard Davidson, MC	
MAJ Paul C. Sowray, MC	MAJ Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	MAJ Robert L. Sheffler, MC	
MAJ Robert B. Ellis, MC	MAJ Richard Tenglin, MC	
CPT Jennifer L. Cadiz, MC	CPT James Hu, MC	
Key Words: neutropenia, fluconazole, amphotericin B		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$1836.00	//

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

Technical Approach: Patients (n=48) with no documented bacterial source of infection who fail to defervesce after 72 hours of antibacterial antibiotic will be randomized into three groups. Group 1 patients with normal renal function will receive intravenous fluconazole, 800 mg day 1, followed by 400 mg IV daily. Group 2 patients with normal renal function will receive oral fluconazole, 800 mg day 1, followed by 400 mg daily and Group 3 patients with normal renal function will receive IV amphotericin B, 0.25 mg/kg Day 1, followed by 0.6 mg/kg/day. Appropriate premedication (e.g., hydrocortisone, meperidine, diphenhydramine, acetaminophen) will be administered as needed. Dosage will be adjusted appropriately (by extent of disease) for renal impairment. Patients who defervesce following initiation of antifungal therapy and in whom no infection is documented will continue therapy until bone marrow recovery occurs. Patients who remain febrile following initiation of antifungal therapy will be monitored closely with repeat cultures, chest radiographs, and other studies as indicated. If no infection is documented, patients will continue receiving antifungal therapy until afebrile and the ANC is above 500/mm³ for two consecutive days. If a fungal infection is documented, patients receiving an antifungal drug to which the organism is sensitive will continue receiving that drug. If the organism is not sensitive to the study drug assigned to the patient, the study will be terminated and an appropriate antifungal agent begun. In either case, therapy will be continued for a length of time consistent with medically accepted guidelines. Dichotomous variables will be analyzed using either the chi square test or Fisher's exact test. Continuous variables will be analyzed using either ANOVA or T test for comparison. The results from patient randomization will be analyzed to ensure no significant differences in patient populations due to the randomization process alone. Beta errors will also be calculated.

Progress: Patient enrollment (1 subject) has been limited at Madigan due to very low numbers of patients eligible for the study. The University of Washington has enrolled over 100 patients.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/020		Status: On-going
Title: Evaluation of the Efficacy and Safety of Glimepiride versus Glyburide in Subjects with Noninsulin-Dependent Diabetes Mellitus (NIDDM)				
Start Date: 01/03/92		Est. Completion Date:		
Department: Medicine		Facility: MAMC		
Principal Investigator: COL David L. Bunner, MC				
Associate Investigators:		LTC (P) Robert E. Jones, MS		
LTC H. Lester Reed, MC		LTC Daniel H. Knodel, MC		
CPT Robert M. Tuttle, MC		CPT Carl A. Gibson, MC		
Key Words: diabetes, noninsulin-dependent, glimepiride, glyburide				
Accumulative		Est. Accumulative		Periodic Review:
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	//

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

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

Progress: Twelve of 17 patients entered remain in the double blind portion of the protocol and are in midtitration (dose adjustment) phase at this time. All who have entered are showing an improvement in glycemic control and have had no significant side effects. Several have had mild transient hypoglycemia.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/059		Status: Terminated	
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 Doreen Saltiel, MC			MAJ Alice M. Mascette, MC		
Key Words: coronary disease,cigarette smoking					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$3525.00
					Periodic Review: 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: Three control patients were entered in this study. It has been exceedingly difficult to enroll patients in the study. Also, there has been a severe shortage of technicians to perform the procedures. Because of these factors, the protocol has been terminated.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/050		Status: On-going	
Title: Effects of Valproic Acid on Semen Parameters in Male Epileptics					
Start Date: 04/03/92			Est. Completion Date:		
Department: Medicine			Facility: MAMC		
Principal Investigator: LTC William L. Clayton III, MC					
Associate Investigators: LTC (P) Robert E. Jones, MS James R. Wright, M.T.			CPT Linda A. Marden, MC CPT Katherine H. Moore, MS Louis A. Matej, B.S.		
Key Words: epilepsy, semen parameters, valproic acid					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
					Periodic Review: //

Study Objective: To prospectively determine the incidence of abnormalities in the semen of epileptic men who are taking valproic acid for seizure prophylaxis and to assess the effects of incubating valproic acid with sperm from nonepileptic donors in vitro.

Technical Approach: Valproic acid, a frequently used antiepileptic, may be linked to a reduction in sperm numbers and sperm function. This possible association is based upon a few case reports and scattered animal studies. In this prospective study, 50 men will be asked to provide two to three ejaculates every three months for one year. These samples will be reviewed for morphology and sperm counts as well as analyzed by computer to assess a variety of motility parameters. Items of particular importance during the computerized evaluation will include morphometric observations as well as movement parameters such as the amplitude of lateral head displacement and swimming velocities. Fixed, stained slides for subjective interpretation of morphology will also be obtained. In addition, the effects of valproic acid on sperm motility and sperm long chain fatty acid:coenzyme A ligase [AMP] will be measured in vitro. The in vitro studies will be conducted using normal semen samples discarded from the clinical semen analysis lab. Sperm concentrations will be handled using a repeated measures ANOVA to determine statistical significance.

Progress: No patients have been entered because very few patients have been newly started on valproate that qualify for the study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/099	Status: On-going
Title: Azithromycin in the Treatment of Nongonococcal Urethritis: A Multicenter Double-Blind, Double-Dummy Study Employing Doxycycline as A Comparative Agent		
Start Date: 11/01/91	Est. Completion Date: Aug 93	
Department: Medicine	Facility: MAMC	
Principal Investigator: LTC Ronald H. Cooper, MC		
Associate Investigators: LTC Rodney A. Michael, MC		
Key Words: nongonococcal urethritis, azithromycin, doxycycline		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: Seventy-five patients have been entered in this study, all in FY 92. The code has not yet been broken because patients are still being entered. There have been good cure rates in both arms of the protocol. No unexpected adverse reactions have occurred.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/103

Status: On-going

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

Start Date: 11/06/92

Est. Completion Date: Oct 93

Department: Medicine

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
CPT Curtis S. Hansen, RPH, MSC

MAJ Kenneth A. Bertram, MC

Key Words: cisplatin, dolasetron mesylate, zofran, antiemetics

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To compare the effectiveness of a 2.4 mg/kg single IV dose of dolasetron mesylate to a 32 mg single IV dose of ondansetron for complete prevention of emesis due to >70 mg/m² of cisplatin chemotherapy and to compare the effectiveness of a 1.8 mg/kg single IV dose of dolasetron mesylate to a 32 mg single IV dose of ondansetron and to the 2.4 mg/kg single IV dose of dolasetron mesylate for complete prevention of emesis due to >70 mg/m² of cisplatin chemotherapy.

Technical Approach: This is a double-blind, randomized, stratified, parallel, multicenter study in which patients with confirmed malignant disease will receive either 1.8 mg/kg or 2.4 mg/kg of dolasetron mesylate or 32 mg of ondansetron. Six hundred patients (20 at MAMC) will be prospectively stratified as to cisplatin dose, i.e., 300 patients receiving 70 to 90 mg/m² versus 300 patients receiving >90 mg/m². The activity and duration of drug action will be evaluated for 24 hours. If the patient experiences at least three emetic episodes during the 24 hour evaluation period after the start of chemotherapy or request alternative antiemetic therapy, the investigator will initiate escape medication according to institutional practice. Safety, tolerance, and patient satisfaction will also be monitored.

Progress: This is a new study that is awaiting approval from HSC before patient entry begins.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/070	Status: Completed
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		
Associate Investigators:		
MAJ Thomas M. Baker, MC	COL Donald H. Kull, MC	
CPT David R. Bryson, MC	MAJ Ruben D. Sierra, MC	
LTC Lauren K. Colman, MC	CPT Margaret M. Barnes, MC	
COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC	
Key Words: nonsmall cell,cancer:lung		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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/M², days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/M², 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/M², days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/M², 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: Two patients were entered in FY 92 for a total of 28 patients. Data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/050

Status: Completed

Title: Sucralfate and Aluminum Absorption

Start Date: 06/14/91

Est. Completion Date:

Department: Medicine

Facility: MAMC

Principal Investigator: CPT Amy E. Ellingson, MC

Associate Investigators:
MAJ Amy M. Tsuchida, MC

MAJ Michael F. Lyons II, MC

Key Words: aluminum, bone absorption, sucralfate

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:

//

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 paired results assessing a difference between paired data with Student's t-test.

Progress: Eight healthy male volunteers with normal renal function participated. The data show that six weeks of sucralfate ingested in the doses routinely prescribed leads to absorption and increases total body stores of aluminum in subjects with normal renal function. A paper was presented at the American Gastroenterology Association in May 1992.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/072	Status: On-going
Title: Prognostic Significance of Oncogene Amplification and Expression in Human Breast Cancer		
Start Date: 06/05/92	Est. Completion Date: Jun 93	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Robert B. Ellis, MC		
Associate Investigators: CPT Robert M. Tuttle, MC MAJ Richard R. Gomez, MC CPT Katherine H. Moore, MS		
Key Words: cancer, breast, oncogene amplification		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

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

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

Progress: Twenty-five cases were selected for initial studies. The investigators have confirmed that mRNA can be extracted from paraffin embedded breast tissue. This mRNA can be used for PCR amplification and subsequent analysis. Currently, the immunohistochemistry assay is being standardized.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/070	Status: On-going
Title: Comparison of TLC D-99 Doxorubicin Liposome Injection versus Doxorubicin Injection in Metastatic Breast Cancer		
Start Date: 07/02/92	Est. Completion Date: Aug 95	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Robert B. Ellis, MC		
Associate Investigators:		
LTC Howard Davidson, MC	COL Joseph A. Paris, MC	
MAJ Luke M. Stapleton, MC	MAJ Paul C. Sowray, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert L. Sheffler, MC	
CPT James Hu, MC	MAJ Richard Tenglin, MC	
Key Words: cancer, breast, TLC D-99 doxorubicin liposome, doxorubicin		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

Technical Approach: This will be a multicenter, randomized, parallel, open, comparative study in patients with metastatic breast cancer to compare the safety and efficacy of TLC D-99 and free doxorubicin HCL. Third party blinding will be implemented for evaluation of all radionuclide cardiac angiographies and cardiac biopsies. Growth Colony Stimulating Factor (G-CSF) therapy will be routinely given to both treatment groups in an effort to reduce the myelosuppression associated with doxorubicin administration. Therapy with either treatment will begin at 75 mg/m². Dose escalation and reduction steps will be done based on patient tolerance of the drug. Separate randomization series will be used for patients with and without previous exposure to doxorubicin. Cardiac toxicity will be monitored by serial EKG's, echocardiograms, and resting and stress radionuclide cardiac angiography. To document pathologic changes seen with doxorubicin exposure, endomyocardial biopsies will be collected at a cumulative dose of 450 mg/m². With any clinical or laboratory evidence of cardiac dysfunction or with progressive disease, treatment will be discontinued and the patient offered an alternate treatment program.

Progress: This is a new study which is awaiting approval from HSC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/019 **Status:** On-going

Title: The Efficay and Safety of Misoprostol for the Prevention of NSAID-Induced GI Complications

Start Date: 01/03/92

Est. Completion Date:

Department: Medicine

Facility: MAMC

Principal Investigator: MAJ Thomas L. Irvin, MC

Associate Investigators:
MAJ L. Dalessandro, MC

MAJ Kathryn K. Riordan, MC

Key Words: gastritis, NSAID-induced, misoprostol

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To determine the efficacy and safety of misoprostol compared to placebo for the prevention of clinically significant and serious nonsteroidal anti-inflammatory drug (NSAID) induced gastrointestinal (GI) events. The events are GI bleeding, ulcer perforation, surgery for ulcer disease, or death due to GU, DU or severe gastrointestinal erosive disease.

Technical Approach: Patients >60 years of age on daily NSAID therapy with rheumatoid arthritis will be enrolled in the study. After baseline demographic and medical information has been recorded, the patients will be randomized to receive either 200 mcg misoprostol or matching placebo four times a day (with meals and a bedtime snack), in addition to the NSAID therapy for six months. Patients may take Amphojel or other nonmagnesium antacids during the study with this usage recorded. Patients will report any GI events to the principal investigator. Patients will be assessed by the principal investigator at three and six months for the occurrence of any of the GI events of interest. Formal statistical testing will be performed on the demographic information (age, gender, vital signs). The primary endpoint is the development of a GI complication during the six months of therapy. A tabular display of the complication development rate across time will be done by institution and then by institutions combined. A survival analysis will be performed to assess the difference in the complication development rate distributions across time. The NSAID-induced GI complication rate will be modeled using logistic regression to assess the significance of risk factors and their impact on treatment outcome. The incidence of adverse events will be tabulated by treatment group, event, and body system. The overall incidence rate will be compared between treatment groups across all patients using the Pearson's chi square test of marginal homogeneity. Vital sign measurement changes from baseline at the end of the study will be analyzed using the t test. Between group differences will be assessed using analysis of variance.

Progress: Fifteen patients have been entered with no major adverse reactions. Several patients withdrew due to GI intolerance.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/013	Status: Completed
Title: Is Continuous Enteral Feeding Alone Adequate Prophylaxis Against Gastroduodenal Bleeding of Stress Induced Mucosal Lesions		
Start Date: 11/01/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Thomas W. Irvine, MC		
Associate Investigators: MAJ Michael F. Lyons II, MC MAJ Amy M. Tsuchida, MC		LTC Anthony S. Sado, MC MAJ Gregory E. Schlepp, MC
Key Words: mucosal lesions, continuous feeding		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 be 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: Fifty patients were entered in this study. Enteral feedings were shown to be effective in the prevention of bleeding from stress-induced mucosal ulcerations in mechanically ventilated patients.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/062	Status: On-going
Title: Determination of the Sensitivity and Specificity of Light Reflection Rheography for the Diagnosis of Deep Venous Thrombosis in the Lower Extremity		
Start Date: 07/28/89	Est. Completion Date: Jun 90	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Duane J. Jeffers, MC		
Associate Investigators:		
Nancy N. Greenfield, M.S.	MAJ Dipankar Mukharjee, MC	
SGT Charles Adams	Michael Bertoglio, B.S.	
	COL Charles A. Andersen, MC	
Key Words: Light reflection rheography, venous thrombosis		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$6000.00	OMA Cost: \$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 patients were entered in this study in FY 92 due to the move to the new hospital and other time constraints on the principal investigator. Seventeen patients have been entered in previous years.

Detail Summary Sheet

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

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

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

Progress: The technique of phospholipid mass spectroscopy is currently being developed. No subjects will be entered until the investigators are confident that they can easily separate and detect phospholipids.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/023		Status: On-going	
Title: Investigations into the Mechanisms of Phospholipid Synthesis in Human Spermatozoa					
Start Date: 11/21/86			Est. Completion Date: Dec 87		
Department: Medicine			Facility: MAMC		
Principal Investigator: LTC (P) Robert E. Jones, MS					
Associate Investigators: CPT Kevin J. Carlin, MC			MAJ Charles J. Hannan, MC COL Stephen R. Plymate, MC		
Key Words: spermatozoa,phospholipid synthesis					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$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 labeled fatty acids, CoASH, ATP, Mg^{2+} , and Tris. The reaction will be terminated by delipidating the sperm with $CHCl_3$: MeOH, and the organic phase will be chromatographed on silica gel TLC plates. These plates will be developed and spots will be scraped and counted. If the labeled fatty acid is found to be contained within a phospholipid region, cofunctioning of ligase and acyl transferase will be assumed to occur. Studies to characterize acyl transferase activity will be performed using an assay based on the liberation of CoASH which reacts with DTNB, resulting in a change in absorption at 414 nm. Either palmitoyl or docosahexaenoyl CoA will be used as the acyl donor to lyso-phosphatidyl choline. The conversion of lyso-phosphatidyl choline to phosphatidyl choline will be chromatographed. This assay will be optimized for pH, ionic strength, substrate levels and amount of enzyme before kinetic constants are determined. For carnitine-dependent transacylation, D, L-palmitoyl carnitine and lyso-phosphatidyl choline will be coincubated with washed sperm, delipidated and the products chromatographed as above. If the amount of lyso-phosphatidyl choline declines while phosphatidyl choline increases, a carnitine dependent mechanism will be presumed to exist. Alternatively, carnitine dependency could be screened by using 3H-palmitoyl carnitine to look for labeled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabeled 22:6 with 3H-16:0 and following the appearance of 16:0 in phosphatidyl choline. Conversely, the effect of 16:0 on 14C-22:6 will be studied.

Progress: The investigators have demonstrated that ether lipids can be synthesized from hexadecanol and phosphatidylethanolamine, presumably through an exchange reaction at the SN-1 position. We are currently attempting to characterize this enzyme. A paper was presented at the Society for the Study of Reproduction in June 1992.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/083		Status: Completed
Title: Influence of Calcium on Phosphatidylcholine Synthesis in Human Spermatozoa				
Start Date: 09/16/88		Est. Completion Date: Sep 89		
Department: Medicine		Facility: MAMC		
Principal Investigator: LTC (P) Robert E. Jones, MS				
Associate Investigators: COL Stephen R. Plymate, MC		MAJ Charles J. Hannan, MC		
Key Words: spermatozoa,phosphatidylcholine,calcium,spermatozoa				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$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 2×10^8 in the isolation buffer. Approximately 1×10^7 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 $MgCl_2$, 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/10⁷ 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: A23187, a calcium ionophore, had no effect on phosphatidylcholine synthesis from free fatty acids and lyso-PC. By contrast, A23187 clearly inhibited phosphatidylethanolamine production from free fatty acids and lyso-PE. A manuscript has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 85/084	Status: Terminated
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 MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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: Attempts at ligase purification have been stymied due to contamination of the crude preparation with acrosomal proteases. Use of anti-proteases (inhibitors) has not been entirely successful. Due to these technical problems, this protocol was terminated.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/038		Status: On-going
Title: Detailed Studies Into Membrane Lipid Synthesis in Human Sperm				
Start Date: 02/16/90		Est. Completion Date: Feb 99		
Department: Medicine		Facility: MAMC		
Principal Investigator: LTC (P) Robert E. Jones, MS				
Associate Investigators: CPT Brenda K. Bell, MC		COL Stephen R. Plymate, MC		
Key Words: lipid synthesis,human sperm				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$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 2×10^8 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, 14C-1-16:0, or 14C-1-22:6. The reaction will be initiated by the addition of 107 sperm. Blank incubations will be performed in the absence of CoASH or the specific starting substrate to investigate the metabolic mechanisms of lipid turnover. Methylation of phosphatidylethanolamine (PE) will be measured by incubating 3H-methyl-S-adenosylmethionine (SAM) with diacyl PE or a 14C labeled fatty acid, 3H-SAM and 1-acyl-2-lyso PE. Another pathway for plasmalogen or ether lipid synthesis in nongerminal tissues will be assessed by incubating sperm with 14C-22:6, 1-palmitoyl32-lyso PI (phosphatidylinositol) or -PC (phosphatidylcholine) and 3H-1-hexadecanol in the aforementioned buffer. Alternatively, 3H-hexadecanol, 14C-22:6, unlabeled 16:0 will be coincubated with dihydroxyacetone phosphate (DHAP). The reaction will be terminated after 1 hour and lipids will be extracted and dried. Incorporation of labeled fatty acids into sphingomyelin (SM) will be determined by detection of the fatty acyl radiolabel in the SM region of the thin layer chromatography (TLC) plates. After resolubilization in chloroform and methanol, lipids will be separated on LK5 TLC plates. Standards will be run on each plate and spots corresponding to standards will be scraped and counted. Plasmalogen formation will be assessed by performing mild acid hydrolysis on the extracted phospholipids prior to TLC or before rechromatography and determining DPM's in the fatty aldehyde and lysophospholipid regions. The presence of ether lipids will be determined by their resistance to alkaline and enzymatic hydrolysis prior to TLC. Mono and diacyl phospholipid synthesis will be assessed by free fatty acid release from SM and by using phospholipases A2 (PLA2) and B (PLB).

Progress: The investigators are presently characterizing acyl transferase activity in fresh human sperm.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 83/081	Status: On-going
Title: Studies on Fatty Acid Activation in Spermatozoa: Kinetics and Localization		
Start Date: 09/16/83	Est. Completion Date: Sep 84	
Department: Medicine	Facility: MAMC	
Principal Investigator: LTC (P) Robert E. Jones, MS		
Associate Investigators: COL Bruce L. Fariss, MC COL Stephen R. Plymate, MC		
Key Words: spermatozoa, fatty acid		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$785.00	04/05/91

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

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

Progress: The investigators are attempting to obtain an enriched sperm membrane preparation in order to further characterize ligase activity.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 88/026

Status: On-going

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

Start Date: 01/15/88

Est. Completion Date: Jun 89

Department: Medicine

Facility: MAMC

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

Associate Investigators:
MAJ Karl E. Friedl, MC

COL Stephen R. Plymate, MC
MAJ Charles J. Hannan, MC

Key Words: spermatozoa, lipids, morphology

**Accumulative
MEDCASE Cost:**

\$40000.00

Est. Accumulative

OMA Cost:

\$2000.00

Periodic Review:

04/05/91

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

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

Progress: Data collection continues.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/070		Status: On-going	
Title: Characterization of Serovar-Specific Ureaplasma Antigens by Analysis with Monoclonal Antibodies					
Start Date: 09/16/88			Est. Completion Date:		
Department: Medicine			Facility: MAMC		
Principal Investigator: LTC (P) Robert E. Jones, MS					
Associate Investigators:			MAJ John E. van Hamont, MS		
Key Words: antigens,ureaplasma,monoclonal antibodies					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$3700.00
					Periodic Review: //

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, mycoplasma assay, and direct fluorescent assay. The monoclonals identified as having type specificity will be used in the analysis of colloidal gold labeling procedures for localization of type-specific antigen by electron microscopy and for affinity column chromatography purification of type specific antigen from ureaplasma cell lysates. The monoclonals and antigens thus characterized will be used in the development of assays for future identification of clinical isolates of *Ureaplasma* and analysis of host serological responses.

Progress: No further work was undertaken on this protocol in FY 92. Abstracts reporting data from this study were presented in 1990 and 1991 and a paper has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/059	Status: On-going
Title: Bleomycin vs. Minocycline in a Randomized Double Blind Prospective Trial of Intrapleural Therapy for Recurrent Malignant Pleural Effusions		
Start Date: 07/02/92	Est. Completion Date: Sep 94	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Lynn M. Keenan, MC		
Associate Investigators: CPT John R. Caton, MC CPT Stacey B. Young, AN CPT Bernard J. Roth, MC		CPT Jennifer L. Cadiz, MC CPT Curtis S. Hansen, RPH, MSC LTC William H. Cragun, MC
Key Words: pleural effusions, bleomycin, minocycline, randomized		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine the efficacy of minocycline versus bleomycin for sclerosis of malignant pleural effusions.

Technical Approach: Eighty patients with advanced malignancy and symptomatic pleural effusion recurrent after at least one prior therapeutic thoracentesis will undergo chest x-ray to confirm freely flowing pleural fluid. A data sheet will be kept recording ECOG performance status, chest radiograph results, and demographic information (age, sex, diagnosis, stage of disease, type of chemotherapy received, side effects to the sclerosant including pain, fever, hypotension, allergic reaction, rash, fatigue, anorexia, nausea, vomiting, diarrhea, elevated liver function tests, anemia, neutropenia, and elevated blood urea nitrogen or creatinine). The patient will be randomized to either bleomycin or minocycline. A chest tube will be placed and when it drains less than 100 cc per 24 hour period, the patient will undergo a test dose of the study drug. If the study drug is tolerated, the patients will undergo sclerotherapy with the assigned drug. The chest tube will be clamped for two hours and then placed onto 20 cm suction which will be maintained for at least 24 hours and until pleural drainage is < 150 ml/day. The chest tube will then be removed. Chest radiographs will be obtained at 72 hours to assess for recurrence of the effusion. If the fluid reaccumulates more than 50% of the original volume, the patient will be considered a treatment failure and removed from the study. Liver function tests, blood urea nitrogen, creatinine, and CBC will be obtained at 24 and 48 hours to monitor for side effects. The side effects listed on the data sheet will be monitored during the first 48 hours after sclerosis has been completed. Chest radiographs will be obtained at 7, 14, 30, 60, and 90 days to assess for response. Analysis of variance and regression analysis will be utilized to review the data obtained.

Progress: Two patients have been entered in this study with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/057	Status: Completed
Title: Do Not Resuscitate: Do Not Provide Care?		
Start Date: 04/03/92	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Lynn M. Keenan, MC		
Associate Investigators:		
CPT Roberta F. Ficke, MC	LTC William H. Cragun, MC	
CPT Jonathan P. Mueller, MC	CPT Pamela Charney, SP	
CPT Robert M. Tuttle, MC	CPT Stacey B. Young, AN	
Key Words: Do not resuscitate orders		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine if the care of the patient with a "Do Not Resuscitate" (DNR) status changes in ways other than explicitly specified by the DNR order or DNR note.

Technical Approach: Charts of 40 patients will be prospectively reviewed by two independent investigators. On day 1, the investigators will begin the data collection which will include the prior 24 and 48 hours of the admission. Then the data collection period will prospectively include the day of the DNR order, the following 24 hours, and 72 hours as well as 7 to 10 days later. Data collection will include: admitting diagnosis, underlying diagnosis, admitting service, ICU or general ward patient, facility, staff writing DNR, number of lab draws, x-rays, procedures and calls to the house officer. Also, type of x-rays and procedures, and content of the physician and nurses notes will be evaluated for the number of problems addressed, documentation of a current physical exam, actual vital signs recorded and specific patient subjective comments recorded. Nutritional care, nutritional supplementation and nutritional consult will also be recorded. The charts will be evaluated for vital signs charting. Patients will be identified by life expectancy: less than 48 hours and less than 6 months and greater than one year. The charts will also be evaluated for the change in the pattern of administration of antibiotics, blood products, pressor agents, dialysis, mechanical ventilation, and invasive hemodynamic monitoring.

Progress: The charts of 61 patients were studied. Those with the DNR note showed a decrease in annotations of physical exam, vital signs, RN pain notations, and doctor problems. There was 36% mortality with only 36% Social Work Service or hospice consults. Only 36% of the DNR notes had a specified treatment plan. An abstract has been accepted for presentation at the Army American College of Physicians Meeting in November.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/098	Status: On-going
Title: Does Laparoscopy Add to the Diagnosis of Nonfocal Liver Disease?		
Start Date: 01/04/91	Est. Completion Date: Apr 92	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Michael F. Lyons II, MC		
Associate Investigators: MAJ Amy M. Tsuchida, MC		CPT Robert J. Lodato, MC MAJ Gregory E. Schlepp, MC
Key Words: liver disease, laparoscopy		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 non-invasive imaging studies (LSS, U/S, or CT) will be done. Immediately prior to laparoscopy, one or more of the associate investigators will assess the non-invasive work-up and form a prelaparoscopy diagnosis for four groups: cirrhosis, chronic hepatitis, normal, and fatty change. Laparoscopy with biopsies will be done, using standard technique. During the laparoscopy (before biopsy results are known), the associate investigators will make a diagnosis based on the non-invasive workup and laparoscopic findings. The two diagnoses pre and post-laparoscopy will then be compared with the histologic diagnosis. The core biopsy histologic diagnosis will be compared to the pinch biopsy result. Four fold tables for chi square analysis will be used to compare the sensitivity, specificity, and positive and negative predictive values of the pre and post-laparoscopic diagnoses. Chi square analysis will be used to compare the accuracy of the pinch biopsy to that of the core biopsy.

Progress: Patients are still being entered on this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/051	Status: Suspended
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 Ulcer Disease		
Start Date: //	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Michael F. Lyons II, MC		
Associate Investigators: MAJ Gregory E. Schlepp, MC MAJ Mark D. Brissette, MC		MAJ Amy M. Tsuchida, MC COL Michael J. Carlon, MC
Key Words: cancer:esophagus,Barrett's,stomach		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	07/02/92

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

Technical Approach: Approximately 200 subjects with a diagnosis of Barrett's esophagus, gastric intestinal metaplasia by prior upper endoscopic biopsy or by history of partial gastrectomy for 10 or more years will be studied. After visualizing the esophagus, stomach, and duodenum, biopsies will be obtained from these areas as dictated by the subject's diagnosis. One half of the biopsy specimen will be processed for histology, classified according to the type of mucosa present, and designated negative, indefinite, or positive for dysplasia. Specimens forwarded for flow cytometry will be processed in the routine fashion. Data will be gathered and analyzed by an on-line computer. Cell cycle parameters will be analyzed using a first order polynomial S phase. By this nonlinear least squares curve-fitting technique, the G1/G0 (2N) and G2/M peaks (4N) are fit using normal distributions and the region between these two peaks is allotted to cells in DNA synthesis (S phase). Aneuploid peaks will be fit by inclusion of additional 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: In July 1992, the principal investigator asked for this protocol to be put in a suspended status until he has the time and resources to make the changes required by the Human Use Committee.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/042		Status: Terminated
Title: Safety and Efficacy of BID and QID Dosing with Tiagabine HCl Versus Placebo as Adjunctive Treatment for Complex Partial Seizures				
Start Date: 06/05/92			Est. Completion Date:	
Department: Medicine			Facility: MAMC	
Principal Investigator: MAJ John W. McBurney, MC				
Associate Investigators:			MAJ Mark A. Lombardo, MC	
Key Words: seizures, tiagabine				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$0.00		\$0.00	//	

Study Objective: To determine the efficacy of BID and QID dosing with tiagabine HCl versus placebo as adjunctive therapy for complex partial seizures.

Technical Approach: This is a randomized, double-blind, placebo-controlled, parallel-group, add-on antiepileptic drug trial. The study consists of a Baseline Phase and a Double-Blind Phase. For the baseline phase, patients will give a medical and neurological history, receive appropriate examinations, and keep a seizure diary. This phase of the study will provide a prospective baseline seizure frequency and determine entry into the double-blind phase. Patients entering the double-blind phase will be randomized to one of three treatment regimens: (1) placebo four times a day (2) 16 mg tiagabine HCl two times a day and placebo two times a day, or (3) 8 mg tiagabine HCl four times a day. The initial dose of tiagabine will be tiagabine HCl 4 mg twice a day, or tiagabine HCl 2 mg four times a day, or placebo. The dosage will be increased in 3 steps during the next 4 weeks until it reaches the constant levels as stated above, i.e., 16 mg twice a day and 8 mg four times a day, after which it will remain constant for the next 8 weeks. Upon completion of the Fixed-Dose Period, all patients will be asked to enter the open-label extension study. Those who are already taking tiagabine will continue to take it with all patients taking the 8 mg QID dosage. Patients who are taking tiagabine who do not wish to enter extension study will be tapered off the tiagabine. Those receiving the placebo who wish to enter the extension phase will take tiagabine, starting at 2 mg four times a day and building up to 8 mg four times a day. Those who are taking the placebo and do not wish to enter the extension study will be dropped from the study. Patients will continue on tiagabine for as long as it is effective in controlling the seizures.

Progress: This study was terminated at MAMC because the sponsor closed the study to patient entry before approval was received to use the investigational drug.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/073	Status: Terminated
Title: Vagal Nerve Stimulation via Neurocybernetic Prosthesis for the Control of Chronic Epilepsy		
Start Date: 11/01/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ John W. McBurney, MC		
Associate Investigators: CPT Renee M. Bernier, MC LTC Joseph P. McCarty, MC		
Key Words: epilepsy, vagal nerve stimulation, neurocybernetic		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: The MAMC investigators felt that they were not provided with the detailed information that they needed to determine which patients this procedure could best be used for and the safety data to back this information up. After further literature review and consideration of the protocol, the investigators did not feel comfortable with the data on the potential long term side effects of the device and terminated MAMC's participation in the study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/094		Status: On-going
Title: Effects of Carnitine on Measures of Cognition, Mood, and Sleep in Adolescents with Epilepsy Treated with Valproate				
Start Date: //		Est. Completion Date: Dec 92		
Department: Medicine		Facility: MAMC		
Principal Investigator: LTC Joseph P. McCarty, MC				
Associate Investigators: None				
Key Words: epilepsy, carnitine, adolescents				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$0.00		\$0.00	//	

Study Objective : To evaluate the effects of L-Carnitine therapy on energy levels and general sense of well-being in adolescent patients who have been previously diagnosed with epilepsy and who are currently receiving valproate as a treatment and to correlate any changes in measures of energy and general well-being with physiologic changes attributable to carnitine.

Technical Approach : Adolescent patients with epilepsy who are currently receiving valproate for control of seizures and who are presently under good control will be eligible for this study. Studies have indicated that one of the metabolic side effects of valproate is lowering of plasma carnitine concentration with a possible negative impact on fatty acid metabolism and resultant decrease in mood and energy levels. Patients will have baseline measures of general sense of well-being and cognition. They will then take carnitine or a placebo for six weeks. At the end of the six week period, data will be collected regarding energy levels and general sense of well-being. The patients will then switch to the opposite experimental treatment for another six week period. At the end of the second six week period the same data will be collected regarding energy level and general sense of well-being. For statistical analysis of psychological measures, changes in mood states and in cognitive scores from period 1 to period 2 in Group A (carnitine) will be compared to Group B (placebo) within each antiepileptic drug condition (valproate monotherapy vs polytherapy). Paired T-tests (parametric) or Wilcoxon Rank Sum tests (non-parametric) will be used for analysis. If changes are seen in the blood chemistry without concomitant changes in behavioral measures, baseline psychological measures will be examined as possible moderating variables.

Progress : This is a new study that is awaiting HSC approval.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/003	Status: Completed
Title: Videx (2',3',-dideoxyinosine, ddi) AIDS Treatment Program		
Start Date: 12/07/90	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: LTC Rodney A. Michael, MC		
Associate Investigators:		LTC Ronald H. Cooper, MC
Key Words: AIDS,Videx,treatment		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: This study was closed by the sponsor because the drug was approved by the FDA. Four patients were entered in this study at MAMC (1 in FY 92). All data have been sent to the sponsor for analysis.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/018	Status: Completed
Title: Open Label, Compassionate Clearance Treatment of Aids-Related Cryptosporidial Diarrhea with Diclazuril (R64,433)		
Start Date: 01/03/92	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: LTC Rodney A. Michael, MC		
Associate Investigators: LTC Ronald H. Cooper, MC		
Key Words: diarrhea, aids-related, cryptosporidial, diclazuril		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective: To provide diclazuril capsules as treatment of AIDS-related cryptosporidial diarrhea.

Technical Approach: Patients will have a history taken and a physical examination, including body weight. The stool will be examined for ova and parasites to confirm the presence of *Cryptosporidium* oocysts before the patient is started on the drug. Patients will be started on 600 mg of diclazuril divided into two daily doses. Patients will be evaluated weekly during the first month and monthly thereafter. The following will be obtained or determined at least monthly during treatment: stool examination for *Cryptosporidium* oocysts average number of bowel movements per day and gastrointestinal symptoms and routine hematology and biochemistry screen. Patients will be given a six week trial of therapy. If there is a favorable clinical response, the patient will be continued indefinitely on diclazuril. In the event of no clinical response, diclazuril will be stopped after six weeks or sooner if poorly tolerated.

Progress: No patients were entered in this study at MAMC. The study has been closed by the sponsor due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/097	Status: On-going
Title: The Use of Thyroid Tissue Obtained by Fine Needle Aspiration (FNA) as Substrate for Polymerase Chain Reaction (PCR) Amplification of Thyroglobulin and the Papillary Thyroid Cancer (PTC) Oncogene		
Start Date: 10/04/91	Est. Completion Date: Apr 92	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Mark E. Peele, MC		
Associate Investigators: CPT Robert M. Tuttle, MC		
Key Words: cancer:thyroid,PCR,thyroglobulin,FNA,PTC oncogene		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$1250.00	//

Study Objective: 1. To show that thyroid tissue obtained by routing fine needle aspiration (FNA) can be used for the polymerase chain reaction (PCR) amplification of thyroidal genomic DNA and messenger RNA transcripts. 2. Utilize PCR to amplify DNA sequences unique to the RET and PTC (papillary thyroid cancer) 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 ul of either RPMI cell culture media or phosphate buffered saline (PBS). Cells will be rapidly pelleted by centrifugation after the rinse to remove excess plasma proteins. The cell pellet will be resuspended in 25 ul DEPC treated water and rapidly chilled to -70 deg C. This material will then be stored until laboratory study begins. PCR will be used to amplify thyroidal genomic and mRNA. The material collected from the FNA will be heated to 65 deg C in the presence of RNasin and hypotonic DEPC treated water to linearize the nucleic acids. The mRNA and DNA will serve as the templates for the PCR amplification. Three sets of PCR primers and oligomers will be synthesized. All the primer sets have an engineered span containing a restriction enzyme site (HINDIII) on the 5' portion to allow insertion of the amplified material into a sequencing vector. Thyroglobulin will be amplified as the positive control, the oncogenes PTC1 and RET will be amplified from aliquots of the same material. The first step in the amplification of the mRNA will be the synthesis of first strand complementary DNA. The cDNA and linearized DNA will be amplified as per standard PCR protocols for 35 cycles. The amplified products are separated on an agar gel and blotted onto a nylon membrane, the

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

Progress: The investigators developed and implemented basic protocols for oligonucleotide synthesis and purification nucleic acid extraction from various tissue preparations to include cell culture, FNA, and paraffin embedded tissue blocks and expression PCR analysis of thyroglobulin, PTC oncogene, and beta 2-microglobulin mRNA transcripts. Clinical aspiration material was collected on six individuals with thyroid neoplasia, 5 with benign nodular disease, and one with papillary thyroid cancer (histology confirmed). All aspirations were adequate for cytologic evaluation.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/068	Status: On-going
Title: The Time Course for Metabolic Responses to Thyroid Hormone: Specific Contributions of Muscle Efficiency and Resting Oxygen Utilization		
Start Date: //	Est. Completion Date: Jan 94	
Department: Medicine	Facility: MAMC	
Principal Investigator: LTC H. Lester Reed, MC		
Associate Investigators: LTC (P) Robert E. Jones, MS		COL David L. Bunner, MC CPT Carl A. Gibson, MC
Key Words: thyroid hormone, muscle efficiency, oxyten utilization		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: The investigators have validated both ergometer and metabolic cart protocols and studied three subjects.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/032

Status: Completed

Title: The Relationship Between Circulating Androgens and Declining Body Weight During Extended Cold Weather Operations

Start Date: 01/03/92

Est. Completion Date:

Department: Medicine

Facility: MAMC

Principal Investigator: LTC H. Lester Reed, MC

Associate Investigators:

CPT Robert M. Tuttle, MC

Key Words: androgens, body weight, cold weather

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To determine the relationship between weight loss and changing serum androgen and gonadotrophin concentrations during cold weather operations.

Technical Approach: In a previous study performed by the principal investigator at the Naval Medical Research Institute, Bethesda, MD, the energy deficits incurred by a group of U.S. Navy SEAL members during an 8 week winter training exercise were determined. This group had an increased energy requirement of 1886 kcal/day and weight loss in eight of the nine men of between 1-5.7 kg. These men lost subcutaneous body fat. The thyroid hormone kinetics of these men have been reported and help to characterize this environmental condition as a combination of extended cold exposure, field operating tension, increased energy expenditure, and a net hypocaloric state. This study would analyze the serum from these nine men collected before and after their training to correlate declines in body weight, bioactive and immunoactive LH, total testosterone and estradiol and sex hormone binding globulin. This pilot study may only establish the relationship between these two variables. Further investigation will be needed to isolate the specific contributions of undernutrition and "stressful" operational involvement in these changes. The statistical analysis will be carried out with Student's t test for paired data with a $p < 0.05$ used as the level of significance.

Progress: The sera from these nine subjects have been analyzed. Body weight and percent body fat declined during the study period even though energy intake did not decline. SHBG increased 54% without changes in serum albumin or thyroid hormone binding globulin. There were no significant changes in serum total testosterone, estradiol, or luteinizing hormone. The calculated free testosterone, based on standard binding characteristics, tended to decrease but did not reach statistical significance. The ratio of free testosterone to estradiol, however, declined 15%. The variable individual changes in estradiol concentrations were highly and positively correlated with individual declines in percent body fat. The relationship of estradiol to total body weight is less clear. The fall in the free testosterone/estradiol ratio was also directly correlated with a fall in percent body fat and total body weight. These data are being included in a manuscript for peer review publication.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/082	Status: Terminated
Title: Iontophoresis Therapy for Rheumatoid Arthritis		
Start Date: 10/04/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Kathryn K. Riordan, MC		
Associate Investigators: MAJ Thomas L. Irvin, MC		
Key Words: arthritis:rheumatoid,iontophoresis		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 long-term data. Reasons for withdrawal from treatment groups will be analyzed and discussed in final data analysis.

Progress: This study has been terminated due to time constraints on the principal investigator. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/083	Status: On-going
Title: Iontophoresis Therapy for Bursitis and Tendinitis		
Start Date: 10/04/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Kathryn K. Riordan, MC		
Associate Investigators: MAJ Thomas L. Irvin, MC		
Key Words: bursitis,tendinitis,iontophoresis		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 0.5 cc will be used in the iontophoresis treatments. Lidocaine hydrochloride 4% will be used in all treatments (including shams).

Progress: Sixteen patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/099	Status: On-going
Title: Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure		
Start Date: 10/19/90	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Bernard J. Roth, MC		
Associate Investigators: LTC William H. Cragun, MC		
Key Words: pleural effusion, albumin, congestive heart failure		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

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

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

Progress: Two subjects were entered in this study in FY 92 for a total of three subjects. One patient had conversion to exudate by Light's criteria, yet remained a transudate by albumin criteria. Accrual on this study is slow because patients who meet the criteria are uncommon.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/015

Status: On-going

Title: Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure

Start Date: 03/01/91

Est. Completion Date:

Department: Medicine

Facility: MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators:
MAJ Bruce S. Grover, MC

LTC William H. Cragun, MC

Key Words: positive pressure ventilation, air flow obstruction, nasal mask

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$260.00

Periodic Review:

//

Study Objective: To determine if one eight hour period per week of ventilatory rest via nasal mask positive pressure ventilation will improve pulmonary function and exercise tolerance in patients with chronic air flow obstruction and chronic respiratory failure marked by an elevated arterial carbon dioxide.

Technical Approach: The study population will be both sexes, age >18 years, with severe COPD. The following baseline values will be obtained: age, weight, height, smoking status, medication list, chest x-ray, spirometry, formal lung volumes, MIP, MEP, DLCO, arterial blood gas measurement, pulse oximetry, end-tidal capnography, thyroid function tests, CBC, electrolytes, Karnofsky scale, dyspnea index, and 12 minutes walking distance. Spirometry, pulse oximetry, and end-tidal capnography will be repeated once weekly for four weeks. After four weeks, baseline studies will be repeated and an overnight polysomnography will be performed which includes electroencephalogram, electromyogram, electro-oculogram, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous 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 nIPPV will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAP and nIPPV patients using Student's T test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or PaCO₂ will be considered a positive result of nIPPV.

Progress: No additional patients have been entered in this study in FY 92. Six patients were entered in previous years. Two prospective subjects may be entered in the next month.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/043		Status: On-going	
Title: The Effects of Testosterone Replacement in Hypogonadal, Malnourished Patients with Chronic Obstructive Pulmonary Disease (COPD)					
Start Date: 09/15/89			Est. Completion Date: Oct 89		
Department: Medicine			Facility: MAMC		
Principal Investigator: CPT Bernard J. Roth, MC					
Associate Investigators: MAJ John P. Kushner, MC			COL Stephen R. Plymate, MC MAJ Bruce S. Grover, MC		
Key Words: CPOD,testosterone,hypogonadal,malnourished					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$65.00		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 FEV1, 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 FEV1 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 patients were studied on Part I of this study (amendment of Sep 89 as stated above) which is a screening tool to determine entry in to Part 2. There appears to be a high rate (53%) of hypogonadism in patients with COPD. A paper was presented at the April 1992 meeting of the American Thoracic Society. Two additional patients were entered in Part 2 of the study in FY 92 for a total of six subjects.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/024

Status: On-going

Title: Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging

Start Date: 01/03/92

Est. Completion Date:

Department: Medicine

Facility: MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators:
MAJ Miquel Rovira, MC
MAJ Frank A. Zimba, MC

MAJ Kevin L. Quinn, MC
MAJ Steven S. Wilson, MC

Key Words: cancer, bronchogenic, MRI

Accumulative
MEDCASE Cost:

\$0.00

Est. Accumulative
OMA Cost:

\$0.00

Periodic Review:
//

Study Objective: To determine the incidence of clinically occult brain metastasis in patients with resectable primary bronchogenic carcinoma.

Technical Approach: The subjects (100) for this protocol will be patients >18 years of age with primary bronchogenic carcinoma, Stage IIIa or less as determined by chest CT, who are neurologically intact. The patient will undergo a complete clinical neurological history and physical exam and enhanced cranial MRI to screen for brain metastasis. Patients with evidence of significant CNS pathology will be divided into four groups: (1) solitary lesion amenable to neurosurgical resection (2) significant brain pathology other than metastatic disease that would delay or preclude therapy (3) brain metastasis and (4) metastasis outside the brain. Patients in group 1 or 2 will undergo neurosurgical and/or radiation therapy evaluation for possible curative or palliative therapy. Patients in group 3 or 4 will undergo radiation therapy and/or hematology-oncology evaluation for possible palliative therapy. Patients in whom MRI revealed suspicious areas which are not definitely characteristic for metastasis will undergo brain biopsy using stereotactic localization. Patients refusing brain biopsy will be followed closely with periodic follow-up enhanced cranial MRI every three months. MRI and clinical data will be evaluated to determine the overall incidence of clinically occult brain metastases and the presence (if any) of any significant differences among primary cell types.

Progress: Thirteen patients have been entered. Data will be reviewed when 50 subjects have been entered. Dr. Quinn was the original principal investigator. The principal investigator was changed to Dr. Roth upon the reassignment of Dr. Quinn.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/036 **Status:** Completed

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

Associate Investigators:	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

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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: Approximately 150 subjects were entered. Data are being analyzed and a paper is being prepared for publication.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/035		Status: Completed
Title: Home Intravenous Antibiotic and Heparin Therapy in a Military Setting				
Start Date: 04/20/90		Est. Completion Date: Feb 91		
Department: Medicine		Facility: MAMC		
Principal Investigator: CPT Phillip S. Schwartz, MC				
Associate Investigators: CPT Anne E. Vockroth, MC		MAJ Richard H. Snyder, MC		
Key Words: IV therapy,antibiotic therapy,heparin therapy				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		05/03/91

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: Eighteen subjects were entered. This method proved to be safe with no adverse effects. The study was put on hold after these 18 patients in order to do some statistics. It was never restarted due to additional duties added to the investigators schedule.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/082	Status: On-going
Title: A Pilot Study of Carboplatin and Daily Oral Etoposide in the Treatment of Advanced Non-Small Cell Lung Cancer		
Start Date: 08/17/90	Est. Completion Date: Jun 93	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
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	
Key Words: cancer:lung:non-small cell,carboplatin,etoposide		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$3000.00	//

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

Technical Approach: Thirty subjects with histologic evidence of non-small cell lung cancer and no prior chemotherapy will be studied. Patients with CNS metastases and simultaneous neoplasms at another site will be excluded. Patients will receive chemotherapy in 28 day cycles. Each cycle will start on day 1. Carboplatin IV will be given on days 1 and 8. The total dose for both days will be determined by the formula $5 \times (\text{creatinine clearance [ml/min]} + 25)$. Etoposide will be given 50 mg/M² 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/M² po days 1-21 for future cycles. Patients will be evaluated for response after two cycles. Those who have at least a 25% reduction in the product of the bidimensional measurement of the marker lesion will receive two more cycles of therapy and then stop all therapy. Those who do not have a 25% reduction in the cross-dimensional product will stop treatment. Those patients who have non-measurable disease will receive two more cycles if there has been no deterioration in the performance status otherwise, they will also stop therapy. Toxicities will be described as the frequency per patient on study and per cycle of treatment. Response rates will be described using standard criteria. Survival will be measured from study entry. Survival will be displayed graphically and described as duration of survival per quartile of patients.

Progress: No patients were entered in FY 92. Nine subjects have previously been entered. A small number of responses has been seen. The significance will be determined when 14 patients have been accrued.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/007	Status: On-going
Title: Treatment of Thrombocytopenia, Hemolytic Anemia, or Neutropenia with Ascorbic Acid		
Start Date: 04/20/90	Est. Completion Date: Oct 91	
Department: Medicine	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: ascorbic acid, thrombocytopenia, hemolytic anemia, neutropenia		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$585.00	//

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

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

Progress: No patients were entered in this study in FY 92 one was entered in FY 91.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/044 **Status:** Terminated

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

Start Date: // **Est. Completion Date:**

Department: Medicine **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	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

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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/M² IV bolus for five consecutive days once very four weeks until maximal response or disease progression occurs. The patients will undergo weekly CBC 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: This protocol was terminated because fludarabine phosphate has been approved by the FDA for use in these patients. Two patients were entered at MAMC in FY 91 with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 84/040		Status: Terminated	
Title: Treatment of Graves' Ophthalmopathy with Cyclosporin					
Start Date: 04/20/84			Est. Completion Date: Sep 86		
Department: Medicine			Facility: MAMC		
Principal Investigator: COL Gary L. Treece, MC					
Associate Investigators:			COL Stanley C. Allison, MC		
COL Francis G. LaPianan, MC			COL Leonard Wartofsky, MC		
LTC (P) Robert E. Jones, MS			CPT Andrew Ahmann, MC		
Key Words: ophthalmopathy:Graves',cyclosporin					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:		\$0.00	OMA Cost:		\$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 T4, T3, 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: This protocol was terminated due to the retirement of the principal investigator. No patients were entered in FY 92. Two patients were entered 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

Date: 30 Sep 92	Protocol No.: 81/056	Status: Completed
Title: The Effect of Nephrosis on Treated Hypothyroidism		
Start Date: 03/17/81	Est. Completion Date: Sep 86	
Department: Medicine	Facility: MAMC	
Principal Investigator: COL Gary L. Treece, MC		
Associate Investigators:		
COL Stephen R. Plymate, MC	COL Stanton R. Brown, MC	
MAJ Howard M. Cushner, MC	CPT Jeffrey Addison, MC	
	MAJ Charles J. Hannan, MC	
Key Words: hypothyroidism, nephrosis		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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, T4, and T3. Fasting samples will be drawn for SMAC-20, T4, T3 resin, T3 by RIA, TSH, THAT (an extra tube will be drawn for free T4, reverse T3, 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 T4 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: This study was closed due to the retirement of the principal investigator. No patients were entered in FY 92. Preliminary results from eight subjects indicate a higher incidence of hypothyroidism associated with the nephrotic syndrome than previously reported.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 82/005 **Status:** Terminated

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

Associate Investigators:

MAJ Robert E. Jackson III, MC
LTC Daniel H. Knodel, MC

COL Bruce L. Fariss, MC

LTC (P) Robert E. Jones, MS

MAJ William R. Sheldon Jr., MC

Key Words: adrenal insufficiency, urinary free cortisol

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$700.00

Periodic Review:

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 under- and 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: This protocol was terminated due to the retirement of the principal investigator. No patients were entered in FY 92. Patient recruitment has been slow due to the rarity of patients with primary adrenal insufficiency. In previous years, four patients were entered.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/045	Status: Terminated
Title: Randomized Trial of Interferon Versus Ursodeoxycholic Acid in the Treatment of Non-A, Non-B, Type C Hepatitis		
Start Date: //	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: MAJ Amy M. Tsuchida, MC		
Associate Investigators: MAJ Gregory E. Schlepp, MC		MAJ Michael F. Lyons II, MC CPT William A. Pearce, MC
Key Words: hepatitis, type C, interferon, ursodeoxycholic acid		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To demonstrate whether ursodeoxycholic acid would have the same, if not better, efficacy when compared to 5 million units three times a week of alpha-interferon 2-B in the treatment of non-A, non-B, type C hepatitis and to determine if analysis of cytokines and growth factors will predict outcome of treatment.

Technical Approach: Twenty-five subjects will have appropriate lab tests to rule out other common causes of chronic hepatitis and metabolic liver diseases. Within six months prior to entry into the study, subjects will be required to have had a liver biopsy which shows changes consistent with chronic active hepatitis and patients must have serum evidence of ongoing liver damage with ALT at least 1.5 times normal. Patients will be randomized to (1) alpha-interferon 2-B, 5 million units SQ or IM three times a week, or (2) ursodeoxycholic acid 10 mg/kg orally daily for nine months. Patients will be followed monthly with clinical evaluations and serum chemistries (glucose, CBC, prothrombin time, liver panel, lytes). Serum will be drawn and saved pretreatment and at three month intervals for protein markers of inflammation and cell injury such as the interleukin proteins and growth factors to see if any markers are detectable to identify responders versus nonresponders to the treatment. Patients who show improvement in laboratory parameters will continue treatment for nine months. At the end of nine months, treatment will be terminated and repeat liver biopsy and clinical assessment will be performed. Patients who show no evidence of response after three months will be crossed over to the other treatment arm and treated with the crossover medication for nine months. All patients will be followed off treatment for six months with repeat liver biopsy and clinical assessment done at the end of the six month follow-up period.

Progress: This study was terminated because the pharmacy could not support the costs of the drugs used in the trial.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/039	Status: Completed
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:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Robert M. Tuttle, MC		
Associate Investigators: COL Stephen R. Plymate, MC		CPT Brenda K. Bell, MC CPT Katherine H. Moore, MS
Key Words: testosterone, stress		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To study insulin induced hypoglycemia as a model of acute stress and to determine if the change in testosterone seen with acute stress is related to cortisol alone or whether it can also be seen with the stimulation of other adrenal precursor products.

Technical Approach: Ten healthy male volunteers (18-35 years) who are without evidence of current acute or chronic illness will have an insulin tolerance test done with blood samples drawn for cortisol, testosterone, immunoactive LH, bioactive LH, estradiol, and glucose, every 15 minutes for one hour prior to the human insulin bolus to establish baseline values. Blood samples will continue to be drawn every 15 minutes for 180 minutes after injection of the insulin. SHBG will be measured on the first and last sample and endorphin levels will be measured at baseline and at times corresponding to maximal hypoglycemia. A standard multiple dose metyrapone test will be performed one month from the insulin tolerance test. Just before the first dose and four hours after the last dose, serum samples will be obtained for cortisol, estradiol, immunoactive LH, bioactive LH, testosterone, ACTH, SHBG, endorphins, and 11-deoxycortisol. The relationship of bioactive LH to immunoactive LH will be compared using the biologic to immunologic ratio both before and during the acute stress. The data from the metyrapone test will be used to determine if metyrapone can cause a decrease in serum testosterone acutely. Again, the B/I ratio will be compared pre and post-test. Changes in serum concentrations of the measured hormones will be analyzed by repeated measures analysis of variance.

Progress: Eight patients were evaluated. The artificial acute stress of hypoglycemia induced by a bolus injection of insulin IV was associated with a rapid decline in serum testosterone (by 90 minutes). LH by RIA was unchanged. However, LH determined by bioassay was dramatically increased in the first 45 minutes of the study. This suggested that the earliest response of the hypothalamic-pituitary-gonadal axis to the artificial stress of insulin-induced hypoglycemia was a transient rise in LH bioactivity that was not accompanied by a rise in serum testosterone, indicating a possible primary testicular defect in this paradigm.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/081	Status: On-going
Title: The Effect of Thyroid Hormone Suppression on Thyroid Nodules Found to be Indeterminate by Fine Needle Aspiration		
Start Date: 10/04/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Robert M. Tuttle, MC		
Associate Investigators: MAJ John P. Kushner, MC MAJ Arnold A. Asp, MC	LTC (P) Robert E. Jones, MS COL Ernest L. Mazzaferri, MC MAJ James H. Timmons, MC	
Key Words: thyroid nodules, thyroid hormone suppression, needle aspiration		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost \$0.00	Periodic Review: //

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

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

Progress: Eight patients were enrolled in FY 92. Patient enrollment continues.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/080	Status: On-going
Title: A Prospective Evaluation of Gonadal Damage in Thyroid Cancer Patients Treated with Radioactive Iodine		
Start Date: 10/04/91	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Robert M. Tuttle, MC		
Associate Investigators: COL Stephen R. Plymate, MC LTC (P) Robert E. Jones, MS MAJ Arnold A. Asp, MC William Bremner, MD, Ph.D.		COL Ernest L. Mazzaferri, MC David Gardner, MD Christina Wang, MD MAJ Charles J. Hannan, MC
Key Words: cancer:thyroid,gonads,radioactive iodine		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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: Two patients have been entered in this study one of them in FY 92.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/043	Status: On-going
Title: Utility of Sinus Tenderness as a Diagnostic Sign in Sinusitis		
Start Date: 10/02/92	Est. Completion Date:	
Department: Medicine	Facility: MAMC	
Principal Investigator: CPT Diana S. Willadsen, MC		
Associate Investigators:		
CPT Thomas F. Burke, MC	CPT Jonathan A. Perkins, MC	
MAJ Danny M. Douglas, MC	MAJ Roderick D. Moe, MC	
MAJ James H. Timmons, MC	COL W. Pierre Andrade	
COL James S. Brown, MC	MAJ Kevin L. Quinn, MC	
Key Words: sinusitis, diagnosis, tenderness		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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

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

Progress: This protocol has not been implemented. It is being revised to meet the Human Use Committee requirements and a new principal investigator will be assigned as Dr. Willadsen has begun an Oncology Fellowship.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF NURSING

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/026	Status: Terminated
Title: The Primary Needs of Relatives of Critically Ill Patients		
Start Date: 02/01/91	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: CPT Brenda C. Conway, AN		
Associate Investigators: CPT Anna I. James, AN CPT Kathy K. Prue-Owens, AN		
Key Words: critically ill patients:needs of relatives		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: Approximately 50 individuals were interviewed. The PI was then reassigned. Since this protocol will need approximately 50 more subjects, it has been terminated at MAMC and the PI will submit the protocol for approval at her new duty station in order to complete the study.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/082

Status: On-going

Title: Evaluation of Aftacare Videotaped Programs on Diabetes, Cancer & Heart Disease for Patient Education as an Intervention in Secondary Prevention of Complications Associated with These Chronic Diseases

Start Date: //

Est. Completion Date: Nov 92

Department: Nursing

Facility: MAMC

Principal Investigator: MAJ Sandra Hellman, AN

Associate Investigators:
Ann Lancaster, CHN

MAJ Muriel Metcalf, AN

Key Words: videotaped education programs, Aftacare, diabetes, cancer, heart disease

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To evaluate the usefulness of Aftacare videotaped programs on diabetes, cancer, and heart disease for patient education as an intervention in secondary prevention of complications associated with these chronic diseases.

Technical Approach: The community health nurse will collect demographic information and administer a pretest concerning the patients knowledge of his/her medical condition, the patients concerns regarding his/her disease state, resources to help the patient understand how to cope with the condition, and what the patient can do to attain the highest level of health possible. Subjects will then be alternately assigned to a videotape educational program group or to a MAMC standard patient education group. Patients in the videotape group will view the video within two weeks after completion of the pretest. After viewing the video, the participants will be given a post-test, essentially obtaining the same information. Patients assigned to the control group will be given the pretest and be referred to the primary nurse who will be responsible for initiating the medical center's patient education. They will be given the same post-test the video group two weeks after completing the pretest. The videotape group will have demographic data collected and means determined for age, education, and income. Data on other demographic variables will be categorized by frequency counts. Qualitative data will be obtained from pre/post tests. Common themes will be identified, categorized, and then described for each group. From this, data will be inspected for trends within each group. The demographic variables for each group will be visually compared to determine group equivalence.

Progress: A total of 42 patients has enrolled in the heart disease section and 33 of these patients have completed the study. A total of 5 patients has enrolled in the cancer section with four completing the study (1 patient expired). Only one patient has enrolled and completed the diabetes section.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 91/031		Status: Completed	
Title: Tracheal Epithelial Injury and Body Core Temperature Changes Related to Ventilator Inspired Gas Temperatures in Piglets					
Start Date: 03/01/91			Est. Completion Date:		
Department: Nursing			Facility: MAMC		
Principal Investigator: Lori A. Loan, AN					
Associate Investigators:			LTC Barbara S. Turner, AN		
Key Words: body core temperature,tracheal epithelail injury,piglets,Animal Study					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
					Periodic Review: 08/07/92

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: Thirty-four animals were randomized as stated in the protocol. There were no statistically significant differences in tracheal injury or body core temperature between the groups, but data suggests a trend toward damage with ventilation at any temperature. No tracheal slides showed evidence of tracheal burning.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/088

Status: Completed

Title: Maternal Adaptation: Concerns, Perceived Social Support, and Health Care Utilization

Start Date: 08/03/92

Est. Completion Date: Oct 92

Department: Nursing

Facility: MAMC

Principal Investigator: MAJ Elizabeth A. Mittelstaedt, AN

Associate Investigators:

LTC Barbara S. Turner, AN

Key Words: postpartum women, social support, health care utilization

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$220.00

Periodic Review:
//

Study Objective: (1) To identify the concerns of postpartum women as they are discharged from the hospital (2) to identify the perceived social support systems of new mothers at the time of discharge (3) to identify the relationship between postpartum maternal concerns and perceived social support at the time of discharge and patterns of health care utilization from discharge to four weeks postpartum and (4) to analyze the relationship between concerns, perceived social support, and patterns of health care utilization and attendance at prenatal education classes.

Technical Approach: In order for physicians and nurses to assist the postpartum patient in her adaptation to motherhood, it is necessary to understand the concerns regarding motherhood of the postpartum patient and her knowledge and understanding of the social support systems that are available. This is especially true for military dependents since contact with an extended family is limited or nonexistent. Term patients whose delivery was normal will complete a five part Maternal Adaptation Questionnaire which will cover the following items: postpartum maternal concerns (self, infant, husband, family, and community are included) the social support network the level of social support demographic data, and a postpartum journal in which the subjects will annotate each time they have a concern or question for which assistance or advice from a health care professional is sought. Descriptive statistics, to include mean and standard deviation, will be utilized to analyze the data.

Progress: The questionnaire was completed by 124 subjects. The data, which will be used for a thesis, are being analyzed.

Detail Summary Sheet

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

Title: The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants

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

Department: Nursing **Facility:** MAMC

Principal Investigator: LTC Michelle T. Renaud, AN

Associate Investigators:
Susan Blackburn, M.D. LTC Barbara S. Turner, AN
MAJ Joanna C. Beachy, MC Karen Thomas, M.D.

Key Words: high risk infants, NICU environment, physiologic and neurobehavioral effect

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

Study Objective : To evaluate the effects of a modified NICU physical environment on the growth and development of three groups of high risk infants.

Technical Approach : Two groups of preterm infants (<31 weeks and 32 to 37 weeks gestational age) and a group of full term infants will be evaluated during hospitalization and post discharge; 120 infants will be randomly assigned to an experimental group (n=60 with 20 in each of the groups) or a control group (n=60 with 20 in each of the groups) once they achieve medical stability. The experimental group will be cared for from entry into the study until discharge in a specially designed NICU with a program of care that includes reduction of sound and light levels and day-night cycling of lighting. Controls will receive routine care in the standard NICU environment. All infants will have dependent measures recorded at the same time intervals. Outcome measures include: weight gain, duration of hospitalization, transition to nipple feeding, duration of organized sleep, amount of quiet sleep, diurnal cycling of heart rate, body temperatures, sleep-wake states, neurobehavioral stress cues, neurobehavioral and neurological assessments, and hearing and vision examinations. Analysis will include descriptive statistics, t-tests, analysis of variance procedures (including repeated measures) and cosinor analysis.

Progress : This is a new study that has not been implemented.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/046

Status: On-going

Title: Pregnancy Attitudes, Ambivalence, and Symptom Distress

Start Date: 02/01/91

Est. Completion Date:

Department: Nursing

Facility: MAMC

Principal Investigator: LTC Irene M. Rich, AN

Associate Investigators:

LTC Susan L. Burroughs, AN

Key Words: pregnancy:attitudes,ambivalence,symptom distress

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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

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

Progress: The data have been analyzed and the principal investigator is completing and will defend her dissertation (for Doctorate in Nursing Science) in April.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/084	Status: Completed
Title: A Study to Evaluate the Effects of Heparinized and Non-heparinized Flush Solutions on the Patency of Arterial Pressure Monitoring Lines		
Start Date: 10/04/91	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: LTC Connie K. Schultz, AN		
Associate Investigators: None		
Key Words: arterial pressure lines, patency, heparin, non-heparin solutions		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 been completed. This was a multicenter protocol and the data has been sent to the American Association for Critical Care Nurses for analysis.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/075

Status: Completed

Title: The Effects of Prolonged Parental-Child Separation on School-Aged Children Due to Military Deployment

Start Date: 07/12/91

Est. Completion Date: Apr 92

Department: Nursing

Facility: MAMC

Principal Investigator: 1LT Pamela S. Smith, AN

Associate Investigators:
MAJ Mary Sue Reagan, AN

MAJ Steven C. Parkison, MS

Key Words: parental,child separation,military deployment,children:school aged

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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: During the Persian Gulf crisis 532,000 troops served in Southwest Asia. Of this number 53% were married. There were 16,337 single parents and 1,231 couples with children serving in Southwest Asia. The sample for this study consisted of 57 families with an active duty member assigned to Madigan and deployed to Southwest Asia with children ages 6-14 years. The children were without developmental delays or a previous history of psychiatric care. There were 20 families with the mother absent, 20 families with father absent, and 17 families with no parent absent from the home. This study indicated that children separated from a parent do have more behavior problems than children who are not separated from a parent. When compared to children with no parent absent from the home and children with the father absent, children separated from their mothers tend to be more anxious/depressed and have more attention behavior problems. Children separated from their fathers tend to have more aggressive problems and delinquent behavior when compared to the non absent group and mother absent group. Further studies are needed to evaluate behavioral changes in children when separated from the mother versus separation from the father.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/028	Status: On-going
Title: The Effect of Two Levels of Hyperoxygenation Given via a Manual Resuscitation Bag and Ventilator During Endotracheal Suctioning of Premature Infants		
Start Date: 05/19/89	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: LTC Barbara S. Turner, AN		
Associate Investigators: None		
Key Words: endotracheal suctioning, infant, resuscitation bag		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: 06/14/91

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 (FIO₂ 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, PO₂/FIO₂ 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 FIO₂ by MRB 20% increase over baseline FIO₂ by MRB 10% increase over baseline FIO₂ by ventilator and 20% increase over baseline FIO₂ by MRB.

Progress: An additional 29 infants were entered in the protocol in FY 92 for a total of 52 infants who have completed the protocol. The anticipated final sample size is 60 infants. The data analyzed to date demonstrate no clinically significant difference in selected physiologic variables attributed to using either the manual resuscitation bag or the ventilator.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/086		Status: On-going
Title: Physiologic Responses to Exogenous Surfactant				
Start Date: 09/04/92			Est. Completion Date: Jul 95	
Department: Nursing			Facility: MAMC	
Principal Investigator: LTC Barbara S. Turner, AN				
Associate Investigators:			MAJ Joanna C. Beachy, MC	
Key Words: surfactant				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		//

Study Objective: To extend prior research on exogenous surfactant administration in premature infants by systematically examining two types of exogenous surfactant, two methods of administration, and the resulting interventions in response to improved pulmonary compliance.

Technical Approach: The sample will consist of 24 intubated and mechanically ventilated premature infants with respiratory distress. The sample will be stratified by two gestational age ranges (<27 wks and 28-30 wks) and then randomized to treatment groups with equal representation in each stratification: Group 1: N=6 for each age range (total 12) Exosurf administered by sideport adapter Group 2: N=3 for each age range (total 6) - Surfactant administered by feeding tube through endotracheal tube Group 3: N=3 for each age group (total 6) - Surfactant administered through a double lumen endotracheal tube. Data from selected physiologic variables will be recorded continuously and simultaneously for a two hour and 25 minute period, beginning prior to administration of exogenous surfactant through two hours post surfactant administration. Ventilatory interventions will be annotated on the wave forms from the recorder. Data will be analyzed for trends based on type of exogenous surfactant, method of administration, and type of interventions instituted. Results from this pilot study will provide data on infants' response to two types of surfactant and methods of administration, as well as intervention patterns. The data will be used to support a larger multisite study examining physiologic responses following surfactant administration.

Progress: Five infants have completed the protocol. No technical difficulties have been encountered that required protocol modification.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/072	Status: On-going
Title: Piglet Tracheal Epithelial Injury and Regeneration Following Endotracheal Suctioning		
Start Date: 05/18/90	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: LTC Barbara S. Turner, AN		
Associate Investigators: LTC Tom E. Wiswell, MC MAJ James G. MacMillan, VC		
Key Words: epithelium, regeneration, endotracheal suctioning, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 I (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 I) or ZEEP (Group II) once every 60 minutes for the six hours of mechanical ventilation. The piglets in Groups I and II 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 protocol was not funded by the NIH. The PI has now submitted the protocol for funding by the special congressional research funds mandated in FY 92.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 91/034		Status: On-going
Title: Impact of Continuous vs Intermittent Negative Pressure on Tracheal Trauma and Regeneration				
Start Date: 03/01/91			Est. Completion Date:	
Department: Nursing			Facility: MAMC	
Principal Investigator: LTC Barbara S. Turner, AN				
Associate Investigators: LTC Tom E. Wiswell, MC			MAJ James G. MacMillan, VC	
Key Words: tracheal trauma, suctioning,Animal Study				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$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).

Technical Approach: The research questions to be answered are (1) what is the immediate (acute) effect on the tracheal epithelium of ETS using INP versus CNP (2) what is the response of the tracheal epithelium (chronic effect) of ETS using INP versus CNP over the 21 days immediately following ETS and (3) are there differences acutely and chronically in the percentage of tracheal epithelial circumferences that are covered by basal cells, ciliated epithelium and goblet cells based on exposure to suctioning using INP versus CNP. The sample will consist of 98 Chester White swine who will be randomly divided into 4 groups: Control (n=14) sham (n=14) Group I - intermittent negative pressure (n=35) and Group II - continuous negative pressure (n=35). Groups I and II will be intubated, mechanically ventilated, and receive 6 controlled ETS procedures (1 /hour) during 6 hours of ventilation. The swine will either be euthanized immediately after the sixth ETS procedure or recovered and euthanized at 3, 7, 10, 14, and 21 days post ETS. Swine in the control and sham groups will be euthanized at the same time points. All tracheas will be harvested and sectioned into 13 sections beginning at the second tracheal ring and extending to the 9th tracheal ring. Each section will be graded using video image analysis for determination of the percentage of circumference denuded, the numbers of cells, types of cells, and ratio of cell types remaining. Injury scores for each swine in each group at each time period will be determined.

Progress: Upon continuing review in July 1992, this protocol was retitled because of the confusion with number #90/72. The original title was "Tracheal Trauma and Regeneration Following Suctioning." The protocol has been approved by the NCI, but the funds have not been received therefore, it has not been implemented.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/036	Status: Completed
Title: Transition of the Preterm Infant to an Open Crib		
Start Date: 04/03/92	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: LTC Barbara S. Turner, AN		
Associate Investigators: Lori A. Loan, AN		Sue Wilson, RN
Key Words: preterm infant, crib		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine the outcome on the very low birth weight infant's weight and temperature when weaned to an open crib using a standardized procedure based on room temperature, incubator temperature, and infant temperature.

Technical Approach: In Part 1, the infant will be dressed in a cap, t-shirt, and diaper, and wrapped in two blankets. The incubator temperature control will be decreased by 1.5 degrees C per day until 28 degrees C is reached and the infant has a stable temperature and weight gain. In Part 2, the infant will be placed in an open crib dressed in a cap, t-shirt, and diaper and wrapped in two blankets. Temperature will be taken every 15 minutes for one hour or until four stable temperature readings are obtained. A continuously monitoring abdominal thermistor probe will be taped to the infants skin and temperature will be recorded every four hours as well as daily weight for the first three days in the open crib. Infant temperatures are to be in the 36.0 to 37.0 degree C range. If it falls below 36.0 for over one hour, the infant will be removed from the study.

Progress: Thirty five infants completed this protocol without adverse effects. Data collection sheets were forwarded to a central data site of the Organization for Obstetric, Gynecologic, and Neonatal Nurses to be compiled with the data from nine other collection sites and analyzed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/078

Status: Comp

Title: Nurses vs. Patients: Views on Nurses Smoking and Its Influence on Patient Health Practice

Start Date: 06/05/92

Est. Completion Date: Sep 92

Department: Nursing

Facility: MAMC

Principal Investigator: 1LT Edward E. Yackel, AN

Associate Investigators:

Lori A. Loan, AN

Key Words: smoking, nurses, patient health practices

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review
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Study Objective: To compare and contrast the attitudes of MAMC nurses and patients relation to views on nurses who smoke, patient counseling on smoking, and the nurse as a role model.

Technical Approach: Two wards will be chosen at random to participate in this study. Forty nurses and twenty patients will be surveyed. Nurse participants will be a convenience sample of every third nurse on the unit roster. Patients will be adult inpatients with an acuity classification of III or less. Nurses will complete a questionnaire that obtains age, educational level, employment status, smoking status, and their opinion of how patients feel about different areas of nurse smoking. The patients will complete a questionnaire obtaining sex, smoking status, educational level, and how they feel about nurses who smoke. Data will be analyzed using chi square analysis to establish statistical significance of educational level, smoking status, sex, and employment status in relation to nurses as role models and counselors on the subject of smoking.

Progress: Initial review of the data suggests the following trends: (1) patient population was predominantly male while nurse population was female (2) while patients felt that nurses who smoked set a bad example, it was their personal choice patients were not to tell which nurses smoked by smell on clothes, etc. about 20% of the patients stated they would like to be counseled by a former smoker nurses felt that patients would not care about a nurse's smoking practice. A manuscript is being written.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/047	Status: Completed
Title: The Relationship of the Sense of Coherence and Hardiness to the Nutritional Status of Anorectic Head and Neck Cancer Patients Currently Undergoing Radiation Therapy		
Start Date: 02/01/91	Est. Completion Date:	
Department: Nursing	Facility: MAMC	
Principal Investigator: CPT Stacey B. Young, AN		
Associate Investigators:		LTC Loretta Forlaw, AN
Key Words: cancer:head & neck,radiation,nutritional status		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: This study was done in conjunction with LTC Loretta Forlaw, AN, who is an active duty doctoral candidate. Only one patient was entered at MAMC. The data regarding this patient was forwarded to LTC Forlaw to be included with data from other institutions in a dissertation which LTC Forlaw is writing for her doctoral degree.

DETAIL SHEETS FOR PROTOCOLS

NUTRITION CARE DIVISION

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/041	Status: Completed
Title: Dental Liquid Ration Evaluation		
Start Date: 04/05/91	Est. Completion Date:	
Department: Nutrition Care	Facility: MAMC	
Principal Investigator: CPT Pamela Charney, SP		
Associate Investigators: None		
Key Words: liquid rations, evaluation, dental		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: The data were sent to US Army Natick Research Center investigators for analysis. The data analysis has been completed and a manuscript has been submitted to the American Dietary Association. The Army has ordered a supply of the ration to use at several hospitals.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF OB/GYN

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/010	Status: On-going
Title: Predictors of Response to Ovulation Induction with Clomiphene Citrate in the Overweight Patient		
Start Date: 02/07/92	Est. Completion Date:	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ Alicia Y. Armstrong		
Associate Investigators: CPT Carl A. Gibson, MC		CPT Nathan J. Hoeldtke, MC
Key Words: ovulation induction, clomiphene citrate, overweight		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$12875.00	//

Study Objective: To determine if aspects of the patient history and endocrine profile (testosterone, androstenedione, DHEAS insulin, and glucose) are predictive of the response to ovulation induction with clomiphene citrate (CC) in the obese patient.

Technical Approach: Patients (n=50), with ovulatory dysfunction documented by basal body temperatures and history, who are > 30% over ideal body weight and not >100% over ideal body weight will be enrolled at the time of the initial infertility visit. At the initial enrollment, patients will complete a detailed menstrual, pregnancy, and weight history, and waist to hip ratio will be done. Weights will be done at initiation and at the third, sixth, and ninth cycles. At the time of enrollment, the patients will have the following serum studies: DHEAS, estrone, androstenedione, testosterone, SHBG, insulin, and 2 hour glucose tolerance test. These studies (with the exception of the 2 hour GTT) will be repeated at the third, sixth, and ninth cycles. A mid-luteal progesterone will also be drawn at the third, sixth, and ninth cycles. Additional documentation of ovulation will be made with urinary luteinizing hormone levels, using ovulation predictor kits and basal body temperatures. Chi square, Student's t test, and regression analysis will be used where appropriate for data analysis.

Progress: Six patients have been enrolled. Five of the patients have had initial laboratory studies. Three of the patients were found to have elevated insulin levels, although none of them have had elevated glucose levels. One patient was found to have markedly elevated androgens, but her evaluation has shown no evidence of an androgen secreting tumor. There has been one pregnancy. There have been no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/093

Status: On-going

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

Start Date: 08/07/92

Est. Completion Date:

Department: OB/GYN

Facility: MAMC

Principal Investigator: MAJ Alicia Y. Armstrong

Associate Investigators:

CPT M. Ahmed, MC

CPT Wilma I. Larsen, MC

CPT H. Harrison, MC

LTC (P) Robert E. Jones, MS

CPT J. Olson, MC

CPT Colleen C. Foos, MC

Key Words: spermatozoa, cryopreservation, hyperactivation

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

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

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

Progress : Semen parameters have been established and these parameters have been entered into the Hamilton Thorne analyzer. Video tapes of the sperm trajectories have been produced and reviewed by three of the investigators. The media and laboratory materials have been ordered.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/022 **Status:** Terminated

Title: Preterm Delivery Prevention

Start Date: 07/28/89

Est. Completion Date: Jun 90

Department: OB/GYN

Facility: MAMC

Principal Investigator: MAJ Philip M. Bayliss, MC

Associate Investigators:

MAJ Glenn D. Jordan, MC

MAJ Douglas A. Milligan, MC

COL Patrick Duff, MC

MAJ W. Kim Brady, MC

MAJ Jerome N. Kopelman, MC

Key Words: preterm delivery prevention

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$5960.00

Periodic Review:

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: Approximately 200 subjects were needed to conduct this study. After two years of enrollment, only 20 subjects had been enrolled. Therefore, it was decided that this protocol would not be feasible due to the length of time needed to accrue enough subjects.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/021		Status: On-going
Title: Amniotic Fluid Index: A Comparison Between Real Time Ultrasound and Color Flow Doppler Ultrasound in its Determination				
Start Date: 04/03/92		Est. Completion Date:		
Department: OB/GYN		Facility: MAMC		
Principal Investigator: CPT Timothy J. Boley, MC				
Associate Investigators:		MAJ Philip M. Bayliss, MC		
MAJ Jerome N. Kopelman, MC		COL John A. Read II, MC		
Key Words: amniotic fluid index, ultrasound, doppler ultrasound				
Accumulative		Est. Accumulative		Periodic Review:
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	//

Study Objective: To determine if the use of color flow doppler ultrasound alters the quantitation of the amniotic fluid index (AFI) when compared to the standard technique of real time ultrasound.

Technical Approach: Perinatal morbidity and mortality are significantly increased in the presence of increased or decreased amniotic fluid. Currently, real time ultrasound is used to determine the AFI on pregnant patients. However, in some cases, falsely elevated AFI levels may be obtained because it is not possible to identify a loop of umbilical cord using real time ultrasound and it is counted as part of the amniotic fluid. Color flow doppler capabilities are now available which allow for simple identification of the umbilical cord. This procedure has not been compared to real time ultrasound in the determination of AFI. Patients (n=100) undergoing antepartum testing for indicated obstetrical reasons will have an AFI determination made using real time ultrasound. A second AFI determination will then be performed using color flow doppler. These AFI measurements will be completed by different physicians without knowledge of the other's measurement. Patients found to have oligohydramnios (an AFI value of 5 cm of less) will be managed by current departmental standards. A paired t test will be used to analyze the data.

Progress: Nine patients have been studied. Dr. Boley replaced Dr. Philip Bayliss as principal investigator in July 1992, due to the reassignment of Dr. Bayliss.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/071	Status: On-going
Title: The Establishment of the Doubly Perfused, Placental Cotyledon Model for the In Vitro Investigation of the Umbilical-Placental Circulation		
Start Date: 06/05/92	Est. Completion Date: Aug 92	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: CPT Timothy J. Boley, MC		
Associate Investigators:		
LTC Arthur S. Maslow, MC	MAJ Philip M. Bayliss, MC	
COL John A. Read II, MC	MAJ Jerome N. Kopelman, MC	
Key Words: umbilical circulation, placental circulation		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To establish an in vitro model using the placental cotyledon perfusion system. This model would simulate as closely as possible the in vivo placenta to study the umbilical-placental circulation.

Technical Approach: A cotyledon chamber will be constructed from Plexiglas. This chamber will consist of a cylinder in which the selected cotyledon will be placed on a supporting mesh screen. The placenta will be examined for tears or gross abnormalities. Suitable chorionic vessels will be identified and followed until they drive down into the placenta. An artery and its adjacent vein will be cannulated with 18 gauge intravenous catheters. Perfusion will be begun into the fetal artery at a rate of 3-8 ml/minutes. Two 21 gauge butterfly needles will be placed into the intervillous space near the site where the chorionic artery and vein enter the cotyledon. Perfusion of the intervillous space will be begun at a rate of 6-10 ml/minute. The perfusate consists of a balanced salt solution to which albumin and heparin have been added. The perfusate will be kept at 38 degrees Celsius and will be bubbled with a gas mixture of 95% oxygen and 5% carbon dioxide throughout the perfusion period. The pH of the solution will be continually monitored and adjusted as needed to keep the pH in the 7.35-7.45 range. Pressure will also be constantly monitored within the system. A second cotyledon will then be cannulated and perfused as above. These two cotyledons will then be separated from the rest of the placenta and placed into a temperature-controlled chamber. Samples will be collected from the system every 30 minutes before and after perfusing the cotyledon. The samples will be assayed for oxygen and glucose consumption, prostacyclin, endothelin, and nitrite levels. Results will be compared between cotyledon pairs and placentas. Total perfusion time is 4-6 hours. Approximately 10 placentas from uncomplicated pregnancies will be perfused to establish baseline levels.

Progress: The placental perfusion lab has been established and sufficient equipment and supplies have been accumulated to carry out basic perfusion experiments and to perform necessary assays. Utilizing methods described in the literature with some adaptations, the investigators have developed a model. Initial perfusion experiments have dealt with developing the techniques and skills of the investigators who are now in the process of collecting samples of effluent from fetal and intervillous perfusion circuits. The perfusion on two normal placentas has been completed and samples have been obtained. The principal investigator was changed from Dr. Bayliss to Dr. Boley in July 1992 due to the reassignment of Dr. Bayliss.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/023

Status: On-going

Title: A Comparison of Amniotic Fluid Collected by Amniocentesis versus Amniotic Fluid Collected Via an Intrauterine Pressure Catheter in the Diagnosis of Chorioamnionitis in Laboring Patients at Term

Start Date: 04/03/92

Est. Completion Date:

Department: OB/GYN

Facility: MAMC

Principal Investigator: CPT Timothy J. Boley, MC

Associate Investigators:
MAJ Philip M. Bayliss, MC

MAJ Jerome N. Kopelman, MC
COL John A. Read II, MC

Key Words:

Accumulative
MEDCASE Cost:

\$0.00

Est. Accumulative
OMA Cost:

\$0.00

Periodic Review:
//

Study Objective: To compare the validity of using amniotic fluid samples collected using an intrauterine pressure catheter versus samples collected by amniocentesis in establishing a diagnosis of chorioamnionitis and to determine the optimum tests to perform on amniotic fluid to establish a diagnosis of chorioamnionitis.

Technical Approach: The study population (n=60) will be divided into Group A, which will consist of term pregnant patients in labor with clinical evidence of chorioamnionitis, and Group B, which will consist of term pregnant patients in labor without evidence of chorioamnionitis. Group A will have a sample collected by amniocentesis and a second sample via an intrauterine pressure catheter. Group A samples will be sent to the lab for gram stain, aerobic and anaerobic cultures, glucose determination, and leukocyte esterase activity. A maternal serum glucose level and CBC will also be done at the time the amniotic fluid sample is drawn. Following delivery, the placenta will be evaluated for evidence of chorioamnionitis. The neonate will be assessed for the presence or absence of neonatal sepsis, and the presence of maternal postpartum endomyometritis will be documented. Group B will have a sample of amniotic fluid collected through an intrauterine pressure catheter which will have the same evaluations as the samples in Group A. A maternal peripheral blood sample will be collected and sent for glucose determination. Results of the data collection for each group will be compared. Differences in results will be evaluated by means of the chi square analysis, paired and unpaired t tests, and logistic regression, as needed.

Progress: Two patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/022	Status: On-going
Title: Continuous Infusion Epidural Analgesia: Its Effects on the Doppler Velocimetry of the Umbilical Arteries of Normotensive and Preeclamptic Patients in Labor		
Start Date: 04/03/92	Est. Completion Date:	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: CPT Timothy J. Boley, MC		
Associate Investigators:		
MAJ Jerome N. Kopelman, MC		LTC Joseph J. Mancuso Jr., MC
MAJ Philip M. Bayliss, MC		COL John A. Read II, MC
Key Words: umbilical arteries velocimetry, epidural analgesia		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	//

Study Objective: To evaluate the effects of continuous infusion epidural analgesia on umbilical artery blood flow in term, laboring pregnancies, including both normotensive and preeclamptic patients.

Technical Approach: Ten normotensive and 10 preeclamptic patients will be studied. The study will involve the measurement of the systolic/diastolic (S/D) ratio of the umbilical arteries in patients electing to have epidural analgesia in labor. All patients will be at term and in the active phase of labor. Continuous infusion epidural technique will be standardized for all patients. The S/D ratio will be determined, using a continuous wave doppler analyzer, in each patient at four intervals: prehydration, posthydration, at the onset of epidural analgesia, and approximately one hour after the epidural is functional. Pain relief will be documented through skin testing with a needle to record the level of the dermatome achieved and through the patient's own subjective grading, using a standard Glasgow Pain Ruler. Analysis of data will be by paired t test.

Progress: No patients have been entered to date due to other priorities. Dr. Bayliss original principal investigator changed to Dr. Boley July 1992 due to reassignment of Dr. Bayliss.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/090		Status: On-going
Title: The Effects of Estradiol and Progesterone on Vasoactive Substances in the Dually Perfused Cotyledon Model				
Start Date: 08/03/92		Est. Completion Date: Dec 92		
Department: OB/GYN		Facility: MAMC		
Principal Investigator: CPT Timothy J. Boley, MC				
Associate Investigators:		MAJ Glenn Markenson, MC		
LTC Arthur S. Maslow, MC		MAJ Jerome N. Kopelman, MC		
COL John A. Read II, MC		MAJ Philip M. Bayliss, MC		
Key Words: cotyledon, estradiol, progesterone				
Accumulative		Est. Accumulative		Periodic Review:
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	//

Study Objective: To document the baseline rate of release/production of estrogens and progesterone in the isolated cotyledon system under varying experimental conditions to delineate the effects of these hormones on the production of eicosanoids and endothelium-derived vasoactive substances and to compare selected other parameters of "viability" of the perfusion system to the steroid production.

Technical Approach: The procedure for initiating, maintaining, and evaluating the integrity/viability of the cotyledon model has been described in the previous protocol "The Establishment of the Doubly Perfused, Placental Cotyledon Model for the In Vitro Investigation of the Umbilical-Placental Circulation." Each substrate listed below will be used in 5 cotyledon perfusions: (1) 17-b-estradiol (E2), 20 ng/ml, and (2) E2, 20 ng/ml plus progesterone (P), 200 ng/ml. Sampling of the fetal and maternal outflow perfusates will be drawn for assays of estradiol, progesterone, and the vasoactive substances TBX2, 6-keto-PGF1, and endothelin 1. Each of these assays will be accomplished with commercially available enzyme immunoassays. Nitric oxide will be measured indirectly from nitrite levels measured in the outflow perfusates. Sampling intervals will be every 15 minutes and the duration of perfusion from the addition of the substrates will be four hours. Each placental cotyledon/lobe will be run as a pair with another cotyledon from the same placenta. This second perfused cotyledon will serve as a control, receiving only the baseline balanced salt solution as a perfusate. Statistical analysis will be performed using the t-test.

Progress: This protocol has not been implemented. It will be started upon the completion of Protocol #92/071 Dr. Timothy Boley, principal investigator.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/064 **Status:** Completed

Title: Role of Color Flow Doppler in Evaluation of Patients with Persistent Trophoblastic Disease

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

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

Principal Investigator: CPT Dwight L. Dyksterhouse, MC

Associate Investigators: LTC Gordon O. Downey, MC
MAJ Philip M. Bayliss, MC MAJ Jerome N. Kopelman, MC

Key Words: cancer, gestational trophoblastic heoplasia, clor flow Doppler

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

Study Objective: To examine the role of endovaginal color flow doppler (CFD) ultrasound as a possible safe and accurate clinical adjuvant in following the response to chemotherapy of patients with persistent trophoblastic disease.

Technical Approach: Gestational trophoblastic disease affects 20% of women after molar pregnancies. These patients require chemotherapy for treatment, the efficacy of which has been followed by observing decreasing BHCG levels. In this study, patients with this disease will be followed for the course of their chemotherapy with serial vaginal color flow doppler ultrasound to help gauge treatment efficacy. This is a rare disease, so less than 10 patients will probably be studied. These ultrasounds will be done weekly, coinciding with the time of drawing the patient's BHCG levels to determine treatment success. No statistical interpretation will be required, rather a direct visual inspection of abnormal areas of color flow will be obtained with ultrasound pictures and compared with the laboratory studies concurrently done. The results will be reviewed for possible presentation and publication.

Progress: Two patients with gestational trophoblastic neoplasia, one with metastatic disease, were studied. Color flow identified areas of intrauterine disease in both patients, which decreased during treatment in close conjunction with the declining BHCG values. The investigators conclude that color flow doppler may serve as a useful clinical parameter in following tumor regression in patients with gestational trophoblastic disease, as well as to assist in the initiation or alteration of different treatment regimens.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/041

Status: On-going

Title: Correlation of Vaginal Ultrasonographic Findings with Pathology in GYN Surgical Patients

Start Date: 09/04/92

Est. Completion Date: Jul 93

Department: OB/GYN

Facility: MAMC

Principal Investigator: CPT Colleen C. Foos, MC

Associate Investigators:

LTC Arthur S. Maslow, MC

CPT Karen M. Nelson, MC

LTC David J. Magelssen, MC

MAJ Jerome N. Kopelman, MC

Key Words: vaginal ultrasonography, histologic diagnosis, GYN surgery

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To correlate the preoperative ultrasonographically determined values (ovarian volume endometrial stripe thickness ovarian morphology, outline, internal structure characteristics pulsatility indices of ovarian arteries and color flow doppler characteristics of ovaries and uterus) with operative findings (ovarian volume, uterine volume and weight, endometrial gross appearance, ovarian and uterine morphology) and postoperative histologic diagnosis in women undergoing gynecology surgery.

Technical Approach: Approximately 200 adult patients undergoing gynecological surgical procedures which involve removal or visualization of the ovaries and/or uterus will undergo a vaginal ultrasound examination in addition to the routine preoperative evaluation. Ovarian volumes will be assessed using ovarian dimensions and computing the volume with the formula of an ellipsoid. Doppler flow and color flow doppler will be used respectively to determine ovarian artery pulsatility indices and blood flow characteristics. Maximum endometrial stripe thickness will be measured and ovarian contour, morphology, and echogenicity will be described. At the time of surgery, intraoperative measurements of ovarian dimensions will be measured in vivo. If removed, the uterus will be bivalved to examine the endometrium. For laparoscopic gynecologic surgeries, three ovarian dimensions will be measured on each ovary using a laparoscopic measuring probe. The uterus will be similarly measured. If the uterus is not to be removed, endometrial biopsy will be performed intraoperatively to sample the endometrium. Postoperatively, the surgical specimens will be evaluated in the routine manner. Again ovarian volume will be determined using the above formula. Statistical evaluation correlating preoperative ultrasonography findings with operative and pathologic findings will be performed.

Progress: Seven subjects have been studied. It is too early to make any conclusions.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/060	Status: On-going
Title: A Randomized Prospective Evaluation of Bladder Flap Closure at Time of Cesarean Section		
Start Date: 05/01/92	Est. Completion Date: Apr 93	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ Jerome N. Kopelman, MC		
Associate Investigators: COL John A. Read II, MC LTC Arthur S. Maslow, MC		
Key Words: Cesarean, bladder		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective: To determine if the type of closure of the vesicouterine peritoneum affects the postoperative course in low transverse Cesarean section patients.

Technical Approach: Approximately 365 patients having a low transverse Cesarean section will be studied. They will be randomized to either closure or nonclosure of the vesicouterine peritoneal at the time of Cesarean section repair. Patients will be evaluated by ultrasound on day of discharge for fluid collection at the lower uterine segment incision site. Parameters of postoperative morbidity will be compared between the two groups.

Progress: Thirty-seven subjects have been studied.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/034	Status: Terminated
Title: Cordocentesis in an Animal Model		
Start Date: 03/16/90	Est. Completion Date: Dec 90	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ Jerome N. F n, MC		
Associate Investigators: Douglas A. Milligan, MC COL John A. Read II, MC		
Key Words: cordocentesis, Animal Study		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: 08/07/92

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 radiological 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: This protocol has been terminated. It was never implemented due to staff shortages.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/101	Status: On-going
Title: Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy		
Start Date: //	Est. Completion Date: Mar 94	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ Jerome N. Kopelman, MC		
Associate Investigators: LTC Glenn C. Tripp, MC Millie Herd, AN		
Key Words: herpes simplex virus, pregnancy		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective : To evaluate infants of sero-converters by means of Denver Developmental Tests and type specific HSV antibodies by Western blot in order to answer the following questions: does maternal HSV-2 seroconversion during pregnancy without evidence of asymptomatic shedding of the virus from the genital tract at the onset of labor or evidence of acute neonatal HSV infection result in significant neurodevelopmental disability in the offspring; and can asymptomatic HSV seroconversion in the newborn occur as a result of in utero infection or undetected perinatal transmission without evidence of acute neonatal infection.

Technical Approach : About 3% of women who are HSV seronegative at the first prenatal visit are HSV seropositive at the time of delivery. If the maternal HSV cultures were negative on admission to the labor suite and the neonatal conjunctival and nasopharyngeal cultures were negative on day 2 of life, the newborns are discharged from the hospital at 1-5 days postpartum. The only long term follow-up performed has been routine pediatric care. However, any long term neurodevelopmental consequences to the uninfected offspring of women experiencing an asymptomatic first episode of genital HSV during pregnancy are unknown. This study will be done in conjunction with Children's Hospital, Seattle, WA, and the University of Washington. Approximately 20 children will be studied at Madigan. At six months of age, the child will be administered the modified Denver Developmental Test, and a blood sample will be drawn to measure type-specific HSV antibodies by Western blot. By six months of age, passively acquired maternal antibody should be completely metabolized. HSV antibody present at this time should represent an asymptomatic congenital or neonatal infection and seroconversion. Information regarding the mother's demographic profile and pregnancy history, her serologic and virologic profiles, and the infant data (e.g., birth weight, gestational age) will also be obtained.

Progress : Twenty-four infants have been identified and consent forms signed. Testing will start as soon as the children are six months of age.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/106	Status: Completed
Title: Evaluation of Efficacy of Twelve Hour Urine Collections in the Diagnosis of Pre-eclampsia		
Start Date: 03/01/91	Est. Completion Date: Dec 90	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: CPT Wilma I. Larsen, MC		
Associate Investigators: MAJ Jerome N. Kopelman, MC CPT Montgomery E. Thorne, Jr., MC		
Key Words: pre-eclampsia, 12 hour urines		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: Each patient collected two consecutive 12 hour urines which were analyzed and then combined to form a 24 hour specimen. The results were compared using a paired t analysis and no significant difference was found. Additionally, using 150 mg of protein in 12 hours as an equivalent of 300 mg in 24 hours, we had 100% sensitivity and 86% specificity in diagnosing proteinuria consistent with preeclampsia. Twelve hour urine collections appear to accurately reflect the amount of protein in a 24 hour specimen and can be used in evaluating patients for possible preeclampsia.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/024 **Status:** Terminated

Title: The Evaluation of an Endocervical Brush Device in a Population of Pregnant Patients

Start Date: 03/01/91

Est. Completion Date:

Department: OB/GYN

Facility: MAMC

Principal Investigator: CPT Karen M. Nelson, MC

Associate Investigators:
MAJ W. Kim Brady, MC

MAJ Jerome N. Kopelman, MC
CPT Stefanie S. Christian, MC

Key Words: endocervical brush, pregnancy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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: Data were collected on approximately 1000 subjects. However, in the transition from the old hospital building to the new building, the data records were lost as well as the listing of patients enrolled. Therefore, the new principal investigator has no way to access the data. Therefore, the protocol has been terminated.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/017		Status: On-going
Title: Surgical Management of the Bowel and Urinary Tract in Gynecologic Surgery (Swine Model)				
Start Date: 01/20/89			Est. Completion Date: Indef.	
Department: OB/GYN			Facility: MAMC	
Principal Investigator: LTC Mark E. Potter, MC				
Associate Investigators: COL Richard P. Belts, MC			LTC David J. Magelssen, MC MAJ John W. Cassels JR, MC	
Key Words: gynecologic surgery,training protocol,swine,bowel,urinary tract,Animal Study				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	Periodic Review:
			\$0.00	08/07/92

Study Objective: To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing and stapling techniques and to familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy, and vascular injury repair.

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

Progress: One session using one pig was held in FY 92. The principal investigator was changed from Dr. Gordon Downey to Dr. Mark Potter in July 1992 due to the retirement of Dr. Downey.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/091	Status: Completed
Title: Quantitative Evaluation of Blood Loss in Parturients With and Without Clinical Chorioamnionitis		
Start Date: 08/03/92	Est. Completion Date: Aug 92	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL John A. Read II, MC		
Associate Investigators: MAJ Jerome N. Kopelman, MC Cheryl A. Yanko		
Key Words: chorioamnionitis, blood loss		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective: To quantitatively investigate the relationship between clinical chorioamnionitis and blood loss.

Technical Approach: This will be a retrospective chart review of all obstetric patients presenting to the Labor and Delivery Unit at MAMC during the period 1 Jan 87 to 31 Dec 91, diagnosed with clinical chorioamnionitis. An equivalent number of control charts will be studied for each year in the study. The groups will be evaluated for equivalence and/or statistical significance in terms of maternal age, sponsor rank, race, gravity/parity, smoking history, overall length of labor, time between phases of labor, drugs received during labor, type of anesthesia, length of time to membrane rupture, and way membranes ruptured. Discrete data will be tested for significance with chi square test or Fisher's exact test. Continuous data will be tested for significance with a two-tailed t-test. Logistic regression analysis will be used to eliminate and/or account for confounding factors and areas of non-equivalence. For the purposes of this study, postpartum hemorrhage will be defined as a change between admission and one day postpartum hematocrit levels > 5% for vaginal delivery and >8% for C-section. This dichotomized blood loss data will be analyzed initially via chi-square testing allowing for establishment of risk ratios. Other data sheet entries (infant data, maternal blood group, amniotic fluid analysis, PML episodes, etc.) are either confirmatory for chorioamnionitis or for informational purposes.

Progress: 513 charts for study patients and 513 charts for controls were studied. Postpartum hemorrhage occurred in 34.9% of study patients and in 13.3% of controls. Case and study groups were compared for other known factors associated with postpartum hemorrhage and no significant differences existed between the groups. Risk analysis showed that parturients with chorioamnionitis who delivered vaginally were 1.82 times more likely to hemorrhage, while patients with chorioamnionitis who delivered by cesarean were 6.92 times more likely to hemorrhage than those without chorioamnionitis.

DETAIL SHEETS FOR PROTOCOLS

PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 80 Sep 92	Protocol No.: 92/027	Status: Completed
Title: Immunization Status Among Two Year Olds and the Role of Missed Opportunities		
Start Date: 01/03/92	Est. Completion Date:	
Department: PM	Facility: MAMC	
Principal Investigator: MAJ Coleen P. Baird, MC		
Associate Investigators: MAJ Margot R. Krauss, MC		
Key Words: immunization status, two year olds, effect		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To elucidate the descriptive epidemiology of missed opportunities for immunization in children assigned to the MAMC catchment area and to determine the factors which may have contributed to or be associated with non vaccination. A missed opportunity (MO) is defined as "any clinic visit which coincided with the chronological age for immunization but at which no immunization occurred.

Technical Approach: The immunization record of children 0-2 years of age will be reviewed to ascertain if the primary series shots were given at the appropriate age. Basic demographic information will be collected from each record as well as the total number of visits and well baby visits the child made and whether the child has any chronic conditions. If shots were given later than indicated, the chart will be reviewed to see if any health care contacts occurred between shots which could be considered a missed opportunity. If a missed opportunity occurred, information on a number of variables will be collected to include whether the child has siblings, was seen at CONUS vs OCONUS, at a MEDDAC/MEDCEN vs outlying clinic, and specialist vs a GMO, by the primary care provider or on a consultation or in the ER, and whether on sick call walk in or by appointment, rank of sponsor, if there was a contraindication to immunization, and if the physician mentioned immunizations in his note. This data will be analyzed to provide the descriptive epidemiology of missed opportunities.

Progress: The survey determined that coverage with the primary series was 76.4% by age two and 72% of children underimmunized had at least one missed opportunity. Nearly half of all children had been late for at least one shot and half of these children had an intervening visit at which time they could have been immunized. Attendance at military daycare was protective for the outcome of full immunization and fully immunized children attended significantly more well baby visit. There was no increased likelihood of full immunization with increasing number of visits. Children seen primarily at Pediatrics were more likely to be underimmunized than those seen primarily at Family Practice. If all visits by underimmunized children were utilized to vaccinate, 93% of children could have been fully immunized by age two.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/028	Status: Completed
Title: Epidemiology of Unintentional Injuries in Infant and Toddler Age Children in a Military Population		
Start Date: 01/03/92	Est. Completion Date:	
Department: PM	Facility: MAMC	
Principal Investigator: MAJ Daniel R. Davidson, MC		
Associate Investigators: Frederik P. Rivara, M.P.H.		MAJ Margot R. Krauss, MC
Key Words: injuries, children, military		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine the number, type, and severity of injuries occurring in children ages 0-4 at Fort Lewis, WA to observe for associations between various demographic factors and injuries to determine the number of hospitalizations and deaths occurring in this population of children and to observe for injury prone children and high priority injuries at Fort Lewis.

Technical Approach: Approximately 800 children with a 2:1 female to male ratio will be randomly selected from the DEERS computer database for five different age groups: <1 and ages 1, 2, 3, and 4. Age, sex, number of injuries by type and etiology, number of clinic visits, need for hospitalization or specialty referrals, and deaths will be extracted from the charts (out-patient and in-patient) of these children. The sponsor's race, rank, marital status, and education will also be recorded. Each injury will be classified according to the diagnosis and etiology of the injury. Injury rates will be calculated for various types of injuries and then recalculated after adjusting for various demographic factors including age, sex, sponsor's rank, race, and marital status. Adjusting these rates is meant to determine if the injury rates are the same after removing the influence of these demographic factors. Injury rates will also be compared for various clinical factors including number of clinical visits, hospital admission, and specialty referrals. Statistical analysis of the data will be performed using chi-square and Mantel Haenszel methods.

Progress: Rates of unintentional injury in children 0-4 at Ft Lewis were higher than those for civilian populations. Black children have less injuries than children of other races. Two year olds have a higher risk of falls. Children of sponsors who have a high school education or less and enlisted personnel have a higher risk of injury than those whose sponsors are college educated or officers. A thesis is being written as one of the requirements for a Masters in Public Health at the University of Washington.

Detail Summary Sheet

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

Title: Early Identification of and Assistance to Pregnant Women Subjected to Domestic Violence

Start Date: 06/05/92

Est. Completion Date: Dec 92

Department: PM

Facility: MAMC

Principal Investigator: CPT Heidi A. Fuery, AN

Associate Investigators:

MAJ Philip M. Bayliss, MC

Key Words: domestic violence, pregnancy

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

Study Objective: To increase early detection of domestic violence and help direct victims to existing networks by increasing the physician's knowledge of assessing for such signs and symptoms in OB clients. This will be accomplished by teaching the physician the necessary interviewing skills to detect domestic violence and the local resources to assist its victims.

Technical Approach: OB physicians will be assigned to an intervention or a nonintervention group. Each group will be asked to fill out a questionnaire designed to determine their level of assessment in interviewing patients about domestic violence at the start of the study. The nonintervention group will be asked to continue using whatever assessments and interventions they currently use. The intervention group will receive a lecture addressing the signs and symptoms of domestic violence and interviewing techniques. They will be given a list of questions that should be asked of all OB patients and written material to make available to the patients. They will be allowed to intervene with whatever domestic violence interventions are appropriate. They will be asked to document if patients are attending any parenting or other classes. At the end of the study, both groups will be asked to complete a questionnaire to see if they subjectively feel an increase in comfort in asking questions to assess for domestic violence. Charts will be reviewed to ascertain the frequency of documented domestic violence in both populations, physician initiated assessments of the presence of domestic violence, and the use of primary prevention classes by any of the patrons and the FACMT-Spouse report will be used to ascertain if any of the enrolled OB patients were reported as victims of domestic violence. Comparison will be made between the two groups of the number of referrals, the referral rate, the documentation of potential or real domestic violence, interventions used, and physicians comfort level in assessing for and assisting victims of domestic violence during the OB visits. Each question on the pre and post test will be compared for each of the subjects to determine the impact of education and willingness to refer to appropriate interventions.

Progress: Approximately 30 subjects were entered. Charts are being reviewed to collect the remainder of the data.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/014

Status: On-going

Title: Assessment of Risk Factors for HIV Infection Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion - Incident Cases

Start Date: 02/16/90

Est. Completion Date: Jun 91

Department: PM

Facility: MAMC

Principal Investigator: MAJ Margot R. Krauss, MC

Associate Investigators:
COL Kevin M. McNeill, MC

MAJ John G. McNeil, MC

Key Words: HIV, risk factors, antibody seroconversion

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost:

\$0.00

01/03/92

Study Objective: To assess demographic and behavioral determinants associated with new HIV infections in order to generate information for implementing changes in education strategies currently in use for populations at risk for HIV infection, particularly in terms of potential new risk factors.

Technical Approach: This multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion of antibody to HIV using ELISA with duplicate Western Blot confirmation. There will be one control for each male subject and three controls for each female subject. Controls will be selected at random from the group of all uninfected active duty personnel at the same installation where cases seroconvert and will be matched for age (± 2 years), gender, ethnicity, rank, and length of service. Controls must have tested negative on or after the date their matched case seroconverted. Subjects and controls will be interviewed by trained interviewers from collaborating civilian health agencies who are blinded to the HIV antibody status of study participants. The interview will be conducted from and HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographics, medical history, risk factors of drug use, sexual history, and other risks. The investigators anticipate that 160 to 230 incident cases will be eligible for recruitment each year and feel that the majority of these cases can be recruited. In any multi-risk factor study such as this, the problem of chance statistical considerations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be performed. These methods will include calculation of measures of effect (e.g. matched odds ratios and confidence intervals) for various risk behaviors as well as matched multivariate analyses (e.g. behavioral hazards, conditional logistic regression).

Progress: This protocol has been reactivated because funding has been reinstated. One patient was entered at MAMC in FY 92 for a total of five patients and seven controls entered.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/033	Status: Completed
Title: STD Recidivism Study		
Start Date: 01/03/92	Est. Completion Date:	
Department: PM	Facility: MAMC	
Principal Investigator: Mark C. Ruberton, MD		
Associate Investigators: MAJ Margot R. Krauss, MC		
Key Words: sexual transmitted disease, recidivism		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To define the spectrum and prevalence of behavioral risk factors associated with recidivism of sexually transmitted diseases (STD) in a military setting.

Technical Approach: Each person seen at the Special Adult Clinic for a two month period will be asked to answer a questionnaire. Two hundred cases and 400 controls will be evaluated. Cases will be defined as two or more diagnoses of GC or NGU (>5 WBCs/HPF) or one diagnosis of GC or NGU (>5 WBCs/HPF) with a history of GC or NGU/Chlamydia by answers to questionnaire. As each survey is completed, a computer file is updated linking the patient's record number (internal to the computer) with the survey number in order to obtain the subjects past STD history and other demographic data. Key variables will be: >4 sexual partners in the last year ethnic/social mixing drug/ETOH use health seeking behavior knowledge of STDs/HIV condom use exposure to behavior change programs and various demographic variables (i.e., race, SES, etc.). Chi-square and Mantel-Haenszel tests for statistical difference of key variables between cases and controls will be performed. Logistic regression models may be applicable to analyze multiple predictor variables.

Progress: The greatest risk for study subjects were: being black, being single, multiple sex partners in the last 12 months, and not knowing the sexual partner as well as the controls did. Eighteen percent of patients diagnosed with STD were recidivist and 45% of those diagnosed with urethritis were recidivist.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/004	Status: Terminated
Title: Tympanometry Guidance for Treatment of Otitis Media		
Start Date: 12/07/90	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: LTC Thomas R. Babonis, MC		
Associate Investigators: COL Marvin S. Krober, MC		LTC Patrick C. Kelly, MC COL Michael R. Weir, MC
Key Words: otitis media, tympanometry		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 30 days later 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: The suggested sample size for this protocol was 450. After two years of enrollment only 15 patients have been enrolled. The protocol has been terminated due to insufficient numbers of subjects.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 91/093		Status: Completed	
Title: Health Habits and Lifestyles in Families of Children Less Than Two Years of Age					
Start Date: 10/04/91			Est. Completion Date:		
Department: Pediatrics			Facility: MAMC		
Principal Investigator: LTC Thomas R. Babonis, MC					
Associate Investigators:			Kathi Kemper, M.D.		
Key Words: health,lifestyle,children:<2 YO					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:		
\$0.00		\$0.00			//

Study Objective: To assess the feasibility of screening women for tobacco, alcohol, and illicit drug use in the setting of 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: 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 and effect modification between variables to arrive at adjusted odds ratios for risk of substance abuse.

Progress: This protocol has been completed. Five pediatric clinics in the Seattle/Tacoma area participated and 667 subjects were enrolled. Information obtained from this study was included in a paper that was published in July 1992: Screening for Maternal Depression in Pediatric Clinics, American Journal of Diseases of Children 146:876-878, 1992.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/049	Status: Completed
Title: Perceptions of Discipline and Child Physical Abuse Among Blacks and Whites		
Start Date: 04/03/92	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: LTC Thomas R. Babonis, MC		
Associate Investigators: Kathi Kemper, M.D. Jodie Buntain-Ricklefs, MSW		
Key Words: child abuse, discipline		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To attempt to answer the questions: (1) do perceptions about the appropriateness of types of discipline differ between Caucasians and African Americans (2) does the self-reported prevalence of specific forms of discipline and physical abuse vary between African Americans and Caucasians do income level and education account for any differences and does the acceptability of different types of discipline differ between those who consider themselves to have been abused as children and those who do not.

Technical Approach: Mothers at MAMC will be asked to participate in this study on parent discipline. They will complete a questionnaire designed to answer the research questions. Subjects will rate the frequency of their disciplinary experiences as a child. Then they will rank the acceptability of each item as a method of child discipline. The last section of the questionnaire asks about demographic information. There are also two questions pertaining to their assessment of whether or not they consider themselves to have been mistreated or physically abused as a child. Independent variables will be age, race, education, and income. Dependent variables will be in two categories: the subjects' ranking on each of the 21 items pertaining to whether or not the method of discipline happened to them or not as a child. Also, their ranking of each of the 21 items as to how acceptable they find each method of discipline to be. Descriptive statistics will be calculated. One way ANOVA for differences in disciplinary experiences and race will be calculated. Logistic regression will be used to predict abused/nonabused controlling for income, education, and race.

Progress: Approximately 180 subjects completed the questionnaire. A paper is being written by the investigators at the University of Washington.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/058		Status: On-going
Title: Neonatal Emergency Procedure Training in the Rabbit Model				
Start Date: 04/20/90		Est. Completion Date: Indef.		
Department: Pediatrics		Facility: MAMC		
Principal Investigator: MAJ Joanna C. Beachy, MC				
Associate Investigators:		LTC Matthew M. Rice, MC		
Key Words: training protocol,neonatal,rabbit,neonatal emergency procedure,Animal Study				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$0.00		\$864.00	08/07/92	

Study Objective: To train physicians who have not been previously trained in emergency management of neonates who will be called upon to perform this function in the Neonatal Intensive Care Unit.

Technical Approach: This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands on attempts by the interns and residents. The animal lab will allow the student to observe and practice to proficiency those lifesaving skills necessary in the management and stabilization of the neonatal patient. Telazol, 15 mg/kg, and xylazine, 5 mg/kg IM, will be administered to induce and maintain anesthesia. Additional anesthesia will be administered in increments as needed. The rabbits will be intubated with a 2-3 mm i.d. endotracheal tube and ventilation will be maintained as necessary with 100% oxygen. Tracheal intubation, venous cutdown, needle thoracocentesis, and chest tube insertion will be performed by each intern or resident in attendance.

Progress: The principal investigator was changed from Dr. Perkins to Dr. Beachy in Aug 92. One training session was held in FY 92 utilizing one rabbit. Upon continuing review, the type/amount of anesthesia and the method of euthanasia were changed in Aug 92 to bring the protocol into compliance with current regulations.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/055	Status: On-going
Title: Use of the Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Symptom Checklist as an Initial screening Interview for Identification of Obsessive Compulsive Disorder (OCD) and Related Behaviors in Childhood		
Start Date: 04/05/91	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: MAJ Robert B. Broadhurst, MC		
Associate Investigators: Jennifer S. Achilles LTC Patrick C. Kelly, MC		
Key Words: OCD, screening, Yale Brown Compulsive Scale, symptom checklist, children: 7 - 18 YO		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective: To determine if the short interview is a clinically useful format for identifying Obsessive Compulsive Disorder (OCD) in childhood and to further evaluate the diagnostic screening properties of the CY-BOCS as a semi-structured interview looking for OCD in childhood.

Technical Approach: Approximately 1000 subjects will be selected for interviewing. This will consist of 500 subjects 7 to 12 years old and 500 subjects 13 to 18 years old. Subjects will be randomly selected from appointment rosters. While the parent(s) and child are waiting in the waiting room, they will be asked about participating in this protocol. We will explain that this will involve a 10 minute interview of parent(s) and child in a private exam room. Using the chi-square test, comparisons will be made between the positive and negative short interview groups, between the positive and negative CY-BOCS interview groups, between the positive and negative physical exam finding groups, between the positive trichotillomania/eating behavior and negative groups. Concordance of all positive groups will be assessed. Demographic data in positive and negative groups will be compared. From analysis of the above groups, information on the selectivity of the short interview versus the CY-BOCS for OCD diagnosis at followup will be formulated. Minimal prevalence rates of OCD will be assessed for this clinic sample. All positive interview groups and physical exam findings will be compared with diagnoses and medical problems at followup evaluation. All diagnoses and medical problems will be determined at followup interview, as the gold standard for establishing any diagnosis or medical problem in this study. Data in all the negative groups will be assessed for frequency of "1" level symptoms, trichotillomania symptoms, and eating disorder symptoms on the CY-BOCS according to age, sex and sponsor rank. This will also be correlated with any later DSM diagnoses, which may come about on followup clinical interviews.

Progress: Ninety-six subjects were entered in FY 92 for a total of 206 entries. Preliminary analysis indicates that OCD is not detectable by the two instruments used in the study. A larger number of interviews is needed to definitely determine the utility of these screening procedures. A paper was presented at the NW Developmental Pediatric Society, 24 Apr 92.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/004		Status: On-going	
Title: Incidence of Group A Beta Hemolytic Streptococcus Colonization and Infection in Association with Varicella					
Start Date: 01/03/92			Est. Completion Date:		
Department: Pediatrics			Facility: MAMC		
Principal Investigator: LT Kenneth L. Brooks, MC					
Associate Investigators:			COL Marvin S. Krober, MC		
Key Words: varicella, streptococcus, colonization, infection					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$748.00
					Periodic Review: //

Study Objective: To determine the frequency at which Group A beta hemolytic streptococcus (GABHS), in association with varicella, will colonize the pharynx, the rectum, and the varicella lesion and to determine the attack rate of GABHS in patients with, or without, positive cultures of GABHS.

Technical Approach: This will be a multicenter study with a total of 520 patients entered. Patients who have been diagnosed with Varicella will have a culture taken from an intact Varicella lesion and from the pharynx and the rectum. Patients will be recultured between days 5 and 7 of the rash with at least 48 hours between cultures. Data to be collected will include: age, sex, day of rash at presentation, treatment before and after enrollment, month of year, first and second culture results from each site, estimate of the number of Varicella lesions, presence or absence of Varicella mucosal lesions, and infectious complications during the Varicella illness, which may include any of the following: local cellulitis, bacteremia/sepsis, osteomyelitis, streptococcal toxic shock-like syndrome, arthritis, pneumonia, gangrenosa, abscess, erysipelas, endocarditis, and acute glomerulonephritis. The end points that will be evaluated include: the culture results in the pharynx and rectum being positive or negative for GABHS, the culture results in the Varicella lesions being positive or negative for Streptococcus and/or Staphylococcus, and the presence or absence of infection with GABHS. Confounders may include: the patient's age, sex, day of presentation, number of lesions, presence or absence of Varicella mucosal lesions, and month of year. Chi square analysis will be used to evaluate the results.

Progress: Principal investigator has been unable to implement study due to other priorities.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/079	Status: On-going
Title: Use of Metoclopramide With Chloral Hydrate for Sedation		
Start Date: 08/17/90	Est. Completion Date: Jan 91	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: CPT Vincent A. Dubravec, MC		
Associate Investigators: CPT George D. Patrin, MC		
LTC Joseph P. McCarty, MC		
Key Words: sedation, metoclopramide, chloral hydrate		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$42.06	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: Two new patients were entered in FY 92 for a total of 25 subjects. Lack of funding and the move to the new hospital building delayed continuation of the study. Original PI was Dr. Patrin.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/044		Status: On-going
Title: Lead Levels and Their Relationship to Attention Deficit Hyperactivity Disorder and Developmental Delay				
Start Date: 06/05/92			Est. Completion Date: Mar 93	
Department: Pediatrics			Facility: MAMC	
Principal Investigator: CPT Cynthia A. Kahn, MC				
Associate Investigators: LTC Patrick C. Kelly, MC			COL Stephen Stephenson, MC	
Key Words: lead, ADHD				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	\$0.00
				Periodic Review: //

Study Objective: To determine if children with attention deficit hyperactivity disorder (ADHD) or developmental delay have elevated lead levels at the time of diagnosis as compared to age matched controls.

Technical Approach: Two hundred controls, 50 children with ADHD, and 50 children with developmental delay will be entered. Controls will be selected at random in the Pediatric Clinic. All newly diagnosed children with ADHD or developmental delay will be asked to participate. Parents will complete a questionnaire after informed consent has been obtained and a blood sample will be obtained from the child for a lead level. The questionnaire will elicit information about the child's attention span, previous testing for lead levels, any diagnosis of anemia, family members or playmates who have had a high lead level, and demographic data to include age, sex, socioeconomic status, length of time in Washington state, other areas lived, and time of year. The following information will be examined: demographic data presence or absence of developmental delay presence or absence of attention problems and lead levels. Using standard statistical tests (chi-square, t-test), comparisons will be made between the control and sample groups based on lead levels. Demographic data will be analyzed with an ANOVA table to insure that these variables are not a cause for difference between groups.

Progress: Eighty-three controls, 11 ADHD children and 2 children with developmental delay have been studied.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/071	Status: On-going
Title: Pyridoxine as Specific Therapy and Prophylaxis in the Treatment of Theophylline-Induced Seizures in Mouse and Rabbit Models		
Start Date: 05/18/90	Est. Completion Date: May 91	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: COL Michael R. Weir, MC LTC Patrick C. Kelly, MC CPT Gregory M. Glenn, MC LTC Joseph P. McCarty, MC		
Key Words: seizures, prophylaxis, pyridoxine, mouse, rabbit, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$420.00	08/07/92

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: No work has been done on this protocol since November 1990. Additional mice are needed for statistical evaluation. A request for revisions will be submitted to the LAUC and work is expected to continue in early 1993.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/108	Status: Terminated
Title: Role of Anticonvulsants in Theophylline Toxicity		
Start Date: 10/19/90	Est. Completion Date: Sep 91	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators:		
LTC Joseph P. McCarty, MC	LTC Patrick C. Kelly, MC	COL Michael R. Weir, MC
Key Words: theophylline toxicity, anticonvulsants, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$916.00	08/07/92

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 was never implemented because available equipment was inadequate to produce the required EEG's in rabbits.

Detail Summary Sheet

Date: 30 Sep 92	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:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: COL Michael R. Weir, MC CPT Katherine H. Moore, MS		LTC Patrick C. Kelly, MC John Enriquez MAJ John W. McBurney, MC
Key Words: seizures, glutamine, 4-aminobutyraldehyde, theophylline toxicity, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	08/07/92

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 in two. EEG recordings will be obtained at 15 minute intervals. Baseline blood samples will be drawn for pyridoxal-5'-phosphate and again after aminophylline, pyridoxine, and glutamin/aminobutyrate. Spinal taps will be attempted on some animals for determinations of GABA and glutamine. The animals will be observed for a period of three hours with EEG monitoring, followed by three days in cages. Consistent presence or absence of effect on the EEG is expected. Analysis of blood levels of PLP and CSF levels of GABA and glutamine will be by repeated measures ANOVA with post-hoc testing by paired t-tests. The resulting paper will be descriptive.

Progress: No work was done on this protocol during FY 92. The principal investigator expects to reactivate the study in early 1993. In previous years, a small number of mice had been treated with various combinations of the study drugs. 4-aminobutyraldehyde appeared to reverse the toxicity caused by theophylline.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/052	Status: Terminated
Title: Role of Anticonvulsants with Pyridoxine in Theophyllin Toxicity in Rabbits		
Start Date: 04/05/91	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: COL Michael R. Weir, MC		LTC Patrick C. Kelly, MC MAJ John W. McBurney, MC
Key Words: anticonvulsants,theophylline toxicity,rabbit,pyridoxine,Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	08/07/92

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 consistent presence or absence of effect on the EEG. resulting paper will be descriptive.

Progress: This study was never implemented because available equipment precluded adequate EEG's of the rabbits.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/076		Status: On-going
Title: Protective Role of Pyridoxine in Gentamicin Nephrotoxicity				
Start Date: 10/20/89		Est. Completion Date: Sep 90		
Department: Pediatrics		Facility: MAMC		
Principal Investigator: COL Marvin S. Krober, MC				
Associate Investigators: COL Michael R. Weir, MC		LTC Jose D. Masi, MC		
Key Words: nephrotoxicity,gentamicin,pyridoxine,Animal Study				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$3135.00		08/07/92

Study Objective: To test whether pyridoxine has a protective effect on gentamicin nephrotoxicity.

Technical Approach: Following a period of quarantine and observation, rabbits will be premedicated with xylazine and ketamine and then taken to the operating suite in groups of seven. One animal will receive 100 mg of pyridoxine as a control. The remaining animals will receive either 20 mg/kg or 60 mg/kg of gentamicin intramuscularly. One animal at each gentamicin dose will then receive either saline or 10 mg pyridoxine or 100 mg pyridoxine. These medications will be repeated daily for five days. Blood will be drawn for pyridoxal 5'-phosphate (PLP), gentamicin, and creatinine on days 1 (before injection), 3, and 5. Following the last injection in the morning, the animals will be sacrificed in the late morning or early afternoon using pentobarbital or suitable substitute, and one kidney from each animal will be recovered for fixation for blinded and pathologic interpretation. In each of two subsequent weeks, seven more animals per week will be studied similarly. This is a descriptive study in which the investigators hope to show that there is a general relationship between renal pathology and the average fall in PLP or, potentially, a relationship between pathology and gentamicin blood levels. BMDP and SPSS will be used to analyze data. If there are striking differences between the renal pathology of the various animals, the pathology will be scored for rank testing versus PLP, creatinine, gentamicin levels, and B6 dose.

Progress: No work has been done on this protocol since March 1991. Delays have ensued because the dose of gentamicin did not produce significant renal pathology and new arrangements are needed for blood PLP assays. Work is expected to continue in January 1993.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/007	Status: On-going
Title: A Comparative Study of the Safety and Efficacy of Clarithromycin and Eryped (Erythromycin Ethylsuccinate) Suspensions in the Treatment of Children with Community-Acquired Pneumonia		
Start Date: 01/03/92	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: MAJ Arlene E. Roots, AN		
COL Donald R. Moffitt, MC		
Key Words: pneumonia, Clarithromycin, Augmentin, children		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$150.00	//

Study Objective: To compare the efficacy and safety of clarithromycin and erythromycin ethylsuccinate suspensions in the treatment of children with community-acquired pneumonia who are suitable candidates for oral macrolide therapy.

Technical Approach: Children from 3 to 12 years of age with community-acquired pneumonia will be treated with either clarithromycin 7.5 mg/kg/dose b.i.d., or 20.0 mg/kg/dose b.i.d., or 13.3 mg/kg three times a day. About 300 patients will be enrolled nation-wide, with approximately 10 patients enrolled at Madigan. Patients must have x-ray confirmation of the diagnosis of pneumonia. They must not have underlying chronic disease, renal disease, or hepatic disease. At the initial visit, the children will have CBC, CRP, blood chemistries, blood culture, sputum culture, and serology and culture for chlamydia and mycoplasma. The children will return in 5-7 days for repeat clinical evaluation. Urine will be obtained to check for compliance. The child will receive antibiotics for 10 days and return to the clinic within 48 hours of stopping treatment. A repeat chest x-ray will be done and sputum will be cultured, if possible. CBC and chemistries will be retested. The patient will be evaluated for culture, x-ray, and clinical response to treatment. Laboratory and clinical side-effects of treatment will be noted. A final visit will be at 4-6 weeks. Convalescent serum will be obtained at that time. Results will be used to compare the safety and efficacy of clarithromycin and erythromycin.

Progress: One patient has been entered in this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/092	Status: On-going
Title: Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses		
Start Date: 07/20/90	Est. Completion Date: Sep 91	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: MAJ Thomas A. Perkins, MC		COL James S. Rawlings, MC MAJ Joanna C. Beachy, MC
Key Words: HIV, diagnostic assays, children		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: Several patients have been studied with the data entered in the central data collection point at WRAIR.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/093	Status: On-going
Title: Epidemiology of HIV in Pediatric and Perinatal Patients: A Natural History Study		
Start Date: 08/17/90	Est. Completion Date: Jul 93	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: MAJ Thomas A. Perkins, MC		COL James S. Rawlings, MC MAJ Joanna C. Beachy, MC
Key Words: HIV, epidemiology, pediatric		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To establish a Pediatric AIDS Center (PAC) to identify at-risk dependents of HIV positive individuals, compile a high-risk HIV pediatric registry, collect basic epidemiological data, and conduct longitudinal follow-up studies to assess the transmission and progression of HIV infection following heterosexual and/or perinatal exposure.

Technical Approach: This is a multicenter study, which originated at Walter Reed Army Medical Center and is being funded by an NIH grant. The Armed Forces are required, by Department of Defense directive, to screen all active duty personnel for antibody to HIV. Army personnel who are positive for HIV antibody are reported to the US Army HIV Data System (USAHDS). The PAC will identify and follow all eligible pediatric beneficiaries of HIV positive soldiers by comparing USAHDS reports with computer linked family records in the Defense Enrollment Eligibility Reporting System data files. Dependents who are identified from matching records will be entered into an HIV high-risk patient registry. To validate the matching process and to facilitate evaluation of high-risk families, a physician network with coordinators at each Army regional medical center will be established. The regional coordinators will work with the PAC to provide an accurate clinical evaluation, obtain appropriate laboratory studies, and organize regular followup for high-risk patients. Each patient will be evaluated for HIV infection with antibody screening, HIV culture, and antigen assay. Infection will be staged according to current Center for Disease Control (CDC) recommendations. Clinical information from the initial evaluation and subsequent follow-up visits will be entered into computer-managed patient files at the PAC. CDC classifications will be updated with results from the most current evaluation. Once the PAC has been established, the investigators anticipate that the HIV registry and PAC could be expanded to follow patients from all three branches of the Department of Defense.

Progress: No further entries pending resolution of funding problems at central WRAIR site.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/107		Status: On-going
Title: Perinatal HIV Infection: Epidemiology and Natural History				
Start Date: 10/19/90			Est. Completion Date: Apr 95	
Department: Pediatrics			Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC				
Associate Investigators: MAJ Thomas A. Perkins, MC MAJ W. Kim Brady, MC			COL James S. Rawlings, MC MAJ Joanna C. Beachy, MC	
Key Words: HIV,epidemiology,natural history				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	\$0.00
				Periodic Review: //

Study Objective: To develop a clinical perinatal center for the diagnosis and management of pregnant women with human immunodeficiency virus (HIV) infection and their newborn infants and to systematically collect clinical, laboratory, and epidemiologic data describing the course and natural history of perinatal HIV infection.

Technical Approach: Preliminary screening will be performed with the ELISA test and positives will be confirmed by Western blot assay, and the women will be staged according to the Walter Reed Staging System. The initial evaluation will include a physical examination, assessment of fetal growth and well being, HIV culture, quantitative T-cell subset analysis, CBC, serology for CMV, toxoplasmosis and herpesvirus, and blood samples for p24 antigen assay, in situ hybridization, and polymerase chain reaction (PCR). Reassessment will be done during each trimester of pregnancy and at the time of birth using the same test measures as in the initial evaluation. At the time of birth, the placenta and a segment of the umbilical cord will be sent for electron-microscopic, histochemical, and immunofluorescent analysis. Postpartum cervical cultures will be obtained for CMV and Herpes virus cultures. A sample of breast milk will be obtained for HIV culture in women who forego suppression of lactation. Infants will be evaluated at birth and then every three months for two years. Laboratory tests will be the same as for the mother with the addition of urine, rectal, and nasopharyngeal cultures for CMV. Physical exam in infants will also include assessment for fetal embryopathy. Subjects will be divided into two subsets: (1) HIV+ mother and HIV+ infant and (2) HIV+ mother and HIV- infant. Descriptive statistics will be used to describe the entire sample and prevalence comparisons will be made for the two major subsets. Analytic methods may involve both univariate and multivariate techniques.

Progress: No further entries pending resolution of funding problems at central WRAIR site.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/018	Status: On-going
Title: Role of Pyridoxine in Gentamicin-Lasix Nephrotoxicity in Rabbits		
Start Date: 02/01/91	Est. Completion Date:	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Marvin S. Krober, MC		
Associate Investigators: COL Michael R. Weir, MC		
Key Words: nephrotoxicity, gentamicin-Lasix, pyridoxine, rabbit, Animal Study		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: 08/07/92

Study Objective: To test whether or not the nephrotoxicity and altered blood-brain barrier associated with a gentamicin-lasix combination can be altered by pyridoxine.

Technical Approach: Twenty-two New Zealand white rabbits will be divided into the following groups: gentamicin + lasix + saline (7 rabbits) gentamicin + lasix + pyridoxine (7 rabbits) pyridoxine only (2 rabbits) gentamicin only (2 rabbits) lasix only (2 rabbits) saline only (2 rabbits). On day one of the study, baseline blood samples will be obtained for measurement of creatinine, gentamicin, and PLP (the active form of pyridoxine) levels. The animals will receive IM injections by group for five days. On days 5, 8, and 12 blood samples will again be obtained to measure creatinine, gentamicin, and PLP levels. The IM injections will be repeated on days 8 - 12. The animals will be sacrificed on day 12 and the kidneys and the brains will be sent to the pathologist who will grade the pathology on the following 5 point scale: (1) no significant pathology (2) focal ATN involving <10% of the tubules (3) mild ATN involving 10-25% of the tubules (4) moderate ATN involving 26-50% of the tubules, widespread ballooning necrosis of tubular epithelium, definite nuclear degeneration (at least focally) proteinaceous material in tubules ± interstitial inflammation and tubular regenerative changes and (5) severe changes involving over 50% of the tubules with changes as in #4 but more wide spread. Changes in blood levels of creatinine, gentamicin, and PLP will be compared between the two study groups by ANOVA.

Progress: Work has not begun on this protocol. Continuation is dependent on implementation of protocol #89/76 also by Dr. Krober. Work is expected to begin in March 1993.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 89/071

Status: On-going

Title: Comparison of Effectiveness of Lidocaine HCL vs Hyaluronidase in the Early Treatment of Soft Tissue Extravasation Injuries in Swine

Start Date: 09/15/89

Est. Completion Date: Oct 89

Department: Pediatrics

Facility: MAMC

Principal Investigator: CPT John S. Scott, MC

Associate Investigators:

COL Michael R. Weir, MC

Key Words: extravasation injuries, lidocaine HCL, hyaluronidase, swine, Animal Study

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$614.00

Periodic Review:

08/07/92

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 principal investigator was changed from Dr. Weir to Dr. Scott in July 1992. Work will begin on this study in the fall of 1992, after the principal investigator completes his chief resident rotation.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/067	Status: On-going
Title: Cervical Human Papillomavirus Infection Prevalence in Female ROTC College Cadets		
Start Date: 07/02/92	Est. Completion Date: Aug 92	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: MAJ Elisabeth M. Stafford, MC		
Associate Investigators:		
CPT Gilbert Teague, MC	COL Terrel J. Michel, MC	MAJ Robert S. Stewart, MS
MAJ Barbara A. Crothers, MC	COL Dan C. Moore, MC	
Key Words: papillomavirus, college cadets		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine the prevalence of cervical HPV (Human Papillomavirus) infection in ROTC college students from a geographically diverse sample.

Technical Approach: Five hundred young adult women reporting for inprocessing ROTC physicals will be asked to participate in this cervical Human papillomavirus infection screening study. Participation will include completion of a questionnaire and processing of an endocervical sample for HPV obtained from the routine PAP smear sampling. PAP smears revealing squamous or glandular cell abnormalities will require cervical colposcopy as standard of care. Cadets with negative PAP smears and positive HPV DNA screen will not undergo colposcopy, but will be informed of the positive result with the recommendation that they make this information available to their private physician. After determining the prevalence of HPV cervical infection, data will be further analysed using chi-square analysis and stepwise logistic regression to determine significant variable associations with HPV status.

Progress: 333 women cadets were enrolled in this study. This represented approximately 95% of the women attending the summer camp. Forty-two states and the District of Columbia were represented. Demographic and gynecologic health data obtained from questionnaires completed by the participants have been entered in a data base. Cervical samples are currently being processed for HPV, with completion of lab analysis expected by the end of 1992.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF RADIOLOGY

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/012 **Status:** Terminated

Title: Nasogastric Tissue Sampling of the Upper Alimentary Tract

Start Date: 01/03/92

Est. Completion Date: Jan 94

Department: Radiology

Facility: MAMC

Principal Investigator: LTC Gregory N. Bender, MC

Associate Investigators:

MAJ Amy M. Tsuchida, MC

CPT John L. Reichle, MC

MAJ James H. Timmons, MC

MAJ Michael F. Lyons II, MC

Key Words: alimentary tract, nasogastric tissue sampling

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0

OMA Cost:

\$24,815.00

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Study Objective: To validate the detection of neoplasia with fluoroscopic guided nasogastric biopsy (FGNB) of the stomach and duodenum.

Technical Approach: Patients with an abnormal upper gastrointestinal series (UGI) will be eligible for this study. Each subject will have an NG tube placed with the tip of the tube in the region of the duodenal sweep or the stomach. The subject will then be given .5 mg IV Glucagon to paralyze the small bowel and stomach. Once adequate hypotonicity of the bowel and stomach is reached, a barium suspension will be introduced through the NG tube to opacify the duodenum and stomach and to delineate the lesions for biopsy. For duodenal biopsy, the biopsy cable will then be introduced into the lumen of the NG tube and directed out of the proximal port in the region of the duodenum. A mucosal biopsy of the duodenum will then be taken with the cable biopsy forceps under fluoroscopic guidance. For gastric biopsy, the NG tube is then withdrawn into the region of the stomach. A barium suspension is then introduced into the stomach through the NG tube to allow fluoroscopic visualization of the entire stomach to direct the biopsy. The biopsy cable is then introduced via the NG tube and up to three tissue samples are taken from the lesion in the stomach. Following each biopsy, the cable, NOT the tube must be withdrawn and again reintroduced for the next sampling. Analysis of the data, following biopsy of 200 patients, will be for sensitivity, positive predictive value, and percentage agreement only for the detection of neoplasia.

Progress: This protocol was terminated because the MEDCASE equipment could not be purchased and because it was determined by HSC that an IDE number would be required.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/013	Status: Terminated
Title: Nasogastric (Gastric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Stomach (Feasibility Study)		
Start Date: 01/03/92	Est. Completion Date: Jan 94	
Department: Radiology	Facility: MAMC	
Principal Investigator: LTC Gregory N. Bender, MC		
Associate Investigators:		
MAJ Amy M. Tsuchida, MC	MAJ James H. Timmons, MC	
CPT Gregory Welle, MC	MAJ Michael F. Lyons II, MC	
CPT Timothy Schofield, MC	CPT John L. Reichle, MC	
Key Words: nasogastric ultrasound, stomach		
Accumulative MEDCASE Cost: \$250,000	Est. Accumulative OMA Cost: \$2,700.00	Periodic Review: //

Study Objective: To determine the clinical feasibility of fluoroscopically guided nasogastric ultrasound (FGNU) of the stomach.

Technical Approach: Twenty patients undergoing gastric endoscopy (EGD) for clinical indications (suspected gastric tumor) will be studied. The FGNU and the EGD will be performed on separate days. Subjects will have a nasogastric tube placed with the tip of the tube in the region of the duodenal sweep or the second portion of the duodenum, or in the stomach. The distal balloon will then be inflated with 15-30 cc of water soluble, iodinated radiographic contrast material to document position under fluoroscopy. 200-400 cc of deaerated water or saline solution will be slowly instilled through the proximal ports of the catheter to fill the duodenum and/or stomach with water proximal to the catheter balloon. An ultrasound cable, 7.5-10 mHZ (endoscopic ultrasound probe), 3 mm in diameter will be inserted through the NG tube with its tip located at the level of the contrast opacified balloon. The patient will be scanned for up to 60 minutes in an attempt to obtain adequate ultrasound images of the entire stomach surface. All pertinent ultrasound images will be recorded on acetate film and on videotape for further review. Fluoroscopy will be used to periodically document the position of the probe as it is pulled back through the nasogastric tube. After completion of imaging, the NG tube balloon will be deflated and the endoscopic ultrasound probe and NG tube will be removed. The data will be recorded as individual trials in list form with side by side columns representing success or failure in placing the nasogastric tube and in visualizing the entire gastric surface and yes or no concerning adequacy of the images obtained by location.

Progress: This protocol was terminated because the MEDCASE equipment request was denied and because HSC determined that an IDE number would be required.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/014	Status: Terminated
Title: Nasogastric (Gastric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Stomach (Validation for Detection of Gastric Carcinoma)		
Start Date: 01/03/92	Est. Completion Date: Jan 94	
Department: Radiology	Facility: MAMC	
Principal Investigator: LTC Gregory N. Bender, MC		
Associate Investigators:		
MAJ Amy M. Tsuchida, MC	MAJ James H. Timmons, MC	
CPT Gregory Welle, MC	MAJ Michael F. Lyons II, MC	
CPT Timothy Schofield, MC	CPT John L. Reichle, MC	
Key Words: nasogastric ultrasound, stomach		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$26,500.00	//

Study Objective: To validate the detection of gastric neoplasia with fluoroscopically guided nasogastric ultrasound (FGNU) of the stomach.

Technical Approach: This study will be a continuance of the feasibility study, MAMC #92/13, and will be conducted in the same manner. If that study is successful, 20 additional patients will be entered in this study. Whereas the previous study collected data to determine if the nasogastric tube could be successfully placed, if the entire gastric surface could be visualized, and if the images obtained would be adequate, this study will be used to determine if the procedure is adequate in determining if a gastric adenocarcinoma/malignancy is present. The results of this procedure will be compared with surgical/biopsy results for validity of the procedure.

Progress: This study was terminated because the MEDCASE request was denied and because HSC determined that an IDE number would be required.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/015

Status: Terminated

Title: Nasogastric (Gastaric/Duodenal/Biliary/Pancreatic) Ultrasound Study of the Pancreas

Start Date: 01/03/92

Est. Completion Date: Dec 94

Department: Radiology

Facility: MAMC

Principal Investigator: LTC Gregory N. Bender, MC

Associate Investigators:

MAJ Amy M. Tsuchida, MC

CPT Gregory Welle, MC

CPT Timothy Schofield, MC

MAJ James H. Timmons, MC

MAJ Michael F. Lyons II, MC

CPT John L. Reichle, MC

Key Words: nasogastric ultrasound, pancreas

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0

OMA Cost:

\$26,500.00

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Study Objective: To validate the detection of pancreatic neoplasia with fluoroscopically guided nasogastric ultrasound (FGNU).

Technical Approach: This study will be performed in the same method as the previous study, MAMC #92/14, except that the subjects will be patients with suspected pancreatic carcinoma and data will be collected to determine the sensitivity of this procedure in recognizing pancreatic carcinoma when compared with surgery and biopsy.

Progress: This study was terminated because the MEDCASE request was denied and because HSC determined that an IDE would be required.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF SURGERY

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/028	Status: On-going
Title: The Influence of Prophylactic Administration of Intravenous Crystalloid and Colloid Solutions on the Incidence of Hypotension Following Subarachnoid Anesthesia		
Start Date: 04/05/91	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Frederick W. Burgess, MC		
Associate Investigators: MAJ David M. Colonna, MC		LTC Douglas M. Anderson, MC LTC Michael J. Sborov, MC
Key Words: anesthesia, hypotension, prophylactic agents		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: This protocol is slowly accruing subjects. Thus far, 33 patients have been randomly assigned to receive crystalloid, Hespan, or no preload prior to anesthesia. None of the patients has experienced any major adverse reactions. Urinary retention has not occurred.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/029 **Status:** Terminated

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:

Department: Surgery

Facility: MAMC

Principal Investigator: MAJ Frederick W. Burgess, MC

Associate Investigators:

LTC Michael J. Sborov, MC

LTC Douglas M. Anderson, MC

COL Charles A. Andersen, MC

Key Words: surgery:abdominal aortic,bupivacaine,fentanyl

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

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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, pO₂ and pCO₂. VAS pain scores will also be quantitated at 6 hour intervals to ascertain that comparable levels of analgesia were provided.

Progress: Unfortunately, many of the clinical practitioners were unwilling to adhere to the protocol guidelines. Since it was not possible to maintain adequate control the protocol was terminated.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/030	Status: Completed
Title: Determination of the Ideal Bupivacaine/Fentanyl Concentration for Continuous Thoracic Epidural Infusion for Postoperative Analgesia in Thoracotomy Patients		
Start Date: 04/05/91	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Frederick W. Burgess, MC		
Associate Investigators: LTC Michael J. Sborov, MC		LTC Douglas M. Anderson, MC COL Daniel G. Cavanaugh, MC
Key Words: thoracotomy, postoperative analgesia, bupivacaine, fentanyl		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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, paO₂, and paCO₂. VAS pain scores will be quantitated at 6 hour intervals to ascertain that comparable levels of analgesia were provided.

Progress: This study evaluated in 40 patients the impact of combining a local anesthetic with the narcotic fentanyl for the management of postoperative thoracotomy pain. It was found that by adding bupivacaine, 0.03, 0.06, and 0.125%, fentanyl use could be decreased by 25-30%. Furthermore, patients in all three bupivacaine treatment groups had significantly less carbon dioxide retention and had an improved acid base balance in the initial 24 hour postoperative period.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 91/035		Status: Completed	
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:		
Department: Surgery			Facility: MAMC		
Principal Investigator: MAJ Frederick W. Burgess, MC					
Associate Investigators: LTC Michael J. Sborov, MC			MAJ Frederick W. Burgess, MC LTC Joseph J. Mancuso Jr., MC		
Key Words: hemorrhagic shock,anesthesia,physiologic response,swine,Animal Study					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		08/07/92	

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 7 ml of 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 minutes 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 (\pm 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: Twenty-one pigs were randomly assigned into the four groups in this study. The study suggests that aggressive volume administration with crystalloid solutions,

prior to hemorrhage, does not ameliorate the hypotensive response to hemorrhage in animals receiving combined epidural/general anesthesia. Combined epidural/general anesthesia appears to increase the risk of hypotension in operations at risk for hemorrhage. Aggressive volume administration may not reduce the risk of hypotension, and may contribute to postoperative fluid overload.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/090 **Status:** On-going

Title: Selective Blockade of the Vagus Nerve to Relieve Referred Shoulder Pain
Associated with Pulmonary Surgery in Human Subjects

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

Department: Surgery **Facility:** MAMC

Principal Investigator: MAJ Frederick W. Burgess, MC

Associate Investigators:
LTC Richard M. Dearman, MC COL Daniel G. Cavanaugh, MC
MAJ James D. Helman, MC LTC Douglas M. Anderson, MC

Key Words: shoulder pain, pulmonary surgery, vagus nerve

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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 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: Five patients have been entered. It is too early for data analysis.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/008	Status: On-going
Title: Influence of Phrenic Nerve Blockade on the Incidence of Referred Shoulder Pain in Patients Undergoing Thoracic Surgery for Pneumonectomy		
Start Date: 02/07/92	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Frederick W. Burgess, MC		
Associate Investigators: LTC Douglas M. Anderson, MC COL Daniel G. Cavanaugh, MC		CPT Michael J. Decker, MC COL Michael J. Barry, MC
Key Words: referred shoulder pain, phrenic nerve		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To evaluate the contribution of the phrenic nerve to the referred shoulder pain associated with thoracic surgery for pneumonectomy.

Technical Approach: Pneumonectomy operations may be associated with referred pain symptoms conducted by the phrenic nerve. Blockade of the phrenic nerve may inhibit these pain symptoms. This will be a double-blind randomized trial using patients greater than 18 years of age who are presenting for thoracotomy. Individuals will be assigned in a random fashion to receive either 0.9% NaCl or 0.5% bupivacaine for infiltration around the phrenic nerve above the hilum prior to closure of the thoracic cavity. There will be 8-10 patients in each group. Postoperative pain management will be provided according to standard MAMC practice with a thoracic epidural infusion of narcotic/local anesthetic. Each patient will be evaluated at 1 and 24 hours postoperatively for the presence of referred shoulder pain. Severity of pain will be assessed by the patient using a visual analog scale. Demographic data on each patient, including height, weight, age, sex, and surgical procedure will be collected and analyzed where appropriate by chi-square analysis or an 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: One patient has been entered. Subject accrual is slow due to the infrequent nature of this type of surgery.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/047	Status: On-going
Title: Identification of the Optimal Bupivacaine Concentration for Epidural Analgesia in Combination with Patient Controlled Epidural Fentanyl Analgesia		
Start Date: 06/05/92	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Frederick W. Burgess, MC		
Associate Investigators: CPT David J. Bower, MC CPT Michael J. Decker, MC		
Key Words: epidural analgesia, bupivacaine, fentanyl		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

Study Objective: To identify the optimal concentration of dilute local anesthetic for continuous epidural analgesia that will produce the greatest reduction in the total amount of narcotic required for postoperative analgesia following major thoracic and upper abdominal surgery.

Technical Approach: At Madigan, virtually all patients undergoing major abdominal or thoracic surgery receive epidural anesthesia for postoperative pain relief. In this study, patients greater than 18 years of age who have been scheduled by the anesthesiologist to receive patient-controlled epidural analgesia for postoperative pain relief will be randomized to four groups: (1) fentanyl plus a placebo, (2) fentanyl plus 0.03% bupivacaine (3) fentanyl plus 0.0625 % bupivacaine or (4) fentanyl plus 0.125% bupivacaine. Patients will rate postoperative pain using a visual analog scale every four hours for 24 hours and arterial blood gases will be obtained at one hour postoperatively and at 24 hours after the start of the epidural infusion. The total amount of fentanyl and the amount of additional fentanyl provided in the form of a bolus will be recorded and totaled for the 24 hour period. Arterial blood gas data and total fentanyl requirements will be analyzed between groups for statistical significance, using analysis of variance and the Student-Newman-Keuls test.

Progress: One patient has been entered. The study has been delayed by the need to institute a hospital-wide in-service program. This training program is now complete and patients are being recruited for the study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/061		Status: On-going
Title: A Double Blind, Placebo-Controlled Comparison Between 0.125%, 0.25%, and 0.5% Ropivacaine, When Used for Post-operative Infiltration in Herniorrhaphies: A Dose Response Study				
Start Date: 05/01/92			Est. Completion Date: May 93	
Department: Surgery			Facility: MAMC	
Principal Investigator: MAJ Frederick W. Burgess, MC				
Associate Investigators:			MAJ Christopher R. Kaufmann, MC	
Key Words: herniorrhaphies, ropivacaine				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	\$0.00
				Periodic Review: //

Study Objective: To establish the dose-response analgesic effect of ropivacaine, given postoperatively by local wound infiltration, using three different concentrations of ropivacaine in equal volumes and saline.

Technical Approach: Male outpatients scheduled for elective inguinal herniorrhaphy will be randomized to receive local infiltration during wound closure with one of three concentrations of ropivacaine (0.125%, 0.25%, or 0.5%) or saline, using equal volumes. Surgery will be performed under a short acting regional block and pre-anesthetic medication will be standardized according to usual practice at Madigan. Infiltration of the surgical wound during closure will be done using 30 ml of the study drug (15 ml in the deep layer and 15 ml in the superficial layer). In the first 32 patients, the plasma concentration of ropivacaine will be followed during the first 2 hours after end of infiltration. Assessments of perceived pain will be assessed by the patient using a visual analogue scale (VAS) at premedication, and at 60, 120, 180, 240, and 300 minutes and at 8 and 24 hours after the end of drug infiltration and again on the first postoperative visit (6-14 days postoperatively). Tolerance to pressure-induced pain will be at the same time periods as the VAS while in the hospital. Postoperative analgesic therapy will be standardized in regard to drug, dose, and minimum interval between doses. The time to first request for analgesics and the amount of analgesics required during the first 6 days postoperatively will be recorded. A follow up VAS and pressure-induced pain test will be done at the first postoperative visit. Adverse events will be recorded intraoperatively, in the post-anesthesia recovery room, at the first postoperative visit, and at a telephone follow-up 2-3 weeks after surgery. The presence of a dose-response relationship (increasing effect with increasing dose) will be the primary analysis and will be done using a regression analysis.

Progress: Four patients have completed the protocol. Results will not be available until the study is complete.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/026	Status: Suspended
Title: Shoulder Morbidity in Head and Neck Surgery		
Start Date: //	Est. Completion Date: Apr 92	
Department: Surgery	Facility: MAMC	
Principal Investigator: CPT Domenic M. Canonico, MC		
Associate Investigators: MAJ Michael R. Morris, MC		1LT David Paulson, MS CPT Jonathan A. Perkins, MC
Key Words: surgery, head & neck, morbidity		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$200.00	//

Study Objective: To compare postoperative shoulder morbidity with regard to strength, work function, and range of motion in patients subjected to radical neck dissection and/or regional musculocutaneous flap reconstruction during the course of treatment for a head and neck malignancy.

Technical Approach: Patients will be examined and the trapezius muscle function and bulk will be noted and each subject will complete a questionnaire as a measure of the patient's perception of the functional results of surgery. Patients will then be identified by groups. Group 1 will include those with post radical neck dissection alone Group 2 will include those with a pectoralis myocutaneous flap only, and group 3 will have had both a radical neck dissection and a pectoralis myocutaneous flap. The three groups will then be evaluated by history, physical exam, and physical therapy protocol. The physical therapist will test for available passive range of motion and active range of motion for shoulder flexion, extension, abduction, and internal and external rotation, as well as scapular mobility. Shoulder/shoulder girdle strength will be tested by a licensed physical therapist and gross strength will be tested using the LIDO isokinetic machine. Each subject will act as his/her own control. The uninvolved side will be compared to the involved side and statistically analysed.

Progress: This protocol was suspended at the principal investigator's request in July 1992 until he has the time to revise the protocol according to the stipulations of the Human Use Committee.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 79/064

Status: Completed

Title: Implantation of Intraocular Lenses

Start Date: 03/16/79

Est. Completion Date: Indef.

Department: Surgery

Facility: MAMC

Principal Investigator: LTC Kevin J. Chismire, MC

Associate Investigators:

LTC David P. George, MC

COL Thomas H. Mader, MC

MAJ Leslie P. Fox, MC

COL Stanley C. Allison, MC

MAJ Anthony R. Truxal, MC

Ronald K. Sugiyama, M.D.

MAJ Lawrence J. White, MC

COL Floyd L. Wergeland Jr., MC

MAJ Mark S. Dwyer, MC

Key Words: intraocular lenses

Accumulative

MEDCASE Cost: \$0.00

Est. Accumulative

OMA Cost: \$200.00

Periodic Review:

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: 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: This was a treatment protocol to provide a means where MAMC patients could be treated with intraocular lenses, all of which were classified as investigational when first put into use. Considering the wide range of lenses that have now been approved by the FDA, MAMC has decided to use only lenses that are FDA approved. Therefore, the protocol has been terminated. Approximately 2000 implants were made in the twelve years that this protocol was active.

Detail Summary Sheet

Date: 30 Sep 92	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		
Associate Investigators:		
COL Jackie L. Finney, MC	COL Richard A. Camp, MC	
LTC Donald B. Blakeslee, MC	COL Thomas G. Griffith, MC	
MAJ Stephen D. Clift, MC	LTC Robert J. Kenevan, MC	
LTC Bruce R. Wheeler, MC	MAJ Viswanatham Piratla, MC	
	MAJ Michael R. Morris, MC	
Key Words: training protocol, microsurgery, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$690.00	08/07/92

Study Objective: To perfect the techniques needed to perform clinical microsurgery and to establish formal training programs in clinical microsurgery at MAMC for use of those surgeons desiring to develop this expertise.

Technical Approach: A schedule of one or two afternoons per week will be set aside for teaching sessions. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques. Staff and residents from the Orthopedic, Plastic Surgery, and Thoracic Surgery Services will train in the following procedures: (1) reimplantation of extremities, (2) re-anastomosis of peripheral vessels and nerves, (3) repair of avulsion wounds, (4) graft transplants, (5) free cutaneous, myocutaneous and composite tissue transfer for traumatic lesions and reconstructive procedures, (6) re-anastomosis of facial nerve lesions. The training will begin with small vessels and nerves in cadaver specimens of small laboratory animals. When the anatomy of the area is learned as well as the use of the microsurgical instruments and the operating microscope, then microsurgical procedures in living rats, guinea pigs, and rabbits can be learned.

Progress: Four training sessions were held in FY 92, using one rat each.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/099

Status: On-going

Title: The Implantation of Bone Morphogenic Protein Using Vascularized Omentum in a Predetermined Size and Shape in Swine

Start Date: //

Est. Completion Date: Dec 92

Department: Surgery

Facility: MAMC

Principal Investigator: MAJ Stephen M. Davis, MC

Associate Investigators:
MAJ Robert J. Wygonski, DC

MAJ Cecil R. Dorsett, DC
MAJ Douglas A. Powell, VC

Key Words: bone protein, omentum, animal study, Animal Study

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$600.00

Periodic Review:
//

Study Objective : To determine if a vascularized graft utilizing omentum with bone morphogenetic protein can induce bone formation in a three dimensional shape; and to determine bone produced in this manner can survive transplantation to a different location.

Technical Approach : Bone grafting is a commonly performed procedure. The best bone graft is a vascular autogenous graft (one obtained from the patient complete with its own blood supply). However, this is not always possible and does have certain risks, even when properly performed. Bone morphogenetic protein (BMP) is a substance which induces new bone to form in intra- or extra-skeletal sites and has recently been cloned by recombinant DNA techniques. Six pigs will be used for this study. Each pig will undergo a laparotomy with the placement of six tubular molds around individual omental pedicles. Two molds will contain only omentum, two will contain omentum and autogenous bone, and two will contain omentum and bone morphogenetic protein. Forty five days after being implanted, each mold will be opened and visually examined. The two molds containing bone morphogenetic protein will have their vascular supply switched by microsurgical techniques. After an additional 45 days, all molds will be harvested and examined to determine if bone has been produced in a three dimensional shape with its own blood supply. If present, an attempt will be made to determine if it is cortical, cancellous, or corticocancellous bone.

Progress : This is a new protocol which has not yet been implemented.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/037	Status: Completed
Title: Metatarsus Proximus: Its Association with Interdigital Neuromas		
Start Date: 02/07/92	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: Timothy S. Grace, M.D.		
Associate Investigators: Donald J. Carlson, D.P.M. MAJ Richard O. Jones, MS		CPT Kevin F. Sunshein, MS Lawrence B. Harkless, D.P.M.
Key Words: metatarsus proximus, interdigital neuromas		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine if there is an increased finding of metatarsus proximus and digital divergence in patients who have a confirmed diagnosis of neuroma as opposed to an asymptomatic control group.

Technical Approach: Operative reports and radiographs from 80 patients who have undergone neuroma surgery will be reviewed. Radiographs of 40 patients without symptoms of neuroma or complaint of other painful foot pathology will be reviewed as a control group. Neuroma will be confirmed through pathologic specimens. Radiographs will be reviewed and measurements taken to show evidence of a relationship between metatarsus proximus and digital divergence and the occurrence of interdigital neuromas. Metatarsus proximus is the obliteration of interdigital space between adjacent metatarsal heads found on anterior posterior radiograph. It is measured in millimeters, from the medial most aspect of one metatarsal head to the lateral most aspect of the adjacent metatarsal head. Metatarsus proximus would be a measurement of zero or a negative number, which would indicate metatarsal head overlap. Digital divergence is measured by the angle between the bisection of proximal phalanges of the affected interspace. It is felt that as the size of the neuroma increases so will the digital divergence angle.

Progress: Results of the study revealed no statistical relationship between the radiologic findings of metatarsus proximus and digital divergence and the occurrence of neuromas. An unexpected finding was an increased intermetatarsal angle of the affected interspace in the neuroma group. A manuscript has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/046	Status: On-going
Title: Can the Combination of Intramuscular Ketorolac and Continuous Epidural Bupivacaine Eliminate the Need for Narcotic Analgesia Post-Thoracotomy		
Start Date: 06/05/92	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: CPT Gary D. Gridley, MC		
Associate Investigators: CPT Ronald L. Hurst, MC		MAJ Frederick W. Burgess, MC COL Daniel G. Cavanaugh, MC
Key Words: thoracotomy, ketorolac, bupivacaine		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To demonstrate a substantial reduction or complete elimination of the need for narcotic analgesics following thoracic surgery, with the analgesic combination of intramuscular ketorolac and a continuous epidural bupivacaine infusion.

Technical Approach: Patients presenting for open thoracotomy who have chosen epidural anesthesia for postoperative pain control will be randomized to one of four groups: (1) fentanyl plus 0.625% bupivacaine plus an IM placebo (saline) every six hours (2) fentanyl plus 0.125% bupivacaine plus an IM placebo (saline) every six hours (3) fentanyl plus 0.625% bupivacaine plus 30 mg ketorolac IM every six hours (4) fentanyl plus 0.125% bupivacaine plus 30 mg ketorolac IM every six hours Groups 1 and 2 will receive a 60 mg injection of placebo prior to awakening from the surgical procedure and Groups 3 and 4 will receive a 60 mg injection of ketorolac before awakening. Patients will control their pain using a Patient Controlled Analgesia Device to administer fentanyl (100 mcg of fentanyl with an initial 10 minutes lock out period). Patients will quantify their pain once every four hours using a visual analog scale (scale of 1-10). For pain more severe than 5 on the scale, a supplemental epidural injection of 50 mcg of fentanyl will be provided. Total fentanyl requirements will be analyzed between groups. VAS pain score will be quantitated at 4 hours intervals to ascertain that comparable levels of analgesia were provided.

Progress: This protocol has not been implemented. The investigators are investigating obtaining a suitable placebo.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/098	Status: On-going
Title: Randomized Prospective Study Comparing Intermittent Pneumatic Compression of the Calf to Intermittent Sequential Pneumatic Compression of the Whole Leg		
Start Date: 01/03/92	Est. Completion Date: Nov 93	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Kurt L. Hansberry, MC		
Associate Investigators: COL Charles A. Andersen, MC MAJ Ian M. Thompson, MC MAJ James H. Timmons, MC		
Key Words: pneumatic compression, intermittent, sequential, calf, leg		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$3055.00	Periodic Review: //

Study Objective: To determine the best mechanical device used to prevent deep venous thrombosis (DVT) and subsequent pulmonary embolism, taking into consideration patient comfort and cost effectiveness.

Technical Approach: Patients undergoing open urologic procedures that wish to participate in the study will sign the consent form and will be categorized by specific organ system. Then using a random numbers table, subjects will be randomized to one of two prophylactic groups within that category. One of these modalities is normally used in these procedures. One day prior to the surgery, a duplex venous scan will be performed on both lower extremities. At the time of surgery, the compression devices will be placed on the subjects and be worn for at least 72 hours post operatively and longer if the patient is not fully ambulatory. Duplex scans will be done on each patient on post operative day 3 or 4 and 7. Appropriate therapy will be instituted (anticoagulants) once a diagnosis is made. Once the patient is discharged from the hospital, surveillance for DVT will cease and that patient's involvement in the protocol will end. Incidence of DVT will be compared using chi-square analysis.

Progress: Twenty-nine patients have been entered, all in FY 92.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/087

Status: On-going

Title: Patient-Controlled Analgesia and the Risk of Postoperative Myocardial Ischemia

Start Date: //

Est. Completion Date: Indef.

Department: Surgery

Facility: MAMC

Principal Investigator: MAJ James D. Helman, MC

Associate Investigators:
LTC Michael J. Sborov, MC
D. Mangano Ph.D, M.D.

MAJ Frederick W. Burgess, MC
CPT Ronald L. Hurst, MC

Key Words: analgesia, myocardial ischemia

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To identify the most efficacious post-operative pain modality which will reduce the incidence and or severity of postoperative myocardial ischemia in high-risk patients undergoing noncardiac surgery.

Technical Approach: This study will evaluate the relative effectiveness of IV patient-controlled analgesia (PAC) morphine sulfate and epidural PCA fentanyl alone or combined with dilute local anesthetic for continuous epidural analgesia in patients with coronary artery disease undergoing upper abdominal surgery. Patients will be randomized in a blinded fashion to receive either IV PCA with morphine sulfate or PCA epidural fentanyl and a separate epidural infusion of saline or to PCA epidural fentanyl and a separate epidural infusion of 0.0625% bupivacaine. The effectiveness will be determined by observing the incidence and severity of myocardial ischemia measured electrocardiographically and the incidence of adverse cardiac outcomes: cardiac-related death, myocardial infarction, and ventricular failure.

Progress: This is a new study which has not yet been implemented.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 85/021	Status: On-going
Title: Advanced Trauma Life Support Course		
Start Date: 01/18/85	Est. Completion Date: Indef.	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Christopher R. Kaufmann, MC		
Associate Investigators: COL Stanley C. Harris, MC		MAJ Leslie W. Yarbrough, VC LTC William E. Eggebrotten, MC
Key Words: training protocol, ATLS, Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$1600.00	08/07/92

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: Two training sessions using four goats each were held in FY 92. The principal investigator was changed in July to Dr. Kaufmann due to the reassignment of Dr. Eggebrotten.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/091

Status: On-going

Title: Transurethral Prostatectomy and Associated Erectile Dysfunction

Start Date: 01/03/92

Est. Completion Date:

Department: Surgery

Facility: MAMC

Principal Investigator: CPT Richard W. Knight, MC

Associate Investigators:
COL John N. Wettlaufer, MC

MAJ Kurt L. Hansberry, MC

Key Words: sexual function, prostatectomy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To use objective data to measure erectile function after transurethral prostatectomy.

Technical Approach: All patients who have medical indications for transurethral resection of the prostate (TURP) will be asked to participate in this study, with the expectation of from 100-200 consenting subjects. Prior to undergoing the surgery the subjects would be asked to answer a questionnaire concerning sexual function/dysfunction. They would then undergo three nights of NPT (nocturnal penile tumescence) measurements at home with a computerized device called the Rigiscan. This device measures the "hardness" (rigidity) of the erect penis and the size (width) of the erect penis and records duration and number of events (erections) each night. The subject would then undergo the TURP. Approximately three to six months after the surgery the subjects will again undergo NPT for three nights, just like the before surgery procedure. Pre-op and post-op NPT measurements will be compared to determine any objective change in erectile function. The questionnaire will also be used to determine any subjective change in function.

Progress: Patients continue to be entered.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/042	Status: Terminated
Title: The Effect of Catheter Tunnelling With and Without Addition of a Subcutaneous Cuff on Catheter-Related Sepsis		
Start Date: 04/05/91	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: CPT Michael J. Mooney, MC		
Associate Investigators: MAJ John C. Schilhab, MS LTC Anthony S. Sado, MC SGT Gregory James		
Key Words: catheter sepsis, catheter tunnelling, subcutaneous cuff		
Accumulative MEDCASE Cost: \$0.00	Est. Accumulative OMA Cost: \$0.00	Periodic Review: //

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: Eight patients were entered in this protocol in previous years. The protocol has been terminated because the ICU no longer uses the 3-lumen catheters required for this protocol.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/005	Status: Completed
Title: An Epidemiological Study of Nasopharyngeal Cancer		
Start Date: 10/21/88	Est. Completion Date: Jan 92	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Michael R. Morris, MC		
Associate Investigators: Thomas L. Vaughan, M.D.		LTC Donald B. Blakeslee, MC
Key Words: cancer,nasopharyngeal		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 Madigan patients participated in this study. A paper is being written by the investigators at Fred Hutchinson Cancer Research Center.

Detail Summary Sheet

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

Title: Evaluation of the Rate of Avascular Necrosis Formation Following Austin Bunionectomy: A Follow-up Study

Start Date: 01/03/92

Est. Completion Date:

Department: Surgery

Facility: MAMC

Principal Investigator: CPT Michael T. Neary, MS

Associate Investigators:

CPT Kevin F. Sunshein, MS

MAJ Richard O. Jones, MS

MAJ John W. Van Manen, MC

Rush A. Youngberg, M.D.

Key Words: necrosis, avascular, Austin bunionectomy

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

Study Objective: To determine the rate of first metatarsal head avascular necrosis following bunion surgery in patients having the Austin bunionectomy without lateral soft tissue release and to analyze the validity of the magnetic resonance imaging testing of subjects having had specific first metatarsal head images following osteotomies.

Technical Approach: The records of 10 patients receiving the Austin (head osteotomy) without the release of lateral soft tissue attachments and 20 patients receiving the Austin (head osteotomy) with the release of lateral soft tissue attachments, all of whom received magnetic resonance imaging studies (MRI) of the first metatarsal following osteotomy will be reviewed. A single MRI evaluation is routinely done 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 of the bone. MRI images will be read blindly by a staff radiologist. The parameters to be analyzed are radiographic findings, MRI findings, and anatomic distribution of avascular necrosis. Descriptive statistics will be used to describe the results.

Progress: A prospective study of 12 consecutive patients with hallux abducto valgus deformity in whom an Austin osteotomy without lateral release was performed. One of the 12 patients following Austin osteotomy without lateral release had changes on MRI consistent with avascular necrosis of the first metatarsal head. These results were then compared to a study of 20 patients that had the Austin Osteotomy with lateral release using the Fisher's exact test, and a value of 0.023 was found (95% confidence level). The Austin osteotomy with lateral release significantly increases the risk of developing avascular necrosis of the first metatarsal head and should only be performed in instances where the soft tissue contracture is largely contributing to the hallux abducto valgus deformity.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/092	Status: On-going
Title: Gram Negative Endotoxin Monoclonal Antibody as an Adjunct to Treating Gram Negative Endophthalmitis in the Rabbit		
Start Date: 08/07/92	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: MAJ Vernon C. Parmley, MC		
Associate Investigators:		
COL Thomas H. Mader, MC	CPT (P) Kent Karren, MC	
MAJ Anthony R. Truxal, MC	LCDR John H. Varga, MC	
CPT Curtis S. Hansen, RPH, MSC	CPT Lilia Fannin, MC	
Key Words: monoclonal antibody, endophthalmitis, animal model, Animal Study		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	//

Study Objective: To determine the tolerance of rabbit retina and corneal endothelium to intraocularly administered gram negative endotoxin monoclonal antibody (GNEMA) and to determine if GNEMA, in combination with intraocularly injected antibiotic, is more effective than intraocularly injected antibiotics alone in decreasing the amount of retinal necrosis associated with gram negative endophthalmitis.

Technical Approach: The study will be conducted in two parts. Part one will determine if GNEMA is safe when administered intraocularly. One rabbit will be injected only with a balance salt solution and serve as a control. The other rabbits will receive a specified amount of GNEMA in both eyes, starting at one fourth the required effective systemic dose needed for treating gram negative sepsis and increasing to four times the required systemic dose. The rabbits will be euthanized and their eyes examined histopathologically for evidence of toxicity.

The second part of the study will determine efficacy. Gram negative bacterial endophthalmitis will be reproduced in the rabbits with two species of bacteria. In 16 rabbits, one eye will serve as a control and be treated according to accepted standard of care with vitrectomy and intraocular antibiotics. The other eye will be treated the same except it will also receive the maximum safe amount of GNEMA that can be injected intraocularly. One rabbit will be a non-infected control. After time intervals of one day and one week, the rabbits will be euthanized and their eyes examined for retinal and corneal viability. The study will be blinded to the pathologist performing the determination of viability. A viability score will be determined based on the normal or abnormal appearance of the retina and cornea. The viability score of each group will be compared with the Fisher exact test or Student's t test to determine statistical significance between the two groups.

Progress: This study will be started as soon as the supplies have been received.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/025	Status: Completed
Title: Neuropeptide Levels in Nasal Secretions and Mucosa of Patients with Chronic Sinusitis and Nasal Polyposis		
Start Date: //	Est. Completion Date:	
Department: Surgery	Facility: MAMC	
Principal Investigator: CPT Jonathan A. Perkins, MC		
Associate Investigators: MAJ Michael R. Morris, MC		CPT Domenic M. Canonico, MC COL W. Pierre Andrade
Key Words: sinusitis, polyposis, neuropeptides		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$2000.00	//

Study Objective: To measure by radioimmunoassay technique levels of substance P and calcitonin gene-related peptide in the nasal secretions and nasal mucosa in patients with nasal polyposis and chronic sinusitis.

Technical Approach: The following patients will be studied: 10 with nasal polyposis 10 with chronic sinusitis and 10 without known nasal or paranasal sinus disease. Patients with antibiotic or steroid treatment of underlying nasal disease within the month preceding testing will not be eligible. A thorough history and physical examination will be conducted on each patient and the exact nature of each patient's symptomatology will be noted as well as underlying atopic disease. Any abnormal physical exam findings will be noted. A laboratory evaluation will include a CBC, total eosinophil count, and nasal smear for eosinophils. Each subject will have a specimen of nasal secretions and nasal mucosa collected for evaluation. The nasal mucosa will be tested for protein content. Quantification of neuropeptides, SP, and CGRP will be performed using radioimmunoassay. The mean and standard error of the mean will be used to describe central tendency and variation throughout the study. ANOVA will be used to test for statistical significance.

Progress: Thirty patients were studied per protocol. A paper was presented at the Annual Meeting of the American Rhinologic Society, Sept 92.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/036

Status: Completed

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:

Department: Surgery

Facility: MAMC

Principal Investigator: LTC Michael J. Sborov, MC

Associate Investigators:

MAJ David M. Colonna, MC

LTC Douglas M. Anderson, MC

MAJ Frederick W. Burgess, MC

LTC Joseph J. Mancuso Jr., MC

Key Words: anesthesia, subarachnoid space, baricity, swine, Animal Study

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
08/07/92

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: A total of five animals was studied per protocol. The results from two animals were discarded secondary to catheter dislodgement. The results from the remaining animals demonstrated that higher plasma levels of bupivacaine were present in the animals treated with the mannitol and dextrose containing solutions. This may indicate that the inhomogenous distribution of the hyperbaric solutions contributes to a faster egress of the bupivacaine from the cerebral spinal fluid and a more rapid redistribution into the systemic compartment.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/007	Status: On-going
Title: General Surgery Stapling Familiarization Lab (Swine Model)		
Start Date: 11/21/86	Est. Completion Date: Oct 87	
Department: Surgery	Facility: MAMC	
Principal Investigator: LTC Clifford L. Simmang, MC		
Associate Investigators:		
COL Stanley C. Harris, MC	COL Preston L. Carter, MC	
MAJ Stephen B. Smith, MC	LTC Richard A. Hall, MC	
COL Michael J. Barry, MC	MAJ Michael J. O'Reilly, MC	
LTC James A. Knight, MC	COL Daniel G. Cavanaugh, MC	
COL Charles A. Andersen, MC	LTC Richard M. Dearman, MC	
Key Words: training protocol, stapling, swine, Animal Study		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$500.00	08/07/92

Study Objective: To familiarize residents in General Surgery with the proper use of surgical stapling devices.

Technical Approach: For each laboratory session, two animals will be anesthetized (ketamine HCl 20 mg/kg body weight and atropine 0.088 mg/kg body weight, IM) as a pre-anesthetic. The animals will then be intubated endotracheally and surgical anesthesia will be induced and maintained using a mixture of Halothane and nitrous oxide. Once a surgical level of anesthesia has been achieved, the abdominal cavity will be entered via a midline incision. A demonstration of stapling techniques (under the direct supervision of staff surgeons and representatives from the staple manufacturer) will be performed on the animal by the surgical residents. After the demonstration, all animals will be euthanized without being allowed to recover from anesthesia.

Progress: Four sessions were held in FY 92. Three pigs and 1 goat were used in these sessions. The principal investigator was changed from Dr. Andersen to Dr. Simmang in July 1992.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/015	Status: On-g
Title: Investigation of Cryotreatment on the Epiphysis of Growing Rabbit Bone		
Start Date: 02/16/90	Est. Completion Date: Jan 91	
Department: Surgery	Facility: MAMC	
Principal Investigator: CPT James S. StLouis, MC		
Associate Investigators: COL D. Scott Smith, MC MAJ Michael Tidwell, MC		CPT Harvey Montigo, MC COL Roberto Barja, MC
Key Words: bone,epiphysis,cryotreat,rabbit,Animal Study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$150.00	08/07/92

Study Objective: To determine if cryotreatment to the epiphysis of 6 week old rabbits stunt growth, slow growth, or cause deformity.

Technical Approach: Number or rabbits studied: 15 The lateral aspect of the distal of the right leg will be exposed and the CT-73 cryosurgical system will be applied w microprobe to freeze the area. The left rear leg will be operated in the same manne except the cryoprobe will not be applied. After a six week period for bone growth, th animals will be euthanized. A pathologist will then determine the gross effect on g plates and any deformities present on the right versus the left femur. Microscopic specimens of the cryotreated epiphyses will be examined to evaluate remaining pot growth of microvascular structures and uniformity of cryological effects. Data will evaluated using a paired t test between right and left sides to compare the legs at a alpha level of 0.05.

Progress: This study has not been implemented because the principal investigator been assigned to Children's Hospital in Seattle, WA, for most of his residency.

DETAIL SHEETS FOR PROTOCOLS

FORT ORD MEDDAC

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/081		Status: Complete
Title: A Benefit-Cost/Utility Analysis of Cervical Cytology During Pregnancy				
Start Date: 07/02/92			Est. Completion Date: Sep 2	
Department: FOrd			Facility: MAMC	
Principal Investigator: MAJ Patrick M. Carter, MC				
Associate Investigators: CPT Michael Luszcak, MC			MAJ Thomas C. Coburn, MC	
Key Words: cervical cytology, pregnancy				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	\$0.00
				Periodic Review: //

Study Objective: To determine the cost effectiveness of performing PAP smears as a routine part of the initial prenatal visit.

Technical Approach: In this study, "benefit" refers to overall monetary savings produced by doing the procedure "utility" refers to the health benefits of doing the procedure and is expressed in terms of "well-years" gained and "cost" refers to the direct monetary cost of performing the procedure as well as additional procedures made necessary by the results of the initial procedure, such as repeat PAP smears and colposcopies. In this study, costs of doing antenatal PAP smears will be determined by chart review of all deliveries done by the Family Practice Service at Silas B. Hayes Arm Community Hospital during 1990. The initial PAP smear results, as well as any repeat PAP smears, colposcopies or other procedures done in response to the initial PAP results will be recorded. Monetary benefits due to discovery and treatment of CIN (cervical intraepithelial neoplasia) at a curable stage will be estimated based on published data on incidence of the stages of CIN and invasive cancer, the rates of transition between the stages, and the difference in cost between treating curable and incurable cervical cancer. Utility of the procedure will be calculated based on expected curable cases found by the initial PAP smear that would have progressed to an incurable stage had the prenatal PAP smear not have been done. Well-years gained from this will be calculated from standard life table data with adjustment for morbidity caused by treatment of the lesions. The benefit-cost/utility ratio calculated from this study will be compared with ratios published for other common procedures to determine the relative cost effectiveness of this test.

Progress: The records of 523 patients were studied. It was determined that routine prenatal cervical cytology is significantly less cost effective than most commonly done medical procedures. If medical funding is limited, elimination of this test for women with normal cervical cytology within the previous 2-3 years should be considered. A paper has been submitted to JAMA for consideration for publication.

DETAIL SHEETS FOR PROTOCOLS

FORT WAINWRIGHT, ALASKA

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/054

Status: On-going

Title: Melatonin and Cortisol Secretion in the Arctic, Effects of Photoperiod on Circadian Rhythms and Mood

Start Date: 06/14/91

Est. Completion Date:

Department: Fort Wainwright

Facility: MAMC

Principal Investigator: COL Matthew E Levine, MC

Associate Investigators:

LT Lawrence K. Duffy, USNR

Key Words: melatonin,arctic,photoperiod,circadian rhythm

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:

Study Objective: To establish basic knowledge and understanding of the effects of extreme latitude on the circadian secretory patterns of the primary hormones of the pineal and adrenal glands, and to determine possible effects on mood and behavior.

Technical Approach: Melatonin and serum cortisol levels will be determined on approximately 100 individuals on a quarterly basis, as close to the solstices and equinoxes as practical, at 0200, 0800, 1030, and 1700 hours on those days. Sufficient blood will be obtained for additional endocrine studies, such as reproductive hormones, and possibly thyroid hormones. Subjects will be screened verbally for recent acute stress or geographic changes, and, if either is present, the blood draw will be delayed by one week to allow for diminution of physiologic stress response or readjustment to arctic photoperiod. On the day of the first sampling, a Seasonal Pattern Assessment Questionnaire will be administered. The Beck Depression Inventory will be administered to each subject at each sampling period. Data will be compared with that from other studies at similar and different latitudes. Seasonal variations in hormone levels and mood rating scores will be compared in individual subjects, as well as in the study group. Relationships between mood behavior, endocrine physiology, and season will be subjected to statistical analysis using a repeated measures multi-variate analysis with season and sex as factors, and age as a co-variant. A posteriori multiple contrasts will be made with Bonferroni tests.

Progress: Fifty-one patients have been entered. In FY 92, serial blood samplings were completed in Dec/Jan and Mar/Apr and the Beck Depression Inventories were also administered at those times. Extensive data analyses from these and earlier samplings have been and continue to be performed. Significant diurnal and seasonal variations in hormone secretion patterns have been found in cortisol, melatonin, and testosterone. Preliminary statistical analysis shows strong correlations between hormonal levels (cortisol and melatonin, possibly testosterone) and sleep, fatigue, and probably other behaviors. Cortisol levels in the fall are high at 0200 and 0800 hours.

DETAIL SHEETS FOR PROTOCOLS

LETTERMAN MEDDAC

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/065

Status: On-going

Title: Racial Differences in Responses to the Rorschach Inkblot Test in a Psychiatric Population

Start Date: 05/01/92

Est. Completion Date:

Department: LAMC

Facility: MAMC

Principal Investigator: Lisa M. Tobin, M.A.

Associate Investigators:

CPT James J. Picano, MS

Key Words: Rorschach Inkblot Test, racial differences

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To examine racial differences in responses to the Rorschach Inkblot Test in a clinical population and to determine if such response differences exist, and whether or not they are a function of clinical diagnosis.

Technical Approach: While inquiry has been made into biases inherent in other areas of psychodiagnostic testing, little has been done to examine racial differences in responses to projective measures, such as the Rorschach. The population will be male and female persons evaluated and diagnosed in a military psychiatric inpatient setting. In this study, approximately 40 records of African-American subjects will be matched for diagnosis, age, education SES, and rank to records of Euro-American subjects. All subjects will have a valid Rorschach protocol in the record. Valid Rorschach protocols will be those that contain 14 or more responses and reflect standardized administration procedures. The following psychiatric variables will be obtained: admission, testing and discharge dates, prior hospitalizations, number of days hospitalized medication used as well as presence/absence of medication at the time of testing an estimate of intellectual abilities, and discharge diagnosis. Descriptive statistics such as frequency distributions on a variety of Rorschach variables will be generated and displayed in table form. In addition, descriptive statistics for demographic and psychiatric variables will be generated, both for the total sample and for black and white subject groups separately.

Progress: The investigator is in the process of reviewing the charts.

DETAIL SHEETS FOR PROTOCOLS

U.S. DEPARTMENT OF AGRICULTURE

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 92/001		Status: On-going
Title: Methods for Assessing Vitamin A Status in Healthy Adults				
Start Date: 10/04/91		Est. Completion Date: Jul 92		
Department: USDA		Facility: MAMC		
Principal Investigator: Betty Jo Burri, Ph.D.				
Associate Investigators:		Andrew J. Clifford, Ph.D.		
Key Words: liver,vitamin A,isotope technique				
Accumulative		Est. Accumulative		Periodic Review:
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	//

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

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

Progress: No further work was done on this study in FY 92 due to other higher priority commitments. Fifty-four subjects have been entered in previous years.

DETAIL SHEETS FOR PROTOCOLS

CHILDRENS CANCER STUDY GROUP

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/009		Status: Terminated
Title: CCG 321P4: "6 in 1" Chemotherapy for Children with Newly Diagnosed Advanced Stage Neuroblastoma				
Start Date: 11/18/88		Est. Completion Date: Indef.		
Department: CCG		Facility: MAMC		
Principal Investigator: Edythe A. Albano, M.D.				
Associate Investigators: None				
Key Words: neuroblastoma,chemotherapy				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$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 CCG 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: This protocol has been terminated because there is no longer an investigator registered to conduct CCG protocols at MAMC. No patients were entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/100	Status: Terminated
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: 03/01/91	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/mm³ and those >100,000/mm³ 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 unfavorable blast cell cytogenetics at diagnosis and patients with an m3 day 14 bone marrow response will be non-randomly assigned to delayed intensification.

Progress: This protocol has been terminated because there is no longer an investigator registered to conduct CCNG studies at MAMC. Two patients, entered in previous years, are in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/101

Status: Terminated

Title: 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

Start Date: 03/01/91

Est. Completion Date: May 95

Department: CCG

Facility: MAMC

Principal Investigator: Edythe A. Albano, M.D.

Associate Investigators: None

Key Words: leukemia:lymphoblastic,chemotherapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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 non-randomly 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: This study has been terminated because there is no longer an investigator registered to conduct CCNG studies at MAMC. No patients were entered on this protocol.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/102	Status: Terminated
Title: CCG 1883: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Infants Less Than 12 Months of Age, Phase III		
Start Date: 03/01/91	Est. Completion Date: Dec 93	
Department: CCG	Facility: MAMC	
Principal Investigator: Edythe A. Albano, M.D.		
Associate Investigators: None		
Key Words: leukemia:lymphoblastic,chemotherapy,infant:(<1 YO)		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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 high dose 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: This study has been terminated because there is no longer an investigator registered to conduct CCNG studies at MAMC. No patients were entered in this study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/103		Status: Terminated
Title: CCG 1884: A Comparison of Idarubicin to Daunomycin in A Multi-Drug Treatment of ALL in Marros Relapse				
Start Date: 03/01/91			Est. Completion Date: Indef.	
Department: CCG			Facility: MAMC	
Principal Investigator: Edythe A. Albano, M.D.				
Associate Investigators: None				
Key Words: ALL, idarubicin, daunomycin,				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review	
\$0.00		\$15000.00	07/12/91	

Study Objective: To compare the efficacy and toxicity of Idarubicin (IDR) and Daunomycin (DNM) when used in combination with vincristine (V), prednisone (P), L-asparaginase (L) to induce second marrow remission in children with acute lymphoblastic leukemia (ALL) who have experienced a first marrow relapse while 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 evaluated for the maintenance vs bone marrow transplant question. All patients who achieve remission on VPL-IDR or VPL-DNM 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/m² (calculating each 12.5 mg/m² of IDR as 45 mg/m² of DNM equivalent) or cardiotoxicity occurs (whichever occurs first). It is recommended that patients going to bone marrow transplant not receive more than 450 mg/m² total prior lifetime dose of anthracycline. Maintenance therapy will be continued for 2 1/2 years if the patient remains disease free.

Progress: This protocol has been terminated because there is no longer an investigator registered to conduct CCNG protocols at MAMC. No patients were entered on this

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/076		Status: Terminated	
Title: 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					
Start Date: 05/15/87			Est. Completion Date: May 92		
Department: CCG			Facility: MAMC		
Principal Investigator: Edythe A. Albano, M.D.					
Associate Investigators:			Maj Kip R. Hartman, MC		
Key Words: Hodgkin's disease					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		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: This protocol has been terminated because there is no longer an investigator at MAMC registered to perform CCNG protocols. No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 87/093

Status: Terminated

Title: CCG 134P: Therapy of Acute Lymphoblastic Leukemia in High Risk Patients

Start Date: 09/18/87

Est. Completion Date: Jul 92

Department: CCG

Facility: MAMC

Principal Investigator: Edythe A. Albano, M.D.

Associate Investigators:

Maj Kip R. Hartman, MC

Key Words: leukemia:lymphoblastic

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review
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 with 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 will 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 consist of vincristine, prednisone, and 6-mercaptopurine. CNS prophylaxis during consolidation will include both I.V. high dose methotrexate and intrathecal Ara-C. A 4 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 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 period which will be repeated 4 times, after which all chemotherapy ceases. The first year of 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: This study has been terminated because there is no longer an investigator at MAMC who is registered to conduct CCNG studies. Two patients were entered in the study in previous years. One subject died of the disease and the other is in the follow-up study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/063		Status: Terminated	
Title: CCG 144: Treatment of Acute Lymphoblastic Leukemia in Average Risk Patients					
Start Date: 10/21/88			Est. Completion Date: Jul 93		
Department: CCG			Facility: MAMC		
Principal Investigator: Edythe A. Albano, M.D.					
Associate Investigators:			Maj Kip R. Hartman, MC		
Key Words: leukemia:lymphoblastic					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:		
\$0.00		\$0.00	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: This protocol has been terminated because there is no longer an investigator at MAMC registered to conduct CCNG protocols. One patient was entered in FY 88 and is in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/014		Status: Terminated
Title: CCG 213: Treatment of Newly Diagnosed Acute Non-lymphoblastic Leukemia for Children Greater than One Month but Less than 21 Years of Age				
Start Date: 11/12/87		Est. Completion Date: Jan 94		
Department: CCG		Facility: MAMC		
Principal Investigator: Edythe A. Albano, M.D.				
Associate Investigators:		Maj Kip R. Hartman, MC		
Key Words: leukemia:nonlymphoblastic				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		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: This protocol has been terminated because there is no longer an investigator at MAMC registered to conduct CCNG protocols. One patient, entered previous to FY 90 is in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/112		Status: Terminated	
Title: CCG 461: Intergroup National Wilms' Tumor Study - 4					
Start Date: 09/18/87			Est. Completion Date: Sep 97		
Department: CCG			Facility: MAMC		
Principal Investigator: Edythe A. Albano, M.D.					
Associate Investigators:			Maj Kip R. Hartman, MC		
Key Words: Wilms' tumor					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
			Periodic Review:		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 chemo 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 receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

Progress: This study has been terminated because there is no longer an investigator registered to conduct CCNG studies at MAMC. Two patients, entered in previous years, are in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/067	Status: Terminate
Title: CCG 8602: Idarubicin for Remission Induction in Patients with Leukemia in Children in Second or Subsequent Marrow Relapse		
Start Date: 05/15/87	Est. Completion Date: May 91	
Department: CCG	Facility: MAMC	
Principal Investigator: Edythe A. Albano, M.D.		
Associate Investigators: Maj Kip R. Hartman, MC		
Key Words: leukemia:marrow relapse, idarubicin		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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/m² and as 30 mg/m², 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: This protocol has been terminated because there is no longer an investigator registered to conduct CCNG protocols at MAMC. No patients were entered on this study.

DETAIL SHEETS FOR PROTOCOLS

GYNECOLOGY ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92

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

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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 non-randomized cases. Amonafide will be administered as a slow intravenous infusion over an hour at an initial dose of 300 mg/m² daily for five days. A serial dose escalation up to 450 mg/m² will be used in patient without toxicity after each cycle of therapy until a Grade 1 hematologic toxicity occurs. All patients will receive therapy until disease progression or until adverse effects prohibit further therapy.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 88/082	Status: On-going
Title: GOG 26EE: A Phase II Trial of Didemnin B (NSC #325319) in Patients with Advanced Pelvic Malignancies		
Start Date: 09/16/88	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: cancer:pelvic,didemnin B		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: 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/m² 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 have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/023		Status: On-going
Title: 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				
Start Date: 01/19/90			Est. Completion Date: Indef.	
Department: GOG			Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC				
Associate Investigators: None				
Key Words: cancer:cervix,fazarabine				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$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 $40 \text{ mg/M}^2/\text{day}$ 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 have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/024		Status: Completed	
Title: GOG 26HH: A Phase II Trial of 5-Fluorouracil and Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies					
Start Date: 01/19/90			Est. Completion Date: Indef.		
Department: GOG			Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC					
Associate Investigators: None					
Key Words: cancer:pelvic,5-Fluorouracil,leucovorin					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$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 $<5 \text{ IU}$. Leucovorin will be given in a dose of 20 mg/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 mg/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

Date: 30 Sep 92

Protocol No.: 90/026

Status: On-going

Title: GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia

Start Date: 01/19/90

Est. Completion Date: Indef.

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: trophoblastic neoplasia, DNA, hydatidiform moles

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

03/01/91

Study Objective: To determine: if aneuploidy identifies a subset of high-risk hydatidiform moles; if ploidy status has sufficient predictive value to justify prophylactic chemotherapy of certain molar pregnancies; if proliferative activity, as estimated from cell cycle distribution, has any prognostic value; the number of paraffin blocks that constitutes an appropriate sampling of a molar pregnancy in order to establish presence of aneuploid cell lines; and if ploidy or proliferative index, as measured on either the mole or subsequent biopsy material, can predict the pattern of post-molar gestational trophoblastic neoplasia to be either metastatic or nonmetastatic and the response to various treatment regimens; and to assess persistence of ploidy status by comparing ploidy of molar tissue with ploidy status of subsequent tissue samples obtained after development of post-molar gestational trophoblastic disease.

Technical Approach: Flow cytometry will be used to measure ploidy and proliferative rate on archival tissues on patients identified as having complete hydatidiform mole pregnancies. These patients have previously been identified by entry on GOG Protocol #55. Results of lab measurements on tissue will be compared to clinical characteristics of post molar course, treatment received, if any, and response to such treatment. The incidence of aneuploidy in tissue samples from staging work-up in those patients who have developed persistent gestational trophoblastic neoplasia will be assessed. Information regarding cell cycle kinetics and growth fraction will be used to correlate tumor responses to treatment regimens in consideration of cell cycle phase specificity for various agents.

Progress: Blocks are being submitted for analysis.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/008	Status: On-going
Title: GOG 26II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies		
Start Date: //	Est. Completion Date:	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: pelvic malignancy, 5-Fluorouracil, leucovorin: high dose		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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/m² 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/m²/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

Date: 30 Sep 92

Protocol No.: 91/009

Status: On-going

Title: 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 Squamous Cell Carcinoma of the Cervix

Start Date: //

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer:cervix,squamous cell,chemotherapy,cisplatin,dibromodulcitol

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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/m² every three weeks; Regimen II: cisplatin 50 mg/m² plus dibromodulcitol, 180 mg/m² daily x 5, every three weeks; Regimen III: cisplatin 50 mg/m² plus ifosfamide 5 gm/m² infused over 24 hours plus mesna 6 gm/m² 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

Date: 30 Sep 92

Protocol No.: 91/010

Status: On-going

Title: 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 Stage IV Epithelial Ovarian Carcinoma

Start Date: //

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer:ovarian,chemotherapy,cyclophosphamide,cisplatin,taxol

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

Study Objective: To determine response rate, response duration, and survival in suboptimal Stage III and Stage IV ovarian cancer treated with different platinum-based combination chemotherapy regimens; to evaluate the relative activity of a new combination (cisplatin/taxol) as compared to the standard regimen (cisplatin/cyclophosphamide); to further evaluate the toxicities of the new combination of cisplatin/taxol in this larger patient population; and to compare the relative toxicities and therapeutic indices of the two regimens.

Technical Approach: Patients with established ovarian epithelial cancer, suboptimal (>1 cm in diameter) Stages III and IV who have had optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue submitted for histologic examination, will be eligible. Following optimal initial surgery, patients will be randomized to either cisplatin plus cyclophosphamide or to cisplatin plus taxol given every 21 days for six courses. Patients with partial response, stable disease, or increasing disease will then go off study to be treated on other appropriate GOG protocols. Patients who are clinically free of disease at the completion of therapy will undergo a reassessment laparotomy to determine disease status unless CA-125 is >100. A 21 item patient self-report questionnaire and a five item nurse 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 were entered in FY 91; both are in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/011

Status: On-going

Title: GOG 112: A Randomized Comparison of Chemoprophylaxis Using Methotrexate versus Routine Surveillance in the Management of the High Risk Molar Pregnancy

Start Date: //

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: molar pregnancy, methotrexate, routine surveillance

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To determine the incidence of post-molar trophoblastic disease after evacuation of the high risk molar pregnancy in those patients receiving chemoprophylaxis versus those randomized to usual post-evacuation surveillance; to evaluate the toxicity associated with chemoprophylaxis; and to develop a clinical pathologic scoring system for risk of post-molar trophoblastic disease which highly correlates with the serum free beta HCG assay.

Technical Approach: Patients who are categorized as at high risk for molar pregnancy and who have a gross and microscopically verified diagnosis of classic (true) hydatidiform mole, obtained by evacuation of the uterus with uterine conservation, will be eligible. Patients will be randomized to either a methotrexate prophylactic regimen or surveillance. Patients will have a pelvic ultrasound performed in the two week period prior to evacuation or in the two week period immediately following evacuation. The first HCG serum determination will be performed in the 48 hour period immediately prior to or after evacuation. HCG serum determinations will be repeated weekly. The methotrexate prophylactic regimen (40 mg/m² 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 entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/064

Status: On-going

Title: 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

Start Date: 07/12/91

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer:cervix,hydroxyurea,5-Fluorouracil,cisplatin

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost:

\$0.00

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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 FY 91 in this study; both are in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 89/036

Status: On-going

Title: GOG 93: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)

Start Date: 05/19/89

Est. Completion Date: Indef.

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer:ovarian,chromic phosphate,laparotomy

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$2416.00

Periodic Review:

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

Date: 30 Sep 92	Protocol No.: 88/081	Status: On-going
Title: GOG 106: Evaluation of the Serum Marker, CA-125, in the Management of Carcinoma of the Endometrium		
Start Date: 09/16/88	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: cancer:endometrial,CA-125,serum marker		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 surgical pathologic criteria (stage, grade, sites); to evaluate the efficacy of CA-125 in monitoring response to therapy (surgery, radiation, chemo, hormonal) in endometrial carcinoma; and to evaluate the efficacy of CA-125 in predicting survival and/or recurrence in endometrial cancer.

Technical Approach: Patients with endometrial carcinoma who are eligible for designated concurrently active GOG treatment protocols for endometrial cancer will be eligible. Specific protocols are selected to obtain a population of patients with tumor burdens and risks for recurrence appropriate to accomplish the study objectives. Serum for CA-125 will be collected according to a schema individually developed for each treatment protocol to be consistent with the regimen and anticipated findings. The collection schedules developed will follow the general schema that follows, modified as appropriate: 1. prior to surgery, if surgery is needed; 2. prior to initiation of therapy; 3. prior to each chemotherapy treatment; 4. monthly during hormonal therapy; 5. prior to initiation of postoperative radiation and at two week intervals during therapy; 6. at the completion of therapy; 7. at regular follow-up intervals, approximately every three months for the first year, every four months the second year, and every six months thereafter, on patients who are free of disease; 8. in patients who progress, follow-up blood samples will not be required after progression is well documented and sera at those time points has been obtained. The duration of this study will be determined by the designated concurrently active GOG treatment protocols with five years of follow-up thereafter.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/037		Status: On-going	
Title: 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					
Start Date: 05/19/89			Est. Completion Date: Indef.		
Department: GOG			Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC					
Associate Investigators: None					
Key Words: cancer:endometrial,doxorubicin,cisplatin					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		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/m² IV every three weeks to a maximum total dose of no greater than 500 mg/m². Regimen II: doxorubicin 60 mg/m² IV every three weeks plus cisplatin, 50 mg/m² IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m². 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

Date: 30 Sep 92	Protocol No.: 89/052	Status: On-going
Title: 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		
Start Date: 04/21/89	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: tumor:uterus,ifosfamide,cisplatin,uroprotector mesna		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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/m²/d IV for 5 days plus Mesna 120 mg/2 IV bolus 15 minutes prior to Ifosfamide, first day only; then 1.5 g/m²/d infusion over 5 days; repeated every 21 days. Regimen II: cisplatin 20 mg/m²/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/m² 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

Date: 30 Sep 92		Protocol No.: 89/038		Status: Completed	
Title: GOG 8803: Flow Cytometrically Determined Tumor DNA Content in Advanced Epithelial Ovarian Cancer					
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: cancer:ovarian:epithelial,DNA,flow cytometry					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$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: This study has been completed; GOG will analyze data.

Detail Summary Sheet

Date: 30 Sep 92	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		
Accumulative IEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	03/01/91

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 one) 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

Date: 30 Sep 92		Protocol No.: 89/041		Status: Completed
Title: GOG 8810: Flow Cytometrically Determined DNA Content in Endometrial Carcinoma				
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: cancer:endometrial,DNA,flow cytometry				
Accumulative		Est. Accumulative		Periodic Review:
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	03/01/91

Study Objective: To 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 #33, 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: This study has been completed. GOG will do the data analysis.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/072	Status: Completed
Title: 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		
Start Date: 07/28/89	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: cancer:cervix,HPV,C-MYC,gene expression		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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 c-myc 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 labeled 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 hybridization controls, respectively.

Progress: This study has been completed; GOG will analyze the data.

Detail Summary Sheet

Date: 30 Sep 92

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 Stromal Tumor)

Start Date: 01/03/92

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: tumor:ovarian stroma,chemo,bleomycin,etoposide,cisplatin

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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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-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

Progress: One patient was entered in this study in FY 91 and is in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/085	Status: On-going
Title: GOG 26KK: A Phase II Trial of Merbarone (NSC336628) in Patients with Advanced and Recurrent Epithelial Ovarian Carcinoma		
Start Date: 02/07/92	Est. Completion Date:	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: None		
Key Words: cancer:ovarian:epithelial,merbarone		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. In this protocol, the agent will be merbarone, a thiobarbituric derivative. The intent of the protocol is to determine the efficacy of this agent in patients whose advanced malignancy has been resistant to high priority methods of treatment.

Technical Approach: Only patients with ovary epithelial, cervical, or endometrial cancer will be eligible. Because of severe phlebitis induced by peripheral infusion, each patient must have a central line prior to administration of merbarone. Patients must have adequate hepatic function as demonstrated by bilirubin and SGOT less than 2 x normal and creatinine must be < 1.5 mg, with a creatinine clearance of 60 ml/min. Merbarone will be administered as a continuous IV infusion via central line at a starting dose of 1000 mg/m²/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

Date: 30 Sep 92

Protocol No.: 91/086

Status: On-going

Title: 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 I-A2, I-B and II-A Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection

Start Date: 01/03/92

Est. Completion Date:

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer:cervix,5-Flourouracil,cisplatin,radiotherapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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 FY 91 and is in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 82/073		Status: On-going	
Title: GOG 26A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies					
Start Date: 11/20/81			Est. Completion Date: Indef.		
Department: GOG			Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC					
Associate Investigators: COL William L. Benson, MC			COL Roger B. Lee, MC		
Key Words: malignancy:pelvic					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$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 eligible patients/disease site/drug or combination studied. The design allows replacement of ineffective regimens by newer agents or combinations. Sections relating to specific agents will be sequentially incorporated into this protocol as these agents are studied. Continuing review will be done for each separate protocol. To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy and a granulocyte count $>1500/\text{mm}^3$, 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 92. GOG 26S for closed due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 82/007

Status: On-going

Title: GOG 26C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies

Start Date: 11/20/81

Est. Completion Date: Indef.

Department: GOG

Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators:
COL William L. Benson, MC

COL Roger B. Lee, MC

Key Words: cancer:pelvic,cisplatinum

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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/M² 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 92. Three patients were entered in previous years and have died of their disease.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 83/024	Status: On-going
Title: GOG 26N: A Phase II Trial of Diahydroxyanthracenedione (DHAD) (NSC #30179) (CL232315) in Patients with Advanced Pelvic Malignancies		
Start Date: 11/19/82	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: COL William L. Benson, MC COL Roger B. Lee, MC		
Key Words: cancer:pelvic,DHAD,diahydroxyanthracenedione		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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/M² I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy. This protocol was closed to uterus/MMT patient entry in Aug. 87.

Progress: No patients entered at MAMC in FY 92. In previous years, three patients were entered and all died of the disease.

Detail Summary Sheet

Date: 30 Sep 92

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
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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/M² I.V. once a week. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patients were entered in FY 92. One patient was entered in FY 85 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 84/064 **Status:** Completed

Title: GOG 26S: A Phase II Trial of Teniposide in Patients with Advanced Pelvic Malignancies

Start Date: 06/15/84

Est. Completion Date: Jun 89

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,teniposide

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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/M² 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: This protocol has been closed to patient entry. No patients were entered in FY 92. Two patients were entered in previous years and died of their disease.

Detail Summary Sheet

Date: 30 Sep 92

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 William L. Benson, MC

COL Roger B. Lee, MC

Key Words: cancer:pelvic,ifosfamide,uroprotector mesna

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
03/01/91

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/M² daily for five days and mesna will be given 400 mg/M² 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

Date: 30 Sep 92	Protocol No.: 86/075	Status: On-going
Title: GOG 26W: A Phase II Trial of Echinomycin in Patients with Advanced Pelvic Malignancies		
Start Date: 07/18/86	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,echinomycin		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 eligible for response and toxicity. Each patient will remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		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 William L. Benson, MC		COL Roger B. Lee, MC		
Key Words: cancer:pelvic,gallium nitrate				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$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: Gallium nitrate will be given as a slow intravenous infusion over 30-60 minutes at a dose of 750 mg/m². 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 entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 81/079	Status: On-going
Title: GOG 40: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas		
Start Date: 05/15/81	Est. Completion Date: Indef.	
Department: GOG	Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC		
Associate Investigators: COL William L. Benson, MC COL Roger B. Lee, MC		
Key Words: sarcoma:uterine		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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: This protocol is closed to patient entry. Six patients were entered in previous years with three of them still being followed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 84/033

Status: On-going

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

Start Date: 02/17/84

Est. Completion Date: Dec 88

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: tumor:ovarian,melphalan,cisplatin

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
03/01/91

Study Objective: To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

Technical Approach: Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

Progress: Study closed to patient entry. Ten patients were entered in previous years and are still being followed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 84/074

Status: On-going

Title: 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 Ovary, Pure and Mixed with Other Elements

Start Date: 08/17/84

Est. Completion Date: Jul 89

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:ovarian,teratoma,tumor:sinus,chemo,bleomycin,cisplatin

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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 eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

Progress: One patient entered in FY 91 and still in follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 87/048**Status:** Completed**Title:** 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**Start Date:** 02/27/87**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

Key Words: cancer:endometrial,papillary,debulked,radiation**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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: This study has been closed to patient entry. Two patients were entered at MAMC in FY 88 and both have died of the disease.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/028		Status: On-going	
Title: 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					
Start Date: 11/21/86			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:ovarian,cyclophosphamide,cisplatin,P32					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
			Periodic Review:		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 progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

Technical Approach: The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m² I.V., on day 1 plus cisplatin, 100 mg/m IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

Progress: Five patients have been entered in previous years. Four have died of the disease.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 87/091

Status: On-going

Title: GOG 99: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

Start Date: 07/17/87

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:endometrial,radiotherapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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: Two patients were entered in previous years. Both are in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92	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 William L. Benson, MC COL Roger B. Lee, MC		
Key Words: hydatidiform moles, monoclonal antibody, free beta HCG, PGTD		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	02/07/92

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 entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 81/035

Status: On-going

Title: GOG 41: Surgical Staging of Ovarian Carcinoma

Start Date: 01/16/81

Est. Completion Date:

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:ovarian,surgical staging

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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; one has died of the disease; one has been entered in another study; two have been lost to follow-up; and five are being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 81/118 **Status:** Completed

Title: 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 and IV.

Start Date: 09/18/81

Est. Completion Date:

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:multiple,doxorubicin,cyclophosphamid

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	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 non-measurable 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: This study is closed to patient entry. Five patients were entered in previous years.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 82/036		Status: On-going
Title: GOG 63: A Clinical Pathologic Study of Stages IIB, III, and IVA Carcinoma of the Cervix				
Start Date: 03/19/82			Est. Completion Date:	
Department: GOG			Facility: MAMC	
Principal Investigator: LTC Gordon O. Downey, MC				
Associate Investigators: COL William L. Benson, MC			COL Roger B. Lee, MC	
Key Words: cancer:cervix,pathologic study				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:	Periodic Review:	
\$0.00		\$0.00	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 IIb, III, and IVa carcinoma of the cervix.

Technical Approach: All eligible patients with invasive carcinoma of the cervix, Stages IIb through IVa, will undergo preoperative clinical staging, including traditional staging as permitted by FIGO rules. Extended clinical staging utilizing sonography, lymphangiography, and computerized transaxial tomography are mandatory. When these tests reveal an aortic nodal metastasis, the patient will have a fine needle biopsy; however, if the tests are negative, the patient will have an aortic lymphadenectomy. Patients who have a positive fine needle biopsy or positive aortic lymphadenectomy will undergo scalene node biopsy before consideration for a GOG treatment protocol. It is anticipated that all patients will be considered for entry into a GOG protocol for which they are suitable when such protocols are available.

Progress: This study is closed to patient entry. Four patients have been entered who are still being followed.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 85/090	Status: Completed
Title: GOG 83: A Clinico-Pathologic Study of Simultaneous Endometrial and Ovarian Carcinomas		
Start Date: 09/20/85	Est. Completion Date:	
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:ovarian,cancer:endometrial,clinico-pathologic study		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	03/01/91

Study Objective: To determine the natural history of patients with synchronous adenocarcinoma presenting in both the endometrium 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 concomitant 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: This study has been closed to patient entry. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 83/041

Status: Completed

Title: 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 Therapy, Para Aortic and Common Iliac Lymphadenectomy and Adjunctive Extrafascial Hysterectomy.

Start Date: 02/18/83

Est. Completion Date: Jun 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,radiotherapy,lymphadenectomy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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: This study has been closed to patient entry. One patient was entered in FY 86 who has been lost to follow-up.

Detail Summary Sheet

Date: 30 Sep 92	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:	Est. Accumulative OMA Cost:	Periodic Review: 03/01/91
\$0.00	\$0.00	

Study Objective: To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

Technical Approach: All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

Progress: One patient entered in FY 88 who is still in follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/106		Status: On-going
Title: GOG 101: A Phase II Evaluation of Preoperative Chemoradiation for Advanced Vulvar Cancer				
Start Date: 08/21/87		Est. Completion Date: Indef.		
Department: GOG		Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC				
Associate Investigators: COL William L. Benson, MC		COL Roger B. Lee, MC COL Donald H. Kull, MC		
Key Words: cancer:vulva,chemoradiotherapy				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		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 T3 primary tumor by using preoperative chemoradiotherapy; the survival rate for patients with Stage III or IV-A disease associated with this technique of therapy; the morbidity of a combined chemoradiosurgical approach to advanced vulvar cancer and to attempt to improve survival in patients with N3 groin nodes.

Technical Approach: Patients with primary, previously untreated, histologically confirmed invasive squamous or adenocarcinoma of the vulva clinically determined to be Stage III or IV will be treated with chemoradiation therapy according to the sub-stage. Regimen I: Patients with T4 or unresectable T3 primary tumor and NO or N1 groin nodes will receive a split course of radiation therapy to the vulva by AP-PA fields. Twice daily fractions of 150 cGY will be given on days 1-4 and 1'-4'; once daily fractions of 180 cGY will be given on days 5, 8-12 and 5', 8'-12'. A 1 1/2 to 2 1/2 week split will be allowed between the two courses. Total midplane dose will be 4560 cGY. During the twice daily radiation (days 1-4 and 1'-4'), patients will receive concurrent chemotherapy of 5-FU, 1000 mg/m² over 24 hours, allopurinol, 300 mg p.o., and cisplatin, 50 mg/m² 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 entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/013	Status: On-going
Title: GOG 90: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors		
Start Date: 11/21/86	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: tumor:germ cell:ovary,cisplatin,etoposide,bleomycin,VAC,vincristine,dactinomycin,cyclophosphamide,BEP		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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 SHEETS FOR PROTOCOLS

NATIONAL CANCER INSTITUTE

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 81/033		Status: On-going	
Title: NCI 7602: All Stage IC and II 9A,B,C) and Selected Stage IAii and IBii Ovarian Cancer					
Start Date: 01/16/81			Est. Completion Date: Jun 85		
Department: NCI			Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC					
Associate Investigators: COL William L. Benson, MC			COL Roger B. Lee, MC		
Key Words: cancer:ovarian,surgery,melphalan,radiotherapy					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$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, 1Aii, 1Bii, or 1Ai or 1Bi with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If IIB, IIC, residual disease is found, will be randomized to pelvic radiotherapy plus melphalan alone. If after 18 months of therapy, the patient remains free of disease, chemotherapy will be discontinued. Second look will be done if the patient is free of disease after 18 months of chemotherapy.

Progress: This protocol was closed to patient entry September 1986. Data are still being collected on some patients.

DETAIL SHEETS FOR PROTOCOLS

PEDIATRIC ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/077 **Status:** Terminated

Title: 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 Sarcome or Primitive Neuroectodermal Tumor off Bone, A Phase III Intergroup Study

Start Date: 12/07/90 **Est. Completion Date:** Indef.

Department: POG **Facility:** MAMC

Principal Investigator: Edythe A. Albano, M.D.

Associate Investigators: LTC Howard Davidson, MC

Key Words: bone, Ewing's sarcoma, tumor: neuroectodermal, chemo

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	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 patients treatment 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: This protocol has been terminated due to the departure of the principal investigator. Two patients, entered in previous years, were in the follow-up stage.

DETAIL SHEETS FOR PROTOCOLS

PUGET SOUND ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/079		Status: On-going	
Title: PSOC 615: Intraperitoneal Consolidation Therapy Following Second-Look Operation in Ovarian Cancer					
Start Date: 06/19/87			Est. Completion Date: Indef.		
Department: PSOC			Facility: MAMC		
Principal Investigator: LTC Gordon O. Downey, MC					
Associate Investigators: COL William L. Benson, MC			COL Roger B. Lee, MC		
Key Words: cancer:ovarian,P32,cisplatin,5-Flourouracil					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	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/m²) and 5-FU (1000 mg/m²) through the Tenckhoff catheter every three weeks for a maximum of four doses unless there are unacceptable side effects.

Progress: One patient was entered in FY 87 and is in the follow-up phase.

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 91/066**Status:** On-going**Title:** PSOC 1007: Adriamycin and Cefoperazone for Treatment of Carcinoma and Sarcoma Refractory to Adriamycin**Start Date:** 11/01/91**Est. Completion Date:****Department:** PSOC**Facility:** MAMC**Principal Investigator:** MAJ Paul C. Sowray, MC**Associate Investigators:**

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

Key Words: adriamycin, cefoperazone**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To determine the complete and partial response rates to a combination of adriamycin and cefoperazone in patients who have had progression of non-Hodgkin's lymphoma, small cell lung carcinoma, sarcoma, breast or ovarian carcinoma while on an adriamycin-containing chemotherapeutic regimen or have progressed within six months of receiving such a regimen and to determine the toxicities of the addition of high dose cefoperazone to adriamycin in the treatment of refractory malignant disease.

Technical Approach: Adriamycin has been used extensively in the therapy of a number of malignancies. In many instances, the malignant cells become resistant and adriamycin becomes ineffective and is one of the agents implicated in multiple drug resistance (MDR). Because of its clinical value, the mode of action of adriamycin and the possible mechanisms of drug resistance have been the subject of extensive research. Cefoperazone has been purported to act as a modulator of MDR. It is hoped that high-dose cefoperazone will block the MDR capability of the cancer cells which will allow the adriamycin to remain within the cancer cells for a longer period of time, thereby allowing patients to go back into remission. All patients will receive intravenous cefoperazone weekly at a dose of 5 grams in 30 minutes, followed by a continuous IV infusion for three hours at 4 grams per hour. After the 30 minutes loading dose, patients will be given a bolus of adriamycin. Patients will be reevaluated after eight weeks. Patients will continue on treatment until there is evidence of disease progression; there is a decrease in ejection fraction by MUGA scan to <40% or a fall of 20 percentage points; or the patient develops symptoms of congestive heart failure.

Progress: One patient has been entered at MAMC in FY 91 with no adverse effects.

DETAIL SHEETS FOR PROTOCOLS

SOUTHWEST ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 92/006**Status:** Completed**Title:** SWOG 9016: Study of External Brain Irradiation and Cisplatin/BCNU Followed by BCNU for the Treatment of Primary Malignant Brain Tumors**Start Date:** 02/07/92**Est. Completion Date:****Department:** SWOG**Facility:** MAMC**Principal Investigator:** MAJ Kenneth A. Bertram, MC**Associate Investigators:**

MAJ Paul C. Sowray, MC
MAJ Luke M. Stapleton, MC
MAJ Robert B. Ellis, MC
CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Robert L. Sheffler, MC
MAJ Richard Tenglin, MC
CPT James Hu, MC

Key Words: cancer, brain, cisplatin, BCNU**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To determine whether this regimen (radiation therapy plus BCNU/cisplatin) can be given safely in a cooperative group setting; to demonstrate that adequate accrual can be achieved with this regimen; and to estimate response, disease stabilization rates, and the probability of one year survival.

Technical Approach: Primary brain tumors account for about 2% of neoplastic deaths. Radiation therapy after primary resection is considered to prolong survival. There is in vivo evidence that BCNU prolongs survival at 12 and 24 months and there is in vitro evidence that cisplatin is active against cultured brain tumor cells. Therefore, patients will have the primary brain tumor resected and then begin combined treatment with radiation therapy (180 cGy per treatment fraction, 5940 cGy total or 5 days a week for 6.5 weeks) plus one course of BCNU (180 mg/M²/d) and cisplatin (33 mg/M²/d) concurrent with Days 1-3 of radiation. Subsequent chemotherapy (both cisplatin and BCNU) will be given weeks 7, 13, and 19; and BCNU only will be given weeks 25 and 31.

Progress: This study was closed to patient entry 1 Jul 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/052 **Status:** On-going

Title: SWOG 9031: A Double Blind Placebo Controlled Trial of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Leukemia, Phase III

Start Date: // **Est. Completion Date:** Jun 94

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Kenneth A. Bertram, MC

Associate Investigators:	LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC	MAJ Luke M. Stapleton, 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

Key Words: cancer, leukemia, myeloid

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

Study Objective: To compare the complete response rates and duration of survival in patients 56 or older with acute myeloid leukemia (AML) when treated with standard doses of cytosine arabinoside (Ara-C) and daunorubicin (DNR), with or without recombinant human granulocyte-colony stimulating factor (rhG-CSF); to assess the frequency and severity of toxicities of the two treatment regimens; to compare the duration of neutropenia and thrombocytopenia, the total number of febrile days, the number of days of antibiotic therapy, the number and type of infection episodes, and the number of hospital days in patients treated with or without rhG-CSF; and to correlate biological parameters including cell surface immunophenotype, ploidy, and cytogenetics with clinical response.

Technical Approach: Patients aged 56 and older with AML will be randomized to receive treatment with either Ara-C/DNR plus rhG-CSF or Ara-C/DNR plus placebo (Ara-C days 1-7, C/DNR days 1-3, and blinded drug begins on day 10) Patients who had regrowth of leukemia during this course of treatment will receive a second identical course of treatment except the blinded drug will not be started until the marrow shows <5% blasts. The blinded drug will not be given in the second induction course if the patient has regrowth of leukemia following the first induction course. Following completion of induction therapy, patients who achieve complete remission will be registered to receive two cycles of post-remission therapy, utilizing the same regimen to which they were originally randomized.

Progress: No patient entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/094	Status: On-going
Title: SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary		
Start Date: 02/07/92	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Kenneth A. Bertram, MC		
Associate Investigators: MAJ Paul C. Sowray, MC MAJ Patrick L. Gomez, MC MAJ Robert B. Ellis, MC CPT Jennifer L. Cadiz, MC		LTC Howard Davidson, MC MAJ Luke M. Stapleton, MC MAJ Robert L. Sheffler, MC MAJ Richard Tenglin, MC CPT James Hu, MC
Key Words: cancer:leukemia,cytogenetic studies		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on SWOG protocols and at various times in the course of treatment; to estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients; and to provide quality control for all SWOG cytogenetic data.

Technical Approach: The complex nature and diversity of numerical and structural chromosomal changes in hematologic malignancies have been increasingly recognized in the last 15 years as cytogenetic techniques have improved and the knowledge base expanded. It has been shown that the majority of malignancies have non-random chromosomal anomalies such that specific cytogenetic aberrations are generally associated with particular leukemia subtypes. Previous studies have shown the remarkable consistency of the recurring chromosome abnormalities in the leukemias and their current and potential usefulness as diagnostic and prognostic indicators. Strong correlations with certain clinical immunological and morphologic features have been shown and in certain cases a molecular mechanism has been discovered. Large prospective studies which include responsiveness to the various treatments have not been done and for most leukemias the molecular mechanisms and correlations remain to be elucidated. Patients on this study must be registered on one of the following SWOG protocols: 8326, 8600, 8612, 9034, 9108, and all new leukemia protocols approved as of 1990 by SWOG. Patients will receive treatment as directed by the treatment protocols and the treatment protocols will specify when specimens are to be submitted for cytogenetic analysis. Bone marrow samples will be submitted whenever possible, unless the treatment protocol specifies otherwise. However, if the marrow is not aspirable ("dry tap"), a peripheral blood sample will be submitted. A patient may only be registered on this protocol once. Data will be collected by major categories of leukemia: first line AML, first line ALL, relapsed AML, chronic phase CML, CML patients in acceleration or blast crisis; and hairy cell leukemia. The study will be open for accrual of patients for a minimum of five years. The smallest group of patients (CML in acceleration or blast crisis) is expected to have at least 100 patients by that time.

Progress: One patient has been entered in this study (FY 92).

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/096	Status: On-going
Title: SWOG 9108 (CALGB-9011, NCIC-CTG CL.1): A Phase III Comparison of Fludarabine Phosphate vs Chlorambucil vs Fludarabine Phosphate Plus Chlorambucil in Previously Untreated B-Cell Chronic Lymphocytic Leukemia		
Start Date: 09/06/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Kenneth A. Bertram, MC		
Associate Investigators:		
MAJ Paul C. Sowray, MC	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	
Key Words: cancer:leukemia,B-cell,fludarabine phosphate,chlorambucil		
Accumulative	Est. Accumulative	Periodic Review:
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: No patients have been entered on this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/095	Status: On-going
Title: SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia		
Start Date: //	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Kenneth A. Bertram, MC		
Associate Investigators:		LTC Howard Davidson, MC
MAJ Luke M. Stapleton, MC		MAJ Patrick L. Gomez, MC
MAJ Robert B. Ellis, MC		CPT Jennifer L. Cadiz, MC
MAJ Richard Tenglin, MC		CPT James Hu, MC
Key Words: cancer, myelogenous, leukemia		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To compare the duration of survival in patients with chronic myelogenous leukemia (CML) in blast phase, when treated with either chemotherapy (Ara-C/Daunomycin) alone or chemotherapy plus the resistance modifier, cyclosporine-A (CyA); to estimate the frequency of P-glycoprotein expression and its association with blast lineage and prognosis; and to compare the frequency and severity of toxicity of the two treatment regimens.

Technical Approach: Patients will be randomized to receive treatment with either Ara-C/Daunomycin alone or Ara-C/Daunomycin + CyA. If the day 14 bone marrow shows less than or equal to a 50% reduction in the absolute blast count per 500 cell differential compared with the pretreatment bone marrow, the patient will be considered a treatment failure and removed from the study. If there is more than a 50% reduction in the blast count as stated above, but the patient has not achieved a complete remission or restored chronic phase status, a second course of the original induction regimen will begin on or after day 21. Patients who do not achieve complete remission or restoration of chronic phase after two inductions will be removed from the protocol. Patients who achieve complete remission or restored chronic phase will receive one course of consolidation therapy (same regimen as for induction therapy).

Progress: No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/060 **Status:** Completed

Title: 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.

Start Date: 05/19/89

Est. Completion Date: Jun 92

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Everardo E. Cobos Jr., MC

Associate Investigators:

COL William D. Belville, MC

LTC John A. Vaccaro, MC

MAJ Mark H. Kozakowski, MC

CPT Denis Bouvier, MC

COL Irwin B. Dabe, MC

COL Victor J. Kiesling, MC

LTC Howard Davidson, MC

MAJ Kenneth A. Bertram, MC

Key Words: cancer:bladder,bacillus Calmette-Guerin,DNA,mitomycin-C

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$0.00

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 BCC; 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: This study was closed to patient entry, 15 May 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/087	Status: Completed
Title: SWOG 8910: Evaluation of Low Dose Continuous 5-Fluorouracil (5-FU) and Weekly Cisplatinium (CCDP) in Advanced Adenocarcinoma of the Stomach		
Start Date: 06/15/90	Est. Completion Date: Jun 93	
Department: SWOG	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
MAJ Paul C. Sowray, MC	MAJ Everardo E. Cobos Jr., MC	
CPT Denis Bouvier, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
Key Word cancer:stomach,5-Fluorouracil,cisplatinium		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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: This study was closed to patient entry 1 Aug 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/047		Status: On-going	
Title: SWOG 8854: Prognostic Value of Cytometry Measurements of Breast Cancer DNA from Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814					
Start Date: 03/16/90			Est. Completion Date: Mar 98		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators: None					
Key Words: cancer:breast,DNA,cytometry,postmenopausal					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$0.00		10/19/90	

Study Objective: To determine if ploidy analysis of breast cancer by routine clinical flow cytometry (CFM) technique can predict response to therapy and survival of patients registered to SWOG 8814 and to determine if ploidy analysis by image processing technique more accurately predicts patient response to therapy and survival than ploidy analysis by flow cytometry.

Technical Approach: Two paraffin blocks, one representing the highest grade region of the primary tumor, the second representing the highest grade regional metastasis in a positive lymph node, will be used. From each of these blocks, two to five sections will be cut and a nuclear suspension prepared. From each suspension, a cytospin preparation will be prepared and stained with Dif-Quik to ensure that the cells present in the H & E slide are represented adequately in the nuclear preparation. A second cytospin preparation will be prepared for staining by the Feulgen technique for image processing DNA analysis. The remainder of the nuclear preparation will be stained with propidium iodide following RNase digestion for FCM DNA analysis. Cox regression modeling will be used to explore the prognostic value of ploidy status as determined by FCM and by image processing, in conjunction with the covariates tumor size, age, ER and PgR levels, and number of nodes.

Progress: This is a companion study using tissue from SWOG 8854. Samples from four patients have been studied.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 88/003

Status: On-going

Title: SWOG 8520: Cis-Diamminedichloroplatinum (II), Methotrexate and Bleomycin in the Treatment of Advanced Epidermoid Carcinoma of the Penis, Phase II

Start Date: 12/11/87

Est. Completion Date: Sep 90

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC

MAJ David M. Dunning, MC

CPT Denis Bouvier, MC

MAJ Thomas M. Baker, MC

LTC Lauren K. Colman, MC

MAJ Ruben D. Sierra, MC

COL William D. Belville, MC

Key Words: cancer:penis,cis-diamminedichloroplatinum,methotrexate,bleomycin

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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/M², 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/M², IV bolus on days 1 and 8 and bleomycin, 10 units/M², IV bolus on days 1 and 8. Courses will be repeated every 21 days provided absolute granulocyte count is >1500/ ml and platelet count is >100,000/ ml. Dosage modifications will be made for all three drugs following the initial and all subsequent cycles of chemotherapy, using standard Southwest Oncology Group chemotherapy toxicity criteria for any of the following toxicities: hematopoietic, renal, pulmonary, and neurotoxicity. Chemotherapy with bleomycin will be discontinued when a total cumulative dose of 200 units/M² has been reached. Two cycles of chemotherapy will constitute an adequate trial. Patients with stable or responding disease will continue on treatment beyond two cycles until evidence of disease progression or unacceptable toxicity. Patients who have achieved a complete remission will discontinue all chemotherapy after six cycles. Patients who achieve a complete response will receive 6 courses of treatment.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 87/033		Status: On-going	
Title: SWOG 8501 (INT 0051): Intraperitoneal Cis-platinum/IV Cyclophosphamide vs IV cis-platinum/IV Cyclophosphamide in Patients with Non-measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III , Intergroup					
Start Date: 02/28/87			Est. Completion Date: Dec 89		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators:					
COL Irwin B. Dabe, MC			MAJ Thomas M. Baker, MC		
MAJ David M. Dunning, MC			LTC Lauren K. Colman, MC		
CPT David R. Bryson, MC			MAJ Ruben D. Sierra, MC		
			COL Roger B. Lee, MC		
Key Words: cancer:ovarian,chemotherapy,IP,IV cyclophosphamide,cisplatinum					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:		OMA Cost:			
\$0.00		\$0.00		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/m² plus IV cyclophosphamide, 600 mg/m² every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m² plus IV cyclophosphamide, 600 mg/m², every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

Progress: This study was closed to patient entry 15 Jul 92. One patient was entered in Dec 86 and refused second-look surgery so he was taken off protocol. This patient is still alive and is being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/021		Status: Completed
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 Ruben D. Sierra, MC COL William D. Belville, MC			MAJ Thomas M. Baker, MC MAJ David M. Dunning, MC CPT Denis Bouvier, MC	
Key Words: cancer:renal cell, resectable Alfa-nl, adjuvant treatment				
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:	\$0.00
				Periodic Review: 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: This study was closed to patient entry, 8 Apr 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 85/073 **Status:** On-going

Title: SWOG 8590: Phase III Study to Determine the Effect of Combining
Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell
Carcinoma of the Head and Neck, Phase III (Intergroup Group)

Start Date: 08/23/85 **Est. Completion Date:** May 87

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	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	

Key Words: head & neck, surgery, chemotherapy, radiotherapy

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	10/19/90

Study Objective: To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

Technical Approach: After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cisplatinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

Progress: This study was closed to patient entry 1 Feb 90. Three patients were entered and are still being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 85/008		Status: Completed	
Title: SWOG 8300: Treatment of Limited Non-small Cell Lung Cancer: Radiation versus Radiation Plus Chemotherapy (FOMi/CAP), Phase III					
Start Date: 11/16/84			Est. Completion Date: Oct 86		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators:			MAJ Thomas M. Baker, MC		
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
CPT David R. Bryson, MC					
Key Words: cancer:lung:non-small cell,radiation,chemotherapy					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$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 rad.

Progress: This study was closed to patient entry 1 Mar 88. Three patients entered and all have expired from their disease.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 85/064	Status: On-going
Title: SWOG 8591: NCI Intergroup #0035, An Evaluation of Levamisole Alone or Levamisole plus 5-Fluorouracil as Surgical Adjuvant Treatment for Resectable Adenocarcinoma of the Colon, Phase III - Intergroup		
Start Date: 06/28/85	Est. Completion Date: Apr 87	
Department: SWOG	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
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	
Key Words: cancer:colon,levamisole,5-Fluorouracil		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: -\$0.09	OMA Cost: \$0.00	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 and six are still being followed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 84/019

Status: Completed

Title: SWOG 8221: Treatment of Advanced Bladder Cancer with Preoperative Irradiation and Radical Cystectomy versus Radical Cystectomy Alone, Phase III

Start Date: 12/14/83

Est. Completion Date: Oct 85

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Donald H. Kull, MC

COL Irwin B. Dabe, MC

MAJ Alfred H. Chan, MC

MAJ Michael D. Stone, MC

COL William D. Belville, MC

COL Friedrich H. Stutz, MC

MAJ Thomas M. Baker, MC

MAJ Timothy J. O'Rourke, MC

Key Words: cancer:bladder,cystectomy,radiotherapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
10/19/90

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 rad 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 1 Nov 89. One patient was entered at MAMC in 1984. The patient was randomized to cystectomy alone and expired in June 1992.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 84/018 **Status:** On-going

Title: SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer

Start Date: 12/14/83 **Est. Completion Date:** Sep 85

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	COL William D. Belville, MC
COL Friedrich H. Stutz, MC	COL Irwin B. Dabe, MC
MAJ Thomas M. Baker, MC	MAJ Alfred H. Chan, MC
MAJ Timothy J. O'Rourke, MC	MAJ Michael D. Stone, MC

Key Words: cancer:bladder,BCG,adriamycin

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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: This study was closed to patient entry, 20 Dec 85. Three subjects were entered in 1984. All three are still alive and being followed.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/069	Status: On-going
Title: SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study		
Start Date: 01/03/92	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
MAJ Paul C. Sowray, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Rahul N. Dewan, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Steven S. Wilson, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
Key Words: cancer:rectum,5-Fluorouracil,leucovorin,levamisole		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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 was entered in FY 91 and two were entered in FY 92.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/084

Status: On-going

Title: SWOG 8719: Evaluations of Didemnin B or Ifosfamide/Mesna in Endocrine Resistant Prostate Cancer and of Ifosfamide/Mesna in Patients Without Prior Endocrine Manipulation, Phase II

Start Date: 06/15/90

Est. Completion Date: May 92

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Mark H. Kozakowski, MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

Key Words: cancer:prostate,Didemnin B,Ifosfamide,Mesna,endocrine resistance

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$0.00

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 entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 83/056

Status: On-going

Title: SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study

Start Date: 03/18/83

Est. Completion Date: Feb 85

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Friedrich H. Stutz, MC

MAJ Timothy J. O'Rourke, MC

MAJ Thomas M. Baker, MC

LTC James E. Congdon, MC

COL Irwin B. Dabe, MC

MAJ Alfred H. Chan, MC

Key Words: cancer:breast,surgery,biological parameters

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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 disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

Technical Approach: Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

Progress: This study was closed to patient entry 15 May 88. Eleven patients were entered at MAMC with data still being collected on 10 patients.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 88/032 **Status:** Completed

Title: 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

Start Date: 02/19/88

Est. Completion Date: Feb 91

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Thomas M. Baker, MC

MAJ Ruben D. Sierra, MC

COL Irwin B. Dabe, MC

MAJ David M. Dunning, MC

CPT Denis Bouvier, MC

Key Words: leukemia:acute,chronic granulocytic,chemotherapy,Ara-C

Accumulative

MEDCASE Cost: \$0.00

Est. Accumulative

OMA Cost: \$0.00

Periodic Review:

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/M², IV infusion every 12 hrs for 6 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/M²/day on days 7, 8, and 9; or ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/M²/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/M², IV infusion every 12 hrs for 3 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/M²/day on day 1; and ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/M²/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: Section 8326 of this study was closed to patient entry 1 May 92. Section 8327 was left open to responders to Section 8326. Since there were no patients on Section 8326, the protocol was completely closed at MAMC.;Two patients were entered on this study in 1988 and both expired within a few months of entry.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/053		Status: Completed	
Title: SWOG 8515: Evaluation of Menogaril (NSC 269148) in Non-Hodgkin's Lymphoma, Phase II					
Start Date: 05/20/88			Est. Completion Date: Apr 91		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators:			COL Irwin B. Dabe, MC		
MAJ Thomas M. Baker, MC			MAJ David M. Dunning, MC		
MAJ Ruben D. Sierra, MC			CPT Denis Bouvier, MC		
Key Words: lymphoma:non-Hodgkin's,menogaril					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	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/M² 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/ml and a platelet count >100,000/ml. 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/ml or thrombocytopenia <50,000/ml, 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: This study was closed to patient entry, 1 Dec 91. One patient had been entered on this study in 1988 and expired 18 months later from the disease. Drug induced phlebitis was reported in this patient.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 87/107 **Status:** On-going

Title: SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III

Start Date: 03/19/88 **Est. Completion Date:** Aug 90

Department: SWOG **Facility:** MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	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

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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 disease free status in patients treated with BCG immunotherapy.

Technical Approach: Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG administration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenance or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study.

Progress: This study was closed to patient entry 15 Dec 88. Eleven patients were entered in the study and 10 are still being followed. One patient was taken off study due to severe urticarial reactions to BCG and one patient was taken off study due to severe hematuria attributed to BCG.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 88/066

Status: On-going

Title: SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)

Start Date: 07/15/88

Est. Completion Date: Jun 91

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
CPT Denis Bouvier, MC

COL Irwin B. Dabe, MC

Key Words: Hodgkin's Disease, chemotherapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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/M² IV, days 1 and 8, Vincristine, 1.4 mg/M² IV, days 1 and 8, Procarbazine, 100 mg/M² PO per day x 14 days, Prednisone 40 mg/M² PO per day x 14 days. ABVD: Adriamycin, 25 mg/M² IV, days 1 and 15, Bleomycin, 10 units/M² IV, days 1 and 15, Vinblastine, 6 mg/M² IV days 1 and 15, DTIC, 375 mg/M² IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/M² IV day 8; bleomycin, 10 units/M² IV day 8; and vinblastine, 6 mg/M² IV, day 8.

Progress: This study was closed to patient entry, 1 Aug 89. One patient was entered in Nov 88 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 88/065		Status: On-going	
Title: SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy					
Start Date: 11/18/88			Est. Completion Date: Jun 91		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators: CPT Denis Bouvier, MC MAJ Rahul N. Dewan, MC			COL Irwin B. Dabe, MC MAJ Steven S. Wilson, MC		
Key Words: lymphoma:non-Hodgkin's,radiotherapy,CHOP,chemotherapy					
Accumulative MEDCASE Cost:		\$0.00	Est. Accumulative OMA Cost:		\$0.00
					Periodic Review: 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 non Hodgkin's lymphoma of intermediate or high grade histology except lymphoblastic lymphoma. Patients must have had all visible tumor removed (excisional biopsy) and must have clinically adequate liver and myocardial function to begin treatment at full doses. Patients with known central nervous system disease, previous cancer with a possibility for recurrence which might affect survival or prior chemo or radiotherapy will be ineligible. All patients will be stratified at the time of initial registration by the following: (1) age (<65 years vs >65 years); (2) Stage (I or Ie vs nonbulky II or IIe); (3) histology (diffuse large cell vs other); (4) location of disease (GI involved vs non-GI, abdominal vs non-GI, other); (5) all disease resected vs residual measurable disease. Patients will be randomized to CHOP* (Arm I) or to CHOP plus radiation therapy (Arm II). A complete course of chemotherapy on Arm I will consist of the administration of CHOP every 21 days for eight consecutive cycles unless progressive disease develops. A complete course of chemotherapy for Arm II will consist of the administration of CHOP every 21 days for three consecutive cycles unless progressive disease develops. Radiation therapy will begin immediately after the third cycle of CHOP. Radiation therapy dose, duration, and treatment volume will be determined jointly by the radiation oncologist and the medical oncologist. All patients will be followed at three month intervals until death. CHOP: Cyclophosphamide, 750 mg/M² IV, day 1; Doxorubicin, 50 mg/M² IV, day 1; Vincristine, 1.4 mg/M² IV, day 1; Prednisone, 100 mg/day po, days 1-5.

Progress: Two patients were entered in FY 92 for a total of six entries. All of these patients are being followed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 88/076

Status: On-going

Title: SWOG 8738: Treatment of Extensive Non-small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III

Start Date: 09/16/88

Est. Completion Date: Sep 91

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Mark H. Kozakowski, MC

MAJ Kenneth A. Bertram, MC

COL Irwin B. Dabe, MC

CPT Denis Bouvier, MC

Key Words: cancer:lung:non-small cell,cisplatin,mitomycin-C

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

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 arms: Arm I: standard dose cisplatin (50 mg/M², IV) every four weeks for a maximum of eight cycles; ARM II: high dose cisplatin alone (100 mg/M², IV) every four weeks for a maximum of four cycles; ARM III: high dose cisplatin (100 mg/M² IV) plus mitomycin-C (8 mg/M² IV) given every four weeks for a maximum of four cycles. All patients will have an initial assessment of response after two cycles and then reassessment after four cycles of therapy. Patients on Arm I who respond to treatment may receive continued therapy to a maximum of eight cycles. Upon progression of disease, unacceptable toxicity, or patient request, patients will be taken off treatment. All patients will be followed until death.

Progress: This study was closed to patient entry 1 Jun 90. Five patients were entered at MAMC. Three have died of their disease and two are still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 89/021 **Status:** On-going

Title: SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin = 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in Selected Patients with Dukes's B or C Colon Cancer - 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

MAJ Kenneth A. Bertram, MC

COL Irwin B. Dabe, MC

CPT Denis Bouvier, MC

MAJ Everardo E. Cobos Jr., MC

Key Words: cancer:colon,resection,chemotherapy,leucovorin,levamisole

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$50.00

Periodic Review:

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/m² + 5-FU 425 mg/m²; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m² + 5-FU 600 mg/m²; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

Progress: Four patients were entered in this study in FY 92 for a total of 17 entries. One patient has died from the disease.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 89/058

Status: On-going

Title: SWOG 8692 (INT 0075): Therapy in Premenopausal Women with Advanced, ER Positive or PgR Positive Breast Cancer: Surgical Oophorectomy vs the LH-RH Analog, Zoladex: Phase III, Intergroup

Start Date: 05/19/89

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Mark H. Kozakowski, MC

MAJ Kenneth A. Bertram, MC

COL Irwin B. Dabe, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

Key Words: cancer:breast,surgical oophorectomy,Zoladex,ER,PgR positive

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 89/045		Status: On-going	
Title: SWOG 8621: Chemohormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III					
Start Date: 03/17/89			Est. Completion Date: Mar 92		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators:			COL Irwin B. Dabe, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
CPT Denis Bouvier, MC			MAJ Kenneth A. Bertram, MC		
Key Words: cancer:breast,postmenopausal,chemohormonal therapy					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:		\$0.00	OMA Cost:		\$2316.00
					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. One patient was entered in May of 91 and is alive and well.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/027

Status: On-going

Title: SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor-Positive Breast Cancer - Intergroup

Start Date: 02/16/90

Est. Completion Date: Dec 99

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

Key Words: cancer:breast,chemotherapy,chemohormonal therapy,premenopausal

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$8200.00

Periodic Review:

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: Three patients were entered in FY 92. All are being followed. No patients were entered in previous years.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/029	Status: On-going
Title: SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History...		
Start Date: 01/19/90	Est. Completion Date: Jan 93	
Department: SWOG	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, 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: cancer:breast,chemotherapy,endocrine therapy		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$5000.00	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: Five patients were entered in this study in FY 92 for a total of nine entries. All patients are alive and being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/056		Status: On-going	
Title: SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide					
Start Date: 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					
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:	
\$0.00		\$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.

Progress: This study was closed to patient entry, 9 Apr 92. Two patients were entered in FY 91 and are still being followed.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/065	Status: Completed
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 Paul C. Sowray, 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: hepatoma,merbarone		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$0.00	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: This study was closed to patient entry, 1 May 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 90/086**Status:** On-going**Title:** SWOG 8894: (INT-0105, EST-2889): A Comparison of Bilateral Orchiectomy with or without Flutamide for the Treatment of Patients with Histologically Confirmed Stage D2 Cancer**Start Date:** 06/15/90**Est. Completion Date:** Apr 93**Department:** SWOG**Facility:** MAMC**Principal Investigator:** LTC Howard Davidson, MC**Associate Investigators:**

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

LTC John A. Vaccaro, MC

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

Key Words: cancer:prostate,orchiectomy,flutamide**Accumulative****MEDCASE Cost:**

\$0.00

Est. Accumulative**OMA Cost:**

\$0.00

Periodic Review:

10/19/90

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: No patients were entered in this study in FY 92. Two patients had previously been entered. One patient is still being followed.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/080	Status: On-going
Title: SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Lymph Nodes and Positive Hormone Receptors.		
Start Date: 10/20/89	Est. Completion Date: Sep 99	
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	
	MAJ Robert L. Sheffler, MC	
Key Words: cancer:breast,chemoendocrine therapy,CAF,tamoxifen		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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: Five patients have been entered in this study (none in FY 92). All are in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92**Protocol No.:** 92/079**Status:** On-going

Title: SWOG 8925: Evaluation of Cisplatin + VP-16 Followed by Mitotane at Progression if no Prior Mitotane or Cisplatin + VP-16 Only if Prior Treatment with Mitotane in Patients with Advanced and Metstatic Adrenal Cortical Carcinoma

Start Date: //**Est. Completion Date:** Jul 97**Department:** SWOG**Facility:** MAMC**Principal Investigator:** LTC Howard Davidson, MC**Associate Investigators:**

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert L. Sheffler, MC

MAJ Richard Tenglin, MC

MAJ Paul C. Sowray, MC

MAJ Kenneth A. Bertram, MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

CPT James Hu, MC

Key Words: cancer, adrenal, cisplatin, mitotane, VP-16**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To evaluate response and response duration of patients with adrenocortical carcinoma treated with combination chemotherapy consisting of cisplatin and etoposide and of patients who receive mitotane after progression on the above chemotherapy (if no prior treatment with mitotane); to evaluate the qualitative and quantitative toxicities of these therapies; and to evaluate and compare tumor morphology of patients with rare tumor.

Technical Approach: Patients will be placed in one of two treatment groups. Patients in Group A will not have received any prior chemotherapy. Patients in Group B will have received prior treatment with Mitotane. Eligible patients in Group A and Group B will be treated with cisplatin plus etoposide every 21 days for a total of 12 months or until progression of disease occurs. Group A patients who develop progressive disease will be treated with Mitotane. Group B patients who progress will be taken off protocol.

Progress: No patients have been entered on this study.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 84/059		Status: On-going	
Title: SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III					
Start Date: 05/18/84			Est. Completion Date: May 86		
Department: SWOG			Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC					
Associate Investigators:			COL Friedrich H. Stutz, MC		
COL Irwin B. Dabe, MC			MAJ Thomas M. Baker, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
Key Words: cancer:breast,chemotherapy,emergency room					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:		\$0.00	OMA Cost:		\$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 post-mastectomy and randomly assigned to receive: Arm I a tapering course of oral prednisone for 6 weeks, weekly IV vincristine for 10 weeks, weekly IV methotrexate, and weekly IV 5-FU plus daily oral cyclophosphamide for a total of one year; or Arm II four cycles of adriamycin (IV day 1), cyclophosphamide (IV day 1), 5-FU (IV days 1 and 8), and methotrexate (IV day 22). Each cycle will be five weeks and total duration of therapy in this arm is approximately 20 weeks. Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy. Added to this protocol will be a sub-study to determine the prognostic significance of circulating human mammary epithelial antigens. This will involve blood tests prior to chemotherapy and then once every three months.

Progress: This study was closed to patient entry 15 Jun 90. Three patients were entered at MAMC and one patient (entered Mar 86) is still being followed.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 79/096

Status: On-going

Title: SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III

Start Date: 09/21/79

Est. Completion Date: Sep 81

Department: SWOG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
Suresh B. Katakhar, M.D., DAC

COL Friedrich H. Stutz, MC
COL Irwin B. Dabe, MC

Key Words: cancer:breast,chemotherapy,modality therapy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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 1yr pre- or postmenopausal ER patients. (2) CMFVP for 2 yr pre- or postmenopausal ER patients. (3) CMFVP for 1 yr premenopausal ER+ patients. (4) Oophorectomy + CMFVP premenopausal ER+ patients. (5) Tamoxifen alone for 1 yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for 1 yr postmenopausal ER+ patients. Patients undergoing segmental mastectomy (lumpectomy) will receive 6 weeks radiation therapy in addition to the treatment they are randomized to receive.

Progress: This study was closed to patient entry, 15 Aug 89. Thirty-five subjects have been entered, with 25 of these subjects alive and still being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 78/047		Status: On-going
Title: SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6				
Start Date: 07/31/78		Est. Completion Date: Jan 88		
Department: SWOG		Facility: MAMC		
Principal Investigator: LTC Howard Davidson, MC				
Associate Investigators: LTC H. Irving Pierce, MC		COL Friedrich H. Stutz, MC Suresh B. Katakhar, M.D., DAC		
Key Words: Hodgkin's disease:Stages III & IV,chemotherapy,modality RX				
Accumulative MEDCASE Cost:		Est. Accumulative OMA Cost:		Periodic Review:
\$0.00		\$0.00		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: This study was closed to patient entry 1 Dec 87. Seven patients were entered at MAMC with data still being collected on five of them.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/039

Status: On-going

Title: SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC +
Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-
1877, CALGB-8891)

Start Date: 02/16/90

Est. Completion Date: Mar 92

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Rodney C. Davis, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

LTC Howard Davidson, MC

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

Key Words: cancer:bladder,cystectomy,M-VAC

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
10/19/90

Study Objective: To study insulin induced hypoglycemia as a model of acute stress and to determine if the change in testosterone seen with acute stress is related to cortisol alone or whether it can also be seen with the stimulation of other adrenal precursor products.

Technical Approach: Ten healthy male volunteers (18-35 years) who are without evidence of current acute or chronic illness will have an insulin tolerance test done with blood samples drawn for cortisol, testosterone, immunoactive LH, bioactive LH, estradiol and glucose, every 15 minutes for one hour prior to the human insulin bolus to establish baseline values. Blood samples will continue to be drawn every 15 minutes for 180 minutes after injection of the insulin. SHBG will be measured on the first and last sample and endorphin levels will be measured at baseline and at times corresponding to maximal hypoglycemia. A standard multiple dose metyrapone test will be performed one month from the insulin tolerance test. Just before the first dose and four hours after the last dose, serum samples will be obtained for cortisol, estradiol, immunoactive LH, bioactive LH, testosterone, ACTH, SHBG, endorphins, and 11-deoxycortisol. The relationship of bioactive LH to immunoactive LH will be compared using the biologic to immunologic ratio both before and during the acute stress. The data from the metyrapone test will be used to determine if metyrapone can cause a decrease in serum testosterone acutely. Again, the B/I ratio will be compared pre and post-test. Changes in serum concentrations of the measured hormones will be analyzed by repeated measure analysis of variance.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/040 **Status:** On-going

Title: SWOG 8793 (EST-3883): Randomized Phase III Evaluation of Hormonal Therapy versus Observation in Patients with Stage D1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prostatectomy

Start Date: 02/16/90

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Rodney C. Davis, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

LTC Howard Davidson, MC

MAJ Mark H. Kozakowski, MC

MAJ Patrick L. Gomez, MC

MAJ Kenneth A. Bertram, MC

LTC John A. Vaccaro, MC

Key Words: cancer:prostate,hormonal therapy,lymphadenectomy

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
10/19/90

Study Objective: To determine the time to progression and survival in patients with histologically confirmed Stage D1 adenocarcinoma of the prostate, following radical prostatectomy and pelvic lymphadenectomy, treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy; to determine the effect of early hormone therapy on local control of D1 prostate cancer; to determine whether the effects of hormonal manipulation on progression or patterns of failure are modified by tumor grade, prior TUR, number and grade of involved nodes; to determine if an initially elevated acid phosphatase level predicts a poor response to therapy; to determine whether pretreatment hypogonadism is predictive of a poor response to hormonal therapy; and to evaluate the role of the prostate specific antigen in assessing response, progression, and survival.

Technical Approach: Patients must have undergone a radical prostatectomy within 12 weeks prior to randomization and must have no evidence of disease. Patients with a history of previous hormonal, radiation, systemic or intravesical chemotherapy, a history of other neoplasms in the past 5 years, and those previously treated for prostate cancer (except for prostatectomy and/or pelvic lymph node dissection) are ineligible. Patients will be randomized to hormonal therapy (Zoladex or orchiectomy) or to observation. The treating physician, after consultation with the patient, will determine if the patient receives Zoladex or orchiectomy therapy. Patients randomized to observation, who subsequently progress systemically, will have hormonal management instituted within 6 weeks of systemic progression. Patients randomized to hormonal therapy or who are later put on hormonal therapy will be taken off study if disease progression occurs.

Progress: No patients have been entered at MAMC. Groupwide, mild renal toxicity, hot flashes, and neurologic toxicity have been common.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/067

Status: On-going

Title: SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients

Start Date: 06/14/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Paul C. Sowray, MC
MAJ Robert L. Sheffler, MC
CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC
MAJ Everardo E. Cobos Jr., MC
MAJ Robert B. Ellis, MC

Key Words: cancer:head & neck,cytometry,DNA

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.

Technical Approach: Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck.

Progress: No patients have entered this study.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/054

Status: On-going

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

Start Date: 04/20/90

Est. Completion Date: Mar 93

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Kenneth A. Bertram, MC

MAJ Michael R. Morris, MC

LTC Howard Davidson, MC

MAJ Mark H. Kozakowski, MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

Key Words: cancer:head & neck,DNA,5-Fluorouracil,cisplatinum

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$8200.00

Periodic Review:

10/19/90

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 have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/055	Status: On-going
Title: SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III		
Start Date: 04/20/90	Est. Completion Date: Mar 93	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Patrick L. Gomez, MC		
Associate Investigators:		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Mark H. Kozakowski, MC	
MAJ Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
MAJ Michael R. Morris, MC	MAJ Robert L. Sheffler, MC	
Key Words: cancer:nasopharyngeal,5-Fluorouracil,cisplatin,radiotherapy		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$3900.00	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 in this study in FY 91 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/110 **Status:** Completed

Title: SWOG 8915: A Phase II Study of 6-Thioguanine Administered as 120 Hour Continuous Infusion for Refractory or Recurrent Small Cell Carcinoma

Start Date: 10/19/90

Est. Completion Date: Apr 93

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Kenneth A. Bertram, MC

LTC Howard Davidson, MC

MAJ Mark H. Kozakowski, MC

CPT Denis Bouvier, MC

MAJ Robert L. Sheffler, MC

Key Words: cancer:small cell,6-thioguanine,continuous infusion

**Accumulative
MEDCASE Cost:**

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

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/M²/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: This study was closed to patient entry 15 Dec 91. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/007

Status: On-going

Title: SWOG 8957: Feasibility Trial of Post-Operative Radiotherapy Plus Cisplatin Followed by Three Courses of 5-FU Plus Cisplatin in Patients with Resected Head and Neck Cancer, Phase II Pilot

Start Date: 04/05/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Luke M. Stapleton, MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert B. Ellis, MC

Key Words: cancer:head & neck,radiotherapy,cisplatin,5-Fluorouracil

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$9130.00

Periodic Review:

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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/M², 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/M², day 1 every 21 days for three courses and 5-FU, 1000 mg/M², days 1-4, every 21 days for three courses.

Progress: This study was closed to patient entry 1 May 92. One patient was entered in April 1992 and is still on study.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/070 **Status:** Completed

Title: SWOG 9046: Evaluation of 10-EdAM in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck

Start Date: 01/03/92

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Luke M. Stapleton, MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert B. Ellis, MC

Key Words: cancer:head & neck,squamous cell,10-EdAM

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

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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/M² IVP 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: This study was closed to patient entry, 1 Apr 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/017

Status: On-going

Title: SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma

Start Date: //

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Kenneth A. Bertram, MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Robert L. Sheffler, MC

MAJ Richard Tenglin, MC

CPT James Hu, MC

Key Words: cancer, non-Hodgkin's lymphoma, CVAD, verapamil, quinine

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

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Study Objective: (1) To evaluate the effectiveness of the CVAD chemotherapy regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) when administered in combination with chemosensitizers (verapamil and quinine) which are intended to block the emergence of multidrug resistance in previously untreated patients with intermediate and high grade non-Hodgkin's lymphoma. The effectiveness of CVAD plus verapamil and quinine will be based on the estimate of the complete response rate and the time to treatment failure. (2) To assess the toxicities and side effects associated with the CVAD regimen when combined with verapamil and quinine. Secondary objectives are to further investigate the utility of the proliferative rate (determined by Ki-67 monoclonal antibody), the importance of cell-cell recognition molecules, the role of host response, and the value of detectable levels of p_glycoprotein as prognostic indicators of outcome in conjunction with companion study SWOG 8819; and to further utilize the central serum repository enabling clinicopathologic correlations with the results of studies on the material collected (see companion study SWOG 8947).

Technical Approach: Currently, regardless of the regimen used, 30 to 60% of advanced stage non-Hodgkin's lymphoma patients will relapse and the emergence of clinical drug resistance is a significant problem in these patients. In this study, patients will receive oral verapamil and quinine on days 1-6 as chemosensitizers. They have been shown to reverse the multidrug resistance associated with P-glycoprotein. Starting on day 2, patients will receive a continuous infusion of Adriamycin and vincristine for four days, Cytosan will be given IV on Day 2 and oral decadron will be given days 2-5. Patients with documented progressive disease at any time will be taken off protocol treatment. Patients with stable disease will receive 2 courses (6 weeks) of chemotherapy. Patients responding to treatment will receive a maximum of 8 courses of chemotherapy. Patients will be restaged upon completion of the treatment program to assess response, with a complete laboratory and radiographic evaluation one month after the completion of therapy. All patients will be followed until death.

Progress: One patient has been entered in this study at MAMC and one transfer patient is being followed at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/006	Status: On-going
Title: SWOG 8952 (INT-0111), (CALG-8952), EST-5487): Treatment of Advanced Hodgkin's Disease - A Randomized Phase III Study Comparing ABVD vs MOPP/ABV Hybrid		
Start Date: 04/05/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ William A. Phillips		
Associate Investigators:		
MAJ Paul C. Sowray, MC	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	
Key Words: Hodgkin's disease, ABVD, MOPP, ABV Hybrid		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 92

Protocol No.: 91/021

Status: On-going

Title: SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver; Surgical Resection of Hepatic Metastases in Combination with Continuous Infusion of Chemotherapy

Start Date: 04/05/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ William A. Phillips

Associate Investigators:

MAJ Paul C. Sowray, MC

MAJ Everardo E. Cobos Jr., MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

COL Joseph F. Homann, MC

Key Words: cancer:colorectal,resection,chemotherapy,liver

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

//

Study Objective: To study the effects of long-term continuous infusion of Floxuridine (FUDR) intra-arterially and 5-FU systemically as therapy for liver metastases from colorectal primaries and to study the incidence of recurrence and time to recurrence in patients with 1-3 hepatic metastases treated with resection and continuous infusion of 5-FU into the systemic venous system and FUDR into the hepatic artery.

Technical Approach: This study attempts to combine surgical resection with long term hepatic artery infusion of chemotherapy and continuous infusion 5-FU. Patients with histologic confirmation of colorectal primary carcinoma and evidence of 1-3 liver metastases wither on CAT scan, liver scan or previous laparotomy, with no metastatic disease other than to the liver will be randomized to either surgery plus observation or sugary plus FUDR and 5-FU. FUDR will be given 0.1 mg/kg/day continuously for 14 days via Infusaid pump or arterial subcutaneous device. This cycle will be repeated every 28 days for 4 cycles. 5-FU will be given 200 mg/M²/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/M²/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 92	Protocol No.: 91/045	Status: On-going
Title: SWOG 9028: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD to VAD/Verapamil/Quinine for Induction; (2) Alpha-2b Interferon or Alpha-2b Interferon Plus Periodic VMCP for Remission Maintenance.		
Start Date: 10/04/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ William A. Phillips		
Associate Investigators:		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Luke M. Stapleton, MC	
MAJ Robert L. Sheffler, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
Key Words: myeloma, alpha 2b interferon, VAD, VMCP		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To determine if multidrug resistance can be prevented during remission induction by adding chemosensitizers (verapamil or quinine) to the VAD (vincristine, adriamycin, and dexamethasone); to determine if Interferon alone or plus VMCP (vincristine, melphalan, cytoxan, and prednisone) represents better maintenance therapy for myeloma; to examine the prognostic significance of pretreatment LDH level, Ki-67 level, and presence of P-glycoprotein; and to evaluate the relationship between the magnitude of cytoreduction and survival.

Technical Approach: Previously untreated patients with all stages of multiple myeloma are eligible. Protein criteria must be present but patients with IgM myeloma are not eligible. Patients must not have symptoms of congestive heart failure and may not be on digitalis preparations, beta blockers, or calmodulin inhibitors. Cardiac ejection fraction must be at least 50%, the EKG must be free of serious cardiac arrhythmias, and systolic blood pressure must be >90 mm/Hg. Patients who have had a prior malignancy within the last five years except for basal or squamous cell carcinoma or in situ cervical cancer are not eligible. Patients will be randomized to VAD every 21 days or to VAD plus verapamil and quinine every 21 days. Patients with >75% disease regression and at least 6 months of treatment and those with at least 50% regression after 9 months of treatment will be randomized to maintenance therapy. Maintenance therapy will consist of either alpha-2B interferon 3 times weekly or to alpha-2B interferon plus CVMCP 3 times weekly every 3 months until relapse.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/104

Status: On-going

Title: SWOG 9110: A Phase II Evaluation of Didemnin B in Central Nervous System Tumors

Start Date: //

Est. Completion Date: Sep 95

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Timothy P. Rearden, MC

Associate Investigators:

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

MAJ Richard Tenglin, MC

LTC Robert D. Vallion, MC

LTC Howard Davidson, MC

MAJ Kenneth A. Bertram, MC

MAJ Mark E. Robson, MC

CPT Jennifer L. Cadiz, MC

CPT James Hu, MC

CPT Diana S. Willadsen, MC

Key Words: cancer:nervous system

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$0.00

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Study Objective: To evaluate the likelihood of response in order to assess whether didemnin B should be advanced to further studies and to evaluate the qualitative and quantitative toxicities of didemnin B.

Technical Approach: Didemnin B will be administered IV over 30 mins once every 28 days. Patients will be evaluated for response at least every two courses of treatment. Those achieving complete response, partial response or stable disease will continue on study. Liver function tests and measurable and evaluable disease will be assessed at least every other course of therapy (every eight weeks). Didemnin B therapy and parameters will continue at these intervals until progression of disease occurs.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/002	Status: On-going
Title: SWOG 9045: Evaluation of Quality of Life in Patients with Advanced Colorectal Cancer Enrolled on SWOG 8905		
Start Date: 10/04/91	Est. Completion Date: Jun 92	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators: None		
Key Words: cancer:colorectal,quality of life		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: (1) To compare the following primary aspects of quality of life according to treatment assignment: treatment specific symptoms, physical functioning, and emotional functioning; and (2) to compare four secondary quality of life variables according to treatment assignment: general symptoms, role functioning, social functioning, and global perception of quality of life.

Technical Approach: This cancer control intervention study measures quality of life in patients with advanced colorectal cancer; specifically, patients registered on SWOG 8905: Phase II/III Study of 5-FU and Its Modulation in Advanced Colorectal Cancer. SWOG 8905 compares survival, response rates, and toxicities of 5-FU given by different schedules and/or with biochemical modulators (seven arms). Thus, the benefits of randomization, uniform patient selection, and treatment standardization are transferred to the quality of life investigation. The comparison of quality of life measurements between treatment arms will complement the analysis of survival and response data for patients registered to SWOG 8905 and become a critical consideration if no difference is demonstrated in survival between the treatment arms. A Quality of Life questionnaire will be administered prior to treatment, and at 6, 11, and 21 weeks after randomization on SWOG 8905.

Progress: Two patients have been entered on this study; one in FY 91 and the other in FY 92.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/045	Status: On-going
Title: SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia		
Start Date: 02/27/87	Est. Completion Date: Feb 90	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
LTC Lauren K. Colman, MC	COL Ir	Dabe, MC
MAJ Thomas M. Baker, MC	LTC H	Davidson, MC
MAJ Ruben D. Sierra, MC	MAJ D&	Dunning, MC
	CPT David R. Bryson, MC	
Key Words: leukemia:non-lymphocytic,Ara-C,daunorubicin,cytosine arabinoside		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	10/19/90

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: Six patients have been entered at MAMC and four of them have expired of their disease, with two still being followed. One transfer patient is also being followed.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 86/007	Status: On-going
Title: SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III		
Start Date: 10/18/85	Est. Completion Date: Sep 87	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
LTC Lauren K. Colman, MC	COL Irwin B. Dabe, MC	
MAJ Thomas M. Baker, MC	LTC Howard Davidson, MC	
CPT David R. Bryson, MC	MAJ Michael D. Stone, MC	
Key Words: leukemia:lymphoblastic,consolidation regimens		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 weeks for 36 months or until relapse. An adequate trial will be the completion of remission induction.

Progress: This study was closed to patient entry 15 Nov 91. Five patients were entered in previous years and all expired from their disease. One transfer patient is currently on protocol.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 89/065	Status: On-going
Title: SWOG 8812: Treatment of Limited Small Cell Lung Cancer With Concurrent Chemotherapy, Radiotherapy, With or Without GM-CSF and Subsequent Randomization To Maintenance Interferon or No Maintenance		
Start Date: 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:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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 $\alpha 2$ a to prolong remission duration and survival; and to evaluate the toxicities of rHuIFN $\alpha 2$ a.

Technical Approach: Patients must have histologically proven small cell carcinoma of the lung. Prior to treatment patients will be staged as to the extent of disease. Only patients with limited disease are eligible for this study. Patients must have evaluable or measurable disease, a pretreatment WBC $>4,000$ ml, absolute granulocyte count >1500 ml, platelet count $>100,000$ /ml, serum creatinine of <2.0 mg%, creatinine clearance of >50 ml/min, and performance state of 0-2 by SWOG criteria. Pregnant patients or those with prior radiation therapy, chemotherapy, colony stimulating factors, or interferon are not eligible. Patients with malignant pericardial or pleural effusions, a past medical history of congestive heart failure, extensive pulmonary disease, poor pulmonary reserve, or a history of seizures are ineligible. Patients will be stratified at initial registration by institution and at second registration according to performance status (0-1 vs 2); sex; response; and induction arm. Patients will be randomized to receive induction chemotherapy (cis-platinum + VP-16) and concurrent chest radiotherapy with or without GM-CSF. Consolidation chemotherapy will be as in induction but with no radiotherapy. Those patients achieving a complete remission will be randomized to receive or not receive maintenance therapy with recombinant alpha interferon. All patients who have achieved a complete response by week 33 will receive prophylactic cranial irradiation to the brain. Patients with stable disease, progression, or relapse at any point will be taken off study.

Progress: This study was closed to patient entry, 1 Jan 92. Three patients were entered in previous years and two have died of their disease. This study was temporarily closed in November 1989 due to excessive toxicity and reopened in December 1989, using reduced doses of CDDP and VP-16.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/111	Status: Completed
Title: SWOG 8694 (CALGB 8582): A Comparison of Pentostatin (NSC-218321) and Alpha-Interferon (NSC-377523) in Splenectomized Patients With Active Hairy Cell Leukemia		
Start Date: 08/21/87	Est. Completion Date: Aug 90	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
LTC Howard Davidson, MC	COL Irwin B. Dabe, MC	
MAJ Thomas M. Baker, MC	LTC Lauren K. Colman, MC	
MAJ Ruben D. Sierra, MC	MAJ David M. Dunning, MC	
	CPT Denis Bouvier, MC	
Key Words: leukemia:hairy cell,pentostatin,alpha-interferon,splenectomized		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	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 (2×10^6 IU/m²) 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/m², 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: This study was closed to patient entry, 15 May 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/078	Status: On-going
Title: SWOG 9111: Post-Operative Adjuvant Interferon Alpha 2 in Resected High-Risk Primary and Regionally Metastatic Melanoma, Intergroup		
Start Date: 01/03/92	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Everardo E. Cobos Jr., MC	LTC Howard Davidson, MC	
MAJ Luke M. Stapleton, MC	MAJ Patrick L. Gomez, MC	
MAJ Robert L. Sheffler, MC	MAJ Kenneth A. Bertram, MC	
CPT Jennifer L. Cadiz, MC	MAJ Robert B. Ellis, MC	
Key Words: melanoma,interferon alpha 2		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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 logrank test stratified by stage of disease. If either one of these primary comparisons crosses the group sequential boundary, then the observation arm may be dropped.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	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:		
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: leukemia:myeloid,carboplatin,CBDCA		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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/M²/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/M²/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/M²/ 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 have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 90/063

Status: On-going

Title: SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors

Start Date: 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: tumor:germ cell,etoposide,cisplatin,carboplatin,CBDCA

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
10/19/90

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 90. One patient was entered in May 90 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/064		Status: On-going	
Title: SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas					
Start Date: 05/18/90			Est. Completion Date: Apr 94		
Department: SWOG			Facility: MAMC		
Principal Investigator: MAJ Paul C. Sowray, MC					
Associate Investigators:			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					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:		\$0.00	OMA Cost:		\$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 histology. Patients will receive 6 cycles of induction chemotherapy (ProMACEMOPP, days 1-8) unless progressive disease develops during this treatment. At the completion of induction therapy, patients will be restaged to assess response. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete radiographic and laboratory evaluation for evidence of persistent lymphoma approximately one month after completion of chemotherapy. If no evidence of disease is found these patients will be randomized to Alpha IFN or observation. Patients in partial response and whose bone marrow remains positive after 6 cycles of induction chemotherapy will receive 2 additional cycles of chemotherapy and then be reevaluated. If the bone marrow remains involved or the patient has less than a partial response after a total of 8 cycles, the patient will be removed from further protocol therapy. If after 8 cycles, the bone marrow is negative and the patient is in partial response, the patient will receive radiotherapy. Complete responders after induction chemotherapy; complete responders after induction chemotherapy plus radiation therapy; and partial responders after chemotherapy plus radiation therapy will be randomized to consolidation alpha interferon or observation, approximately one month after completion of therapy.

Progress: Two patients have been entered in this study; one in FY 90 and one in FY 91. Both are still in the follow-up stage.

Detail Summary Sheet

Date: 30 Sep 92		Protocol No.: 90/088		Status: Completed	
Title: SWOG 8923: "Neo-Fac" for Poor Prognosis Stage IV Breast Cancer, A Phase II Pilot Study					
Start Date: 08/17/90			Est. Completion Date: Apr 93		
Department: SWOG			Facility: MAMC		
Principal Investigator: MAJ Paul C. Sowray, MC					
Associate Investigators:			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: cancer:breast,Neo-Fac					
Accumulative		Est. Accumulative		Periodic Review:	
MEDCASE Cost:	\$0.00	OMA Cost:	\$0.00	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: This study was closed to patient entry, 7 Feb 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/112 **Status:** On-going

Title: SWOG 8931 (EST-3189): Phase III Comparison of Cyclophosphamide, Doxorubicin, and 5-Fluorouracil (CAF) and One 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

Associate Investigators:	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

Accumulative	Est. Accumulative	Periodic Review:
IEDCASE Cost: \$0.00	OMA Cost: \$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/M²), and leucovorin, given weeks 1, 5, 7, 9, 11, 13, and 15, with 5-FU, 300 mg/M², given on alternate weeks.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92

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:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

Key Words: cancer:breast,prognostic factors,recurrence,survival

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

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: One patient has been entered (Aug 92).

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/076 **Status:** Completed

Title: SWOG 8936: Evaluation of Piroxantrone in Gastric Carcinoma, Phase II

Start Date: 01/03/92

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

Key Words: cancer:gastric,piroxantrone

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$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: This study was closed to patient entry 15 Jun 92. One patient entered in Oct 91 and expired in Feb 92 of the disease.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/077

Status: On-going

Title: SWOG 9039: Evaluation of Quality of Life in Patients with Stage D2 Cancer of the Prostate Enrolled on SWOG 8894

Start Date: 01/03/92

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ William A. Phillips

MAJ Everardo E. Cobos Jr., MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

Key Words: cancer:prostate,quality of life

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
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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 92 **Protocol No.:** 91/033 **Status:** On-going

Title: SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for Patients with Local Regional Disease, Phase III-Intergroup.

Start Date: 05/03/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ William A. Phillips

MAJ Patrick L. Gomez, MC

MAJ Robert B. Ellis, MC

COL Joseph F. Homann, MC

MAJ Everardo E. Cobos Jr., MC

LTC Howard Davidson, MC

MAJ Luke M. Stapleton, MC

MAJ Robert L. Sheffler, MC

CPT Jennifer L. Cadiz, MC

COL Daniel G. Cavanaugh, MC

Key Words: cancer:esophagus,chemotheray,surgery,modality therapy

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

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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 cisplatin and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatin and 5-FU, starting two to six weeks after surgery.

Progress: One patient was entered in this study at MAMC in March 1992.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/053

Status: On-going

Title: SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II

Start Date: 05/01/92

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ Luke M. Stapleton, MC

MAJ Patrick L. Gomez, MC

MAJ Robert L. Sheffler, MC

MAJ Richard Tenglin, MC

LTC Howard Davidson, MC

MAJ Kenneth A. Bertram, MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

CPT James Hu, MC

Key Words: cancer, soft tissue sarcoma, chemotherapy

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

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Study Objective: To evaluate, in patients with high grade soft tissue sarcoma of the extremity, the trunk, or the head and neck, the efficacy of primary chemotherapy, wide surgical resection, adjuvant chemotherapy, and radiotherapy on local control, metastasis free survival, and overall survival; To evaluate the utility of tumor response to primary chemotherapy as an indicator of local and systemic disease control in high grade soft tissue sarcoma; and to evaluate the toxicity of primary chemotherapy, surgery, adjuvant chemotherapy, and radiation therapy in this patient population. Secondary objectives include those listed for SWOG 9136, a companion protocol studying biologic parameters.

Technical Approach: Patients with a high grade soft tissue sarcoma of the extremity, trunk, or head and neck area are eligible. Patients will receive chemotherapy using the drugs adriamycin, DTIC, and ifosfamide, given concurrently for three cycles at 21 day intervals. Patients will then undergo wide surgical excision of the primary tumor. Following recovery from surgery, patients with partial or complete response or stable disease will receive another three courses of therapy, followed four weeks after completion of chemotherapy by radiation therapy to the whole area (days 1-5 for 6-8 weeks).

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/056 **Status:** On-going

Title: SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients

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

Department: SWOG **Facility:** MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	LTC Howard Davidson, MC
MAJ Luke M. Stapleton, 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
MAJ George F. Hodges, MC	

Key Words: cancer, soft tissue sarcomas, biologic parameters

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

Study Objective: (1) To develop a cooperative group mechanism to study biologic parameters of soft-tissue sarcomas in patients entered onto companion SWOG protocols (see SWOG 9119).; (2) To determine cellular DNA content parameters (DNA CCP) (DNA Ploidy, S-Phase Fraction) of soft tissue sarcomas and to evaluate the effect of these parameters on disease free survival and overall survival. To study the changes in DNA CCP as a result of chemotherapy, and the relationship of these changes to prognosis in patients with soft tissue sarcoma.; (3) To characterize cytogenetic aberrations of soft-tissue sarcomas in the study population. To evaluate the relationship of defined cytogenetic abnormalities to prognosis.; (4) To estimate the level of expression of the multi-drug resistant (MDR) phenotype in untreated soft-tissue sarcoma, and the effect of chemotherapy treatment on the expression of MDR. To evaluate the impact of MDR expression on response to chemotherapy, disease free survival, and overall survival. ; (5) To provide a repository of frozen tissue for future molecular studies in this group of patients.

Technical Approach: As a companion protocol to SWOG 9119 (adjuvant soft-tissue sarcoma trial), DNA CCP, tumor karyotypes, and estimation of the expression of the MDR phenotype of sarcomas entered onto trial will be done.

Progress: No samples have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/054	Status: On-going
Title: SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II		
Start Date: //	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, 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	
Key Words: cancer, osteogenic sarcoma		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To estimate the time to treatment failure and survival rate of the three drug combination, Adriamycin, cisplatin, and ifosfamide, as an adjunctive treatment of osteosarcoma of the extremity; to evaluate histopathologic tumor necrosis following preoperative therapy with this regimen; to assess the feasibility of determining histopathologic tumor necrosis in a cooperative group setting; to assess the influence of clinical prognostic variables on disease outcome; and to assess the toxicity of this regimen.

Technical Approach: Primary osteosarcoma is an uncommon malignancy but it is associated with only a 20% cure rate, if no more than surgery is used. Chemotherapy increases survival to above 50%, but whether or not this survival could be further increased has to be determined. The current study uses three drugs (Adriamycin, cisplatin, and ifosfamide) in an alternating fashion with the intent of optimizing treatment prior to surgery. Once four cycles of treatment have been completed, surgery will be undertaken. After recovery from surgery, four more cycles of chemotherapy will be given.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/080	Status: On-going
Title: SWOG 9151: Evaluation of Topotecan in Hepatoma, Phase II		
Start Date: //	Est. Completion Date: Jun 95	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, MC	MAJ Kenneth A. Bertram, MC	
MAJ Robert L. Sheffler, MC	MAJ Robert B. Ellis, MC	
MAJ Robert L. Sheffler, MC	CPT Jennifer L. Cadiz, MC	
MAJ Richard Tenglin, MC	CPT James Hu, MC	

Key Words: cancer, hepatoma, topotecan

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

Study Objective: To evaluate the response rate of hepatomas treated with topotecan and to evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study.

Technical Approach: Hepatoma is an uncommon malignancy which is usually far advanced by the time diagnosis is made. The median survival after diagnosis is six months. There is no effective chemotherapeutic regimen for this disease. Topotecan is a new chemotherapeutic agent which has been shown to have activity in early cancer trials. An attempt will therefore be made to see whether or not topotecan will be effective against hepatomas. Patients will receive topotecan through an IV for five consecutive days. This treatment will be repeated every three weeks. Patients will continue on this schedule as long as they show either complete response, partial response, or stable disease. If the disease progresses, the patient will be taken off study.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/055	Status: On-going
Title: SWOG 8842: Dihydroxyazacytidine in Malignant Mesothelioma, Phase II Study		
Start Date: 05/01/92	Est. Completion Date: Dec 94	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, 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	

Key Words: cancer, mesothelioma

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

Study Objective: To assess the response rate and survival of patients with unresectable malignant mesothelioma treated with Dihydroxyazacytidine (DHAC, NSC-264880); to further evaluate the toxicity of DHAC given by continuous infusion; and to prospectively evaluate the use of CA-125 as a tumor marker in mesothelioma.

Technical Approach: Mesothelioma is an uncommon tumor and, if not localized, is not amenable to therapy with either surgery or radiation therapy. Chemotherapy has shown moderately good response rates. Whether there has been any benefit in survival is unclear. Therefore, use of a new agent which may have activity against mesothelioma will be undertaken. DHAC causes an inflammatory response in the pleura and it is felt that in the presence of a malignancy of the pleura, this anti-trial continuity response may be tumoricidal. Therefore, all patients on the study will receive two cycles of DHAC by continuous infusion over five days. Cycles will be repeated every four weeks. Patients will continue to receive treatment if they have a partial response or stable disease; otherwise they will be taken off the medication.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/088	Status: Completed
Title: SWOG 8900: A Phase II Pilot of VAD and VAD/Verapamil for Refractory Multiple Myeloma		
Start Date: 08/02/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Kenneth A. Bertram, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Robert B. Ellis, MC	MAJ Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard Tenglin, MC	
MAJ Patrick L. Gomez, MC	CPT James Hu, MC	
Key Words: myeloma, Verapamil, VAD		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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: This study was closed to patient entry, 1 Dec 91. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/095	Status: Completed
Title: SWOG 9012: Evaluation of Low Dose Alpha-Interferon in Patients with Advanced Renal Cell Carcinoma, Phase II		
Start Date: 09/06/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
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	
Key Words: cancer:renal cell,alpha-interferon		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

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 protocol was closed to patient entry, 1 May 92. No patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 92/016 **Status:** Completed

Title: SWOG 9009: Pilot Study for Analysis of Lymphocyte Sub-Set in Natural Killer Activity After Treatment with Levamisole

Start Date: 02/07/92

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:

MAJ Luke M. Stapleton, MC

MAJ Kenneth A. Bertram, MC

MAJ Robert B. Ellis, MC

CPT Jennifer L. Cadiz, MC

LTC Howard Davidson, MC

MAJ Patrick L. Gomez, MC

MAJ Robert L. Sheffler, MC

MAJ Richard Tenglin, MC

CPT James Hu, MC

Key Words: cancer, Duke's carcinoma, lymphocyte, levamisole

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost:

\$0.00

OMA Cost:

\$0.00

//

Study Objective: To analyze selected aspects of the immune response to adjuvant levamisole in patients with surgically resected Duke's Stage C or high risk Duke's Stage B2 colon carcinoma including the following: the effect of levamisole on lymphocyte subsets in the peripheral blood over time and to describe the effect of levamisole on peripheral blood "natural killer" cytotoxicity over time.

Technical Approach: Levamisole is felt to affect the immune system but how it interacts with the immune system to decrease the recurrence of colon cancer is unclear. In order to study this, blood samples will be drawn from patients registered on SWOG 8899 (treatment protocol for Duke's B and C colon cancer) at the following time points: pretreatment, 3, 6, and 12 months, and at three months after completion of treatment. The samples will be analyzed to display the distribution of percent change from baseline at each of the four time points for both response and cytotoxicity. A one sample t-statistic will be used to determine whether significant evidence exists that levamisole induces changes from baseline measurements.

Progress: This protocol has been completed. No subjects were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 92/040	Status: On-going
Title: SWOG 9030: Phase II Study of High Dose Ara-C/Mitoxantrone for the Treatment of Relapsed/Refractory Acute Lymphocytic Leukemia		
Start Date: 02/07/92	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	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	
Key Words: cancer, leukemia, lymphocytic, ara-C, mitoxantrone		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$0.00	//

Study Objective: To assess the complete response rate achieved in adult patients with relapsed or refractory ALL using the combination of high-dose Ara-C with mitoxantrone and to evaluate the toxicities associated with this induction regimen.

Technical Approach: Patients who have relapsing or refractory acute lymphocytic leukemia (ALL) have only one chance of being cured, and that is by a bone marrow transplant, which is available only to about one in four patients. For those patients without the possibility of bone marrow transplant, more effective chemotherapy regimens need to be developed. Preliminary studies suggest the effectiveness of high-dose Ara-C and mitoxantrone, in combination. On this study, patients would receive Ara-C once daily for five days and mitoxantrone will be given as a 30 min infusion beginning 12-20 hours after the first dose of Ara-C (one dose only). Both drugs will be given at very high doses. This will be a one time only regimen that will not be repeated.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/087	Status: On-going
Title: SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954		
Start Date: 08/02/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
MAJ Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., 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	
MAJ Kenneth A. Bertram, MC	CPT James Hu, MC	
Key Words: lymphoma:tissue procurement		
Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0.00	OMA Cost: \$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: This is a companion protocol to SWOG studies using tissue from patients on SWOG studies 8516, 8736, 8809, 8907, and 8954. Tissue samples from two patients have been studied.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 91/089	Status: On-going
Title: SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816		
Start Date: 08/02/91	Est. Completion Date:	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Luke M. Stapleton, MC		
Associate Investigators:		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., 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	
MAJ Kenneth A. Bertram, MC	CPT James Hu, MC	
Key Words: lymphoma:serum repository		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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: Serum from two patients has been entered in this study.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 87/109	Status: Completed
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, Intergroup.		
Start Date: 09/18/87	Est. Completion Date: Aug 90	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	MAJ Mark H. Kozakowski, MC	
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LTC Howard Davidson, MC	CPT Denis Bouvier, MC	
Key Words: cancer:esophagus,radiation,chemotherapy		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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/m² the first day of weeks 1, 5, 8, and 11, 5-FU, 1000 mg/m² 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. Two patients were entered and both have expired.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 90/030	Status: On-going
Title: SWOG 8905: Phase II/III Study of Fluorouracil and Its Modulation in Advanced Colorectal Cancer		
Start Date: 01/19/90	Est. Completion Date: Jun 92	
Department: SWOG	Facility: MAMC	
Principal Investigator: MAJ Paul C. Sowray, MC		
Associate Investigators:		
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Key Words: cancer:colorectal,5-Fluorouracil,leucovorin,PALA		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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 in this study in FY 92 for a total of two entries. One patient has died from the disease.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 90/028 **Status:** Completed

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

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Key Words: cancer:lung:small cell,chemotherapy,PCI,CAV,cisplatin,

Accumulative

Est. Accumulative

Periodic Review:

MEDCASE Cost: \$0.00

OMA Cost: \$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/m² days 1 and 8 (IV), VP-16 50 mg/m²/day for 14 days (PO); Regimen B: Cytosan 60 mg/m²/day for 21 days (PO), Adriamycin 20 mg/m²/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. Three patients were entered and all have died of their disease.

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 91/020

Status: On-going

Title: SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II

Start Date: 05/03/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

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Key Words: mycosis fungoides, retinoic acid, interferon-A

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$0.00

Periodic Review:

//

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, 3×10^6 microgm/m² 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: One patient was entered in this study in Nov of 91 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 92 **Protocol No.:** 91/032 **Status:** On-going

Title: SWOG 8956: A Phase II Study of Cisplatin and 5-Fluorouracil Infusion for Treatment of Advanced and/or Recurrent Metastatic Carcinoma of the Urinary Bladder

Start Date: 05/03/91

Est. Completion Date:

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

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MAJ Luke M. Stapleton, MC

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Key Words: cancer:bladder,cisplatin,5-Fluorouracil

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

Study Objective: To assess efficacy and feasibility of utilizing cisplatin (CDDP) and 5-fluorouracil infusion (5-FU-I) in patients with advanced and/or recurrent carcinoma of the urinary bladder and to evaluate the toxicity of cisplatin and 5-FU in this group of patients.

Technical Approach: Bladder cancer is the sixth most common cancer in the United States, accounting for 10,000 deaths per year. Treatments have been developed which provide 15% long term disease-free survival equated with cure. However, the toxicities have been profound, including treatment related mortalities. As a consequence, this potential less toxic regimen has been devised for evaluation in metastatic bladder cancer. In this study, all patients will receive the same treatment which includes cisplatin on the first day of treatment and continuous infusion of 5-FU on each of the first five days of treatment. These treatments will be repeated every 21 days. Patients response to treatment will be assess every other course (every six weeks). The patients will continue on therapy until they have progression of disease.

Progress: No patients entered at MAMC.;

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 92/051

Status: On-going

Title: SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II

Start Date: 09/04/92

Est. Completion Date: Mar 95

Department: SWOG

Facility: MAMC

Principal Investigator: MAJ Luke M. Stapleton, MC

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Key Words: cancer, gastric, adenocarcinoma, chemoradiation

**Accumulative
MEDCASE Cost:**

\$0.00

**Est. Accumulative
OMA Cost:**

\$0.00

Periodic Review:
//

Study Objective: To evaluate the possible benefit of adjuvant chemoradiation therapy in patients with resected gastric cancer to include: comparison of overall and disease free survival between patients being treated with surgical resection only and those being treated with surgery plus adjuvant therapy; comparison of incidence and patterns of disease failure between surgery and surgery plus adjuvant therapy treated patients; and assessment of patient tolerance of upper abdominal chemoradiation after gastric resection.

Technical Approach: Patients will be randomized to either observation or adjuvant therapy. Adjuvant therapy will consist of one course of 5-FU and Leucovorin given IV. Four weeks later the patient will receive a second course of 5-FU with Leucovorin with concomitant radiation therapy. While receiving radiation therapy, the patient will receive a third course of 5-FU and Leucovorin, which will occur during the fifth week of radiation therapy. After completing radiation therapy, the patient will receive two additional courses of chemotherapy to begin approximately 35 days after completion of radiotherapy.

Progress: No patients have been entered at MAMC.

DETAIL SHEETS FOR PROTOCOLS

UNIVERSITY OF WASHINGTON
NEURO-ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 92

Protocol No.: 89/013

Status: On-going

Title: UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System

Start Date: 09/15/89

Est. Completion Date: Nov 92

Department: UWNG

Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

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Key Words: lymphoma:central nervous system,chemoradiotherapy,methotrexate

Accumulative

MEDCASE Cost:

\$0.00

Est. Accumulative

OMA Cost:

\$328.00

Periodic Review:

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/m², 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 was entered in this study in FY 88 and is well at this time. No other patients have been entered.

Detail Summary Sheet

Date: 30 Sep 92	Protocol No.: 88/073	Status: On-going
Title: UWNG 86-01: Phase II Study of External Brain Irradiation and Hydroxyurea Followed by Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Primary Malignant Brain Tumors		
Start Date: 08/19/88	Est. Completion Date: Jul 91	
Department: UWNG	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: COL Irwin B. Dabe, MC CPT Denis Bouvier, MC		
Robert Goodkin, M.D. MAJ Joseph H. Piatt, MC		
Key Words: tumor:brain,irradiation,PCV,procarbazine,CCNU,vincristine		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$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/M² every six hours. PCV treatment will begin within two weeks after radiotherapy. CCNU, 110 mg/M² po, will be given on day one of each course. Procarbazine, 60 mg/M² po will be given days 8-14. Vincristine, 1.4 mg/M², 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 have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 92	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		
Associate Investigators:		
COL Michael W. Potter, MC	Robert Goodkin, M.D.	
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MAJ Ruben D. Sierra, MC	MAJ David M. Dunning, MC	
MAJ Thomas M. Baker, MC	CPT Denis Bouvier, MC	
Key Words: tumor:brain,chemotherapy,TPDCFH		
Accumulative MEDCASE Cost:	Est. Accumulative OMA Cost:	Periodic Review:
\$0.00	\$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. Exceptions may be made to restart when WBC >3600/cu mm for patients with chronically depressed bone marrow.

Progress: No patients have been entered on this study.

INDEX OF AUTHORS AND INVESTIGATORS

Aaron GR	68, 69, 72	Bertram KA	11, 54, 104, 109, 113, 146,
Achilles J	204		147, 327, 328, 329, 330, 331,
Adams C	116		332, 333, 344, 351, 352, 353,
Addison J	150		354, 355, 356, 357, 358, 359,
Ahmann A	149		360, 361, 365, 366, 368, 369,
Ahmed MA	177		370, 373, 377, 381, 383, 384,
Alba E	10		385, 386, 387, 393, 394, 395,
Albano EA	13, 263, 264, 265, 266, 267,		396, 397, 398, 399, 400, 401,
	268, 269, 270, 271, 272, 273,		402, 403, 405, 406, 407, 409,
	322, 411		411
Allison SC	149, 237	Bigham WF	14
Altamore R	98	Blackburn S	162
Andersen CA	116, 228, 242, 252	Blakeslee DB	238, 247, 338
Anderson DM	227, 228, 229, 232, 233, 251	Bloodworth KE	16
Anderson M	21	Blount BW	15
Anderson PL	13, 21	Blumhardt R	13, 21
Andrade WP	13, 102, 156, 250	Boehm B	21
Armstrong AY	176, 177	Boley TJ	179, 180, 181, 182, 183
Armstrong PJ	21	Bousfield GR	18
Aronson NE	11	Bouvier DP	147, 332, 333, 335, 337, 344,
Asp AA	154, 155		346, 347, 348, 349, 350, 351,
Babonis TR	13, 21, 46, 53, 200, 201, 202		352, 353, 354, 355, 356, 357,
Baird CP	194		358, 359, 360, 365, 366, 368,
Baker TM	110, 335, 336, 337, 338, 339,		369, 370, 381, 382, 384, 385,
	340, 341, 342, 345, 346, 347,		386, 387, 404, 406, 411, 412,
	348, 362, 379, 380, 382, 404,		413
	413	Bower DJ	234
Barja R	253	Bowne JR	14
Barnes MM	110	Boyd DB	74, 75
Barry MJ	233, 252	Brady WK	12, 20, 178, 190, 217
Bauman JM	13	Branch B	102
Baun M	12	Brantner LM	78
Bayliss PM	20, 96, 178, 179, 180, 181,	Brantner RD	77, 78
	182, 183, 184, 196	Bratloff B	11
Beachy JC	162, 167, 203, 215, 216, 217	Bremner W	155
Beattie MT	16	Brennan MF	23
Beck RA	13	Brisette MD	128
Bell BK	19, 20, 57, 121, 153	Broadhurst RB	21, 204
Bellows WH	14, 22	Brooks DE	21
Belts RP	191	Brooks KL	205
Belville WD	13, 332, 335, 337, 341, 342,	Brown CR	65
	348	Brown FH	10
Bender GN	222, 223, 224, 225	Brown JS Jr	15, 102, 156
Bennett E	21	Brown RF	16
Benson WL	12, 296, 297, 298, 299, 300,	Brown SR	150
	301, 302, 303, 304, 305, 306,	Browner W	22
	307, 308, 309, 310, 311, 312,	Brucia J	12
	313, 314, 315, 316, 317, 318,	Brunader JA	11, 15
	320, 324	Brunader RE	11, 15
Bentley T	43	Brundage JF	11, 12
Berger TG	15	Bryson DR	110, 336, 338, 339, 340, 379,
Bergin-Sperry MJ	66		380
Bernier RM	18, 103, 130	Bunner DL	18, 105, 136
Bertoglio M	116	Buntain-Ricklefs J	202
		Burchett S	70

INDEX OF AUTHORS AND INVESTIGATORS

Burgess FW	21, 66, 75, 227, 228, 229, 230, 232, 233, 234, 235, 241, 243, 251	Coles EF	15
Burke TF	18, 156	Colman LK	110, 335, 336, 348, 379, 380, 382, 404, 413
Burkle F	86	Colonna DM	227, 251
Burri BJ	15, 261	Congdon JE	345
Burroughs SL	163	Conley LD	80
Butcher JD	79	Conn VS	11
Byrne RA	46	Conway BC	158
Cadiz JL	104, 113, 125, 148, 325, 327, 328, 329, 330, 331, 343, 361, 367, 371, 372, 373, 374, 375, 376, 377, 383, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 407, 408, 409	Cooper RH	108, 132, 133
		Copley JB	11
Cameron S	21	Cornett PA	14
Camp RA	238	Cosio MQ	238
Canonic DM	22, 236, 250	Cragun WH	125, 126, 140, 141
Carlin KJ	118	Craig DB	11
Carlson MJ	128	Crothers BA	220
Carlson DJ	240	Curr A Jr	15
Carter PL	13, 252	Cushner HM	11, 13, 150
Carter PM	255	Dabe IB	110, 332, 335, 336, 337, 338, 339, 340, 341, 342, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 362, 363, 379, 380, 381, 382, 404, 411, 412, 413
Carter P	21, 22		
Casey B	11	Daines MC	11, 74
Casler JD	15	Dalesandro MM	11
Casper ES	23	Dalessandro L	114
Cassels JW	191	Danielson RW	22
Caton JR	125	Davidson DR	195
Cavanaugh DG	229, 232, 233, 241, 252, 392	Davidson H	11, 104, 109, 110, 113, 146, 147, 148, 322, 325, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 409, 411, 412, 413
Chamusco RF	106, 144		
Chan AH	341, 342, 345	Davis C	11
Charney PJ	126, 174	Davis J	100
Cherkin D	98	Davis RC	13, 21, 144, 365, 366
Chismire KJ	237	Davis SM	239
Christenson CJ	14	Dea-man RM	232, 252
Christian JS	12	Decker MJ	233, 234
Christian SS	190	DeFraites RF	12, 13
Ciceri DP	16	Della-Giustina D	78
Clark TS	10, 47	Deshon GE Jr	15
Clayton WL	107	Dettori JR	10
Clifford AJ	261	Dewan RN	343, 350, 409
Clift SD	238	Deyo GA	14
Clingan TA	10	Diaz JM	14
Clinghan TA	46		
Cobos E	146, 147, 148, 325, 332, 333, 343, 344, 352, 353, 354, 355, 356, 357, 358, 359, 360, 365, 366, 367, 368, 369, 370, 371, 372, 374, 375, 376, 381, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 398, 402, 403, 405, 406, 407, 408, 411		
Coburn TC	255		
Coleridge ST	86		

INDEX OF AUTHORS AND INVESTIGATORS

Dietz JW	22, 91	Fries PD	15
Dixon ZR	15	Frohna WJ	11, 81
Dodrill CB	10	Fry PJ	15
Donahue A	22	Fuery HA	196
Donatucci CF	15	Gardner D	155
Dorsett CR	66, 239	Gardner LI	11
Douglas DM	156	Garrett WL	14, 15
Downey GO	20, 184, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 320, 324	Gatrell CB	86, 87, 144
Dronen SC	86	Gelnett J	13
Dubrave VA	206	Gendron BP	85
Duff P	12, 178	George DP	237
Duffy LK	23, 257	Gernon WJ	338
Dunbar BS	18	Gibson CA	105, 136, 176
Dunning DM	110, 335, 336, 337, 346, 347, 348, 379, 382, 404, 413	Glaubiger DL	15
Dwyer MS	237	Glenn GM	208
Dyksterhouse DL	20, 184	Goho CD	71
Ebbeling WL	102	Goins B	13, 21
Eggebroten WE	244	Gomez PL	104, 113, 146, 147, 148, 325, 327, 328, 329, 330, 331, 333, 343, 344, 355, 356, 357, 358, 359, 360, 361, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 405, 406, 407, 408, 409
Ellingson AE	111	Gomez RR	112
Ellingson AR	18	Goodkin R	14, 411, 412, 413
Elliott	18	Gorie C	44
Ellis RB	104, 148, 112, 113, 325, 327, 328, 329, 330, 331, 343, 361, 367, 371, 372, 373, 374, 375, 376, 377, 383, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 407, 408, 409	Grace TS	240
Engel CC Jr	15	Gradwohl SE	16
Engibous PJ	67	Grajcar MS	79, 91
Enriquez J	211	Greenfield NN	116
Excheverria P	13	Greteman A	21
Fannin L	249	Gridley GD	241
Fariss BL	122, 151	Griffin JM	66, 75
Ferraris VA	16	Griffin PR	10
Ferrell R	13	Griffith TG	238
Ficke RF	126	Grover BS	20, 141, 142
Finney JL	238	Guertler AT	11, 82, 89
Fitzpatrick D	97, 98	Guille JT	14
Flanagan JC	14	Guise JM	12
Fleming JL	12, 44	Gunzenhauser JD	12
Flynn FG	19	Haberberger RL	13
Foos CC	177, 185	Hajdu SI	23
Forlaw L	172	Hall RA	252
Foutch RG	10	Hammes CS	14
Fox LP	237	Hammond G	57
Friedl KE	10, 123	Hannan CJ	10, 118, 119, 120, 123, 150, 155
		Hansberry KL	242, 245
		Hansen CS	109, 125, 249
		Hansen JE	10, 51
		Harkless LB	240

INDEX OF AUTHORS AND INVESTIGATORS

Harris SC	244, 252	Kemper K	13, 21, 201, 202
Harrison H	177	Kenevan RJ	238
Hartman KR	268, 269, 270, 271, 272, 273	Kettler TM	10
Heath G	10	Kiesling VJ	13, 332, 348
Hellman S	159	Kinney JB	13
Helman JD	14, 21, 22, 232, 243	Kiser WR	93, 94
Helmer F	413	Kittle PE	68, 69, 70, 71, 73
Herd M	188	Klaus-Hagen A	47
Herpolsheimer AH	12	Klipper R	13, 21
Hetherington HE	22	Klusman LE	16
Hobbs CJ	11, 57	Knight JA	252
Hodges G	11, 13, 394	Knight RW	245
Hoeldtke NJ	176	Knodel DH	105, 151
Hollinger JO	22	Koenig KG	11
Holmes KD	83	Koenig TE	12
Homann JF	375, 392	Kopelman JN	12, 20, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 192
Homer LD	11		
Hoop RC	57	Kortepeter C	13
Hornbostel LK	16	Kossoy AF	102
Howse J	14	Kowalski KR	11
Hu J	104, 113, 327, 328, 329, 330, 331, 361, 373, 377, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 409	Kozakowski MH	147, 332, 344, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 365, 366, 368, 369, 370, 381, 384, 385, 386, 387, 404, 405, 406, 411
Hurley WT	78, 80	Krauss MR	12, 60, 194, 195, 197, 198
Hurst RL	241, 243	Krober AS	18
Irby PB	16	Krober MS	13, 200, 205, 208, 210, 211, 212, 213, 214, 215, 216, 217, 218
Irvin TL	114, 138, 139		
Irvine TW	79, 115	Kruse RW	14
Jackson RE	151	Kugler JP	11, 15, 16, 94, 97, 98, 99
Jahnke AH Jr	15	Kull DH	110, 315, 316, 317, 341
James AI	158	Kushner JP	20, 142, 154
James G	246	Lagutchik MS	11
Jeffers DJ	116	Lancaster A	159
Jensen H	14	LaPiana FG	149
Johns MC	43	LaPorta AJ	14
Johnson JJ	92	Larsen WI	20, 177, 189
Johnson KR	84	Ledbetter D	15
Johnson MP	79	Lednar WM	14
Johnson RN	14, 16	Ledoux RA	102
Jones HL	65, 67, 68, 69	Lee RB	296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 320, 324, 336
Jones RE	11, 19, 20, 105, 107, 117, 118, 119, 120, 121, 122, 123, 124, 136, 149, 151, 154, 155, 177		
		Lehman R	10
Jones RO	14, 240, 248	Leung J	14, 22
Jordan GD	12, 178	Levine ME	23, 257
Joslin S	19	Lewis EL	17, 95
Kadakis AS	15	Lewis SM	20
Kadakis SC	15	Li J	22
Kahn CA	207	Liebenberg SP	86
Karren K	249	Light DE	11, 96
Katakhar SB	363, 364		
Kaufman C	13, 21, 22, 23, 235, 244		
Keenan LM	19, 125, 126		
Kelly PC	21, 46, 87, 200, 204, 207, 208, 210, 211, 212		

INDEX OF AUTHORS AND INVESTIGATORS

Lillegard WA	79, 91	Milligan DA	12, 178, 187
Lillis-Hearne PK	15	Milliron AN	23
Lin FL	102	Mittelstaedt EA	161
Lindbert JS	11	Moe RD	156
Loan LA	160, 170, 171	Moffitt DR	214
Lodato RJ	19, 127	Montigo H	253
Lombardo MA	19, 20, 129	Mooney MJ	14, 246
Loop S	20, 57	Moore DC	10, 18, 49, 50, 51, 52, 53, 220
Lovins DE	97, 98	Moore J	12
Lubin GI	15	Moore KH	10, 18, 20, 51, 54, 55, 57, 58, 63, 107, 112, 153, 211
Luszczyk M	255		
Lynn MJ	22	Morris ER	18
Lyons MF	18, 19, 20, 111, 115, 127, 128, 152, 222, 223, 224, 225	Morris MR	22, 236, 238, 247, 250, 368, 369
Maccario M	14	Moulton JM	16
MacDonald HR	14	Moyer D	102
MacMillan JG	10, 13, 168, 169	Mueller JP	126
Mader TH	14, 22, 237, 249	Muggelberg ML	102
Magelssen DJ	185, 191	Mukharjee D	116
Magelssen MD	10, 85	Munsinger HL	10
Mancuso JJ	182, 230, 251	Murphy GS	13
Mangano D	22, 243	Nagy M	148
Marden LA	19, 103, 107	Neary MT	248
Markenson G	183	Neidlinger TR	15
Martin DG	11	Nelson KM	185, 190
Martin M	102	Newman RA	52
Martinelli AM	16	Nottestad SE	11, 144
Martyak T	144	Nuchtern J	15
Mascette AM	11, 81, 106, 144	Nuovo JA	10
Masi JD	213	O'Reilly MJ	14, 252
Maslow AS	180, 183, 185, 186	O'Rourke TJ	338, 339, 340, 341, 342, 345, 362
Matej LA	18, 54, 55, 63, 107		
May E	19	Olson J	177
May TC	85	Opheim GS	12
Mazzaferri EL	154, 155	Ostenson RC	20
Mazzoli RA	14	Pace SA	81
McBiles M	16	Padalino PK	1
McBurney JW	19, 20, 77, 211, 212, 129, 130	Page MG	73
McCarty JP	130, 131, 206, 208, 210	Paris JA	113, 144
McDonald HR	16	Parkison SC	46, 165
McEnany MT	14	Parmley VC	14, 249
McGahren E	15	Patience TH	10, 61
McLachlan RI	10	Patrin GD	206
McNeil JG	11, 12, 197	Paulsen CA	10
McNeill KM	197	Paulson D	236
Meadors LW	72	Payne LE	89
Mercado DL	13	Pearce WA	82, 152
Mereish KA	18	Peele ME	134
Metcalf M	159	Perkins D	21
Michael RA	108, 132, 133	Perkins JA	22, 156, 236, 250
Michel TJ	220	Perkins TA	215, 216, 217
Michels TC	17, 99	Perren RS	83
Milazzo MJ	11	Petra PH	10, 18, 55
Miller GJ	14	Petrucelli BP	13
Miller RN	12		

INDEX OF AUTHORS AND INVESTIGATORS

Phillips WA	148, 325, 371, 372, 374, 375, 376, 388, 389, 390, 391, 392, 407, 408	Rowsey JJ	14
Phillips WT	13, 21	Rubertone MC	198
Piatt JH	411, 412, 413	Rudolph AS	13
Picano JJ	16, 259	Rudy EB	12
Pierce HI	148, 364	Rusinko JB	88
Pineda N	14, 22	Russell KM	83
Pinson RH	43	Ruvalcaba RHA	10
Piratla V	238	Sado AS	115, 246
Place R	22	Saltiel D	106, 144
Plymate SR	10, 11, 19, 20, 21, 57, 63, 118, 119, 120, 121, 122, 123, 142, 150, 153, 155	Sanchez JL	13
		Satava R	15
Polzin WJ	12	Sborov MJ	21, 227, 228, 229, 230, 243, 251
Potter ME	191	Schaller R	15
Potter MW	413	Schatz H	14, 16
Powell DA	59, 239	Schilhab JC	246
Pratt DH	10	Schlepp GE	18, 19, 20, 115, 127, 128, 152
Protzko EE	14, 16	Schofield T	223, 224, 225
Provencher MA	43	Schultz CK	164
Prue-Owens KK	158	Schwartz PS	145
Quinn KL	13, 143, 156	Scott JS	219
Radentz WH	11	Seguin SM	13
Rae RE	12	Self DJ	94
Rawlings JS	13, 215, 216, 217	Sexton DL	12
Raymond WR IV	14, 16	Sheffler RL	104, 113, 146, 147, 148, 325, 327, 328, 329, 330, 333, 343, 344, 355, 356, 357, 358, 359, 360, 361, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 405, 406, 407, 408, 409
Read JA	12, 179, 180, 181, 182, 183, 186, 187, 192		16
Reagan MS	165	Shehata BM	151
Rearden TP	377	Sheldon WR	110, 335, 336, 337, 346, 347, 348, 379, 382, 404, 413
Rebecca G	144	Sierra RD	252
Redfield RR	11		253
Reed HL	11, 105, 136, 137	Simmang CL	14
Reed JE	88	Smith DS	17, 165
Reed WW	15	Smith KG	252
Reeves JD	14	Smith PS	21
Reichle JL	222, 223, 224, 225	Smith SB	77
Renaud MT	162	Snodgrass G	145
Render PJ	16	Snuffin WJ	16
Renfer LG	20	Snyder RH	104, 113, 146, 147, 148, 325, 327, 328, 329, 330, 333, 343, 344, 355, 356, 357, 358, 359, 360, 361, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399,
Rice MM	86, 87, 203	Sondeen JL	
Rich IM	163	Sowray PC	
Richards KM	16		
Richards TB	14		
Riordan KK	114, 138, 139		
Rivara FP	195		
Roach GW	14		
Robertson CA	92		
Robinson MD	86		
Robinson RD	12		
Robson ME	377		
Rodkey WG	21		
Roots AE	214		
Roth BJ	20, 125, 140, 141, 142, 143		
Rovira M	143		

INDEX OF AUTHORS AND INVESTIGATORS

Spaulding SA	400, 401, 402, 403, 404, 405, 406, 407, 408	Tran L	22
Spector J	11, 16	Treece GL	20, 149, 150, 151
Spring WB	19	Tripp GC	188
Stafford EM	12	Truxal AR	237, 249
Stapleton LM	220	Tsuchida AM	18, 19, 20, 111, 115, 127, 128, 152, 222, 223, 224, 225
	104, 113, 148, 325, 327, 328, 329, 330, 331, 361, 371, 372, 373, 374, 375, 376, 377, 383, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 407, 408, 409	Tuer WF	102
Stephan M	21	Turner BS	12, 160, 161, 162, 166, 167, 168, 169, 170
Stephenson S	207	Turner TS	13
Stevenson JG	13	Tuttle RM	20, 55, 105, 112, 126, 134, 137, 153, 154, 155
Stewart RS	60, 61, 62, 220	Uyemura MC	100
Stewart WB	14	Vaccaro AR	44
StLouis JS	253	Vaccaro JA	13, 57, 332, 357, 359, 366
Stone KS	12	Vallion RD	377
Stone MD	338, 339, 340, 341, 342, 362, 380	van Hamont JE	55, 70, 124
Stoneceipher KG	14	Van Manen JW	248
Stowe HO	12	Vanderlinde J	89
Stracener JC	53	Varga JH	249
Strampel W	12	Vaughan TL	247
Strand JA	14, 340	Velanovich V	13, 14, 15, 21, 22, 23
Stulting RD	22	Velasco W	22
Stutz FH	338, 339, 340, 341, 342, 345, 362, 363, 364	Vockroth AE	145
Styner MJ	57, 62, 63	Vordermark JS	16
Sugiyama RK	237	Wade CE	16, 21
Sunshein KF	240, 248	Wall K	11
Sutherland RS	14	Walz S	13
Swanson CA	16	Wang C	155
Swanson KR	15	Ward DN	18
Tapper EM	15	Warden D	19
Taylor SG	11	Waring GO	22
Teague G	220	Wartofsky L	149
Tenglin R	104, 113, 327, 328, 329, 330, 331, 361, 373, 377, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 409	Watson RC	15
Thomas K	162	Weber CR	66, 74
Thompson IM	242	Weber RW	102
Thomsen-Archer KL	63	Weber SE	23
Thorne ME	20, 189	Weir MR	13, 200, 208, 210, 211, 212, 213, 218, 219
Thrasher JB	14	Welle GJ	13, 223, 224, 225
Tidwell M	253	Wergeland FL	237
Tier C	84	Westphal KW	15
Tighe JF Jr	15	Wettlaufer JN	14, 245
Timmons JH	13, 21, 53, 154, 156, 222, 223, 224, 225, 242	Wharton WW III	16
Tobin LM	259	Wheeler BR	238
Tollefson D	23	White DC	83
		White LJ	237
		Willadsen DS	20, 156, 377
		Williard WC	23
		Wilson LA	22
		Wilson SK	170
		Wilson SS	143, 343, 350
		Winkler T	23
		Wiren KM	58
		Wiswell TE	168, 169

INDEX OF AUTHORS AND INVESTIGATORS

Wortham D	144	
Wright JR	18, 19, 57, 63, 70, 107	
Wygonski RJ	75, 239	
Yackel EE	171	
Yancey MK	12	
Yanko CA	192	
Yarborough LW	14, 244	
Yates JR	10	
Young-McCaughan SB	12, 125, 126, 172	
Youngberg RA	10, 248	
Yuan R	22	
Yuo HS	15	
Zerwekh JE	11	
Zhang W	10	
Zimba FA	14, 143, 411	
Zold A	10	
Zych KA	10, 47	

INDEX OF KEYWORDS

10-EdAM	372	arthritis	
12 hour urines	189	rheumatoid	138
4-aminobutyraldehyde	211	ascorbic acid	147
5-Fluorouracil	278, 280, 284, 295, 324, 333, 340, 343, 368, 369, 371, 388, 405, 408	asthma	
		acute	83
6-thioguanine	370	asthma	78
	181, 267, 406	ATLS	244
ABV Hybrid	374	Augmentin	214
ABVD	374	Austin bunionectomy	248
acute injuries	84	autorefractors	43
adenocarcinoma	409	avascular	248
ADHD	46, 207	aviators	97, 98
adjuvant treatment	337	azithromycin	108
adolescent(s)	49, 53, 131	B-cell	330
female	95	bacillus Calmette-Guerin	332
adrenal insufficiency	151	back pain	97, 98
adrenal	361	baricity	251
adriamycin	325, 342	Barrett's	128
advance directives	92	BCG	342, 348
Aftacare	159	BCNU	327
aids-related	133	behavior	73
AIDS	70, 132	benzocaine-induced	82
air flow obstruction	141	BEP	318
albumin	140	biologic parameters	394
alimentary tract	59, 222	biological parameters	345
ALL	267	bladder	186
alpha 2b interferon	376	bleomycin	125, 293, 306, 318, 335, 357
alpha-interferon	382, 386, 399	blood loss	192
aluminum	111	body core temperature	160
ambivalence	163	body weight	137
aminothiadiazole	299	bone absorption	111
amniotic fluid index	179	bone protein	239
amonafide	275	bone	253, 322
amphotericin B	104	bowel	191
analgesia	243	boys	52
androgens	137	brain	327
anesthesia	75, 227, 230, 251	breast biopsy	61
animal model	249	breast cancer	54
animal Study	55, 58, 59, 85, 86, 87, 88, 160, 168, 169, 187, 191, 203, 208, 210, 211, 212, 213, 218, 219, 230, 238, 239, 244, 249, 251, 252, 253	breast	112, 113
antibiotic therapy	145	bronchodilator	78
antibody seroconversion	197	bronchogenic	143
anticonvulsants	210, 212	bupivacaine	228, 229, 234, 241
antiemetics	109	bursitis	139
antigens	124	C-MYC	292
anxiety levels	72	CA-125	286
Ara-C	346, 379, 401	CAF	360
arctic	257	calcium	119
arterial pressure lines	164	calf	242
		cancer	59, 112, 113, 143, 159, 184, 247, 327, 328, 331, 361, 373, 393, 394, 395, 396, 397, 400, 401, 409

INDEX OF KEYWORDS

bladder	332, 341, 342, 348, 365, 408	322, 336, 338, 339, 346, 349, 350, 352, 355, 356, 357, 362, 363, 364, 375, 381, 386, 392, 393, 404, 406, 413
breast	334, 345, 353, 354, 355, 356, 360, 362, 363, 387, 388, 389	312
cervix	277, 281, 284, 292, 295, 313, 315, 316	multiple 81
colon	340, 352	chest pain 100, 202
colorectal	375, 378, 405	child abuse 100
endometrial	286, 287, 291, 307, 309, 314	child neglect 165
esophagus	128, 392, 404	child separation 67, 195, 214, 215
gastric	390	children 264
head & neck	172, 367, 368, 371, 372	2-9 YO 204
leukemia	329, 330	7 - 18 YO 201
lung		<2 YO 165
non-small cell	146, 339, 351	school aged 206
small cell	381, 406	chloral hydrate 330
lung	110	chlorambucil 350
nasopharyngeal	369	CHOP 192
nervous system	377	chorioamnionitis 285
ovarian		chromic phosphate 346
epithelial	289, 294	chronic granulocytic 106
ovarian	282, 285, 306, 308, 311, 312, 314, 320, 324, 336	cigarette smoking 257
pelvic	275, 276, 278, 297, 298, 299, 300, 301, 302, 303	circadian rhythm 335
penis	335	cis-diamminedichloroplatinum 109, 281, 282, 284, 287, 288, 293, 295, 305, 306, 308, 318, 324, 327, 351, 357, 361, 369, 371, 385, 406, 408
prostate	57, 344, 359, 366, 391	cisplatin 297, 333, 336, 368
rectum	343	cisplatinum 214
renal cell	337, 399	Clarithromycin 314
small cell	370	clinico-pathologic study 176
stomach	333	clomiphene citrate 184
testicular	357	clor flow Doppler 120
thyroid	134, 155	CoASH ligase 137
vulva	317	cold weather 220
carbohydrate composition	58	college cadets 205
carboplatin	146, 384, 385	colonization 140
carnitine	131	congestive heart failure 380
catheter sepsis	246	consolidation regimens 115
catheter tunnelling	246	continuous feeding 370
CAV	406	continuous infusion 187
CBDCA	384, 385	cordocentesis 89
CCNU	412	corneal abrasion 106
cefoperazone	325	coronary disease 183
cerebral perfusion	88	cotyledon 142
cervical cytology	255	CPOD 92
Cesarean	186	CPR 170
chemoendocrine therapy	360	crib 158
chemohormonal therapy	354, 355	critically ill patients 253
chemoradiation	409	needs of relatives 133
chemoradiotherapy	317, 411	cryotreat 373
chemotherapy	263, 264, 265, 286, 281, 282, 293, 306,	cryptosporidial CVAD

INDEX OF KEYWORDS

cyclophosphamid	312	epidemiology	216, 217
cyclophosphamide	282, 308, 318, 388	epididymus	117
cyclosporin	149	epidural analgesia	182, 234
cyropresavation	177	epilepsy	107, 130, 131
cystectomy	341, 365	epiphysis	253
cytogenetic studies	329	epithelium	168
cytometry	334, 367	equine inhibin	58
cytosine arabinoside	379	ER	353
dactinomycin	318	estradiol	183
daunomycin	267	etoposide	146, 293, 318, 385
daunorubicin	379	evaluation	174
debulked	307	Ewing's sarcoma	322
delayed maturation and growth	52	extravasation injuries	219
dental implications	65	family function	95
dental	68, 69, 174	fatty acid	
dentist attire	72	long chain	120
dentistry	67, 72	fatty acid	122
deployed soldiers	96	fazarabine	277
depression	96	fentanyl	228, 229, 234
deslorelin	50	ferret	87
dexamethasone		flow cytometry	289, 290, 291
optimum dose	74	fluconazole	104
DHAD	298	fludarabine phosphate	148, 330
diabetes	105, 159	flutamide	359
diagnosis	156	FNA	134
diagnostic assays	215	free beta HCG	310
dihydroxyanthracenedione	298	gallium nitrate	303
diarrhea	133	gastric	409
dibromodulcitol	281	gastritis	114
diclazuril	133	gene expression	292
didemnin B	276, 344	gentamicin-Lasix	218
discipline	202	gentamicin	213
DNA	61, 279, 289, 290, 291, 332, 334, 367, 368	gestational trophoblastic heoplasia	184
Do not resusitate orders	126	glimepiride	105
dolasetron mesylate	109	glutamine	211
domestic violence	196	glyburide	105
doppler ultrasound	179	GM-CSF	381
doxorubicin	113, 287, 312, 388	gonads	155
doxycycline	108	growth factor	63
drug survey	65	GYN surgery	185
Duke's carcinoma	400	gynecologic surgery	191
ECG	81	head & neck	236, 338
echinomycin	302	headache	77, 103
EDD	85	health	201
edema		heart disease	159
prevention	74	health care utilization	161
effect	194	helium-oxygen mixture	78
emergency room	80, 86, 362	hemolytic anemia	147
endocervical brush	190	hemorrhagic shock	230
endocrine resistance	344	heparin therapy	145
endocrine therapy	356	heparin	164
endophthalmitis	249	hepatitis	152
endotracheal suctioning	166, 168	hepatoma	358, 396
endotracheal tube placement	85	herniorraphies	235
		herpes simplex virus	188

INDEX OF KEYWORDS

high risk infants	162	hairy cell	382
histologic diagnosis	185	lymphoblastic	264, 265, 266, 269, 270, 380
HIV	70, 197, 215, 216, 217	marrow relapse	273
Hodgkin's disease		myeloid	384
Stages III & IV	364	non-lymphocytic	379
Hodgkin's disease	268, 349, 374	nonlymphoblastic	271
hormonal therapy	366	levamisole	340, 343, 352, 400
hormone receptors	61	LH	50
HPV	292	isoforms	51
human sperm	121	lidocaine HCL	219
hyaluronidase	219	lifestyle	201
hydatidiform moles	279, 310	Light reflection rheography	116
hydroxyurea	284	lipid synthesis	121
hyperactivation	177	lipids	123
hypogonadal	142	liquid rations	174
hypotension	227	liver disease	127
hypothyroidism	150	liver	261, 375
hysterectomy	316	Low back pain	44, 91
idarubicin	267, 273	low malignant potential	290
ifosfamide	288, 301, 344, 357	lymphadenectomy	315, 316, 366
immunization status	194	lymphocyte	400
immunotherapy	348	lymphocytic	401
impact on facility	91	lymphoma	
induction	75	central nervous system	411
infant	166	non-Hodgkin's	347, 350
(<1 YO)	266	serum repository	403
infarct artery patency	144	tissue procurement	402
infection	205	lymphoma	386
informed consent	69	M-VAC	365
injuries	195	malignancy	
interdigital neuromas	240	pelvic	296
interferon alpha 2	383	malnourished	142
interferon-A	407	mammography	99
interferon	152, 381	management	44
intermittent	242	melanoma	383
internship	79, 94	melatonin	257
intraocular lenses	237	melphalan	305, 320
intubation	87	menogaril	347
iontophoresis	138, 139	merbarone	294, 358
IP	336	Mesna	344
irradiation	412	mesothelioma	397
isotope technique	261	metatarsus proximus	240
IV cyclophosphamide	336	methemoglobinemia	82
IV therapy	145	methohexital-isoflurane-nitrous oxide	75
ketorolac tromethamine	77	methotrexate	283, 335, 411
ketorolac	241	metoclopramide	206
laparoscopy	127	microsurgery	238
laparotomy	285	military deployment	165
lead	207	military population	47, 99
leg	242	military	195
leucovorin		minocycline	125
high dose	280	misoprostol	114
leucovorin	278, 343, 352, 405	mitomycin-C	332, 351
leukemia	328, 331, 401	mitotane	361
acute	346	mitoxantrone	401
chronic lymphocytic	148		

INDEX OF KEYWORDS

modality RX	364	orthognathic surgery	74
modality therapy	363, 392	osteogenic sarcoma	395
molar pregnancy	283	otitis media	200
molecular microbiology assay	62	overweight	176
monoclonal antibodies	124	ovulation induction	176
monoclonal antibody	249, 310	oxandrin	52
MOPP	374	oxygen consumption	88
moral reasoning	94	oxyten utilization	136
morbidity	236	P32	308, 324
morphology	123	PALA	405
mouse	208	pancreas	225
MRI	143	papillary	307
mucosal lesions	115	papillomavirus	220
muscle efficiency	136	parent participation	95
mycosis fungoides	407	parental desire	68
myelogenous	331	parental preferences	84
myeloid	328	parental	165
myeloma	376, 398	patching	89
myocardial ischemia	243	patency	164
nasal mask	141	pathologic study	313
nasogastaric tissue sampling	222	patient health practices	171
nasogastaric ultrasound	224	PCI	406
nasogastric tissue sampling	59	PCR	134
nasogastric ultrasound	223, 225	PCV	412
nasopharyngeal	247	pediatric dentistry	73
natural history	217	pediatric dentists	71
necrosis	248	pediatric pain	84
needle aspiration	154	pediatric patients	65, 70
Neo-Fac	387	pediatric	216
neonatal emergency procedure	203	pediatrics	87
neonatal	203	pelvic malignancy	280
nephrosis	150	penicillin skin testing	102
nephrotoxicity	213, 218	pentostatin	382
neuroblastoma	263	PgR positive	353
neurocybernetic	130	PGTD	310
neuropeptides	250	phosphatidylcholine	119
neuropsychological instruments	47	phospholipid synthesis	118
neutropenia	104, 147	phospholipid	117
NICU environment	162	photoperiod	257
non-heparin solutions	164	phrenic nerve	233
non-Hodgkin's lymphoma	373	physiologic and neurobehavioral effect	162
nongonococcal urethritis	108	physiologic response	230
noninsulin-dependent	105	physiologic toll	79
nonsmall cell	110	pig	88
NSAID-induced	114	piglets	160
nurses	171	pirozantrone	390
nutritional status	172	placental circulation	180
OCD	204	plasminogen activator	144
omentum	239	pleural effusion	140
oncogene amplification	112	pleural effusions	125
ondansetron	66	pneumatic compression	242
ophthalmopathy		pneumonia	214
Graves'	149	polymerase chain reaction	60
optometry	43	polyposis	250
orchiectomy	359	position	88

INDEX OF KEYWORDS

positive pressure ventilation	141	sarcoma	
postmenopausal	334, 354	uterine	304
postoperative analgesia	229	screening	204
postoperative complications	67	sedation	206
postoperative nausea	66	seizures	129, 208, 211
postoperative vomiting	66	semen parameters	107
postpartum women	161	sequence	58
power of attorney	92	sequential	242
pre-eclampsia	189	serum marker	286
precocious puberty	50, 51	sexual function	245
prediction	100	sexual transmitted disease	198
pregnancy	96, 103, 188, 190, 196,	SHBG	54
	255	carbohydrate function	55
adolescent	95	characterization	55
attitudes	163	regulation	57
test	80	shoulder pain	232
premenopausal	355	sinusitis	250
preterm delivery prevention	178	sinusitis	156
preterm infant	170	smoking	171
procarbazine	412	social support	161
procine	85	soft tissue sarcoma	393
progesterone	183	soft tissue sarcomas	394
prognostic factors	389	specialty choice	93
ProMACE-Mopp	386	spermatozoa	117, 118, 119, 120,
prophylactic agents	227		122, 123, 177
prophylaxis	208	splenectomized	382
propofol-nitrous oxide	75	squamous cell	281, 372
prostate carcinoma	63	stapling	252
prostatectomy	245	steroids	
protein	63	IV	83
psychometric procedures	46	oral	83
PTC oncogene	134	stimulant medication	46
pulmonary surgery	232	stomach	128, 223, 224
pyridoxine	208, 212, 213, 218	streptococcus	205
quality of life	378, 391	stress	79, 153
quinine	373	subarachnoid space	251
rabbit	203, 208, 212, 218, 253	subcutaneous cuff	246
racial differences	259	sucralfate	111
radiation	172, 307, 339, 404	suctioning	169
radioactive iodine	155	surfactant	167
radiotherapy	295, 309, 315, 316,	surgery	
	320, 338, 341, 350,	abdominal aortic	228
	369, 371, 381	surgery	236, 320, 338, 345, 392
randomized	125	surgical oophorectomy	353
recidivism	198	surgical staging	311
recurrence	389	survival	389
referred shoulder pain	233	swine	191, 219, 230, 251, 252
regeneration	168	symptom checklist	204
resectable Alfa-nl	337	symptom distress	163
resection	352, 375	tamoxifen	360
resuscitation bag	166	taxol	282
retinoic acid	407	tenderness	156
risk factors	197	tendinitis	139
ropivacaine	235	teniposide	300
Rorschach Inkblot Test	259	teratoma	306
routine surveillance	283	testosterone	142, 153

INDEX OF KEYWORDS

theophylline toxicity	210, 211, 212	vincristine	318, 412
thoracotomy	229, 241	vitamin A	261
thrombocytopenia	147	VMCP	376
thyroglobulin	134	VP-16	361
thyroid hormone suppression	154	waste anesthetic gas	71
thyroid hormone	136	weighted scale	100
thyroid nodules	154	Wilms' tumor	272
thyroid size	49	Yale Brown Compulsive Scale	204
thyroid volume	53	zofran	109
tiagabine	129	Zoladex	353
TLC D-99 doxorubicin liposome	113		
topotecan	396		
TPDCFH	413		
tracheal epithelail injury	160		
tracheal trauma	169		
training protocol	86, 87, 191, 203, 238, 244, 252		
treatment	132		
trophoblastic neoplasia	279		
tumor			
brain	412, 413		
germ cell			
ovary	318		
germ cell	385		
neuroectodermal	322		
ovarian stroma	293		
ovarian	290, 305		
sinus	306		
uterus	288		
two year olds	194		
tympanometry	200		
type C	152		
ultrasound	53, 179		
umbilical arteries	182		
umbilical circulation	180		
ureaplasma	124		
urethritis	60		
urinary free cortisol	151		
urinary tract	191		
urine	80		
uroprotector mesna	288, 301		
ursodeoxycholic acid	152		
utilization	99		
VAC	318		
VAD	376, 398		
vagal nerve stimulation	130		
vaginal ultrasonography	185		
vagus nerve	232		
valproic acid	107		
varicella	205		
velocimetry	182		
venous thrombosis	116		
verapamil	373, 398		
videotaped education programs	159		
Videx	132		

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